ICoLA 2019 by KSoLA

Plenary Lecture 1

Chairperson

Joong-Yeol Park | University of Ulsan, Korea

Date & Time: September 6 (Fri.), 11:30-12:10
Place: Room 1+2+3 (3F)

Plenary Lecture 1

Stefano Del Prato

Organization

University of Pisa

Position & Title

Director, Department of Endocrinology and Metabolism, Orthopaedics, Traumatology, Occupational Health, University of Pisa, Italy

» Educational Background & Professional Experience

Year	Name of institution	Position
1982-1992	General Hospital of Padova	Assistant Professor of Metabolic Disease
1984-1992	University of Padova (Italy)	Professor of "Diabetes Physiopatology" at the Post-Graduate Course of Diabetolo
1988-1990	University of Texas	Associate Professor of Medicine
1990-2006	University of Texas	Clinical associate Professor of Medicine
1992-2000	University of Padova (Italy)	Associate Professor of Metabolic Diseases
2000-2002	University of Pisa (Italy)	Associate Professor of Endocrinology
2000-Present	University of Pisa (Italy)	Chief - Section of Diabetes and Metabolic Diseases, Department of Endocrinology & Metabolism,
2000-Present	University of Pisa (Italy)	Post-Graduate Course of Endocrinology and Metabolic Diseases, Section of Diabetes
2002-Present	University of Pisa (Italy)	Professor of Endocrinology
2012-Present	Universidad Peruana Cayetano Heredia, Lima, Peru	Honorary Professor

» Research Interests

Physiopathology and therapy of type 2 diabetes and insulin resistance

» Honors & Awards

- 2014 Cherubino Order - University of Pisa
- 2016 26th DMDSC Gold Medal Oration Award, Chennai, India
- 2018 Celso Prize of the Italian Society of Diabetology for outstanding carrer in the diabetes scientificstudy

» Publications

1. AVOGARO A., MIOLA M., VALERIO A., TOFFOLO G., COBELLI C., TIENGO A., DEL PRATO S. Intracellular lactate- pyruvate-interconversion rates are increased in muscle tissue of non-insulin dependent diabetic individuals. J. Clin Invest. 98:108-115, 1996 (8.788,)
2. BRUTTOMESSO D, PIANTA A, MARI A, VALERIO A, MARESCOTTI M-C, AVOGARO A, TIENGO A, DEL PRATO S. Restoration of early rise in plasma insulin levels improves the glucose tolerance of Type 2 diabetic patients. Diabetes, 48:99-105, 1999 (7.616)
3. MARCHETTI P, DEL GUERRA S, MARSELLI L, LUPI R, MASINI M, POLLERA M, BUGLIANI M, BOGGI U, MOSCA F, DEL PRATO S. Pancreatic islets from Type 2 diabetic patients have functional and survival defects which are ameliorated by metformin. J Clin Endocrinol Metab. 89:5535-5541, 2004
4. BIANCHIC, MICCOLI R, BONADONNA RC, GORGINO F, FRONTONI S, FALOIA E, MARCHESINI G, DOLCI MA, CAVALOT F, CAVALLO GM, LEONETTI F, DEL PRATO S; GENFIEV Investigators. Pathogenetic mechanisms and cardiovascular risk: differences between HbA(1c) and oral glucose tolerance test for the diagnosis of glucose tolerance. Diabetes Care. 35(12):2607-12, 2012.
5. KAHN SE, COOPER ME, DEL PRATO S. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present, and future.Lancet. 2014 Mar 22;383(9922):1068-83. doi: 10.1016/S0140-6736(13)62154-6
6. Hernandez AF, Green JB, Janmohamed S, D'Agostino RB Sr, Granger CB, Jones NP, Leiter LA, Rosenberg AE, Sigmon KN, Somerville MC, Thorpe KM, McMurray JJV, Del Prato S; Harmony Outcomes committees and investigators.Albiglutide and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease (Harmony Outcomes): a double-blind, randomised placebo-controlled trial. Lancet. 2018 Oct 27;392(10157):1519-1529. doi: 10.1016/S0140-6736(18)32261-X. Epub 2018 Oct 2.
7. DANIELE G,GAGGINI M,COMASSI M,BIANCHI C,BASTA G, DARDANO A, MICCOLI R, MARI A, GASTALDELLI A, DEL PRATO S. Glucose Metabolism in HighWRisk Subjects for Type 2 Diabetes Carrying the rs7903146 TCF7L2 Gene Variant. 2015 Aug;100(8):E1160W7. doi:10.1210/jc.2015W1172.

Abstract

THE BENEFITS OF GLP1RA AND SGLT2 INHIBITORS FOR THE CV OUTCOMES: WHAT IS SIMILAR, WHAT IS DIFFERENT?

Stefano Del Prato

Department of Clinical & Experimental Medicine, University of Pisa, Italy
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In spite of therapeutic advances and progressive decline in cardiovascular (CV) morbidity and mortality, subjects with type 2 diabetes continue to have a 2-fold higher risk than those without diabetes. Intensive glycemic control has been shown to provide marginal benefit though most of the studies addressing the question were based on traditional glucose lowering agents. In the past 20 years, new pharmacologic agents have been introduced and almost all of them have been assessed in dedicated CV outcome trials (CVOT) to test their safety and potential CV benefit in large populations of type 2 diabetic subjects. These trails have provided evidence for CV safety of DPP4 inhibitors and demonstrate superiority of SGLT2 inhibitors (SGLT2i) and GLP1-receptor agonists (GLP1-RAs) in term of risk reduction for major adverse cardiovascular events (3 point MACE: CV mortality, nonfatal myocardial infarction, nonfatal stroke). Therefore, among the currently available classes of glucose lowering agents, two have the potential for reducing CV risk in type 2 diabetic subjects. Nonetheless, some difference between SGLT2i and GLP1-RAs are worth to consider. The first trial to show a beneficial CV effect was EMPA-REG. The trial showed that empagliflozin not only was associated with a significant reduction in the 3-point MACE but also reduced dramatically the risk of hospitalization for heart failure. This effect was then confirmed with the use of canagliflozin (CANVAS program) and dapagliflozin (DECLARE) as well as in real world studies. On the contrary, no such a beneficial effect was detected in the GLP1RA CV outcome trials. This difference has been noted by the extensors of the most recent ADA/EASD consensus for the management of hyperglycemia in type 2 diabetes. The experts of the two organizations first suggested that assessment of the presence of a CV condition is compelling in selecting patient's individualized treatment. If the subject has a prevalent atherosclerotic CV disease a SGLT2i or a GLP1-RA with proven CV effects should be considered upon treatment failure with metformin. On the contrary, if heart failure is the main CV manifestation then a SGLT2i should be preferred.

Of interest, the beneficial effect of SGLT2i appear to occur much earlier than that provided by GLP1RAs. This may suggest that the mechanisms through which these drugs confer CV protection is different. Several potential mechanisms have been postulated, but a main hemodynamic effect seems to be the most likely explanation for the beneficial CV effects of SGLT2i, while an anti-atherosclerotic action may be predominant for GLP1-RAs. The hemodynamic action of the SGLT2i has been interpreted as a direct effect on the target organ of these drugs, i.e the kidney. SGLT2i promotes natriuresis and osmotic diuresis, leading to plasma volume contraction and reduced preload, and decreases in blood pressure, arterial stiffness, and afterload as well, thereby improving subendocardial blood flow in patients with heart failure. SGLT2 inhibition is also associated with preservation of renal function. Of interest the latter seems to be exerted for all degree of initial renal function as a renal protection has been reported in type 2 diabetic subjects with preserved glomerular filtration rate (eGFR >90 ml/min/1.73 m^2) as well as those with impaired (eGFR 60 – 90 ml/min/1.73 m^2) and those with reduced eGFR (<60 ml/min/1.73 m^2). A renal protective effect has been also observed with GLP1-RAs. However, such an effect seems to be less pronounced as compared to SGLT2i and more apparent in those with albuminuria. In line with this, the recent results of the REWIND trial show a more pronounced reduction of albumin excretion rate than maintenance of eGFR.

EMPA-REG was the first trail suggesting a CV protection for SGLT2i, but it was the trial that, unexpectedly, show no effect of SGT2i on the risk for nonfatal stroke. A similar finding has been observed with the ensuing SGLT2i trials. On the contrary, a consistent reduction in the risk of stroke has been reported with GLP1-RAs.

In summary, both SLT2i and GLP1-RAs provide CV protection, but differences can be identified between the two classes. These differences also extend to the safety profile. SGLT2i may expose to the risk of urinary and genital infection, euglycemic ketoacidosis, fractures and amputations of the extremities of the lower limbs, and Fournier gangrene. GLP1-RAs' most common adverse events remain nausea and vomiting. While it may be important for the physician to keep in mind these differences, they may also be useful for a better positioning of these pharmacological approaches in the treatment algorithm of people with type 2 diabetes. Finally, given the complementarity of the safety/efficacy profiles of the two classes of drugs, one could hypothesize their concomitant use to exploit their cardiorenal protection. This will require, however, had hoc CV outcome trials.

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Plenary Lecture 2

Chairperson

Jeong-Taek Woo | Kyung Hee University, Korea

Date & Time: September 7 (Sat.), 11:30-12:10
Place: Room 1+2+3 (3F)

Plenary Lecture 2

Ira J. Goldberg

Organization

New York University

Position & Title

Professor of Medicine

» Educational Background & Professional Experience

Year	Name of institution	Position
2014-	New York University School of Medicine	Professor and Director
2005-2014	Columbia University	Professor of Medicine
2000-2014	Division of Preventive Medicine & Nutrition, Columbia University	Chief
1996-2014	Columbia University	Professor of Medicine
1990-1996	Columbia University	Associate Professor of Medicine
1990-1996	Columbia University	Assistant Professor of Medicine

» Research Interests

Diabetes and lipid metabolism and their cardiovascular complications

» Publications

1. Novel Reversible Model of Atherosclerosis and Regression Using Oligonucleotide Regulation of the LDL Receptor. Basu D, Hu Y, Huggins LA, Mullick AE, Graham MJ, Wietecha T, Barnhart S, Mogul A, Pfeiffer K, Zirlik A, Fisher EA, Bornfeldt KE, Willecke F, Goldberg IJ. Circ Res. 2018 122:560-567. PMID:29321129
2. Ni-Huiping Son N-H, Basu D, Samovski D, Pietka TA, Willecke F, Fang X, Yu S-Q, Scerbo D, Drosatos K, Yeh ST, Mullik A, Shoghi KI, Gumaste N, Lhakhang T, Abumrad NA, Goldberg IJ. Endothelial cell CD36 regulates tissue fatty acid and glucose uptake. J Clin Invest. 2018. 128:4329-4342. PMID:30047927
3. Neutrophil-derived S100 calcium-binding proteins A8/A9 promote reticulated thrombocytosis and atherogenesis in diabetes. Kraakman MJ, Lee MK, Al-Sharea A, Dragoljevic D, Barrett TJ, Montenont E, Basu D, Heywood S, Kammoun HL, Flynn M, Whillas A, Hanssen NM, Febbraio MA, Westein E, Fisher EA, Chin-Dusting J, Cooper ME, Berger JS, Goldberg IJ, Nagareddy PR, Murphy AJ. J Clin Invest. 2017 127:2133-2147. PMID: 28504650
4. Drosatos K, Pollak NM, Pol CJ, Ntziachristos P, Willecke F, Valenti MC, Trent CM, Hu Y, Guo S, Aifantis I, Goldberg IJ. Cardiac myocyte klf5 regulates ppara expression and cardiac function. Circ Res. 2016. 118:241-53. PMID: 26574507 PMCID: PMC4886555
5. Gordts PLSM, Nock R, Son N-H, Gonzales JC, Lew I, Thacker BE, Lee RG, Mullick AE, Graham MJ, Goldberg IJ, Crooke RM, Witztum JL, Esko JD. Reduction of hypertriglyceridemia by apoC-III anti-sense oligonucleotides requires low density lipoprotein family receptors. J Clin Invest, 2016; 126:2855-66 PMID:27400128
6. Kolwicz SC, Jr., Liu L, Goldberg IJ, Tian R. Enhancing cardiac triacylglycerol metabolism improves recovery from ischemic stress. Diabetes. 2015. 64:2817-27. PMID: 25858561 PMCID: PMC4512225.
7. Nagareddy PR, Gorman DJ, Stirzaker RA, Grant R, Hong ES, Smyth SS, Choi SH, Korner J, Bornfeldt KE, Fisher EA, Dixit V D, Tall AR, Goldberg IJ *, Murphy A J * (*co-senior authors). Adipose tissue macrophages promote myelopoiesis and monocytosis in obesity. Cell Metabolism 2014; 6;19:821-35. PMID: 24807222 PMCID: PMC4048939. *co-senior authors

Abstract

MY SWEET HEART WAS BROKEN: FAT METABOLISM AND DIABETES IN THE HEART

Ira J. Goldberg

Endocrinology, Diabetes, and Metabolism, New York University, USA
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Production of triglycerides is how we evolved to circulate calories from the gut, to the liver, to the tissues. Triglyceride supplies our heart and skeletal muscles with fuel, and allows our adipose to efficiently store fat. Each triglyceride molecule supplies more than ten times the energy of a molecular of glucose; failure to transport, acquire and use triglyceride leads to energy deficiency and often death. But as is often the case, we can have too much of a good thing. In the blood excess triglyceride leads to pancreatitis, a clinical condition most often seen with poorly control Type 2 diabetes. In the heart excess triglyceride causes cardiomyopathy. My laboratory has focused on the transport, uptake, storage and pathological consequences of too much fat in the wrong places. 1) In the circulation, triglyceride is transported in lipoproteins and cleared via the actions of lipoprotein lipase (LpL) and hepatic triglyceride lipase. By inhibiting these enzymes we showed that triglyceride metabolism regulates LDL and HDL; hepatic lipase inhibition shifts LDL to larger, more buoyant particles and LpL inhibition reduces HDL cholesterol by >50%. 2) Genetic variations that regulate the activity of LpL correlate with cardiovascular risk, as do circulating triglyceride levels. LpL is expressed by macrophages within the arterial wall and, in contrast to its anti-atherosclerotic effects when expressed in muscle, macrophage LpL deficiency reduces macrophage function and atherosclerosis. 3) In the heart, oxidation of fatty acids from triglyceride produces to majority of ATP. Cardiomyocyte-specific LpL deletion leads heart failure with aging and with increased afterload. However, excess lipid accumulation can cause lipotoxic heart failure and ventricular fibrillation. Another source of heart lipids, non-esterified fatty acids, are also used by the heart and their efficient uptake requires endothelial cell expression of CD36. By defining the pathways mediating heart lipid uptake, we will test whether these forms of heart failure can be prevented. Heart disease(s) are about more lipids than cholesterol.

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Keynote Lecture 1

Chairperson

Chee Jeong Kim | Chung-Ang University, Korea

Date & Time: September 6 (Fri.), 09:00-09:30
Place: Room 1+2+3 (3F)

Keynote Lecture 1

Kenneth Walsh

Organization

University of Virginia

Position & Title

Lockhard B. McGuire Professor of Internal Medicine

Director, Hematovascular Biology Center (HBC)

» Educational Background & Professional Experience

Year	Name of institution	Position
2018-	University of Virginia	Lockhard B. McGuire Professor of Internal Medicine
2018-	University of Virginia	Director, Hematovascular Biology Center (HBC)
2008-2018	Boston University	Aram V. Chobanian Distinguished Professor of Cardiovascular Medicine
2008-2018	Boston University	Director, Whitaker Cardiovascular Institute
2001-2008	Boston University	Head, Molecular Cardiology, Whitaker Cardiovascular Institute
2000-2001	Tufts University	Professor of Medicine

» Research Interests

Kenneth Walsh is the director of the Hematovascular Biology Center at the University of Virginia. The Walsh Lab broadly examines the molecular events that drive cardiovascular cell growth, differentiation and cell death. At the forefront of this science, his newest studies have investigated how clonal hematopoiesis functions as a new causal risk factor for CVD. He obtained his PhD in Biochemistry from the University of California, Berkeley.

» Honors & Awards

- 2011 Distinguished Investigator of the American Heart Association
- 2009-2015 Charter Member, CCHF Study Section, National Institutes of Health
- 2004-2016 Associate Editor, Circulation

» Publications

1. S. Sano, Y. Wang, Y. Yura, M. Sano, K. Oshima, Y. Yang, Y. Katanasaka, K.-D. Min, S. Matsuura, K. Ravid, G. Mohi, K. Walsh (2019). *JAK2*^{V617F}-mediated clonal hematopoiesis accelerates pathological remodeling in murine heart failure. ***JACC Basic Transl. Sci.*** In press.
2. S. Sano, Y. Wang, M. Evans, Y. Yura, M. Sano, H. Doviak, K. Walsh (2019). Lentiviral CRISPR/Cas9-mediated genome editing for the study of hematopoietic cells in disease models. ***J. Vis. Exp.*** In press.
3. S. Sano, Y. Wang, K. Walsh (2018). Clonal hematopoiesis and its impact on cardiovascular disease. ***Circ. J.*** 83:2-11.
4. S. Sano, K. Oshima, Y. Wang, Y. Katanasaka, M. Sano, K. Walsh (2018). CRISPR-mediated gene editing to assess the roles of Tet2 and Dnmt3a in clonal hematopoiesis and cardiovascular disease. ***Circ. Res.*** 123:335-341.
5. S. Sano, K. Oshima, Y. Wang, S. MacLauchlan, Y. Katanasaka, M. Sano, M. A. Zuriaga, M. Yoshiyama, D. Goukassian, M. A. Cooper, J. J. Fuster, K. Walsh (2018).Tet2-mediated clonal hematopoiesis accelerates heart failure through a mechanism involving the IL-1β/NLRP3 inflammasome. ***J. Am. Coll. Cardiol.*** 71:875-886.
6. J. J. Fuster, K. Walsh (2018). Somatic mutations and clonal hematopoiesis: unexpected potential new drivers of age-related cardiovascular disease. ***Circ. Res.*** 122:523-532.
7. J. J. Fuster, S. MacLauchlan, M. A. Zuriaga, M. N. Polackal, A. C. Ostriker, R. Chakraborty, C.-L. Wu, S. Sano, S. Muralidharan, C. Rius, J. Vuong, S. Jacob, V. Muralidhar, A. A. B. Robertson, M. A. Cooper, V. Andrés, K. K. Hirschi, K. A. Martin, K. Walsh (2017). Clonal hematopoiesis associated with Tet2 deficiency accelerates atherosclerosis development. ***Science*** 355:842-847.

Abstract

KILLER CLONES: CLONAL HEMATOPOIESIS AS A NEW CAUSAL RISK FACTOR FOR CARDIOVASCULAR DISEASE

Kenneth Walsh

Hematovascular Biology Center (HBC), Robert M. Berne Cardiovascular Research Center, University of Virginia – School of Medicine, USA
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Somatic DNA mutations accumulate with age in many tissues and lead to genomic mosaicism. However, the causal role of genomic mosaicism in the diseases of the elderly other than cancer remains relatively unexplored. Large exome sequencing studies in humans have shown that aging is associated with an increased frequency of acquired mutations in pre-leukemic "driver" genes within hematopoietic cells. These "driver" gene mutations provide a competitive growth advantage to the mutant hematopoietic cell and therefore allow its clonal expansion (i.e. clonal hematopoiesis). Unexpectedly, these somatic mutations have been found to be associated with greater risk of coronary heart disease and stroke, suggesting a previously unrecognized link between somatic mutations in the hematopoietic system and cardiovascular disease. One of the genes that is frequently mutated in clonal hematopoiesis is the epigenetic regulator *TET2*. Using *TET2* as a test case, we explored whether the expansion of mutant hematopoietic cells promotes atherosclerosis in hyperlipidemic mice. More recently we have extended these analyses to additional cardiovascular disease processes and additional driver gene mutations including *DNMT3A* and *JAK2*^{V617F}. Overall, these findings support the concept that clonal hematopoiesis represents a new mechanism of cardiovascular disease that shares features with hematologic malignancy, and that evaluating an individual's clonal hematopoiesis status could add to the predictive capabilities of the traditional risk factors. Further research in the area of hemato-vascular biology could provide a mechanistic framework for the development of personalized medicines for cardiovascular disease that are tailored for individuals who carry specific somatic mutations in their hematopoietic cells.

Keywords
Hematopoiesis, genomic mosaicism, somatic mutations, cardiovascular disease, TET2, DNMT3A, JAK2^{V617F}

ICoLA 2019 by KSoLA

Keynote Lecture 2

Chairperson

Kyong Soo Park | Seoul National University, Korea

Date & Time: September 7 (Sat.), 09:00-09:30
Place: Room 1+2+3 (3F)

Keynote Lecture 2

Gregory G. SCHWARTZ, MD PhD

Organization

University of Colorado School of Medicine, Aurora, Colorado USA

Position & Title

Professor of Medicine

» Educational Background & Professional Experience

Year	Name of institution	Position
1999-Present	University of Colorado School of Medicine Rocky Mountain Regional VA Medical Center, Aurora, Colorado USA	Professor of Medicine Chief, Cardiology Section
1994-1999	University of California, San Francisco (UCSF)	Associate Professor of Medicine
1988-1994	University of California, San Francisco (UCSF)	Assistant Professor of Medicine
1986-1988	University of California, San Francisco (UCSF)	Fellow, Cardiovascular Disease
1982-1986	University of Colorado School of Medicine Denver, Colorado USA	Resident and Chief Resident in Internal Medicine
1976-1982	Duke University, Durham, North Carolina USA	MD (1981), PhD (Physiology, 1982)

» Research Interests

Lipid and metabolic interventions in coronary heart disease, studied in experimental models and in clinical trials

» Honors & Awards

- Section Editor, Journal of the American College of Cardiology
- Fellow, Council on Basic Cardiovascular Science, American Heart Association
- Outstanding Faculty Teaching Award, Division of Cardiology, University of Colorado School of Medicine

» Publications

1. **Schwartz GG**, Steg P, Szarek M, et al. Alirocumab and cardiovascular outcomes after acute coronary syndrome. *N Engl J Med* 2018;379:2097-2107.
2. **Schwartz GG**, Ballantyne CM, Barter PJ, et al. Association of lipoprotein (a) with risk of recurrent ischemic events following acute coronary syndrome. *JAMA Cardiol* 2018; 3:164-168
3. Lu L, Ye S, Scalzo R, Reusch JEB, Greyson CR, **Schwartz GG**. Metformin preserves energetics and prevents ventricular fibrillation during myocardial ischemia in normal pigs. *Diabetologia* 2017; 60:1550-1558.
4. **Schwartz GG**, Abt M, Bao W, Dimicco D, Kallend D, Miller M, Mundl H, Olsson AG. Triglycerides predict recurrent ischemic events after acute coronary syndrome. *J Am Coll Cardiol* 2015; 65:2267-75
5. Lincoff AM, Tardif J-C, **Schwartz GG**, et al. Aleglitazar and cardiovascular outcomes after acute coronary syndrome in patients with type 2 diabetes mellitus. *JAMA* 2014; 311:1515-25
6. **Schwartz GG**, Olsson AG, Abt M, et al. Effects of dalcetrapib in patients with recent acute coronary syndrome. *N Engl J Med* 2012; 367:2089-2099
7. **Schwartz GG**, Olsson AG, Ezekowitz MD, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: The MIRACL study, a randomized controlled trial. *JAMA* 2001; 285:1711-1718.

Abstract

METFORMIN: IS IT A CARDIOVASCULAR DRUG?

Gregory G. SCHWARTZ, MD PhD

Division of Cardiology University of Colorado and Rocky Mountain Regional VA Medical Center Aurora, Colorado, USA
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Metformin has been in clinical use for 61 years and is the most commonly prescribed medication for type 2 diabetes, taken by more than 100,000,000 people worldwide. Most international guidelines recommend metformin as the foundational drug therapy for type 2 diabetes. That guidance is based primarily on findings of reduced death and cardiovascular events with metformin in the United Kingdom Prospective Diabetes Study, an unblinded study with usual care control group performed in 753 patients between 1977 and 1991. Although subsequent observational data and meta-analyses of small trials have also suggested a clinical benefit of metformin, it has never been corroborated in a randomized, placebo-controlled cardiovascular outcomes trial.

Over the past 15 years, a growing body of experimental data has suggested that metformin, acting through AMP-activated protein kinase and possibly other mechanisms, has favorable cardiovascular effects in animal models with or without diabetes. These include anti-atherogenic effects, reduction of myocardial infarct size, improvement in vascular endothelial function, and attenuation of ischemic ventricular arrhythmias. Because placebo-controlled clinical trials of metformin are difficult to perform in patients with established type 2 diabetes, investigators have evaluated the drug's cardiovascular effects in patients without diabetes using surrogate endpoints. Metformin has been shown to improve coronary endothelial function, modify the progression of coronary arterial calcification, and reduce LV mass. However, other studies have shown neutral effects of metformin versus placebo on carotid intima-media thickness and left ventricular function after myocardial infarction. Thus, there is equipoise regarding metformin's role as a cardiovascular therapy.

The Investigation of Metformin in Pre-Diabetes on Atherosclerotic Cardiovascular OuTcomes (VA-IMPACT; clinicaltrials.gov NCT02915198; sponsored by VA Cooperative Studies Program) is testing the hypothesis that metformin, compared with placebo, reduces death and major adverse cardiovascular events in patients with pre-diabetes and established cardiovascular disease. Planned enrollment is 7868 patients followed for a median of 4 years to the accrual of 1360 primary endpoint events. Upon completion, this trial may provide an answer to the longstanding question of whether metformin is a cardiovascular drug.

Keywords
Metformin, AMP-activated protein kinase, cardiovascular disease, pre-diabetes, clinical trial

ICoLA 2019 by KSoLA

Special Lecture 1

Chairperson

Myung-A Kim | Seoul National University, Korea

Date & Time: September 6 (Fri.), 13:20-13:50
Place: Room 1+2+3 (3F)

Special Lecture 1

Laurent YVAN-CHARVET

Organization

INSERM

Position & Title

Director of Research

(eq. to 'tenure track' Full Professor)

» Educational Background & Professional Experience

Year	Name of institution	Position
Since 2015	Inserm	Director of Research
2013-2015	Inserm	Team leader ATIP-AVENIR
2012-2013	Pfizer CVMED	Joint appointment with Columbia University
2009-2013	Columbia University	Associate Professor
2005-2009	Columbia University	Postdoctoral fellowship
2002-2005	Université Paris – Les Cordeliers	PhD

» Research Interests

Hematometabolism, cardiometabolic diseases, atherosclerosis

» Honors & Awards

- 2015 Daniel Steinberg Early Career Investigator AHA
- 2013 EAS young Investigator Award European Athero Society
- 2010 Roger Davis Award Kern Aspen Conference

» Publications

1. Yvan-Charvet et al., Immunometabolic function of cholesterol in cardiovascular disease and beyond. Cardiovasc Res (2019) in press
2. Yvan-Charvet L, Swirski FK. Is defective cholesterol efflux an integral inflammatory component in myelopoiesis-driven cardiovascular diseases? Eur Heart J. (2018) 39(23):2168
3. Yvan-Charvet L, Cariou B. Poststatin era in atherosclerosis management. Curr Opin Lipidol. (2018). 32 :448
4. Viaud et al., Lysosomal Cholesterol Hydrolysis Couples Efferocytosis to Anti-Inflammatory Oxysterol Production. Circ Res. 2018;122(10):1369
5. Tall AR, Yvan-Charvet L. Cholesterol, inflammation and innate immunity. Nat Rev Immunol. (2015). 15 :104-16.
6. Sarrazy V et al., Disruption of Glut1 in hematopoietic stem cells prevents myelopoiesis and enhanced glucose flux in atheromatous plaques of ApoE-/- mice. Circ Res. (2016). 118:1062-77
7. Yvan-Charvet L, et al., ATP binding cassette transporters and HDL suppress hematopoietic stem cell proliferation. Science. (2010), 328: 1689

Abstract

METABOLIC REPROGRAMMING OF MACROPHAGE IN ATHEROSCLEROSIS: IS IT ALL ABOUT CHOLESTEROL?

Laurent YVAN-CHARVET

Institut National de la Santé et de la Recherche Médicale (Inserm) U1065, Université Côte d'Azur, Department of Molecular Medicine (C3M), Atip-Avenir, Fédération Hospitalo-Universitaire (FHU) Oncoage, 06204 Nice, France
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Heart disease kills more people than any other worldwide. In an effort to understand the underlying mechanisms that cause heart disease, at least two distinct lines of thinking have emerged. First, obesity, diabetes, hypertension, high triglycerides, and low HDL cholesterol – the key constituents of the metabolic syndrome – have been recognized as major risk factors. Second, inflammation – the immune system's ancient defense program against infection and injury – has surfaced as a critical component accompanying most stages of disease. Although metabolism and inflammation are essential to survival, involving all tissues throughout life, we still know very little how these processes influence each other. After a contribution to the development of new therapeutics for cardiovascular diseases at Pfizer, the research work of Dr Yvan-Charvet has mainly been focused on how metabolic regulation of the hematopoietic tree occurs in chronic inflammatory diseases such as atherosclerosis – a new area of research for cardiovascular diseases. More recently, a hypothesis-driven selection of biochemical pathways linking metabolism and inflammation has emerged by filtering 'Omics' studies through a 'metabolic pathways' analysis bioinformatic tools. The metabolic reprogramming of macrophage in atherosclerosis beyond cholesterol will be discussed.

Keywords
Hematometabolism, cardiometabolic diseases, atherosclerosis

ICoLA 2019 by KSoLA

Special Lecture 2

Chairperson

Young-Bae Park | Seoul National University, Korea

Date & Time: September 7 (Sat.), 13:20-13:50
Place: Room 1+2+3 (3F)

Special Lecture 2

Sripal Bangalore

Organization

New York University School of Medicine

Position & Title

Professor of Medicine

Director, Complex Coronary Intervention, Bellevue

Director of Research, Cardiac Catheterization Laboratory

Director, Cardiovascular Outcomes Group

» Educational Background & Professional Experience

Year	Name of institution	Position
2018.8-Present	New York University School of Medicine	Professor of Medicine (Tenured)
2013.9-2018.7	New York University School of Medicine	Associate Professor of Medicine
2010.9-2013.8	New York University School of Medicine	Assistant Professor of Medicine
2008.7-2010.6	Brigham and Women's Hospital	Fellowship: Interventional Cardiology
2005.7-2008.6	St Luke's Roosevelt Hospital and Columbia University	Fellowship: Cardiovascular Medicine
2003.7-2005.6	St Luke's Roosevelt Hospital and Columbia University	Residency: Internal Medicine

» Research Interests

Research interest are in comparative effectiveness studies for cardiovascular diseases, particularly stable ischemic heart disease, acute coronary syndromes, hypertension and dyslipidemia

» Honors & Awards

- 2009-2010 Dr. Gregory Braden Memorial Interventional Cardiology Fellow of the Year Award from the Society of Angiography and Intervention
- 2009-2010 Thomas J. Linnemeier Spirit of Interventional Cardiology Young Investigator Award finalist (TCT 2009)
- 2016 Douglas P. Zipes Distinguished Young Scientist Award, American College of Cardiology

» Publications

1. Messerli FH, Hofstetter L, Rimoldi SF, Rexhaj E, Bangalore S. Risk Factor Variability and Cardiovascular Outcome: JACC Review Topic of the Week. J Am Coll Cardiol. 2019 May 28;73(20):2596-2603. doi: 10.1016/j.jacc.2019.02.063. Review.PMID: 31118154
2. Bangalore S, Fayyad R, DeMicco DA, Colhoun HM, Waters DD.Body Weight Variability and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus. Circ Cardiovasc Qual Outcomes. 2018 Nov;11(11):e004724. doi: 10.1161/CIRCOUTCOMES.118.004724. PMID: 30571333
3. Waters DD, Bangalore S, Fayyad R, DeMicco DA, Laskey R, Melamed S, Barter PJ. Visit-to-visit variability of lipid measurements as predictors of cardiovascular events. J Clin Lipidol. 2018 Mar - Apr;12(2):356-366. doi: 10.1016/j.jacl.2017.12.003. Epub 2017 Dec 20. PMID: 29310989
4. Bangalore S, Breazna A, DeMicco DA, Wun CC, Messerli FH; TNT Steering Committee and Investigators. Visit-to-visit low-density lipoprotein cholesterol variability and risk of cardiovascular outcomes: insights from the TNT trial. J Am Coll Cardiol. 2015 Apr 21;65(15):1539-48. doi:10.1016/j.jacc.2015.02.017.PMID: 25881936
5. Bangalore S, Fayyad R, Laskey R, DeMicco DA, Messerli FH, Waters DD. Body-Weight Fluctuations and Outcomes in Coronary Disease. N Engl J Med. 2017 Apr 6;376(14):1332-1340. doi: 10.1056/NEJMoa1606148. PMID: 28379800
6. Bangalore S, Guo Y, Samadashvili Z, Blecker S, Xu J, Hannan EL. Everolimus-eluting stents or bypass surgery for multivessel coronary disease. N Engl J Med. 2015 Mar 26;372(13):1213-22. doi: 10.1056/NEJMoa1412168. Epub 2015 Mar 16.PMID: 25775087

Abstract

CARDIOVASCULAR RISK FACTORS - IT'S TIME TO FOCUS ON VARIABILITY

Sripal BANGALORE

Department of Medicine, Division of Cardiology, New York University School of Medicine, New York, NY, USA
Sripalbangalore@gmail.com

Until recently, intraindividual visit-to-visit variability of cardiovascular risk factors has been dismissed as random fluctuation. This simplistic concept was challenged by demonstrating that visit-to-visit blood pressure variability, independent of average blood pressure, was a powerful risk factor for stroke. Subsequently, variability of other cardiovascular risk factors such as cholesterol, glycemia, and body weight was documented to increase risk independent of their absolute values. Variability of these risk factors has been demonstrated to be a powerful predictor for all-cause and cardiovascular mortality, stroke, coronary artery disease, heart failure, end-stage renal disease, and dementia. With the notable exception of heart rate, cardiovascular risk factors must now be defined by 2 components: the magnitude and duration of sustained risk factor elevation and, equally important, the variability of the same risk factor over time.

Keywords
blood pressure; body weight; cholesterol; glycemia; heart rate; mortality

ICoLA 2019 by KSoLA

Symposium 1

Chairpersons

Hyonggin An | Korea University, Korea
Young-Hak Kim | University of Ulsan, Korea

Date & Time: September 5 (Thu.), 16:00-18:00
Place: Room 4 (5F)

Symposium 1

Hyonggin An

Organization

Korea University

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2015-Present	Korea University	Professor
2009-2015	Korea University	Associate Professor
2004-2009	Korea University	Assistant Professor
2008-2010	University of Iowa	Adjunct Assistant Professor
2004-2008	University of Iowa	Assistant Professor

» Research Interests

Clinical Trials, Missing Data Analysis, Longitudinal Data Analysis, Bayesian Statistics, Causal Inference, Skewed Data Analysis, Health Policy Data Analysis, Epidemiologic Data Analysis, Infectious Disease Modeling, Health cost analysis

» Honors & Awards

- 2018 Korea University Lecture Award (2018 Korea University, Korea)
- 2016 Korea University Seoktop Lecture Award (2016 Korea University, Korea)

» Publications

1. Han KM, Jee HJ, **An H**, Shin C, Yoon HK, Ko YH, Ham BJ, Kim YK, Han C., Intimate partner violence and incidence of depression in married women: A longitudinal study of a nationally representative sample. *J Affect Disord*. 2019 Feb 15;245:305-311
2. Lee HA, Chang JM, Goh HG, Kim TH, Lee YS, Suh SJ, Jung YK, Choi HS, Kim ES, Kim JH, **An H**, Seo YS, Yim HJ, Jeen YT, Yeon JE, Chun HJ, Byun KS, Um SH, Kim CD. Prognosis of patients with gastric variceal bleeding after endoscopic variceal obturation according to the type of varices. *Eur J Gastroenterol Hepatol*. 2019 Feb;31(2):211-217
3. Kim TH, Lee HA, Seo YS, Lee YR, Yim SY, Lee YS, Suh SJ, Jung YK, Kim JH, **An H**, Yim HJ, Yeon JE, Byun KS, Um SH. Assessment and prediction of acute kidney injury in patients with decompensated cirrhosis with serum cystatin C and urine N-acetyl-β-D-glucosaminidase. J *Gastroenterol Hepatol*. 2019 Jan;34(1):234-240
4. Gu DH, Kim MY, Seo YS, Kim SG, Lee HA, Kim TH, Jung YK, Kandemir A, Kim JH, **An H**, Yim HJ, Yeon JE, Byun KS, Um SH., Clinical usefulness of psoas muscle thickness for the diagnosis of sarcopenia in patients with liver cirrhosis. *Clin Mol Hepatol*. 2018 Sep;24(3):319-330
5. Kim TH, Ku DH, Um SH, Lee HA, Park SW, Chang JM, Yim SY, Suh SJ, Jung YK, Seo YS, Kim JH, Yim HJ, Yeon JE, Byun KS, **An H**, How can we improve the performance of Model for End-Stage Liver Disease sodium score in patients with hepatitis B virus-related decompensated liver cirrhosis commencing antiviral treatment?, *J Gastroenterol Hepatol*. 2018 Feb 20
6. Cho, EY and **An H**, Analysis of the Relationship between Regional Prevalence and the Average Concentration of Particulate Matter using Beta Regression, *Journal of The Korean Data Analysis Society*, 2018, vol.20, no.4, pp. 1791-1800
7. Seo YS, Park SY, Kim MY, Kim SG, Park JY, Yim HJ, Jang BK, Park SH, Kim JH, Suk KT, Kim JD, Kim TY, Cho EY, Lee JS, Jung SW, Jang JY, **An H**, Tak WY, Baik SK, Hwang JS, Kim YS, Sohn JH, Um SH, Serum cystatin C level: An excellent predictor of mortality in patients with cirrhotic ascites. *J Gastroenterol Hepatol*. 2018 Apr;33(4):910-917.
8. Han KM, Han C, Shin C, Jee HJ, **An H**, Yoon HK, Ko YH, Kim SH., Social capital, socioeconomic status, and depression in community-living elderly. *J Psychiatr Res*. 2018 Mar;98:133-140
9. Choi Y, Yun MS, Lim SH, Lee J, Ahn JH, Kim YJ, Park KH, Park YS, Lim HY, **An H**, Suh DC, Kim YH., Gemcitabine and Docetaxel Combination for Advanced Soft Tissue Sarcoma: A Nationwide Retrospective Study, *Cancer Res Treat*. 2018 Jan;50(1):175-182

Abstract

THE ROLE OF BIOSTATISTICS IN PRECISION MEDICINE AND BIG DATA ERA

Hyonggin An

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Precision medicine is an approach to maximization of health care by customizing the health-care process with medical decisions, treatments, or drugs being tailored to the individual patient. In precision medicine a tool such as diagnostic testing or imaging is used for choosing optimal therapies based on a patient's special characteristic. The potential optimal action could be the specific drug use, the dose selection, the timing of treatment, or other aspects of treatment or care. The role of biostatistics in precision medicine is somewhat different from classical medicine. In classical medicine, statistics is used for the inference based on population. However, in precision medicine, statistics focuses on estimation and testing for treatment regimes that maximize some cumulative clinical outcomes. In precision medicine, there are some statistical strategies in study design and data analysis such as biomarker, adaptive patients enrichment, patients subgroup, and multiplicity adjustment. In this talk, I provide a brief review of this area of research and discuss statistical challenges in precision medicine.

Keywords
Biostatistics, Precision Medicine, Big Data

Symposium 1

Young-Hak Kim

Organization

Asan Medical Center, College of Ulsan Medical School

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2018-Current	Asan Medical Center, Seoul, Korea	Department of Bioinformatics
2017-Current	Asan Medical Center, Korea	Director of Health Innovation Bigdata center chair
2014-Current	Division of Cardiology, Asan Medical Center, University of Ulsan College of Medicine, Korea	Professor of Medicine
2008-2014	Division of Cardiology, Asan Medical Center, University of Ulsan College of Medicine, Korea	Associate professor of Medicine
2006-2007	Cardiovascular Research Foundation, University of Columbia, New York	Research Fellow
2003-2008	Division of Cardiology, Asan Medical Center, University of Ulsan College of Medicine, Korea	Assistant professor of Medicine
2001-2005	Kyungpook National University, College of Medicine, Korea	Ph.D.
1996-1998	University of Ulsan, College of Medicine, Korea	M.S.
1987-1993	Kyungpook National University, College of Medicine, Korea	M.D.

» Research Interests

- Clinical trials related percutaneous coronary intervention and cardiac imaging
- Approval for clinical trials in medicine and device
- Medical Big Data Regulations and Infrastructure Development
- Cardiovascular disease
- Healthcare Information Tec
- Health Informatics, Artificial Intelligence

» Honors & Awards

- 2014 Best Scientific Exhibition Award-Winning Posters, Gold Medal, 2014 Asian Society of Cardiovascular Imaging
- 2014 Certificate of Merit, 2014 Radiological Society of North America

» Publications

1. Harrison's Principles of Internal Medicine (19th edition). McGraw-Hill Professional, 2016
2. COMPLEX ANGIOPLASTY 5th Edition. Shin-Won Publishing, 2012
3. Advanced Applied Interventional Cardiology. Saunders, 2010

Abstract

MEDICAL BIG DATA: HYPE OR HOPE?

Young-Hak KIM

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Advancements in information and communication technology (ICT) has enabled convergence among industries and the pace of innovation is accelerating day by day. As new types of large-scale, real-time data are generated across all industries, techniques to store, analyze, and utilize the data have been developed widely so that it is possible to derive meaningful insights from the data.

Artificial intelligence (AI) will be the most popular among various analytical techniques applied to derive meaning from big data. Artificial intelligence, which is able to learn a lot of data efficiently and shows the ability to overcome human performance in some fields, is applied to various industries and technologies to improve human life quality.

Growing levels of adoption in big data and AI are bringing ever more hope especially for healthcare industry leading to better health outcomes, lower cost of care, and realization of precision medicine. AI has a great influence on the paradigm shift in healthcare as a core technology basis not only for assisting healthcare professionals through clinical decision support such as medical image reading but also for offering personalized treatment and care experience for patients or even improving the efficiency of hospital operation.

However, a number of challenges still lies ahead for successful adoption of medical big data both in and out of hospitals, such as ambiguity of data ownership, privacy and security concern, regulatory and governance. Moreover, as AI is not dependent on a specific program or set of codes, but learns from the data itself, the amount and quality of data are a very important factor in the development of artificial intelligence and that the performance of AI-based services (or solutions) to be developed according to the data collection and preprocessing process can be controlled. As the phrase "garbage in, garbage out" (GIGO) implies, ensuring accurate and complete data will be the keys to competence in the era of artificial intelligence, and the expected worth increase exponentially as the amount of data gathered continues to grow.

Keywords
Medical Big Data, Artificial Intelligence, Paradigm Shift in Medicine

Symposium 1

Chan Joo Lee

Organization

Yonsei University College of Medicine

Position & Title

Clinical Assistant Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2019.3-Present	Division of Cardiology, Department of Internal Medicine, Severance Hospital Yonsei University College of Medicine	Clinical Assistant Professor
2017.3-2019.2	Department of Health Promotion, Severance Hospital Yonsei University College of Medicine	Clinical Assistant Professor
2016.3-2017.2	Division of Cardiology, Department of Internal Medicine, Severance Hospital Yonsei University College of Medicine	Clinical Research Assistant Professor
2015.3-2016.2	Division of Cardiology, Department of Internal Medicine, Severance Hospital Yonsei University College of Medicine	Fellow
2010.3-2015.2	Yonsei University, Seoul, Republic of Korea	Ph.D

» Publications

1. Lee CJ, Ryu J, Kim HC, Ryu DR, Ihm SH, Kim YJ, Shin JH, Pyun WB, Kang HS, Park JH, Hwang J, Park S. Clinical Benefit of Treatment of Stage-1, Low-Risk Hypertension.: Korean National Health Insurance Database Analysis. Hypertension 2018;72(6):1285-1293
2. Lee CJ, Hwang J, Lee YH, Oh J, Lee SH, Kang SM, Choi D, Kim HC, Park S. Blood Pressure Level Associated with Lowest Cardiovascular Event in Hypertensive Diabetic Patients. Journal of Hypertension. 2018; 36(12):2434-2443
3. Seo J, Lee CJ, Hwang J, Oh J, Lee SH, Kang SM, Kim HC, Park S. Optimal Blood Pressure in Elderly Hypertensive Subjects: A Korean National Health Insurance Service Health Examinee Cohort Study. American Journal of Hypertension. 2018; E-pub (Co-first author)
4. Lee CJ, Kim JY, Shin E, Hong SH, Lee M, Jeon Y, Park S. The effects of diet alone or in combination with exercise in patients with prehypertension and hypertension: a randomized controlled trial. Korean Circulation Journal. 2018; E-pub
5. Lee CJ, Oum CY, Lee Y, Park S, Kang SM, Choi D, Jang Y, Lee JH, Lee SH. Variants of Lipolysis-related Genes in Korean Patients with Very High Triglycerides. Yonsei Medical Journal. 2018;59(1):148-153
6. Lee CJ, Hwang J, Oh J, Lee SH, Kang SM, Kim HC, Park S. Relation between blood pressure and clinical outcome in hypertensive subjects with previous stroke. Journal of American Heart Association. 2017;6(12)
7. Oh J, Lee CJ, Kim DI, Rhee MY, Lee BK, Ahn Y, Cho BR, Woo JT, Hur SH, Jeong JO, Jang Y, Lee SH. Target achievement with maximal statin-based lipid-lowering therapy in Korean patients with familial hypercholesterolemia: A study supported by the Korean Society of Lipidology and Atherosclerosis. Clinical Cardiology. 2017;40(12):1291-1296

Abstract

BENEFIT OF ASPIRIN AND STATIN IN LOW RISK HYPERTENSION: NHIS DATA ANALYSIS

Chan Joo Lee

Yonsei University, Korea
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INTRODUCTION: To determine whether the addition of aspirin to a statin regimen is beneficial in reducing cardiovascular mortality, we analyzed data for uncomplicated hypertensive patients included in the Korea National Health Insurance sample cohort.

METHOD: Among the 758 433 eligible participants aged 20 years or older in 2005, 31 115 participants were selected and divided into four groups: no-treatment group (N = 19 628); aspirin alone group (N = 4814); statins alone group (N = 4717); and combined treatment group (N = 1956). The mean follow-up duration was 94 ± 13 months. The primary outcome of the study was all-cause and cardiovascular mortality from 2007 to 2013.

RESULTS: Treatment with aspirin alone [hazard ratio (HR), 0.62; 95% confidence interval (CI), 0.55-0.70; P < 0.001), treatment with statins alone (HR, 0.48; 95% CI, 0.41-0.57; P < 0.001), and combined treatment (HR, 0.43; 95% CI, 0.34-0.55; P < 0.001) were independently associated with reductions in all-cause mortality. Treatment with aspirin alone (HR, 0.66; 95% CI, 0.53-0.84; P < 0.001), treatment with statins alone (HR, 0.46; 95% CI, 0.33-0.64; P < 0.001), and combined treatment (HR, 0.50; 95% CI, 0.31-0.79; P = 0.003) were also independently associated with reductions in cardiovascular mortality. The addition of aspirin to statins was not associated with an additive benefit in reducing total mortality or cardiovascular mortality.

CONCLUSION: Primary prevention with aspirin and/or statins is beneficial in reducing both all-cause and cardiovascular mortality in uncomplicated hypertensive participants. Nevertheless, as aspirin administration is associated with an increased risk of major bleeding, care must be taken to assess the risk/benefit of using aspirin in primary prevention.

Symposium 1

Ga Eun Nam

Organization

Department of Family Medicine,
Korea University Anam Hospital,
Korea University College of Medicine

Position & Title

Clinical Assistant Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2018.12-	Korea University Anam Hospital	Clinical Assistant Professor
2016.9-2018.12	Sahmyook Medical Center	Chief of Department
2011.3-2016.8	Korea University Ansan Hospital	Clinical Assistant Professor, Clinical Instructor
2012.3-2015.2	Korea University College of Medicine	Ph.D.
2010.3-2012.2	Korea University College of Medicine	M.S.
1999.3-2006.2	Korea University College of Medicine	M.D.

» Research Interests

Obesity, Metabolic syndrome, Epidemiology

» Honors & Awards

· 2018, 2017, 2014 Academic award, The Korean Academy of Family Medicine

» Publications

1. Nam GE, Park YG, Han K, Kim MK, Koh ES, Kim ES, Lee MK, Kim B, Hong OK, Kwon HS. BMI, Weight Change, and Dementia Risk in Patients With NewOnset Type 2 Diabetes: A Nationwide Cohort Study. Diabetes Care. 2019;42(7):1217-1224.
2. Nam GE, Kim SM, Han K, Kim NH, Chung HS, Kim JW, Han B, Cho SJ, Yu JH, Park YG, Choi KM. Metabolic syndrome and risk of Parkinson disease: A nationwide cohort study. PLoS Med. 2018;15(8):e1002640.
3. Nam GE, Kim NH, Han K, Choi KM, Chung HS, Kim JW, Han B, Cho SJ, Jung SJ, Yu JH, Park YG, Kim SM. Chronic renal dysfunction, proteinuria, and risk of Parkinson's disease in the elderly. Mov Disord. 2019 Apr 25. doi: 10.1002/mds.27704.
4. Nam GE, Cho KH, Han K, Han B, Cho SJ, Roh YK, Kim SM, Choi YS, Kim DH, Kim YH, Park YG. Impact of body mass index and body weight variabilities on mortality: a nationwide cohort study. Int J Obes (Lond). 2019;43(2):412-423.
5. Nam GE, Cho KH, Han K, Kim CM, Han B, Cho SJ, Jung SJ, Kwon Y, Kim YH, Kim DH, Kim SM, Choi YS, Roh YK, Park YG. Obesity, abdominal obesity and subsequent risk of kidney cancer: a cohort study of 23.3 million East Asians. Br J Cancer. 2019;121(3):271-277.
6. Nam GE, Han K, Kim DH, Huh Y, Han B, Cho SJ, Park YG, Park YM. Associations between Breastfeeding and Type 2 Diabetes Mellitus and Glycemic Control in Parous Women: A Nationwide, Population-Based Study. Diabetes Metab J. 2019;43(2):236-241.
7. Nam GE, Hwang SY, Chung HS, Choi JH, Lee HJ, Kim NH, Yoo HJ, Seo JA, Kim SG, Kim NH, Baik SH, Choi KM. Implication of Nonalcoholic Fatty Liver Disease, Metabolic Syndrome, and Subclinical Inflammation on Mild Renal Insufficiency. Int J Endocrinol. 2018;2018:1835486.

Abstract

UNSTABLE OBESITY PARAMETERS AND HEALTH OUTCOMES BASED ON NHIS DATABASE

Ga Eun Nam

Department of Family Medicine, Korea University Anam Hospital, Korea University College of Medicine, Republic of Korea
namgaaa@daum.net

Recently, the association between intra-individual variability in cardiometabolic parameters and health outcomes has attracted increasing interest. There has been limited evidence regarding the longitudinal associations of variabilities in obesity measures including weight, body mass index, waist circumference with cardiovascular outcomes and mortality. Using the South Korean National Health Insurance Service (NHIS) database, we have sought to examine the associations between obesity parameters and myocardial infarction, ischemic stroke, and mortality in the general population as well as in patients with type 2 diabetes. We found consistently positive associations between unstable obesity parameters and the health outcomes. Our results indicated that fluctuations in obesity measures may be considered risk factors of cardiovascular outcomes and mortality. In this lecture, I will introduce our study results regarding the association between unstable obesity parameters and health outcomes based on the South Korean NHIS database.

Keywords
Weight, waist circumference, variability, fluctuation, cardiovascular disease, mortality

Symposium 1

Sungsoo Cho

Organization

Dankook University, College of Medicine

Position & Title

Assistant Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2006-2007	Severance Hospital, Yonsei University	Intership
2007-2011	Internal Medicine, Severance Hospital, Yonsei University	Residency
2014-2015	Cardiology, Severance Cardiovascular Hospital, Yonsei University	Fellow
2015-2018	Cardiovascular Medicine, Dankook University Hospital	Clinical Assistant Professor
2018-	Cardiovascular Medicine, Internal Medicine, College of Medicine, Dankook University	Assistant Professor

» Research Interests

Intervention cardiolgy

» Honors & Awards

- 2014 Early career Poster winner, American Heart Association
- 2016 ENCORE winner of the Case prestation

» Publications

1. Sungsoo Cho, Tae Soo Kang, Jung-Sun Kim, MD, et al., Long-term clinical outcomes and optimal stent strategy in left main coronary bifurcation stenting. J Am Coll Cardiol Intv 2018;11:1247-58
2. Sungsoo Cho, Wonkyung Lee, Seong-Hoon Lim, and Tae Soo Kang. Relationship between Clinical Outcomes and Cardiopulmonary Resuscitation Time in Patients with Acute Myocardial Infarction Treated by Extracorporeal Membrane Oxygenation-Assisted Primary Percutaneous Coronary Intervention. Korean Cir J 2018 Aug;48(8):705-715
3. Sungsoo Cho, Hoguen Kim, Jung-Sun Kim, Byeong-Keuk Kim, Yangsoo Jang, Myeong-Ki Hong. In Vivo Demonstration of Frail Neointimal Tissue Embolization After Angioplasty With a Drug-Coated Balloon Confirmed by Optical Coherence Tomography and Histology. Circulation. 2015;132:144-145
4. Sungsoo Cho, Jung-Sun Kim, Jinyong Ha, Dong-Ho Shin, Byeong-Keuk Kim, Young-Guk Ko, MD, Donghoon Choi, Yangsoo Jang, and Myeong-Ki Hong. Three-Dimensional Optical Coherence Tomographic Analysis of Eccentric Morphology of the Jailed Side-Branch Ostium in Coronary Bifurcation Lesions Canadian Journal of Cardiology (2015) 1-6

Abstract

THE USE OF MACHINE LEARNING ALGORITHMS FOR THE IDENTIFICATION OF STABLE OBSTRUCTIVE CORONARY ARTERY DISEASE

Sungsoo Cho, MD, PhD[1], Jun Tae Kim, MD[1], Su Yeon Lee, MD[1], Dongmin Kim, MD[1], Seong-Hoon Lim, MD, PhD[1], Tae Soo Kang, MD, PhD[1], Myung-Yong Lee, MD, PhD[1]

[1]Division of Cardiovascular Medicine, Department of Internal Medicine, Dankook University Hospital, Dankook University College of Medicine, Cheonan-si, Choongcheongnam-do, Korea
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Background: Machine learning (ML) might be useful to analysis various clinical information to make more accurate predictions. The purpose of this study is to develop prediction models using ML algorithms for identification of stable obstructive coronary artery disease (CAD).

Methods: We retrospectively analyzed 2012 patients who visited outpatient department for stable angina or angina equivalent symptom and underwent coronary angiography from August 2014 to January 2016. We analyzed dataset using the most predictive algorithm among five ML algorithms, determine the most significant predictors in 10 variables. We compared between ML algorithm based model and established prediction model (CAD consortium model). Predictive accuracy was assessed by area under the 'receiver operating curve' (AUC). The entire data were randomly split into a training (80%) and a validation set (20%).

Result: Of the 1312 enrolled patients, 861 were patients with obstructive CAD on coronary angiography. The XGBoost algorithm model showed the best performance compared to the other four algorithms (AUC 0.805 95% Confidence interval [CI] 0.744-0.866). The XGBoost algorithm model improved risk prediction compared to CAD consortium clinical model (AUC 0.740 95% CI 0.712-0.768). The accuracy of ML based model was 80.2%. Age, troponin T, and HbA1c were important variables.

Conclusion: ML based models provide high accuracy for the prediction of stable obstructive CAD and find out new association among variables. ML based models improve identification of stable obstructive CAD over established CAD consortium clinical model.

Keywords
machine learning algorithm; coronary artery disease, stable angina pectoris

ICoLA 2019 by KSoLA

Symposium 2

Chairpersons

Goo Taeg Oh | Ewha Womans University, Korea
Laurent Yvan-Charvet | INSERM, France

Date & Time: September 5 (Thu.), 16:00-18:00
Place: Room 5 (5F)

Symposium 2

Laurent YVAN-CHARVET

Organization

INSERM

Position & Title

Director of Research

(eq. to 'tenure track' Full Professor)

» Educational Background & Professional Experience

Year	Name of institution	Position
Since 2015	Inserm	Director of Research
2013-2015	Inserm	Team leader ATIP-AVENIR
2012-2013	Pfizer CVMED	Joint appointment with Columbia University
2009-2013	Columbia University	Associate Professor
2005-2009	Columbia University	Postdoctoral fellowship
2002-2005	Université Paris – Les Cordeliers	PhD

» Research Interests

Hematometabolism, cardiometabolic diseases, atherosclerosis

» Honors & Awards

- 2015 Daniel Steinberg Early Career Investigator AHA
- 2013 EAS young Investigator Award European Athero Society
- 2010 Roger Davis Award Kern Aspen Conference

» Publications

1. Yvan-Charvet et al., Immunometabolic function of cholesterol in cardiovascular disease and beyond. Cardiovasc Res (2019) in press
2. Yvan-Charvet L, Swirski FK. Is defective cholesterol efflux an integral inflammatory component in myelopoiesis-driven cardiovascular diseases? Eur Heart J. (2018) 39(23):2168
3. Yvan-Charvet L, Cariou B. Poststatin era in atherosclerosis management. Curr Opin Lipidol. (2018). 32 :448
4. Viaud et al., Lysosomal Cholesterol Hydrolysis Couples Efferocytosis to Anti-Inflammatory Oxysterol Production. Circ Res. 2018;122(10):1369
5. Tall AR, Yvan-Charvet L. Cholesterol, inflammation and innate immunity. Nat Rev Immunol. (2015). 15 :104-16.
6. Sarrazy V et al., Disruption of Glut1 in hematopoietic stem cells prevents myelopoiesis and enhanced glucose flux in atheromatous plaques of ApoE-/- mice. Circ Res. (2016). 118:1062-77
7. Yvan-Charvet L, et al., ATP binding cassette transporters and HDL suppress hematopoietic stem cell proliferation. Science. (2010), 328: 1689

Abstract

MACROPHAGE GLUTAMINOLYSIS, THE GOOD, THE BAD AND THE UMAMI

Laurent YVAN-CHARVET

Institut National de la Santé et de la Recherche Médicale (Inserm) U1065, Université Côte d'Azur, Department of Molecular Medicine (C3M), Atip-Avenir, Fédération Hospitalo-Universitaire (FHU) Oncoage, 06204 Nice, France
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Macrophage plasticity and adaptability to local environmental cues rely on a rapid metabolic rewiring. Glutaminase (GLS) converts glutamine to glutamate to fuel anabolic processes and support redox and epigenetic reactions. Here, we identify a key role for GLS in macrophage effector functions. Loss of GLS1 diminished alternative macrophage polarization and reduced efferocytosis. This was not associated with canonical glutamate dehydrogenase (GLUD1)-dependent conversion of glutamate into α-ketoglutarate in the mitochondria to fuel the tricarboxylic acid cycle or classical mTor-dependent metabolic reprogramming. GLS1 deficient macrophages rather refocused cellular metabolism to a high redox state and a low transamination-dependent mitochondrial efficiency. Targeted deletion of GLS1 in myeloid cells resulted in failure of apoptotic cell uptake leading to accelerated atherosclerosis. Our findings position glutaminase-dependent metabolic reprogramming as a critical process that enables continued clearance of ACs by macrophages to avoid the pathologic consequences of defective efferocytosis in vivo.

Keywords
Hematometabolism, cardiometabolic diseases, atherosclerosis

Symposium 2

Edward Thorp

Organization

Northwestern University

Position & Title

Associate Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
1999-2004	Loyola University Chicago	PhD
2005-2011	Columbia University	Postdoctoral Fellow

» Research Interests

Cardiovascular Immunology

» Honors & Awards

· FAHA

» Publications

1. Zhang S, Weinberg S, DeBerge M, Gainullina A, Schipma M, Kinchen JM, Ben-Sahra I, Gius DR, Yvan-Charvet L, Chandel NS, Schumacker PT, **Thorp EB**. *Efferocytosis Fuels Requirements of Fatty Acid Oxidation and the Electron Transport Chain to Polarize Macrophages for Tissue Repair*. Cell Metab. 2019 Feb 5;29(2):443-456.e5. PubMed PMID: 30595481.
2. DeBerge M, Yeap, X, Dehn S, Zhang S, Grigoryeva L, Misener L, Procissi D, Zhou X, Lee D, Muller W, Luo X, Rothlin C, Tabas I, & **Thorp EB**. *MerTK Cleavage on Resident Cardiac Macrophages Compromises Repair after Myocardial Ischemia Reperfusion Injury*. Circ Res. ’17 Sep 29;121(8):930-940. doi: 10.1161/CIRCRESAHA.117.311327. Epub 2017 Aug 29. PMID: 28851810. PMCID: PMC5623080.
3. DeBerge M, Shah SJ, Wilsbacher L, **Thorp EB**. *Macrophages in Heart Failure with Reduced versus Preserved Ejection Fraction*. Trends Mol Med. 2019 Apr;25(4):328-340. doi: 10.1016/j.molmed.2019.01.002. Epub 2019 Feb 5. Review. PubMed PMID: 30737012.

Abstract

PHAGOCYTE IMMUNOMETABOLISM IN HEART

Edward Thorp PhD

Northwestern University, Chicago USA
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A timely question pertains to how metabolic phagocytic signaling regulates the signature anti-inflammatory macrophage response. Our studies newly reveal the metabolome of activated macrophages during cardiac tissue injury to reveal an interleukin-10 (IL-10) cytokine escalation that is independent of glycolysis yet bolstered by apoptotic cell fatty acids and mitochondrial β-oxidation, the electron transport chain, and heightened coenzyme NAD+. Loss of IL-10 due to mitochondrial complex III defects was remarkably rescued by adding NAD+ precursors. Il-10 activation by the respiratory chain was also important in vivo, as phagocyte mitochondrial dysfunction led to cardiac rupture after myocardial injury. These findings highlight a new paradigm whereby macrophages leverage injury metabolites and electron transport for anti-inflammatory reprogramming that culminates in organ repair.

Symposium 2

Young-Tae Chang

Organization

POSTECH Chemistry and Center for Self-Assembly & Complexity, IBS

Position & Title

Associate Director(CSC)/ Professor(POSTECH)

» Educational Background & Professional Experience

Year	Name of institution	Position
2017-	POSTECH, Republic of Korea	Professor
2017-	Center for Self-Assembly and Complexity, IBS, Republic of Korea	Associate Director
2007-2017	Laboratory of Bioimaging Probe Development, SBIC, A*STAR, Singapore	Head
2012-2017	National University of Singapore, Singapore	Professor
2007-2017	Medicinal Chemistry Program, National University of Singapore, Singapore	Director
2014-2015	University of Malaya, Malaysia	High Impact Research (HIR) Icon
2007-2011	National University of Singapore, Singapore	Associate Professor
2010	Kyoto University, Japan	Visiting professor
2006 Fall	National University of Singapore, Singapore	Visiting professor
2006 Summer	Broad institute, USA	Visiting professor
2005-2007	New York University, USA	Associate professor
2000-2005	New York University, USA	Assistant Professor
1999-2000	The Scripps Research Institute, USA	Post-Doc
1997-1999	University of Califonia, Berkeley, USA	Post-Doc
1995-1997	POSTECH, Republic of Korea	Ph.D.
1993-1995	POSTECH, Republic of Korea	M.S.
1987-1991	POSTECH, Republic of Korea	B.S.

» Research Interests

Fluorescence Library for Live Cell Imaging & Probe development

» Honors & Awards

- 2012 Outstanding Scientist Award, Faculty of Science, NUS
- 2005 NSF Career Award
- 2003 Society of Boimedical Research (SBR)/CKD Bioscience Award

» Publications

1. Development of Targetable Two-Photon Fluorescent Probes to Image Hypochlorous Acid in Mitochondria and Lysosome in Live Cell and Inflamed Mouse Model, Yuan, L.; Wang, L.; Agrawalla, B. K.; Park, S. J.; Zhu, H.; Sivaraman, B.; Peng, J.; Xu, Q. H.; Chang, Y. T.* *J. Am. Chem. Soc*. 2015, 137, 5930-5938.
2. Surface Enhanced Raman Scattering in Cancer Detection and Imaging, Vendrell, M.; Maiti, K. K.; Dhaliwal, K.; Chang, Y. T. *Trends Biotechnol*. 2013, 31, 249-257.
3. Multiplex Targeted in vivo Cancer Detection Using Sensitive Near-Infrared SERS Nanotags, Maiti, K. K.; Dinish, U. S.; Samanta, A.; Vendrell, M.; Soh, K. S.; Park, S. J.; Olivo, M.; Chang, Y. T.* *Nano Today* 2012, 7, 85-93.
4. Ultrasensitive Near-Infrared Raman Reporters for SERS-based in vivo Cancer Detection, Samanta, A.; Maiti, K. K.; Soh, K. S.; Liao, X.; Vendrell, M.; Dinish, U. S.; Yun, S. W.; Bhuvaneswari, R.; Kim, H.; Rautela, S.; Chung, J.; Olivo, M.; Chang, Y. T.* *Angew. Chem., Int. Ed. Engl*. 2011, 50, 6089-6092.
5. Synthesis of a bodipy library and its application to the development of live cell glucagon imaging probe, Lee, J. S.; Kang, N. Y.; Kim, Y. K.; Samanta, A.; Feng, S.; Kim, H. K.; Vendrell, M.; Park, J. H.; Chang, Y. T.* *J. Am. Chem. Soc*. 2009, 131, 10077-10082. Highlighted at JACS Select #10: Supramolecular and Chemical Cascade Approaches to Molecular Sensing
6. Combinatorial rosamine library and application to in vivo glutathione probe, Ahn, Y. H.; Lee, J. S.; Chang, Y. T.* *J. Am. Chem. Soc.* 2007, 129, 4510-4511.
7. Forward chemical genetic approach identifies new role for GAPDH in insulin signaling, Min, J. K.; Kim, Y. K.; Cipriani, P. G.; Kang, M.; Khersonsky, S. M.; Walsh, D. P.; Lee, J. Y.; Niessen, S.; Yates, J. R.; Gunsalus, K.; Piano, F.; Chang, Y. T.* *Nat. Chem. Biol.* 2007, 3, 55-59. Highlighted at "New diabetes target, C&En News, 2006 (December 4), 84 (49), p 63" & "NYU, Scripps Finding offers New Path For Treatment of Diabetes, Medical News Today, 2006 (November 30)"

Abstract

DEVELOPMENT OF MOLECULAR PROBES FOR THE STUDY OF ATHEROSCLEROSIS

Young-Tae CHANG[1,2]

[1] POSTECH, Department of Chemistry, Republic of Korea
[2] IBS, Center for Self-Assembly & Complexity, Republic of Korea
ytchang@postech.ac.kr

Conventional sensor development requires defining the target and design of sensor, which is so-called hypothesis driven approach. While powerful, this approach cannot be applied to unknown target or difficult to be applied to complex of analytes. To overcome the limitation, we have devised a Diversity Oriented Fluorescence Library Approach (DOFLA) where a combinatorial synthesis of fluorescent dye is combined with unbiased screening to accelerate the sensor development. More than 10,000 synthetic organic dyes were constructed as a tool box, and numerous analytes have been tested, yielding systematic platform for sensor development for almost everything. Complex or unknown target problem with biological systems were also challenged, and various cell type selective probes for live bioimaging were developed. In this presentation, especially the recently developed probe CDg16 for activated macrophages and its application to atherosclerosis will be mainly discussed with a novel gate-oriented mechanisms. The sensors and probes developed in this study will be freely available for the chemical and biological community for common usage

Keywords
Fluorescence, Bioimaging, Chemical Biology, Sensor, Probe, Artificial Cell, Molecular Evolution

Symposium 2

Chang Hyun Byon

Organization

Chonnam National University Hospital

Position & Title

Research Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2018.8-Present	Chonnam National University, Korea	Research Professor
2014.9-2018.7	University of Alabama at Birmingham, USA	Research Associate
2010.1-2014.8	University of California at Los Angeles, USA	Postdoctoral Fellow
2004.8-2009.12	University of Alabama at Birmingham, USA	Doctor of Philosophy
2002.4-2004.7	Asan Institute of Life Sciences, Korea	Research Scientist
2000.3-2002.3	Pohang University of Science and Technology, Korea	Research Scientist

» Research Interests

Vascular calcification in cardiovascular symptoms

» Honors & Awards

- 2016 Young Investigator Award, Arteriosclerosis, Thrombosis and Vascular Biology Annual Conference
- 2009 Cardiovascular Pathophysiology Award for the Outstanding, UAB
- 2008 Merit Award for Young Investigators, Arteriosclerosis, Thrombosis and Vascular Biology Annual Conference

» Publications

1. Sun Y, Byon CH et al. Dietary potassium regulates vascular calcification and arterial stiffness. JCI Insight. 2017 Oct 5;2(19)
2. Byon CH et al. Redox signaling in cardiovascular pathophysiology: A focus on hydrogen peroxide and vascular smooth muscle cells. Redox Biol. 2016 Oct;9:244-253
3. Byon CH et al. Txnip Ablation Reduces Vascular Smooth Muscle Cell Inflammation and Ameliorates Atherosclerosis in Apolipoprotein E Knockout Mice. Atherosclerosis. 2015 Aug;241(2):313-21
4. Byon CH et al. Molecular Mechanisms of Vascular Calcification in Chronic Kidney Disease: The Link between Bone and the Vasculature. Curr Osteoporos Rep. 2015 Aug;13(4):206-15
5. Sun Y, Byon CH et al. Smooth muscle cell-specific runx2 deficiency inhibits vascular calcification. Circ Res. 2012 Aug 17;111(5):543-52
6. Byon CH et al. Runx2-Upregulated Receptor Activator of Nuclear Factor {kappa}B Ligand in Calcifying Smooth Muscle Cells Promotes Migration and Osteoclastic Differentiation of Macrophages. Arterioscler Thromb Vasc Biol. 2011 Jun;31(6):1387-96

Abstract

VASCULAR CALCIFICATION IN CARDIOVASCULAR PATHOLOGIES: ROLE OF O-GLCNAC MODIFICATION

Chang Hyun Byon[1,2]*, Yong Sun[2], Chen Yabing[2], and Soo Wan Kim[1]

[1] Nephrology, Chonnam National University Hospital, Korea
[2] Pathology, University of Alabama at Birmingham, USA
changhyunbyon@gmail.com

Vascular calcification is prevalent in patients with atherosclerosis, diabetes mellitus and chronic kidney disease, which increases the risk of cardiovascular events and mortality. Recent studies have further demonstrated that increased vascular calcification in diabetes is associated with elevated protein O-linked GlcNAc modification (O-GlcNAcylation). As O-GlcNAc transferase (OGT) is the key enzyme that control O-GlcNAcylation by adding O-GlcNAc onto proteins, we determined the effects of inhibition of OGT on diabetic vascular calcification and the underlying molecular mechanisms. By using new inducible smooth muscle-specific OGT deletion mice, we demonstrated that smooth muscle-specific OGT deletion did not affect blood glucose, but significantly inhibited protein O-GlcNAcylation exclusively in smooth muscle layer and inhibited vascular calcification in diabetic mice. Inhibition of vascular calcification by OGT ablation was associated with inhibition of Runx2, the key osteogenic transcription factor that is essential for vascular smooth muscle cell calcification. Further analysis showed that inhibition of Runx2 O-GlcNAcylation by site-directed mutagenesis was found to decrease Runx2 transactivity and alter intracellular localization of Runx2. Our studies have provided novel molecular insights into Runx2 regulation by OGT-dependent O-GlcNAcylation in diabetic vascular calcification, which may shed lights on novel targets that are amenable to drug discovery for diabetic vascular calcification.

Keywords
Vascular calcification, O-GlcNAcylation, Smooth muscle cells, Runx2, Atherosclerosis, Diabetes, Chronic kidney disease

ICoLA 2019 by KSoLA

Symposium 3

Chairpersons

Bong-Soo Cha | Yonsei University, Korea
Brian A. Ference | University of Cambridge, UK

Date & Time: September 6 (Fri.), 09:40-11:10
Place: Room 1 (3F)

Symposium 3

Sripal Bangalore

Organization

New York University School of Medicine

Position & Title

Professor of Medicine

Director, Complex Coronary Intervention, Bellevue

Director of Research, Cardiac Catheterization Laboratory

Director, Cardiovascular Outcomes Group

» Educational Background & Professional Experience

Year	Name of institution	Position
2018.8-Present	New York University School of Medicine	Professor of Medicine (Tenured)
2013.9-2018.7	New York University School of Medicine	Associate Professor of Medicine
2010.9-2013.8	New York University School of Medicine	Assistant Professor of Medicine
2008.7-2010.6	Brigham and Women's Hospital	Fellowship: Interventional Cardiology
2005.7-2008.6	St Luke's Roosevelt Hospital and Columbia University	Fellowship: Cardiovascular Medicine
2003.7-2005.6	St Luke's Roosevelt Hospital and Columbia University	Residency: Internal Medicine

» Research Interests

Research interest are in comparative effectiveness studies for cardiovascular diseases, particularly stable ischemic heart disease, acute coronary syndromes, hypertension and dyslipidemia

» Honors & Awards

- 2009-2010 Dr. Gregory Braden Memorial Interventional Cardiology Fellow of the Year Award from the Society of Angiography and Intervention
- 2009-2010 Thomas J. Linnemeier Spirit of Interventional Cardiology Young Investigator Award finalist (TCT 2009)
- 2016 Douglas P. Zipes Distinguished Young Scientist Award, American College of Cardiology

» Publications

1. Messerli FH, Hofstetter L, Rimoldi SF, Rexhaj E, Bangalore S. Risk Factor Variability and Cardiovascular Outcome: JACC Review Topic of the Week. J Am Coll Cardiol. 2019 May 28;73(20):2596-2603. doi: 10.1016/j.jacc.2019.02.063. Review.PMID: 31118154
2. Bangalore S, Fayyad R, DeMicco DA, Colhoun HM, Waters DD.Body Weight Variability and Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus. Circ Cardiovasc Qual Outcomes. 2018 Nov;11(11):e004724. doi: 10.1161/CIRCOUTCOMES.118.004724. PMID: 30571333
3. Waters DD, Bangalore S, Fayyad R, DeMicco DA, Laskey R, Melamed S, Barter PJ. Visit-to-visit variability of lipid measurements as predictors of cardiovascular events. J Clin Lipidol. 2018 Mar - Apr;12(2):356-366. doi: 10.1016/j.jacl.2017.12.003. Epub 2017 Dec 20. PMID: 29310989
4. Bangalore S, Breazna A, DeMicco DA, Wun CC, Messerli FH; TNT Steering Committee and Investigators. Visit-to-visit low-density lipoprotein cholesterol variability and risk of cardiovascular outcomes: insights from the TNT trial. J Am Coll Cardiol. 2015 Apr 21;65(15):1539-48. doi:10.1016/j.jacc.2015.02.017.PMID: 25881936
5. Bangalore S, Fayyad R, Laskey R, DeMicco DA, Messerli FH, Waters DD. Body-Weight Fluctuations and Outcomes in Coronary Disease. N Engl J Med. 2017 Apr 6;376(14):1332-1340. doi: 10.1056/NEJMoa1606148. PMID: 28379800
6. Bangalore S, Guo Y, Samadashvili Z, Blecker S, Xu J, Hannan EL. Everolimus-eluting stents or bypass surgery for multivessel coronary disease. N Engl J Med. 2015 Mar 26;372(13):1213-22. doi: 10.1056/NEJMoa1412168. Epub 2015 Mar 16.PMID: 25775087

Abstract

BLOOD PRESSURE VARIABILITY

Sripal BANGALORE

Department of Medicine, Division of Cardiology, New York University School of Medicine, New York, NY, USA
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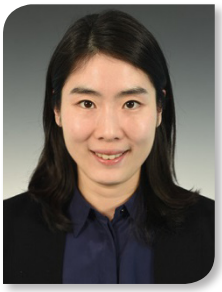
For a given patient, there is second to second, minute to minute, hour to hour, diurnal and seasonal variation in blood pressure. Until recently, intraindividual visit-to-visit variability of blood pressure has been dismissed as random fluctuation. This simplistic concept was challenged by demonstrating that visit-to-visit blood pressure variability, independent of average blood pressure, was a powerful risk factor for stroke. Moreover, other studies have consistently shown adverse outcomes with high variable blood pressure both in patients with and without coronary artery disease. In addition, antihypertensive therapies are currently available with lower blood pressure variability (the smoothness index). It is therefore time to focus not just on blood pressure but also on its variability to optimize care.

Keywords
blood pressure; mortality; variability

Symposium 3



Tae Jung Oh

Organization

Seoul National University, Seoul National University Bundang Hospital

Position & Title

Assistant Professor, Division of Endocrinology and Metabolism

» Educational Background & Professional Experience

Year	Name of institution	Position
2003-2007	Seoul National University College of Medicine	M.D
2010-2012	Postgraduate School, Seoul National University College of Medicine	Master of Medical Science
2012-2015	Postgraduate School, Seoul National University College of Medicine	Ph.D. in Medical Science
2015-2017	Seoul National University Bundang Hospital	Full-time lecturer, Clinical professor
2017-	Seoul National University Bundang Hospital	Assistant Professor

» Research Interests

Diabetic complications, obesity, metabolic surgery

» Publications

1. Oh TJ, Kang S, Lee J, Moon JH, Choi SH, Lim S, Jang HC. Association between deterioration in muscle strength and peripheral neuropathy in people with diabetes. J Diabetes Complicat 2019 Aug
2. Oh TJ, Lee J, Choi SH, Jang HC. Association between Body Fat and Diabetic Peripheral Neuropathy in Middle-Aged Adults with Type 2 Diabetes Mellitus: A Preliminary Report. J Obes Metab Syndr 2019 Jun
3. Oh TJ, Kim YG, Kang S, Moon JH, Kwak SH, Choi SH, Lim S, Park KS, Jang HC, Hong JS, Cho NH. Oral Glucose Tolerance Testing Allows Better Prediction of Diabetes in Women with a History of Gestational Diabetes Mellitus. Diabetes Metab J. 2019 Jun
4. Oh TJ, Yu JM, Min KW, Son HS, Lee MK, Yoon KH, Song YD, Park JY, Jeong IK, Cha BS, Kim YS, Baik SH, Kim IJ, Kim DM, Kim SR, Lee KW, Park JH, Lee IK, Park TS, Choi SH, Park SW. Efficacy and Safety of Voglibose Plus Metformin in Patients with Type 2 Diabetes Mellitus: A Randomized Controlled Trial. Diabetes Metab J. 2019 Jun
5. Oh TJ, Moon JH, Choi SH, Lim S, Park KS, Cho NH, Jang HC. Body-weight fluctuation and incident diabetes mellitus, cardiovascular disease, and mortality: a 16-year prospective cohort study. J Clin Endocrinol Metab. 2019 Mar
6. Ahn CH, Oh TJ, Kwak SH, Cho YM. Sodium-glucose cotransporter-2 inhibition improves incretin sensitivity of pancreatic β-cells in people with type 2 diabetes. Diabetes Obes Metab 2018 Feb
7. Oh TJ, Ahn CH, Kim BR, Kim KM, Moon JH, Lim S, Park KS, Lim C, Jang H, Choi SH: Circulating sortilin level as a potential biomarker for coronary atherosclerosis and diabetes mellitus. Cardiovascular Diabetol. 2017 Jul

Abstract

BODY WEIGHT FLUCTUATION

Tae Jung OH

[1]Department of Internal Medicine, Seoul National University Bundang Hospital, [2]Seoul National University College of Medicine, Korea
ohtjmd@gmail.com

Previous studies have tested whether body-weight fluctuation (weight cycling) is a prognostic marker for mortality in individuals with high cardiovascular risk, including middle-aged men, obese postmenopausal women, and older adults. A more recent study showed that body-weight variability, which was defined as average successive variability (ASV), was significantly associated with a coronary event and mortality in a post hoc analysis of the Treating to New Target trial. In this background, we examined whether body-weight fluctuation can associate incident diabetes mellitus and cardiovascular events, and mortality in a Korean population from the Korean Genome and Epidemiology Study. Subjects with a high ASV of body weight were more obese and had poor metabolic parameters than those with a low ASV of body weight. A 1-unit increase in ASV of body weight was associated with increase in mortality. However, the effect of bodyweight fluctuation on incident diabetes mellitus depended on the presence of obesity at baseline. In this lecture, I will focus on recent data on body-weight fluctuation and health outcomes.

Keyword
Body-weight fluctuation, diabetes mellitus, cardiovascular disease, mortality

Symposium 3

Jae Hyeon Kim

Organization

Division of Endocrinology and Metabolism, Department of Medicine, Samsung Seoul Hospital, Sungkyunkwan University School of Medicine

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2016-	Samsung Seoul Hospital, Sungkyunkwan University School of Medicine, Korea	Professor
2010-2015	Samsung Seoul Hospital, Sungkyunkwan University School of Medicine, Korea	Associate Professor
2009-2010	Samsung Seoul Hospital, Sungkyunkwan University School of Medicine, Korea	Assistant Professor
2005-2008	Boramae Hospital, Seoul National University, Korea	Assistant Professor
2003-2007	Graduate school, Seoul National University College of Medicine, Seoul, Korea	MS, PhD
1989-1995	Seoul National University College of Medicine, Korea	MD

» Research Interests

Type 1 diabetes, glycemic variability, islet cell transplantation, adrenal disease

» Publications

1. Jin SM, Lee HS, Haque MR, Kim HN, Kim HJ, Oh BJ, Lee KW, Kim G, Kim HS, Lee DY, Park JB, Kim SJ, Byun Y, Kim JH. Multi-layer surface modification of pancreatic islets for magnetic resonance imaging using ferumoxytol. Biomaterials. 2019 Sep;214:119224
2. Jun JE, Lee SE, Lee YB, Ahn JY, Kim G, Hur KY, Lee MK, Jin SM, Kim JH. Continuous glucose monitoring defined glucose variability is associated with cardiovascular autonomic neuropathy in type 1 diabetes. Diabetes Metab Res Rev. 2019 Feb;35(2):e3092.
3. Kim G, Lee SE, Lee YB, Jun JE, Ahn J, Bae JC, Jin SM, Hur KY, Jee JH, Lee MK, Kim JH. Relationship between relative skeletal muscle mass and non-alcoholic fatty liver disease: A 7-year longitudinal study. Hepatology. 2018 Nov;68(5):1755-1768.
4. Oh BJ, Jin SM, Hwang Y, Choi JM, Lee HS, Kim G, Kim G, Park HJ, Kim P, Kim SJ, Kim JH. Highly Angiogenic, Nonthrombogenic Bone Marrow Mononuclear Cell-Derived Spheroids in Intraportal Islet Transplantation. Diabetes. 2018 Mar;67(3):473-485.
5. Jun JE, Lee SE, Lee YB, Ahn JY, Kim G, Jin SM, Hur KY, Lee MK, Kim JH. Glycated albumin and its variability as an indicator of cardiovascular autonomic neuropathy development in type 2 diabetic patients. Cardiovasc Diabetol. 2017 Oct 10;16(1):127.
6. Jin SM, Shim W, Oh BJ, Oh SH, Yu SJ, Choi JM, Park HJ, Park JB, Kim JH. Anakinra Protects Against Serum Deprivation-Induced Inflammation and Functional Derangement in Islets Isolated From Nonhuman Primates. Am J Transplant. 2017 Feb;17(2):365-376.
7. Jin SM, Oh SH, Oh BJ, Shim W, Choi JM, Yoo D, Hwang YH, Lee JH, Lee DY, Kim JH. Feasibility of islet magnetic resonance imaging using ferumoxytol in intraportal islet transplantation. Biomaterials. 2015 Jun;52:272-80.

Abstract

GLYCEMIC VARIABILITY AND CARDIOVASCULAR OUTCOMES

Jae Hyeon KIM[1]*, Ji Eun JUN[2], Gyuri KIM[1] and Sang Man JIN[1]

[1] Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, South Korea
[2] Department of Endocrinology and Metabolism, Kyong Hee University at Gangdong, Kyuong Hee University School of Medicine, South Korea
jaehyeonkim26@gmail.com

Diabetes increases the risk of cardiovascular diseases. Although chronic hyperglycemia is a major determinant of macrovascular complications in diabetes, glycemic variability (GV) and hypoglycemia have also a strong influence on the cardiovascular system. GV relates to fluctuations in glycemia and reflects risk of hypoglycemia. The GV is associated with pancreatic beta cell function, and GV is more increased in Type 1 diabetes (T1D) compared with Type 2 diabetes (T2D). Diabetes Control and Complication Trial (DCCT) showed that the maintenance of higher C-peptide secretion, irrespective of the insulin treatment, led to a lower frequency of hypoglycemic events and microvascular complications in T1D. We also found that T1D was associated with higher risk for MI, atrial fibrillation, hospitalized heart failure, and death compared with T2D using the Korean National Health Insurance Service database. Previous studies reported that GV assessed by continuous glucose monitoring (CGM) significantly correlated with endothelial dysfunction, measured by brachial-artery flow-mediated dilation and carotid intima-media thickness, in diabetic patients. Furthermore, GV predicted rapid progression of coronary plaque in patients with acute coronary syndrome (ACS). In another observational study, GV was associated with the presence and severity of CAD, in patients with newly diagnosed type 2 diabetes (T2D). Moreover, a longitudinal study reported that GV assessed by CGM is a predictor of long-term prognosis in patients with ACS without severe diabetes. We also reported that GV assessed by CGM is associated with cardiovascular autonomic neuropathy in T1D and T2D. In this lecture, recent studies related with GV and CV outcomes will be summarized and possible strategies to reduce GV will be discussed.

Keywords
Glycemic variability, continuous glucose monitoring, cardiovascular outcome

Symposium 3

Seung-Hwan Lee

Organization

The Catholic University of Korea

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2019-	Division of Endocrinology and Metabolism, Seoul St. Mary's hospital, The Catholic Univ. of Korea	Professor
2016-2018	Cardiovascular Research Institute, UC San Francisco	Visiting Professor
2013-2018	Division of Endocrinology and Metabolism, Seoul St. Mary's hospital, The Catholic Univ. of Korea	Assistant/Associate Professor
2011-2013	Beth Israel Deaconess Medical Center and Harvard Medical School	Research Fellow
2013	Graduate School of Medicine, The Catholic Univ. of Korea	Ph.D.
2011	The Catholic Univ. of Korea, College of Medicine	M.D.

» Research Interests

Diabetes, Obesity, Adipose tissue metabolism

» Honors & Awards

· 2018 Young Investigator Award (Korean Diabetes Association)

» Publications

1. Mee Kyoung Kim, Kyungdo Han, Yong-Moon Park, Hyuk-Sang Kwon, Gunseog Kang, Kun-Ho Yoon, Seung-Hwan Lee*. Associations of variability in blood pressure, glucose and cholesterol concentrations, and body mass index with mortality and cardiovascular outcomes in the general population. *Circulation* 138:2627-2637, 2018 (*corresponding author)
2. Eun Young Lee, Yeoree Yang, Hun-Sung Kim, Jae-Hyoung Cho, Kun-Ho Yoon, Wook Sung Chung, Seung-Hwan Lee*, Kiyuk Chang*. Effect of visit-to-visit LDL- and HDL-, and non-HDL cholesterol variability on mortality and cardiovascular outcomes after percutaneous coronary intervention. *Atherosclerosis* 279:1-9, 2018 (*corresponding author)
3. Hu Huang*, Seung-Hwan Lee*, Inês Sousa-Lima*, Sang Soo Kim*, Won Min Hwang, Yossi Dagon, Won-Mo Yang, Sungman Cho, Min-Cheol Kang, Ji A Seo, Munehiko Shibata, Hyunsoo Cho, Getachew Debas Belew, Jinhyuk Bin, Bhavna N. Desai, Min Jeong Ryu, Minho Shong, Peixin Li, Hua Meng, Byung-Hong Chung, Daehee Hwang, Min Seon Kim, Kyong Soo Park, Maria Paula Macedo, Morris White, John Jones, Young-Bum Kim. Rho-kinase/AMPK axis regulates hepatic lipogenesis during overnutrition. *J Clin Invest* 128:5335-5350, 2018 (co-first author)
4. Mee Kyoung Kim, Kyungdo Han, Hun-Sung Kim, Yong-Moon Park, Hyuk-Sang Kwon, Kun-Ho Yoon, Seung-Hwan Lee*. Cholesterol variability and the risk of mortality, myocardial infarction and stroke: a nationwide population-based study. *Eur Heart J* 38:3560-3566, 2017
5. Mee Kyoung Kim, Kyungdo Han, Eun Sil Koh, Hun-Sung Kim, Hyuk-Sang Kwon, Yong-Moon Park, Kun-Ho Yoon, Seung-Hwan Lee*. Variability in total cholesterol is associated with the risk of end-stage renal disease: a nationwide population-based study. *Arterioscler Thromb Vasc Biol* 37:1963-1970, 2017 (*corresponding author)
6. Yeoree Yang, Tae-Hoon Kim, Kun-Ho Yoon, Wook Sung Chung, Youngkeun Ahn, Myung-Ho Jeong, Ki-Bae Seung, Seung-Hwan Lee*, Kiyuk Chang*. The stress hyperglycemia ratio, an index of relative hyperglycemia, as a predictor of clinical outcomes after percutaneous coronary intervention. *Int J Cardiol* 241:57-63, 2017 (*corresponding author)

Abstract

CHOLESTEROL VARIABILITY AND HEALTH OUTCOMES

Seung-Hwan Lee

Division of Endocrinology and Metabolism, Department of Internal Medicine, The Catholic University of Korea, Korea
hwanx2@catholic.ac.kr

Recently, visit-to-visit or day-to-day variability in biological parameters has emerged as a previously unrecognized residual risk factor, which is related to the development of various health outcomes. For example, higher blood pressure variability, lower heart rate variability and higher glucose or HbA1c variability have been linked to cardiovascular events and mortality. These effects remained significant after adjusting for the mean levels of the parameters, suggesting that not only managing the absolute value but also reducing the fluctuation should be targeted to improve health outcomes. Using a large nationwide population-based cohort and a hospital-based cohort database, we examined the prognostic significance of increased variability of cholesterol on various health outcomes including mortality, myocardial infarction, stroke, diabetes, end-stage renal disease and dementia. We showed that high variability in lipid levels is associated with these adverse health-related outcomes suggesting that lipid variability is an important and novel risk factor in the general population.

Keywords
Cholesterol, Variability, Mortality, Cardiovascular disease

ICoLA 2019 by KSoLA

Symposium 4

Chairpersons

Hong Seog Seo | Korea University, Korea
Christoph J. Binder | Medical University of Vienna, Austria

Date & Time: September 6 (Fri.), 09:40-11:10
Place: Room 2 (3F)

Symposium 4

Khurram Nasir

Organization

Center for Healthcare Outcomes and Evaluation (CORE)
Division of Cardiovascular Medicine
Yale University and Yale New Haven Health

Position & Title

Associate Professor

Director, Population Health & Health Systems Research

» Educational Background & Professional Experience

Year	Name of institution	Position
2018.2-Present	Section of Cardiovascular Medicine, Yale University School of Medicine, New Haven, CT	Associate Professor
2018.2-Present	Center for Outcomes Research and Evaluation	Director, Population Health & Health Systems Research
2010.7-2012.6	Dept. of Cardiology, Yale-New Haven Medical Center, New Haven, CT	Fellow
2006.7-2008.6	Dept. of Radiology, Massachusetts General Hospital, Boston, MA	Postdoctoral Fellow
2003.7-2005.4	Dept. of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD	Postdoctoral Fellow

» Research Interests

CVD prevention, imaging, population health, precision medicine

» Honors & Awards

- Johns Hopkins University, Distinguished Alumnus Award
- Multiethnic Study of Atherosclerosis, Investigator

» Publications

1. **Nasir K**, Bittencourt M, Blaha MJ, Budoff MJ, Blankstein RB, Agatston A, Shaw LJ, Sibley CT, Blumenthal RS, Krumholz HM. Implications of Coronary Artery Calcium Testing Among Statin Candidates According to American College of Cardiology/American Heart Association Cholesterol Management Guidelines. **J Am Coll Cardiol.** 2015;66:1657–68
2. Blaha MJ, Cainzos-Achirica M, Greenland P, McEvoy JW, Blankstein R, Budoff MJ, Dardari Z, Sibley CT, Burke GL, Kronmal RA, Szklo M, Blumenthal RS, **Nasir K**. Role of Coronary Artery Calcium Score of Zero and Other Negative Risk Markers for Cardiovascular Disease: The Multi-Ethnic Study of Atherosclerosis (MESA). **Circulation**. 2016;133:849-58
3. Hong JC, Blankstein R, Shaw LJ, Padula WV, Arrieta A, Fialkow JA, Blumenthal RS, Blaha MJ, Krumholz HM, **Nasir K**. Implications of Coronary Artery Calcium Testing for Treatment Decisions Among Statin Candidates According to the ACC/AHA Cholesterol Management Guidelines: A Cost-Effectiveness Analysis. **JACC Cardiovasc Imaging**. 2017;10:938-952
4. **Nasir K**. Message for 2018 Cholesterol Management Guidelines Update: Time to Accept the Power of Zero. **J Am Coll Cardiol**. 2018 pii: S0735-1097

Abstract

HOW CORONARY ARTERY CALCIUM TESTING CAN GUIDE MANAGEMENT DECISIONS FOR PRIMARY CARDIOVASCULAR PREVENTION

Khurram Nasir MD MPH MSc

Director, Population Health & Health Systems Research, Division of Cardiovascular Medicine, Center for Healthcare Outcomes and Evaluation (CORE), Yale University and Yale New Haven Health 1 Church Street, Suite 200 New Haven, CT, 06512
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The use of traditional risk factors and laboratory markers to estimate 10-year risk for atherosclerotic cardiovascular disease (ASCVD) remains the cornerstone of clinical decision making for primary prevention of ASCVD in asymptomatic persons. Emerging guidelines suggest measurement of subclinical atherosclerosis provides the strongest risk stratification to guide management decisions. In this regard, coronary artery calcium (CAC) testing is preferred over other imaging methods as provide greater prognostication, discrimination, and reclassification of ASCVD risk. Apart from identifying those truly high-risk persons in whom most ASCVD events occur, an absence of CAC confers a very low risk for future events. A CAC score of 0 has been established to reclassify borderline- to intermediate-risk patients into a category in which lipid-lowering therapy is no longer recommended, a concept termed *the power of zero*. In summary, CAC testing is now a guideline-endorsed decision aid for borderline- to intermediate-risk patients who seek more definitive risk assessment as part of a clinician–patient discussion. This testing can reduce low-value treatment and focus primary prevention therapy on those most likely to benefit.

Keywords
CVD, prevention, CAC, statin, risk stratification, guidelines

Symposium 4

Sang-Hak Lee

Organization

Yonsei University College of Medicine

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2007-Present	Division of Cardiology, Yonsei University College of Medicine	Assistant Professor ~ Professor
2010-2012	Department of Medicine, UC San Diego, USA	Visiting Scholar & Postdoc Fellow
2003-2007	Division of Cardiology, Hallym University College of Medicine	Assistant Professor
2002-2005	Yonsei University Graduate School	PhD
1997-1999	Yonsei University Graduate School	Master
1988-1994	Yonsei University College of Medicine	Bachelor

» Research Interests

Lipoprotein metabolism, vascular biology, cardiovascular genetics

» Publications

1. Lee CJ, et al. *CETP*, *LIPC*, and *SCARB1* variants in individuals with extremely high high-density lipoprotein-cholesterol levels. Sci Rep. In press.
2. Roh JW, et al. Pravastatin versus fluvastatin after statin intolerance: the PRUV-Intolerance study with propensity score matching. Am J Med. In press.
3. Kim K, et al. Statin and clinical outcome of primary prevention in individuals aged >75 years: The SCOPE-75 study. Atherosclerosis 2019;284:31-36
4. Cheon EJ, et al. Novel association between *CDKAL1* and cholesterol efflux capacity: replication after GWAS-based discovery. Atherosclerosis 2018;273:21-27
5. Jung S, et al. Metabolic phenotyping of human atherosclerotic plaques: metabolic alterations and their biological relevance in plaque-containing aorta. Atherosclerosis 2018;269:21-28
6. Shin DG, et al. Clinical features of familial hypercholesterolemia in Korea: predictors of pathogenic mutations and coronary artery disease-a study supported by the Korean Society of Lipidology and Atherosclerosis. Atherosclerosis 2015;243(1):53-58.
7. Ann SJ, et al. PPARα agonists inhibit inflammatory activation of macrophages through upregulation of β-defensin 1 Atherosclerosis 2015;240(2):389-397

Abstract

WHAT CAN LIPID GENETICS DO FOR PATIENTS WITH DYSLIPIDEMIA?

Sang-Hak Lee

Division of Cardiology, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
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In the past decade, many studies on lipid genetics have been performed to identify novel signals associated not only with hereditary dyslipidemia, but also with potential treatment targets or drug response.

Classic examples of genetic disorders of lipid metabolism include familial hypercholesterolemia. However, genome-wide association studies and newer sequencing studies regarding other lipid phenotypes discovered or validated several new targets for lipid-lowering therapy. Some of them were used to develop specific therapeutics: i.e. *PCSK9*, *NPC1L1*, *APOC3*, or *ANGPTL3*.

Some genetic variants have been reported to be associated with efficacy and safety of lipid lowering agents. They include genes that code proteins participating in pharmacokinetics. In patients with familial hypercholesterolemia, drug response partly depends on the class of mutations. Because lipid lowering is crucial for these patients, genetic information may be very helpful to choose appropriate treatment intensity in this population.

Although application of genetic information has not been widespread in patients with dyslipidemia, lipid genetics is being used in many places for treating these patients more effectively and precisely.

Keywords
Genomics, pharmacology, atherosclerosis, lipoproteins

Symposium 4

Jung-Won Suh

Organization

Seoul National University

Position & Title

Professor, MD, PhD

» Educational Background & Professional Experience

Year	Name of institution	Position
2017-	Seoul National University Bundang Hospital	Professor
2012-2017	Seoul National University Bundang Hospital	Associate Professor
2008-2012	Seoul National University Bundang Hospital	Assistant Professor
2007-2008	Gangnam center, Seoul National University Hospital	Assistant Professor
2004-2006	Postgraduate School, Seoul National University	Ph.D. of Medical Science
2002-2004	Postgraduate School, Seoul National University	Master of Medical Science

» Research Interests

Platelet biology and antiplatelet agents, Congenital and structural heart disease, Thrombosis, Intracoronary imaging

» Publications

1. Seo WW, Suh JW, Oh IY, Yoon CH, Cho YS, Youn TJ, Chae IH, Choi DJ. Efficacy of IntraCoronary Erythropoietin Delivery BEfore Reperfusion-Gauging Infarct Size in Patients with Acute ST-segment Elevation Myocardial Infarction (ICEBERG). Int Heart J. 2019 Mar 20;60(2):255-263.
2. Choi W, Chang HW, Kang SH, Yoon CH, Cho YS, Youn TJ, Chae IH, Kim DJ, Kim JS, Park KH, Kim HS, Lim C, Suh JW (corresponding author). Comparison of Minimally Invasive Direct Coronary Artery Bypass and Percutaneous Coronary Intervention Using Second-Generation Drug-Eluting Stents for Coronary Artery Disease-Propensity Score-Matched Analysis. Circ J. 2019 Jun 25;83(7):1572-1580.
3. Lee W, Suh JW, Park JJ, Yoon CH, Cho YS, Youn TJ, Chae IH. Effect of tailored use of tirofiban in patients with non-ST-elevation acute coronary syndrome undergoing percutaneous coronary intervention: a randomized controlled trial. BMC Cardiovasc Disord. 2018;18:201
4. Suh JW, Yun B. Breast arterial calcification: A potential surrogate marker for cardiovascular disease. J Cardiovasc Imaging. 2018;26:125-34.
5. Yoon YE, Kim KM, Bola Yun, Suh JW (corresponding author) et al. Prediction of subclinical coronary artery disease with breast arterial calcification and low bone mass in asymptomatic women. Registry for the women health cohort for breast, bone and coronary artery disease substudy. J Am Coll Cardiol Img. 2018 Aug 6. pii: S1936-878X(18)30551-5. doi: 10.1016/j.jcmg.2018.07.004. [Epub ahead of print]
6. Kim YG, Suh JW (corresponding author), Sibbing D, et al. A laboratory association between hemoglobin and VerifyNow P2Y12 reaction unit: A systematic review and meta-analysis. Am Heart J. 2017;188:53-64.
7. Kim YG, Suh JW (corresponding author), Kang SH, et al. Cigarette Smoking Does Not Enhance Clopidogrel Responsiveness After Adjusting VerifyNow P2Y12 Reaction Unit for the Influence of Hemoglobin Level. JACC Cardiovasc Intv. 2016;9:1680-90.

Abstract

MHEALTH CAN IMPROVE DYSLIPIDEMIA CARE

Jung-Won SUH[1], Si-Hyuck KANG[1], Sooyoung YOO[2], In-Ho CHAE[1]

1 Department of Internal Medcine, Seoul National University Bundang Hospital, Republic of Korea
2 Office of eHealth and Business, Seoul National University Bundang Hospital, Republic of Korea
suhjw1@gmail.com

Dyslipidemia is a major risk factor for atherosclerotic cardiovascular disease (ASCVD). In the last decades, an increase in the use of cholesterol lowering drug has been associated with a decrease in the prevalence of dyslipidemia, but much less progress has been made with lifestyle changes. While traditional 'physician-patient encounters' continues to play an important role in the management of dyslipidemia, alternative approaches are being explored. Mobile health, or mHealth, is one alternative approach that is being investigated for its low cost and wide reach.

mHealth is defined as the use of mobile phone and wireless technologies to support the achievement of health objectives. Rapidly advancing mobile technology and its ability to reach more than 85% of the world's population has led to an increase in popularity of mHealth as a tool to improve risk factor control and patient outcomes. Email and websites were utilized in earlier studies, whereas short message service and mobile applications have been utilized more often in recent studies.

In this talk, I would like to review some recent studies which used mHealth to improve lifestyle and medication adherence. In addition, ongoing studies which use smartphone apps to enhance the physician-patient interaction in patients with ASCVD will be introduced.

Keywords
Atherosclerotic cardiovascular disease, Dyslipidemia, mHealth, lifestyle changes

ICoLA 2019 by KSoLA

Symposium 5

Chairpersons

Yangha Kim | Ehwa Womans University, Korea
Manohar Garg | University of Newcastle, Australia

Date & Time: September 6 (Fri.), 09:40-11:10
Place: Room 3 (3F)

Symposium 5

Sunmin Park

Organization

Hoseo University

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
1981-1985	Ewha Women's University, Dept. of Food & Nutrition	BS
1985-1987	Ewha Women's University, Dept. of Food & Nutrition	MS
1988-1992	Ohio State University, Dept. of Human Nutrition	Ph.D.
1992-1994	Ohio State University, Dept. of Statistics	MS
2013.1-Present	Journal of Medicinal Food	Editor
2015.2-Present	Korean Academy of Science and Technology	Member

» Research Interests

Diabetes, Obesity, Metabolic syndrome, Nutrigenomics

» Honors & Awards

· Mary K. Iacocca Senior Scientist Fellowship, Joslin Diabetes Center, Harvard Medical School

» Publications

1. Jun-Yu Zhou, Mi Young Song, Sunmin Park. Carbohydrate and Na intake and physical activity interact with genetic risk scores of four genetic variants mainly related to lipid metabolism to modulate metabolic syndrome risk in two Korean cohorts
2. Sunmin Park, Xin Zhang, Suna Kang. *FADS1* and *FADS2* minor alleles are positively associated with the risk of metabolic syndrome, especially in middle-aged adults consuming high saturated and monounsaturated fatty acids. Eur J Nutri 2019
3. James W. Daily, Meiling Liu, Sunmin Park. High genetic risk scores of SLIT3, PLEKHA5 and PPP2R2C variants increased insulin resistance and interacted with coffee consumption in middle-aged adults. Nutrition, Metabolism and cardiovascular diseases 2019;29(1):79-89.
4. Meiling Liu, Hyun Seok Jin, Sunmin Park. Protein and fat intake interacts with the haplotype of *PTPN11*_rs11066325, *RPH3A*_rs886477 and OAS3_rs2072134 to modulate serum HDL concentrations in middle-aged people Clinical Nutrition
5. Sunmin Park, Jaeouk Ahn, Byung-Kook Lee. Very-low-fat diets may be associated with increased risk of metabolic syndrome in the adult population. Clin Nutr 2016 Oct;35(5):1159-67.
6. Sunmin Park, Jung-O Ham, Byung-Kook Lee. Effects of total vitamin A, vitamin C, and fruit intake on risk for metabolic syndrome in Korean women and men. Nutrition. 31 (1) (2015) 111–118
7. Sunmin Park, Kyung Min Yoo, Joo Suk Hyun, Suna Kang. Intermittent fasting reduces body fat but exacerbates hepatic insulin resistance in rats regardless of high protein and fat diets. J Nutr Biochem 40:14-22. 2017

Abstract

INTERACTION OF GENETIC AND LIFESTYLES IN DYSLIPIDEMIA RISK IN KOGES

Sunmin PARK

Food & Nutrition, Hoseo University, Korea
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Metabolic syndrome (MetS) is a complex disturbance of lipid (obesity, dyslipidemia), carbohydrate (glucose intolerance), and protein (microalbuminuria and hyperuricemia) metabolisms and arterial hypertension. People with MetS are susceptible to developing obesity, hyperglycemia, hypertension, dyslipidemia, hypertension, and hyperinsulinemia. The common factor related to MetS is increased insulin resistance. MetS increases the incidence of cardiovascular disease (CVD) which has become the world's leading cause of death and is the second most common cause of death in Korea. Dyslipidemia is a major modifiable risk factor for CVD. The prevalence of CVD has been increasing in Korea and it is partly related to dyslipidemia. A very-low-fat (<15 energy %) and high carbohydrate intake (>70 energy %) increases the risk of metabolic syndrome in Korean adults. High-carbohydrate diets (>57.4 energy % in men and >59.1 energy % in women) are associated with a low serum HDL-C in US men and high serum triglyceride in US women. These nutrient intakes and lifestyles can interact with genetic variants to lead to the development of MetS. Interactions with environmental factors, including nutrient intake, can be explained by identifying multiple genetic variants that explain the environmental impacts on the prevalence of MetS in Asians. Interestingly, genetic variants that influence MetS risk are mainly associated with lipid metabolism and they interact with lifestyles. Korean carriers of the *FADS1*_rs174547 and *FADS2*_rs2845573 minor alleles have a greater susceptibility to MetS and moderate fat intake protected against the risk of MetS in carriers of the *FADS1* major alleles. The carriers mainly exhibit decreased serum HDL-cholesterol and increased triglyceride levels and blood pressure after adjusting for MetS-related confounders. Carriers with *APOA5*_rs651821, *EFCAB4B*_rs4766165, and *APOBEC1*_rs10845640 also have increased risk of MetS, and they have interactions with carbohydrate intake and daily physical activity. In conclusion, genetic variants related to lipid metabolism are the major genetic factors which affect MetS risk and they have interactions with lifestyles. Asians who are genetically susceptible to MetS need to consume moderate fat and carbohydrate (about 65-70 %) diet and have daily physical activities to reduce the risk of MetS, especially dyslipidemia.

Keywords
Personalized dietary guideline, Genetic variants, Interaction, Nutrient intake, Lifestyles.

Symposium 5

Kazumasa YAMAGISHI

Organization

Department of Public Health Medicine, University of Tsukuba

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2019-	University of Tsukuba, Japan	Professor
2016-2019	University of Tsukuba, Japan	Associate Professor
2007-2009	University of Minnesota	Visiting Assistant Professor
2004-2016	University of Tsukuba, Japan	Assistant Professor

» Research Interests

Epidemiology and prevention of cardiovascular disease

» Honors & Awards

- 2016.11 Medical Research Encouragement Prize, Japan Medical Association
- 2014.11 Young Investigator's Award, Japanese Society of Public Health
- 2014.07 Young Investigator's Award, Japan Atherosclerosis Society

» Publications

1. Yamagishi K, et al. Fish intake and risk of mortality due to aortic dissection and aneurysm: A pooled analysis of the Japan Cohort Consortium. ***Clin Nutr*** 2019; 38:1678-1683.
2. Yamagishi K, et al. Blood pressure levels and risk of cardiovascular disease mortality among Japanese men and women: The Japan Collaborative Cohort Study for Evaluation of Cancer Risk (JACC Study). ***J Hypertens*** 2019; 37:1366-1371.
3. Yamagishi K, et al. The Circulatory Risk in Communities Study (CIRCS): A long-term epidemiological study for lifestyle-related disease among Japanese men and women living in communities. ***J Epidemiol*** 2019; 29:83-91.
4. Yamagishi K, et al. Serum coenzyme Q10 and risk of disabling dementia: the Circulatory Risk in Communities Study (CIRCS). ***Atherosclerosis*** 2014;237:400-403.
5. Yamagishi K, et al. Dietary intake of saturated fatty acids and incident stroke and coronary heart disease in Japanese communities: The JPHC Study. ***Eur Heart J*** 2013; 34:1225-1232.
6. Yamagishi K, et al. Dietary intake of saturated fatty acids and mortality from cardiovascular disease among Japanese: The JACC Study. ***Am J Clin Nutr*** 2010; 92:759-765.
7. Yamagishi K, et al. Fish, ω-3 polyunsaturated fatty acids, and mortality from cardiovascular diseases in a nationwide community-based cohort of Japanese men and women: The JACC Study. ***J Am Coll Cardiol*** 2008; 52:988-996.

Abstract

EPIDEMIOLOGY OF DIETARY AND LIFESTYLE FACTORS AND CARDIOVASCULAR DISEASE: EXPERIENCES FROM JAPANESE POPULATION-BASED STUDIES

Kazumasa YAMAGISHI

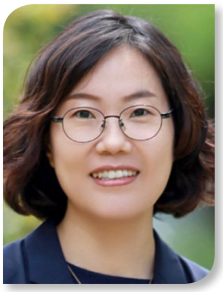
Department of Public Health Medicine, Faculty of Medicine, and Health Services Research and Development Center, University of Tsukuba, Japan
k-yamagishi@umin.net

Asians have high mortality from stroke (especially from intraparenchymal hemorrhage and lacular infarction) and low mortality from coronary heart disease, while Caucasians have the opposite trend. This difference in disease profile can be explained by different types of vascular pathology, that is, arterioloscrerosis and atherosclerosis. Lifestyles, especially dietary habits, in Western populations are more likely to cause atherosclerosis-based diseases such as coronary heart disease and large-artery occlusive cerebral infarction (corresponding to atherothrombotic infarction), while traditional diet and lifestyles in East Asia are likely to cause arteriolosclerosis-based disease such as cerebral hemorrhage and infarction at perfolator's arteries area.

Another possible explanation of difference in disease profile between the East and West is that the large difference in distribution of diet and lifestyle-related factors of cardiovascular disease, such as obesity, lipid profiles, dietary intake of carbohydrate, saturated fat, n-3 polyunsaturated fat, calcium, and sodium. In this context, several Japanese large cohort studies, including Circulatory Risk in Communities Study (CIRCS), Japan Public Health Center-based Prospective (JPHC) Study, and Japan Collaborative Cohort (JACC) Study for Evaluation of Cancer Risk, have identified dietary and lifestyle factors, some of which are unique for East-Asian populations.

Keywords
epidemiology, diet, stroke, heart disease, dementia

Symposium 5



Yunkyoung Lee

Organization

Jeju National University

Position & Title

Associate Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2017-Present	Jeju National University, Korea	Associate Professor
2013-2017	Jeju National University, Korea	Assistant Professor
2010-2013	Research and development center at Maeil Dairies Co	Senior scientist
2008-2010	Obesity and metabolism lab, Human nutrition research center on Aging, Tufts University	Postdoctoral fellow
2003-2008	Integrative Biosciences Pennsylvania State university	Ph.D.
2001-2003	Nutritional Sciences Pennsylvania State university	M.S.

» Research Interests

Functional foods, seaweeds, polysaccharides, inflammation, obesity, diabetes, gut health

» Honors & Awards

- 2018 Best Teaching award, Jeju National University
- 2017 Outstanding scientific research paper award, The Korean Federation of Science and Technology Societies
- 2016 Best presentation award, The Korean Nutrition Society 2016

» Publications

1. Zhang C, Li Z, Zhang C-Y, Li M, **Lee Y**, and Zhang G (2019) Extract Methods, Molecular Characteristics, and Bioactivities of Polysaccharide from Alfalfa (*Medicago sativa L.*) *Nutrients* 11(5), 1181.
2. Yang HS, Haj FG, Lee M, Kang I, Zhang G, and **Lee Y*** (2019) Laminaria japonica Extract Enhances Intestinal Barrier Function by Altering Inflammatory Response and Tight Junction-Related Protein in Lipopolysaccharide-Stimulated Caco-2 Cells. *Nutrients*, 11(5), 1001.
3. Seo SH, Jo SM, Kim J, Lee M, **Lee Y**, and Kang I (2019) Peanut sprouts extracts attenuate triglyceride accumulation by promoting mitochondrial fatty acid oxidation in adipocytes. *International Journal of Molecular Sciences*, 20(5), 1216.
4. Lee M, Sorn SR, **Lee Y**, and Kang I (2019) Salt induces adipogenesis/lipogenesis and inflammatory adipocytokines secretion in adipocytes. *International Journal of Molecular Sciences* 20, 160; doi:10.3390/ijms20010160
5. **Lee Y***, Oh H, and Lee M (2018) Anti-inflammatory effects of Agar free-Gelidium amansii (GA) extracts in high-fat diet-induced obese mice. *Nutrition Research and Practice* 12(6): 479-485.
6. Kang S, Kim E, Kang I, Lee M, and **Lee Y*** (2018) Anti-diabetic effects and anti-inflammatory effects of Laminaria japonica and Hizikia fusiforme in Skeletal muscle: in vitro and in vivo model. *Nutrients* 10, 491; doi:10.3390/nu10040491
7. Choi J, Lee M, Kim HJ, Kown JI and **Lee Y*** (2017) Effects of Black Soybean and Fermented Black Soybean Extracts on Proliferation of Human Follicle Dermal Papilla Cells. *Journal of the Korean Society of Food Science and Nutrition* 46(6): 671-680.

* indicates either the first or corresponding author.

Abstract

DIETARY FACTORS AND PREVENTION OF DYSLIPIDEMIA

Yunkyoung LEE

Department of Food Science and Nutrition, Jeju National University, South Korea
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Obesity is a major worldwide health problem which is highly associated with coronary artery disease, hypertension, type 2 diabetes mellitus, respiratory disorders and dyslipidemia. Dyslipidemia typically involves hypertriglyceridemia and high levels of low-density lipoprotein (LDL) cholesterol. Especially so called atherogenic cholesterol including non-high-density lipoprotein cholesterol and LDL cholesterol has been the focus to be controlled in order to ameliorate the risk for atherosclerotic cardiovascular disease. In this presentation, the evidence base dietary approaches for managing dyslipidemia which were derived from randomized controlled trials (RCTs), meta-analyses of results from RCTs, and review of results from observational, genetic, metabolic, and mechanistic studies will be demonstrated. Briefly, the following topics of lifestyle therapies will be discussed: (1) targets and rationale for lifestyle therapies; (2) dietary patterns to reduce dyslipidemia; (3) replacement of saturated fatty acids; and (4) dietary cholesterol. Although the lifestyle therapies alone are not sufficient to treat and prevent the dyslipidemia, combination of lifestyle therapies and drug therapies certainly can synergistically improve patients' conditions to postpone having further complications.

Keywords
Dietary factors, dyslipidemia, unsaturated fatty acids, cholesterol, lifestyle therapies

ICoLA 2019 by KSoLA

Symposium 6

Chairpersons

Jaehoon Choi | Hanyang University, Korea
Edward Thorp | Northwestern University, USA

Date & Time: September 6 (Fri.), 09:40-11:10
Place: Room 4 (5F)

Symposium 6

Hae-Ock Lee

Organization

Sungkyunkwan University, Korea

Position & Title

Chief Researcher, PhD

» Educational Background & Professional Experience

Year	Name of institution	Position
2013-	Samsung Medical Center	Chief Researcher
2016-2018	Seoul National University, Korea	Research Professor
1993-1999	Northwestern University (Evanston, IL., US.)	PhD
1989-1993	Microbiology, Seoul National University, Korea	B.S.

» Research Interests

Single cell genomics in cancer

» Publications

1. Kim N, Chung W, Eum HH, Lee HO, Park WY: Alternative polyadenylation of single cells delineates cell types and serves as a prognostic marker in early stage breast cancer. *PLoS One* 2019, 14:e0217196.
2. Fan J, Lee HO, Lee S, Ryu DE, Lee S, Xue C, Kim SJ, Kim K, Barkas N, Park PJ, et al: Linking transcriptional and genetic tumor heterogeneity through allele analysis of single-cell RNA-seq data. *Genome Res* 2018, 28:1217-1227
3. Chung, W., Eum, H. H., Lee, H. O., Lee, K. M., Lee, H. B., Kim, K. T., Ryu, H. S., Kim, S., Lee, J. E., Park, Y. H., et al. (2017). Single-cell RNA-seq enables comprehensive tumour and immune cell profiling in primary breast cancer. Nature communications 8, 15081
4. Lee, J. K., Wang, J., Sa, J. K., Ladewig, E., Lee, H. O., Lee, I. H., Kang, H. J., Rosenbloom, D. S., Camara, P. G., Liu, Z., et al. (2017). Spatiotemporal genomic architecture informs precision oncology in glioblastoma. Nature genetics 49, 594-599
5. Kim KT, Lee HW, Lee HO, Song HJ, Jeong da E, Shin S, Kim H, Shin Y, Nam DH, Jeong BC, et al: Application of single-cell RNA sequencing in optimizing a combinatorial therapeutic strategy in metastatic renal cell carcinoma. *Genome Biol* 2016, 17:80
6. Kim KT, Lee HW, Lee HO, Kim SC, Seo YJ, Chung W, Eum HH, Nam DH, Kim J, Joo KM, Park WY: Single-cell mRNA sequencing identifies subclonal heterogeneity in anti-cancer drug responses of lung adenocarcinoma cells. *Genome Biol* 2015, 16:127.
7. Min JW, Kim WJ, Han JA, Jung YJ, Kim KT, Park WY, Lee HO, Choi SS: Identification of Distinct Tumor Subpopulations in Lung Adenocarcinoma via Single-Cell RNA-seq. *PLoS One* 2015, 10:e0135817

Abstract

BASIC OF SINGLE CELL RNA SEQUENCING AND APPLICATION TO CANCER STUDIES

Hae-Ock Lee

[1] Samsung Genome Institute, Samsung Medical Center, Seoul Korea
[2] Department of Health Sciences and Technology, Samsung Advanced Institute for Health Sciences & Technology, Sungkyunkwan Univerisity, Seoul Korea
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Transcriptome analysis at single cell resolution enables explicit characterization of heterogeneous cell populations, and became an essential tool to study cellular composition and dynamics in normal and disease conditions. Currently, the transcriptome analysis has been extended to incorporate genetic, epigenetic, and protein expression data as well as spatial contexts. Here, we applied massively parallel single cell RNA sequencing to multiple tumor types to define alterations in cancer cells and associated microenvironment during cancer progression. The results demonstrate alterations in cellular composition and gene expression changes in diverse cells types. Expansion of regulatory T cells and myofibroblasts were commonly observed in many cancer types indicating shared manner of tumor antigen presentation to immune cells as well as activation of tissue remodeling. Alterations in cancer cells reflected a deviation from normal differentiation axis as well as an adaptation to the metastatic microenvironment. Collectively, our study demonstrates the power of single cell RNA sequencing in the characterization of cancer as a complex ecosystem, and also promotes development of treatment strategies targeting different cellular components,

Keywords
Single cell RNA sequencing, Cellular atlas, Cancer, Microenvironment

Symposium 6

Jong Kyoung Kim

Organization

DGIST

Position & Title

Assistant Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2016-	DGIST, Korea	Assistant Professor
2011-2016	EMBL-EBI, UK	Research Scientist
2010-2011	POSTECH, Korea	Postdoctoral Fellow
2006-2010	POSTECH, Korea	Ph.D.
2004-2006	POSTECH, Korea	M.S.
1999-2004	POSTECH, Korea	B.S.

» Research Interests

Single-cell Genomics, Bioinformatics, Machine Learning

» Honors & Awards

- 2019 Excellent Research Award, DGIST
- 2009 TJ Park Bessemer Science Fellowship, POSCO TJ Park Foundation
- 2006 Microsoft Research Asia Fellowship, Microsoft Research Asia

» Publications

1. Y. Huang*, J. K. Kim*, D. V. Do, C. Lee, C. A. Penfold, J. J. Zylicz, J. C. Marioni, J. A. Hackett, M. A. Surani, STELLA modulates transcriptional and endogenous retrovirus programs during maternal-to-zygotic transition, eLife 6:e22345, 2017
2. T. Ilicic*, J. K. Kim*, F. O. Bagger, D. McCarthy, A. A. Kolodziejczyk, J. C. Marioni, S. A. Teichmann, Classification of low quality cells from single cell RNA-seq data, Genome Biology 17:29, 2016
3. J. K. Kim, A. A. Kolodziejczyk, T. Ilicic, S. A. Teichmann, J. C. Marioni, Characterizing noise structure in single-cell RNA-seq distinguishes genuine from technical stochastic allelic expression, Nature Communications, 6:8687, 2015.
4. A. A. Kolodziejczyk*, J. K. Kim*, J. C. Tsang, T. Ilicic, J. Henriksson, K. N. Natarajan, A. C. Tuck, X. Gao, M. Buhler, P. Liu, J. C. Marioni, S. A. Teichmann, Single cell RNA-Sequencing of pluripotent states unlocks modular transcriptional variation, Cell Stem Cell, 17:471-485, 2015
5. P. Brennecke*, S. Anders*, J. K. Kim*, A. A. Kolodziejczyk, X. Zhang, V. Proserpio, B. Baying, V. Benes, S. A. Teichmann, J. C. Marioni, M. G. Heisler, Accounting for technical noise in single-cell RNA-seq experiments, Nature Methods 10(11):1093-1095, 2013
6. J. K. Kim, J. C. Marioni, Inferring the kinetics of stochastic gene expression from single-cell RNA-sequencing data, Genome Biology 14(1):R7, 2013
7. J. K. Kim and S. Choi, Clustering sequence sets for motif discovery, in Advances in Neural Information Processing Systems (NIPS), 2009

Abstract

DISSECTING CELLULAR HETEROGENEITY USING SINGLE-CELL RNA-SEQ

Jong Kyoung Kim

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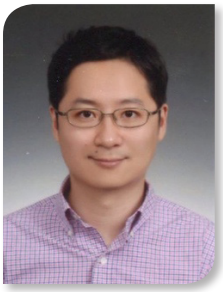
Cell-to-cell variability in gene expression exists even in a homogeneous population of cells. Dissecting such cellular heterogeneity within a biological system is a prerequisite for understanding how a biological system is developed, homeostatically regulated, and responds to external perturbations. Single-cell RNA sequencing (scRNA-seq) allows the quantitative and unbiased characterization of cellular heterogeneity by providing genome-wide molecular profiles from tens of thousands of individual cells. In this talk, I present an overview of scRNA-seq, and apply this approach to dissect cellular heterogeneity in stomach and adipose tissues.

Keywords
Single-cell RNA-seq, Cellular heterogeneity, Cellular plasticity, Adult stem cells

Symposium 6



Sungho Park

Organization

Ulsan National Institute of Science and Technology

Position & Title

Assistant Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2018-2019	Hospital for Special Surgery	Assistant Professor
2012-2018	Weill Cornell Medical School	Instructor and Post-doc
2007-2012	Weill Cornell Medical School	PhD
2003-2005	Seoul National University	MS
1996-2003	Yonsei University	BS

» Research Interests

Innate Immunity, Cytokine Imprints, Macrophage, Inflammation

» Honors & Awards

- 2010 Travel Award / International Conference on Osteoimmunology
- 2011 Outstanding Research Award in Immunobiology / Weill Cornell
- 2013 Rosensweig Genomics Fellowship / Hospital for Special Surgery

» Publications

1. Kusnadi A*, Park SH*, Oliver D, Park-min K, Ivashkiv LB (2019) TNF promotes SREBP activity to regulate macrophage polarization and tissue repair. *: co-first authors. ***Immunity***, In Press.
2. Roh C*, Park SH*#, Lee A, Loupasakis K, Ivashkiv LB#, Kalliolias GD#. (2019) Transient and tolerized inflammatory TNF response in macrophage is sustained in fibroblast-like synoviocytes. ***Annals of the Rheumatic Diseases***, # Co-Corresponding authors, May 16, Epub ahead of print]
3. Park SH, Kang K, Giannopoulou E, Qiao Y, Kang K, Kim G, Park-Min KH and Ivashkiv LB. (2017) Type I IFNs and TNF Cooperatively Reprogram Epigenomic Landscape of Human Macrophages to Promote Inflammatory Activation. ***Nat Immunol*** 18(10):1104-1116.
4. Park SH, Park-Min K, Chen J, Hu X & Ivashkiv LB. (2011) Tumor necrosis factor induces GSK3 kinase–mediated cross-tolerance to endotoxin in macrophages. ***Nat Immunol*** 12(7):607-15.

Abstract

TNF PROMOTES SREBP ACTIVITY AND BINDING TO INFLAMMATORY GENES TO ACTIVATE MACROPHAGES AND LIMIT TISSUE REPAIR

Sung-Ho Park[1] and Lionel Ivashkiv*[2]

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[2] Hospital for Special Surgery, USA
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Cytokine TNF-mediated macrophage polarization is important for inflammatory disease pathogenesis, but the mechanisms regulating polarization are not clear. We performed transcriptomic and epigenomic analysis of the TNF response in primary human macrophages and revealed late phase activation of SREBP2, the master regulator of cholesterol biosynthesis genes. TNF stimulation extended the genomic profile of SREBP2 occupancy to include binding to and activation of inflammatory and interferon response genes independently of its functions in sterol metabolism. Genetic ablation of SREBP function shifted the balance of macrophage polarization from inflammatory to a reparative phenotype in peritonitis and skin wound healing models. Genetic ablation of SREBP activity in myeloid cells or topical pharmacological inhibition of SREBP improved skin wound healing under homeostatic and chronic inflammatory conditions. Our results identify a function and mechanism of action for SREBPs in augmenting TNF-induced macrophage activation and inflammation, and open therapeutic avenues for promoting wound repair.

Keywords
TNF; SREBP2; macrophage polarization; tissue repair; inflammation

ICoLA 2019 by KSoLA

Symposium 7

Chairpersons

In Ho Chae | Seoul National University, Korea
Gregory G. Schwartz | University of Colorado, USA

Date & Time: September 6 (Fri.), 14:00-15:30
Place: Room 1 (3F)

Symposium 7

Soo-Joong Kim, M.D., Ph.D.

Organization

Kyung Hee University, Kyung Hee University Hospital

Position & Title

Full Professor of Internal Medicine (Cardiology)

» Educational Background & Professional Experience

Year	Name of institution	Position
2015-Present	Internal Medicine (Cardiology), College of Medicine, Kyung Hee University, Kyung Hee University Hospital, Seoul, Korea	Full Professor
2011-2012	Cardiology, Massachusetts General Hospital, Harvard Medical School	Research scholar
2010-2015	Internal Medicine (Cardiology), College of Medicine, Kyung Hee University, Kyung Hee University Hospital, Seoul, Korea	Associate Professor
2006-2010	Internal Medicine (Cardiology), College of Medicine, Kyung Hee University, Kyung Hee University Hospital, Seoul, Korea	Assistant Professor
2005-2006	Internal Medicine (Cardiology), Kyung Hee University Hospital, Seoul, Korea	Clinical Assistant Professor
2004.3-2006.2	Kyung Hee University Graduate School, Seoul, Korea	Doctor`s Degree
2003-2004	Internal Medicine (Cardiology), Kyung Hee University Hospital, Seoul, Korea	Clinical Fellow
2000-2003	Korean Navy	Medical officer
1999.3-2004.2	Kyung Hee University Graduate School, Seoul, Korea	Master of Science
1995-2000	Department of Internal medicine, Kyung Hee University Hospital, Seoul, Korea	Internship and Residency
1988.3-1995.2	Kyung Hee University Medical College, Seoul, Korea	Medical Degree

» Research Interests

Intravascular imaging (OCT) of coronary artery

» Honors & Awards

- 2000-present Member of the Korean Society of Internal Medicine
- 2004-present Member of the Korean Society of Circulation
- 2005-present Member of the Korean Society of Interventional Cardiology

» Publications

1. S-amlodipine plus chlorthalidone vs. S-amlodipine plus telmisartan in hypertensive patients unresponsive to amlodipine monotherapy: study protocol for a randomized controlled trial. Jo SH, Park SJ, Kim EJ, Kim SJ, Cho HJ, Song JM, Shin J, Park JJ, Shin JH, Han KR, Choi DJ. Trials. 2018 Jun 20;19(1):324. doi: 10.1186/s13063-018-2636-1.
2. Efficacy and Safety of Fixed-dose Combination Therapy With Telmisartan and Rosuvastatin in Korean Patients With Hypertension and Dyslipidemia: TELSTA-YU (TELmisartan-rosuvaSTAtin from YUhan), a Multicenter, Randomized, 4-arm, Double-blind, Placebo-controlled, Phase III Study. Oh GC, Han JK, Han KH, Hyon MS, Doh JH, Kim MH, Jeong JO, Bae JH, Kim SH, Yoo BS, Baek SH, Rhee MY, Ihm SH, Sung JH, Choi YJ, Kim SJ, Hong KS, Lee BK, Cho J, Shin ES, Rhew JY, Kim H, Kim HS. Clin Ther. 2018 May;40(5):676-691.e1. doi: 10.1016/j.clinthera.2018.03.010. Epub 2018 Apr 17.
3. The Use Pattern and Clinical Impact of Novel P2Y12 Receptor Antagonists for Acute Myocardial Infarction in Korea. Kim SJ. Korean Circ J. 2017 Nov;47(6):864-867. doi: 10.4070/kcj.2017.0302.
4. Liraglutide and Renal Outcomes in Type 2 Diabetes. Mann JFE, Ørsted DD, Brown-Frandsen K, Marso SP, Poulter NR, Rasmussen S, Tornøe K, Zinman B, Buse JB; LEADER Steering Committee and Investigators. N Engl J Med. 2017 Aug 31;377(9):839-848. doi: 10.1056/NEJMoa1616011.
5. Clinical Significance of Lipid-Rich Plaque Detected by Optical Coherence Tomography: A 4-Year Follow-Up Study. Xing L, Higuma T, Wang Z, Aguirre AD, Mizuno K, Takano M, Dauerman HL, Park SJ, Jang Y, Kim CJ, Kim SJ, Choi SY, Itoh T, Uemura S, Lowe H, Walters DL, Barlis P, Lee S, Lerman A, Toma C, Tan JWC, Yamamoto E, Bryniarski K, Dai J, Zanchin T, Zhang S, Yu B, Lee H, Fujimoto J, Fuster V, Jang IK. J Am Coll Cardiol. 2017 May 23;69(20):2502-2513. doi: 10.1016/j.jacc.2017.03.556.

Abstract

WHY SHOULD WE CONSIDER EZETIMIBE IN LIPID GUIDELINES?

Soo-Joong Kim, MD, PhD

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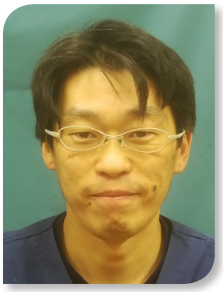
Dyslipidemia, with elevated low-density lipoprotein cholesterol (LDL-C) as its main, is a well-established risk factor for atherosclerotic cardiovascular disease (ASCVD) and statins are the first-line therapy for its management in patients with elevated LDL-C and increased cardiovascular risk. However, many at-risk patients do not achieve the target goal of LDL-C with statin monotherapy or do not tolerate statins due to side effects including muscular symptoms and new onset diabetes. In addition, some patients have residual risk for ASCVD despite maximizing statin therapy. Insufficient LDL-C reduction and residual risk in a significant proportion of statin-treated patients signify that additional therapies are required to deliver more effective treatment of cardiovascular diseases. In this respect, ezetimibe, cholesterol absorption inhibitor, may be used to supplement statin therapy, or used alone in cases of statin intolerance. Emerging evidence from IMPROVE-IT study (Improved Reduction of Outcomes: Vytorin Efficacy International Trial) suggests that adding ezetimibe to statin therapy is associated with further reduction of ASCVD events than statin only treatment, particularly in patients with significantly elevated atherosclerotic cardiovascular disease risk and elevated LDL level. We will discuss about the effects and clinical benefit of ezetimibe for ASCVD.

Symposium 7



Yu Kataoka

Organization

National Cerebral & Cardiovascular Center

Position & Title

Chief Consultant at Department of Cardiovascular Medicine

» Educational Background & Professional Experience

Year	Name of institution	Position
2015-Present	Department of Cardiovascular Medicine, National Cerebral & Cardiovascular Center, Suita, Japan	Chief consultant

» Research Interests

Atherosclerosis, lipids, diabetes, intravascular imaging, prevention

» Honors & Awards

- 2016 Takeda Foundation, Clinical Research Grant Program
- 2016 The 5th international congress of lipid metabolism and atherosclerosis, travel fellowship
- 2016 Kondo Foundation research grant program

» Publications

1. Shishikura D, **Kataoka Y**, Honda S, Takata K, Kim SW, Andrews J, Psaltis PJ, Sweeney M, Kulikowski E, Johansson J, Wong NCW, Nicholls SJ. The Effect of Bromodomain and Extra-Terminal Inhibitor Apabetalone on Attenuated Coronary Atherosclerotic Plaque: Insights from the ASSURE Trial. ***Am J Cardiovasc Drugs***. 2019;19:49-57.
2. Shishikura D, **Kataoka Y**, Pisaniello AD, Montarello JK, Nicholls SJ, Worthley SG. The Extent of Aorta Atherosclerosis Predicts the Occurrence, Severity and Recovery of Acute Kidney Injury after Trans-catheter Aortic Valve Replacement: Volumetric Multi-slice Computed Tomography Analysis. ***Circ Cardiovasc Interv*** 2018;11:e006367.
3. Doi T, **Kataoka Y**, Noguchi T, Shibata T, Fujino M, Nakashima T, Kawakami S, Nakao K, Nagai T, Kanaya T, Tahara Y, Asaumi Y, Tsuda E, Nakai M, Nishimura K, Anzai T, Kusano K, Shimokawa H, Goto Y, Yasuda S. Coronary artery ectasia predicts future cardiac events in patients with acute myocardial infarction. ***Arterioscler Thromb Vasc Biol***. 2017;37:2350-2355.
4. **Kataoka Y**, Harada-Shiba M, Nakao K, Nakashima T, Kawakami S, Fujino M, Kanaya T, Nagai T, Tahara Y, Asaumi Y, Hori M, Ogura M, Goto Y, Noguchi T, Yasuda S. Mature Proprotein Convertsase Subxilisin/kexin Type 9, Coronary Atheroma Burden and Vessel Remodeling in Heterozyogous Familial Hypercholesterolemia. ***J Clin Lipidol***. 2017;11:413-21.
5. **Kataoka Y**, Andrews J, MyNgan D, Nguyen T, Schwarz N, Fendler J, Puri R, Butters J, Keyserling C, Paolini JF, Dasseux JL, Nicholls SJ. Regression of Coronary Atherosclerosis with Infusions of the High-Density Lipoprotein Mimetic CER-001 in Patients with More Extensive Plaque Burden. ***Cardiovasc Diagn Ther***. 2017;7:252-263.
6. **Kataoka Y**, Puri R, Hammadah M, Duggal B, Uno K, Kapadia SR, Tuzcu EM, Nissen SE, King P, Nicholls SJ. Sex Differences in Nonculprit Coronary Plaque Microstructures on Frequency-Domain Optical Coherence Tomography in Acute Coronary Syndromes and Stable Coronary Artery Disease. ***Circ Cardiovasc Imaging***. 2016;9:e004506.
7. **Kataoka Y**, St John J, Wolski K, Uno K, Puri R, Tuzcu EM, Nissen SE, Nicholls SJ. Atheroma progression in hyporesponders to statin therapy. ***Arterioscler Thromb Vasc Biol***. 2015;35:990-995.

Abstract

ROLE OF PCSK9 INHIBITORS IN LIPID GUIDELINES AND FUTURE

Yu Kataoka, MD, PhD, FESC, FACC, FJCC

Department of Cardiovascular Medicine, National Cerebral & Cardiovascular Center
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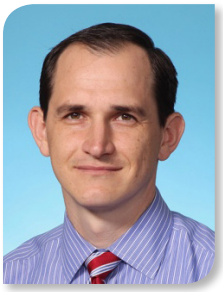
Recent studies demonstrated that proprotein convertase subxilisin/kexin type 9 (PCSK9) inhibitor substantially lowers LDL-C levels and reduces the occurrence of atherosclerotic cardiovascular events in subjects who received high-intensity statin. This suggests PCSK9 as an important therapeutic target to further reduce atherosclerotic cardiovascular risks. PCSK9 is a serine-protease which is associated with LDL metabolism. Pathophysiollogically, two different subtypes exist in circulation; mature and furin-cleaved PCSK9. These subtypes differ in their ability to degrade LDL receptor and promote atherosclerosis. These observations indicate the importance to evaluate each PCSK9 subtype with regard to LDL metabolism and atherogenesis. Further studies will be required to elucidate how we could allocate PCSK9 inhibitor to appropriate patients.

Keywords
PCSK9, coronary atheroma, matured and furin-cleaved PCSK9, intravascular imaging

Symposium 7



Joshua D. Mitchell

Organization

Washington University School of Medicine in St. Louis

Position & Title

Assistant Professor of Medicine

» Educational Background & Professional Experience

Year	Name of institution	Position
2018-	Washington University School of Medicine	Assistant Professor (Cardiology)
2017-2018	Washington University School of Medicine	Fellow, Cardio-Oncology
2015-2018	Washington University School of Medicine	Fellow, Cardiovascular Disease
2013-2015	Walter Reed National Military Medical Center	Assistant Professor (IM)
2011-2013	75th Ranger Regiment, US Army	3D Ranger Battalion Surgeon
2008-2011	Walter Reed Army Medical Center	Resident, Internal Medicine

» Research Interests

Prevention, cardiotoxicity from cancer therapy, cardiac amyloidosis

» Honors & Awards

- Bronze Star Medal with Oak Leaf Cluster, Operation Enduring Freedom
- Alpha Omega Alpha Honor Society
- Burton E. Sobel Award, Excellence in Clinical Cardiovascular Research

» Publications

1. Mitchell JD, Fergestrom N, Gage BF, Paisley R, Moon P, Novak E, Cheezum M, Shaw LJ, Villines TC. Impact of Statins on Cardiovascular Outcomes Following Coronary Artery Calcium Scoring. Journal of the American College of Cardiology. 2018; 72(25):3233-3242. NIHMSID: NIHMS1508981
2. Mitchell JD, Paisley R, Moon P, Novak E, Villines TC. Coronary Artery Calcium and Long-Term Risk of Death, Myocardial Infarction, and Stroke: The Walter Reed Cohort Study. JACC. Cardiovascular imaging. 2018; 11(12):1799-1806.
3. Mitchell JD, Brown DL. Harmonizing the Paradigm With the Data in Stable Coronary Artery Disease: A Review and Viewpoint. Journal of the American Heart Association. 2017; 6(11).
4. Mitchell JD, Collen JF, Petteys S, Holley AB. A simple reminder system improves venous thromboembolism prophylaxis rates and reduces thrombotic events for hospitalized patients. Journal of thrombosis and haemostasis : JTH. 2012; 10(2):236-43.
5. Hulten EA, Carbonaro S, Petrillo SP, Mitchell JD, Villines TC. Prognostic value of cardiac computed tomography angiography: a systematic review and meta-analysis. Journal of the American College of Cardiology. 2011; 57(10):1237-47.

Abstract

IMPACT OF THE CORONARY ARTERY CALCIUM SCORE ON PATIENT SELECTION FOR STATIN THERAPY

Joshua D. MITCHELL[1]*, Nicole FERGESTROM[2], Brian F. GAGE[3], Robert PAISLEY[4], Eric NOVAK[1], and Todd C. VILLINES[5]

[1] Cardiovascular Division, Washington University School of Medicine in St. Louis, USA
[2] Center for Advancing Population Science, Medical College of Wisconsin, USA
[3] General Medical Sciences, Washington University School of Medicine in St. Louis, USA
[4] Cardiovascular Division, Texas Heart Institute, USA
[5] Cardiology Service, Walter Reed National Military Medical Center, USA
jdmitchell@wustl.edu

Patient selection for primary prevention statin therapy has long been founded on the use of traditional risk scores to estimate a patient's hazard for future atherosclerotic cardiovascular events. Yet, this process has an important inherent limitation. Traditional risk scores rely on a single measurement in time of a handful of risk factors and are therefore incapable of fully accounting for a patient's prior lifetime risk exposure. Comparatively, coronary artery calcium (CAC) scoring integrates a patient's risk exposure to date by quantifying their cumulative atherosclerotic burden. Not surprisingly, multiple studies have shown that CAC improves the accuracy of cardiovascular risk prediction above traditional risk scores. Even more powerfully, the absence of CAC (a CAC of zero) has been shown repeatedly to confer a very low risk of future cardiovascular events over a period of at least 10 years.

The widespread acceptance of CAC for patient selection of statin therapy has been tempered by the lack of a randomized controlled trial proving benefit. In the absence of randomized data, observational data continues to grow, though, that CAC is able to optimally select patients most likely to confer benefit from statins. Most recently, our group has shown that in a propensity weighted sample of 13,644 primary prevention patients, CAC presence and severity helped stratify patients most likely to have reduced cardiovascular events with statin therapy. Patients without any CAC showed no benefit from statin therapy over a nearly 10-year follow-up in the primary analysis.

In this lecture, we will review the current state of the evidence and guidelines for incorporating the CAC score into patient selection for statin therapy, including our recent study results. Along the way, important limitations and future directions will be addressed.

Keywords
Calcium score, cardiovascular risk, screening, primary prevention, atherosclerotic cardiovascular disease

Symposium 7

Su-Jin Jeong

Organization

Sejong General Hospital

Position & Title

Endocrinology and metabolism doctor

» Educational Background & Professional Experience

Year	Name of institution	Position
2007-Present	Division of endocrinology and metabolism, Sejong general hospital	Endocrinology doctor
2003-2012	Medical college of Chonbuk National University hospital	Ph.D.
2006-2007	Medical college of Chonbuk National University hospital	Fellowship
1995-2001	Medical college of Chonbuk National University	M.D

» Research Interests

Diabetes complication

» Publications

1. Lee SJ, Jeong SJ, Lee YC, Lee YH, Lee JE, Kim CH, Min KW, Cha BY. Effects of High-Dose α-Lipoic Acid on Heart Rate Variability of Type 2 Diabetes Mellitus Patients with Cardiac Autonomic Neuropathy in Korea. Diabetes Metab J. 2017 Aug;41(4):275-283
2. Cho HA, Jung YL, Lee YH, Lee YC, Lee JE, Lee SJ, Jeong SJ, Kim CH Efficacy of Body Weight Reduction on the SGLT2 Inhibitor in People with Type 2 Diabetes Mellitus. J Obes Metab Syndr. 2017 Jun;26(2):107-113.
3. Myung Shin Kang, Chong Hwa Kim, Su Jin Jeong and Tae Sun Park2 Dietary Sodium Intake in People with Diabetes in Korea: The Korean National Health and Nutrition Examination Survey for 2008 to 2010. Diabetes Metab J. 2016 Aug; 40(4): 290–296.
4. Yu-Chang Lee, Su-Jin Jeong, Sol-Jae Lee, Chong-Hwa Kim, Yong-Hoon Lee, Jung-Eun Lee and Hye-Ji Seo A Case of Teratoma of Thyroid Gland in Adolescence Int J Thyroidol. 2017 May;10(1):61-65

Abstract

LDL TARGET IN LIPID GUIDELINES?

Su-Jin JEONG

Department of Endocrinology and Metabolism, Sejong Gerenal hospital, Bucheon, Korea
tusyle@naver.com

Large clinical studies have clearly established that the link between lowering low-density lipoprotein cholesterol (LDL-C) and risk reduction of cardiovascular events in patients with and those without cardiovascular disease. Consequently, treatment guidelines have been developed that identify LDL-C as a causative factor for cardiovascular disease and as a target for lipid-lowering therapy. A meta-analysis by the Cholesterol Treatment Trialists (CTT) reported that a reduction of 1 mmol per liter in LDL-cholesterol levels results in a consistent 20% to 25% decrease in the risk of the major cardiovascular events as well as the total mortality decreasing by 12 percent. Recently, Low and extremely low LDL have been beneficial to decrease cardiovascular events as RCTs by ezetimibe and PCSK9 inhibitors. This lecture is to look into lipid guideline history and LDL target in recent lipid guidelines.

Keywords
LDL- cholesterol, Cardiovascular events, lipid guidelines

ICoLA 2019 by KSoLA

Symposium 8

Chairpersons

Jeong Bae Park | JB Clinic & Lab, Korea
Jongwon Ha | Yonsei University, Korea

Date & Time: September 6 (Fri.), 14:00-15:30
Place: Room 2 (3F)

Symposium 8

Thomas WEBER, MD, Associate Professor, FESC

Organization

Cardiology Department, Klinikum Wels-Grieskirchen

Position & Title

Deputy Medical Director Cardiology Department

» Educational Background & Professional Experience

Year	Name of institution	Position
2018-	Cardiology Department, Klinikum Wels-Grieskirchen, Austria	Deputy Medical Director
2002-2018	Cardiology Department, Klinikum Wels-Grieskirchen, Austria	Senior Physician
2008	Paracelsus Medical University Salzburg, Austria	Habilitation (Venia legend)
2004	Klinikum Wels-Grieskirchen, Austria	Specialist Cardiology
2001	Klinikum Wels-Grieskirchen, Austria	Specialist Internal Medicine
1990	Medical University Vienna, Austria	Graduation Dr. med.

» Research Interests

Arterial stiffness, pulsatile hemodynamics, hypertension, heart failure, pulse wave reflections, aortic dissection, renal denervation

» Honors & Awards

- Vice president, ARTERY society
- Past president, Austrian Society of Hypertension
- Honorary member, Hungarian Society of Hypertension

» Publications

1. **Weber T**, Wassertheurer S, Hametner B, Moebus S, Pundt N, Mahabadi AA, Roggenbuck U, Lehmann N, Jöckel KH, Erbel R, on behalf of the Heinz Nixdorf Recall investigative group. Cross-sectional analysis of pulsatile hemodynamics across the adult life span – reference values, healthy and early vascular aging. The Heinz Nixdorf Recall and the Multigeneration study. J Hypertens 2019; in press
2. **Weber T**, Chirinos J. Pulsatile hemodynamics in heart failure. *Eur Heart J 2018; 39:3847-54*
3. **Weber T**, Wassertheurer S, Schmidt-Trucksäss A, Rodilla E, Ablasser C, Jankowski P, Muiesan ML, Giannattasio C, Mang C, Wilkinson I, Kellermair J, Hametner B, Pascual JM, Zweiker R, Czarnecka D, Paini A, Salvetti M, Maloberti A, McEniery C. Relationship between 24 hour ambulatory central systolic blood pressure and left ventricular mass – a prospective multicentre study. *Hypertension 2017;70:1157-1164*
4. **Weber T**, Wassertheurer S, O´Rourke MF, Haiden A, Zweiker R, Rammer M, Hametner B, Eber B. Pulsatile hemodynamics in patients with exertional dyspnea – potentially of value in the diagnostic evaluation of suspected heart failure with preserved ejection fraction. *J Am Coll Cardiol 2013; 61:1874-83*
5. Townsend RR, Wilkinson IB, Schiffrin EL, Avolio AP, Chirinos JA, Cockcroft JR, Heffernan KS, Lakatta EG, McEniery CM, Mitchell GF, Najjar SS, Nichols WW, Urbina EM, **Weber T**; American Heart Association Council on Hypertension. Recommendations for Improving and Standardizing Vascular Research on Arterial Stiffness: A Scientific Statement From the American Heart Association. *Hypertension 2015;66:698-722*
6. **Weber T**, Auer J, O´Rourke MF, Kvas E, Lassnig E, Lamm G, Stark N, Rammer M, Eber B. Increased arterial wave reflections predict severe cardiovascular events in patients undergoing percutaneous coronary interventions. *Eur Heart J 2005; 26:2657-63*
7. **Weber T**, Auer J, O´Rourke MF, Kvas E, Lassnig E, Berent R, Eber B. Arterial stiffness, wave reflections and the risk of coronary artery disease. *Circulation 2004; 109:184-189*

Abstract

PULSATILE HEMODYNAMICS IN HEART FAILURE

Thomas WEBER

Cardiology Department, Klinikum Wels-Grieskirchen, Austria
thomas.weber3@liwest.at

Due to the cyclic function of the human heart, pressure and flow in the circulation are pulsatile rather than continuous. Investigating pulsatile hemodynamics starts with the most simple measurement, brachial pulse pressure. Brachial pulse pressure, despite its simplicity and wide availability, is related to development and treatment of heart failure. However, pulse pressure is often confounded in patients with established heart failure, because it depends not only on arterial properties, but also on stroke volume. The next step of analysis consists of central (rather than brachial) pressures, and, more importantly, of wave reflections. Wave reflections are closely related to left ventricular late systolic afterload, ventricular remodeling, diastolic dysfunction, exercise capacity, and, in the long term, the risk of new-onset heart failure. Wave reflection may also represent a therapeutic target. Treatments for heart failure with preserved and reduced ejection fraction, based on a reduction of wave reflection, are emerging. A full understanding of ventricular-arterial coupling, however, requires complex analysis of time-resolved pressure and flow signals, which can be accomplished with contemporary non-invasive imaging and modeling techniques. This presentation provides a summary of our current understanding of pulsatile hemodynamics in heart failure.

Keywords
Pulsatile hemodynamics, wave reflections, heart failure

Symposium 8

Jin-Sun Park

Organization

Ajou University School of Medicine

Position & Title

Assistant professor

MD, PhD

» Educational Background & Professional Experience

Year	Name of institution	Position
2015-	Ajou University School of Medicine	Assistant professor
2012-2015	Ajou University School of Medicine	Clinical Assistant professor
2010-2012	Ajou University School of Medicine	Clinical Instructor
2008-2010	Ajou University School of Medicine	Fellow
2004-2008	Ajou University School of Medicine	Resident
2003	Ajou University School of Medicine	Intern

» Publications

1. Jin-Sun Park, Kyoung-Woo Seo, Byoung-Joo Choi, So-Yeon Choi, Myeong-Ho Yoon, Gyo-Seung Hwang, Seung-Jea Tahk, Joon-Han Shin: Importance of prognostic value of neutrophil to lymphocyte ratio in patients with ST-elevation myocardial infarction. Medicine (Baltimore). 2018; 97(48): e13471.
2. Jin-Sun Park, Jeoung-Sook Shin, You-Hong Lee, Kyoung-Woo Seo, Byoung-Joo Choi, So-Yeon Choi, Myeong-Ho Yoon, Gyo-Seung Hwang, Seung-Jea Tahk, Joon-Han Shin: Prognostic impact of left ventricular mass change in patients with ST-elevation myocardial infarction. Medicine (Baltimore). 2018; 97(4):e9748.
3. Jin-Sun Park, Moo-Yong Rhee, June Namgung, Sung Yun Lee, Deok-Kyu Cho, Tae-Young Choi, Seok Yeon Kim, Jang Young Kim, Sang Min Park, Jae Hyuk Choi, Jae Hang Lee, Hae-Young Kim: Comparison of Optimal Diagnostic Thresholds of Hypertension With Home Blood Pressure Monitoring and 24-Hour Ambulatory Blood Pressure Monitoring. Am J Hypertens. 2017; 6;30(12):1170-1176.
4. Jin-Sun Park, You-Hong Lee, Kyoung-Woo Seo, Byoung-Joo Choi, So-Yeon Choi, Myeong-Ho Yoon, Gyo-Seung Hwang, Seung-Jea Tahk, Joon-Han Shin: Echocardiographic epicardial fat thickness is a predictor for target vessel revascularization in patients with ST-elevation myocardial infarction. Lipids Health Dis. 2016; 16; 15(1): 194.
5. Jin-Sun Park, Gyo-Seung Hwang, Sun-Mi Kim, Kyoung-Woo Seo, Byoung-Joo Choi, So-Yeon Choi, Myeong-Ho Yoon, Joon-Han Shin, Seung-Jea Tahk: Time Variance of Electrocardiographic Transmural Dispersion in Acute Myocardial Infarction. Int J Arrhythm. 2016; 17(4): 174-180.
6. Jin-Sun Park, Joon-Han Shin, Taek-Jong Hong, Hong-Seog Seo, Wan-Joo Shim, Sang-Hong Baek, Jin-Ok Jeong, Youngkeun Ahn, Woong-Chol Kang, Young-Hak Kim, Sang-Hyun Kim, Min-Su Hyon, Dong-Hoon Choi, Chang-Wook Nam, Tae-Ho Park, Sang-Chol Lee, Hyo-Soo Kim: Efficacy and safety of fixed-dose combination therapy with olmesartan medoxomil and rosuvastatin in Korean patients with mild to moderate hypertension and dyslipidemia: an 8-week, multicenter, randomized, double-blind, factorial-design study (OLSTA-D RCT: OLmesartan rosuvaSTAtin from Daewoong). DDDT. 2016; 10: 2599-2609
7. Jin-Sun Park, Byoung-Joo Choi, So-Yeon Choi, Myeong-Ho Yoon, Gyo-Seung Hwang, Seung-Jea Tahk, Joon-Han Shin: Echocardiographically measured epicardial fat predicts restenosis after coronary stenting, Scand Cardiovasc J 2013; 47(5): 297-302

Abstract

ARTERIAL STIFFNESS AND CIRCARDIAN PATTERN OF BLOOD PRESSURE

Jin-Sun PARK

Department of Cardiology, Ajou University School of Medicine, Korea
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Arterial stiffness is a risk factor for cardiovascular morbidity and mortality. The relationship between the arterial stiffness and the circadian pattern of blood pressure (BP) has been controversial. The objective of the present study was to investigate the relationship between arterial stiffness by pulse wave analysis (PWA) and variables of 24-hour ambulatory BP monitoring (ABPM) in patients with high normal BP or hypertension (HTN).

Five hundred forty eight patients (304 males, 48 ± 12 year-old) with high normal BP or HTN were enrolled. BP was measured at the outpatient clinic and 24-hour ABPM was performed. Using radial applanation tonometry, PWA was performed for evaluation of systemic arterial stiffness. Patients were classified into four groups according to the dipping patterns: a nocturnal dipping group, an isolated systolic non-dipping group, an isolated diastolic non-dipping group and a both systolic and diastolic non-dipping group. For adjustment of age, population was divided to 2 groups: old group ≥ 55 year-old (n = 158, 75 males), young group <55 year-old (n = 390, 229 males).

According to the dipping patterns, augmentation pressure (AP), augmentation index (AI) and heart rate (75bpm) adjusted AI (AI@HR75) showed statistically significant difference (P = 0.011, 0.009 and 0.018, respectively). Multivariate analysis showed that isolated diastolic non-dipping was correlated with arterial stiffness expressed as AI and AI@HR 75, only in young group (β-coefficient = 12.6, P = 0.04 and β-coefficient = 7.503, P = 0.028, respectively).

Arterial stiffness might be closely related with the pattern of non-dipping in young patients with HTN and high normal BP.

Keywords
Arterial stiffness, Circadian pattern, blood pressure, pulse wave analysis, hypertension

Symposium 8

MASANORI MUNAKATA

Organization

Japan Organization of Occupational Health and Safety Tohoku Rosai Hospital

Position & Title

Director, Research Center for lifestyle-related disease and Center for the Promotion of Health and Employment Support, and Division of Hypertension, Tohoku Rosai Hospital

Clinical professor, Division of Nephrology, Endocrinology and Vascular Medicine Tohoku University Graduate School of Medicine

» Educational Background & Professional Experience

Year	Name of institution	Position
2016-2019	Research Center for lifestyle-related disease and Center for the Promotion of Health and Employment Support, Tohoku Rosai Hospital	Director
2014-2019	Division of Nephrology, Endocrinology and Vascular Medicine Tohoku University Graduate School of Medicine	Clinical professor
2009-2014	Japan Labor Health and Welfare Organization	Chief researcher
2003-2009	Preventive medical center, Tohoku Rosai Hospital	Director
2003-2019	Division of Hypertension, Tohoku Rosai Hospital	Director

» Research Interests

Pulse wave velocity, stress & hypertension, epidemiology

» Publications

1. Steno-Stiffness Approach for Cardiovascular Disease Risk Assessment in Primary Prevention. Tomiyama H, Ohkuma T, Ninomiya T, Mastumoto C, Kario K, Hoshide S, Kita Y, Inoguchi T, Maeda Y, Kohara K, Tabara Y, Nakamura M, Ohkubo T, Watada H, Munakata M, Ohishi M, Ito N, Nakamura M, Shoji T, Vlachopoulos C, Aboyans V, Yamashina A; Collaborative Group for J-BAVELs (Japan Brachial-Ankle Pulse Wave Velocity Individual Participant Data Meta-Analysis of Prospective Studies). Hypertension. 2019 Mar;73(3):508-513.
2. Physiological Diagnostic Criteria for Vascular Failure. Tanaka A, Tomiyama H, Maruhashi T, Matsuzawa Y, Miyoshi T, Kabutoya T, Kario K, Sugiyama S, Munakata M, Ito H, Ueda S, Vlachopoulos C, Higashi Y, Inoue T, Node K; Physiological Diagnosis Criteria for Vascular Failure Committee. Hypertension. 2018 Nov;72(5):1060-1071.
3. Clinical significance of stress-related increase in blood pressure: current evidence in office and out-of-office settings. Munakata M. Hypertens Res. 2018 Aug;41(8):553-569.
4. Brachial-Ankle Pulse Wave Velocity and the Risk Prediction of Cardiovascular Disease: An Individual Participant Data Meta-Analysis. Ohkuma T, Ninomiya T, Tomiyama H, Kario K, Hoshide S, Kita Y, Inoguchi T, Maeda Y, Kohara K, Tabara Y, Nakamura M, Ohkubo T, Watada H, Munakata M, Ohishi M, Ito N, Nakamura M, Shoji T, Vlachopoulos C, Yamashina A; Collaborative Group for J-BAVEL (Japan Brachial-Ankle Pulse Wave Velocity Individual Participant Data Meta-Analysis of Prospective Studies)*. Hypertension. 2017 Jun;69(6):1045-1052.
5. Relationship between subtle urinary albumin excretion and risk of incident hypertension: modification by glomerular filtration rate. Munakata M, Hattori T, Konno S. Hypertens Res. 2017 Dec;40(12):994-998.
6. Increased double product on Monday morning during work. Kimura G, Inoue N, Mizuno H, Izumi M, Nagatoya K, Ohtahara A, Munakata M; Workplace Hypertension Co-operative Study by 29 Rosai Hospitals belonging to the Japan Organization of Occupational Health and Safety.Hypertens Res. 2017 Jul;40(7):671-674.
7. Brachial-Ankle Pulse Wave Velocity: Background, Method, and Clinical Evidence. Munakata M.Pulse (Basel). 2016 Apr;3(3-4):195-204.

Abstract

THE CLINICAL USEFULLNESS OF BRACHIAL-ANKLE PULSE WAVE VELOCITY

Masanori MUNAKATA

[1] Research Center for Lifestyle-related Disease
[2] Center for the promotion of Health and Employment Support
[3] Division of Hypertension Japan Organization of Occupational Health and Safety, Tohoku Rosai Hospital, Sendai, Japan
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Atherosclerotic cardiovascular disease is a leading cause of death and disability in many developed countries in which ageing is a major risk of CVD. In aged societies, assessment of total vascular risk is important, because elderly peoples are usually associated with multiple risks. Pulse wave velocity (PWV) is a useful measure for the assessment of total cardiovascular risks, since it increases with advancing age, high blood pressure, hyperglycemia, renal functional decline and so on. Brachial-ankle PWV (baPWV) is a most common measure for systemic arterial stiffness routinely used in Japan. The measurement is easy, and its reproducibility is good. The generality and validity of the methodology is guaranteed. The baPWV has been reported to consistently increase with most traditional cardiovascular risk factors except dyslipidemia. Prognostic significance has been confirmed not only in Japanese but also in other Asian population. Recent individual participant data meta-analysis including 14673 Japanese participants has shown that every 1 SD or 3.85 m/sec increase in brachial-ankle PWV was associated with 19% increase in the risk of cardiovascular disease. Moreover, simultaneous evaluation of the ankle-brachial index with baPWV, or steno-stiffness approach could allow further risk stratification of high-risk individuals. Confirmation of normal circulation is also mandatory to ensure the validity of PWV measurement in the target arterial territory. In this lecture, the clinical usefulness of the baPWV will be overviewed according to the latest evidence.

Keywords
Brachial-ankle PWV, Cardiovascular disease, Steno-stiffness approach,

Symposium 8

Hack-Lyoung Kim

Organization

SMG-SNU Boramae Medical Center

Position & Title

Associate Professor, MD, PhD

» Educational Background & Professional Experience

Year	Name of institution	Position
2018-	Seoul National University, Korea	Associate Professor
2012-2018	Seoul National University, Korea	Assistant Professor

» Research Interests

Arterial stiffness

» Publications

1. Jaehoon Chung*, **Hack-Lyoung Kim*** (*co-first author), Myung-A Kim. et al. Association between invasively measured aortic pulse pressure and orthostatic hypotension in patients undergoing invasive coronary angiography. J Hypertens 2019 [in press]
2. **Hack-Lyoung Kim**, Sang-Hyun Kim. Pulse wave velocity in atherosclerosis. Front Cardiovasc Med. 2019 Apr 9;6:41.
3. **Hack-Lyoung Kim**, Jung Pyo Lee, Woo-Hyun Lim, et al. Association between the level of serum soluble ST2 and invasively measured aortic pulse pressure in patients undergoing coronary angiography. Medicine (Baltimore). 2019 Feb;98(8):e14215.
4. In-Chang Hwang, Kwang Nam Jin, **Hack-Lyoung Kim** (corresponding author), et al. Additional Prognostic Value of Brachial-Ankle Pulse Wave Velocity to Coronary Computed Tomography Angiography in Patients with Suspected Coronary Artery Disease. Atherosclerosis 2018 Jan;268:127-137
5. Kyeongmin Jang, **Hack-Lyoung Kim** (corresponding author), Miri Park, et al. Additional value of brachial-ankle pulse wave velocity to single photon emission computed tomography in the diagnosis of coronary artery disease. J Atheroscler Thromb. 2017 Dec 1;24(12):1249-1257.
6. Kim KJ*, **Hack-Lyoung Kim*** (*co-first author), Kim MJ, et al. Gender Difference in the Association between Aortic Pulse Pressure and Left Ventricular Filling Pressure in the Elderly: an Invasive Hemodynamic Study. J Card Fail. 2017 Mar;23(3):224-230.
7. **Hack-Lyoung Kim**, Woo-Hyun Lim, Jae-Bin Seo, et al. Association between arterial stiffness and left ventricular diastolic function in relation to gender and age. Medicine (Baltimore). 2017 Jan;96(1):e5783.

Abstract

ARTERIAL STIFFNESS AND CORONARY ARTERY DISEASE

Hack-Lyoung KIM

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khl2876@gmail.com

Although there have been marked improvements in both diagnostic and therapeutic interventions over several decades, coronary artery disease (CAD) remains the leading cause of death worldwide. Intensive modification of classic risk factors, such as hypertension, diabetes mellitus, dyslipidemia and cigarette smoking, has significantly reduced the development of CAD, however, the high prevalence of residual cardiovascular events requires improvement in the identification and risk stratification strategies. In this context, arterial stiffness, which reflects arterial aging, damage and arteriosclerosis, has emerged as an important risk factor for cardiovascular disease. The measurements of arterial stiffness are easy to make using several noninvasive methods, such as pulse wave velocity. The clinical utility of the measures has been validated in many prior studies. Recent evidence has suggested that the measures of arterial stiffness are correlated with the presence and extent of CAD. More important, increased arterial stiffness is an independent predictor of CAD-related morbidity and mortality beyond classic risk factors. Considering its noninvasiveness, simplicity and reliability, arterial stiffness could serve as a useful marker of CAD, and help identify high-risk patients who may benefit from more aggressive management.

Keywords
Arterial stiffness; coronary artery disease

ICoLA 2019 by KSoLA

Symposium 9

Chairpersons

Min-seon Kim | University of Ulsan, Korea
Ira J. Goldberg | New York University, USA

Date & Time: September 6 (Fri.), 14:00-15:30
Place: Room 3 (3F)

Symposium 9

Man-Ho Choi

Organization

Korea Institute of Science and Technology (KIST)

Position & Title

Principal Scientist/ Head of Research Center

» Educational Background & Professional Experience

Year	Name of institution	Position
1998-2002	Sungkyunkwan University, Korea	Ph.D.
2002-2004	MIT	Post-Doc
2004-Present	KIST	Principal Scientist

» Research Interests

Steroidogenesis in clinical endocrinology

» Honors & Awards

- Associate Editor: Journal of Steroid Biochemistry and Molecular Biology
- Editor: Molecular and Cellular Endocrinology
- Editor: Tohoku Journal of Experimental Medicine

» Publications

1. Increased biosynthesis and accumulation of cholesterol in maternal plasma, but not amniotic fluid in pre-eclampsia. *Sci. Reports*, 9, 1550 (2019)
2. Mass spectrometry-based metabolic signatures of sex steroids in breast cancer. *Mol. Cell. Endocrinol.*, 466, 81 (2018)
3. Ad4BP/SF-1 regulates cholesterol synthesis to boost the production of steroids. *Commun. Biol.*, 1, 18 (2018)
4. Differential lactate and cholesterol synthetic activities in XY and XX sertoli cells. *Sci. Rep.*, 7, 41912 (2017)
5. Profiling of cholesterol and sex steroid hormone metabolism in urological diseases. *Endocr. Relat. Cancer*, 23, R455 (2016)
6. Sex hormone establish a reserve pool of adult muscle stem cells. *Nat. Cell. Biol.*, 18, 930 (2016)
7. Metabolic profiling of steroid conjugates reveals an association between decreased levels of steroid sulfates and adiposity in obese girls. *J. Steroid Biochem. Mol. Biol.*, 162, 100 (2016)

Abstract

CHOLESTEROL EVERYWHERE: ANALYTICAL AND CLINICAL ASPECTS

Man-Ho CHOI

Molecular Recognition Research Center, Korea Institute of Science and Technology, Korea
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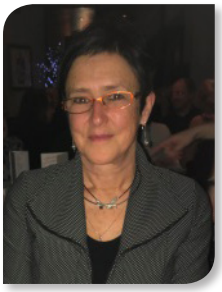
In contrast to immunoaffinity-based methods, that mainly focus on single enzyme or single metabolic reactions, the chromatographic profiling provides quantitative results for a broad spectrum in metabolic dynamics associated with physiological changes of interest. Abnormalities in cholesterol metabolism are associated with physiological changes in various clinical diseases, including hypertensive and lipid storage disorders, as well as reproductive functions. Mass spectrometric detection combined with chromatographic separation of precursors and metabolites of cholesterol has been developed to provide metabolic signatures in clinical and biological applications. This technique can be useful for mining diagnostic/prognostic biomarkers in vasospastic angina, preeclampsia, obesity, and sitosterolemia as well as making pathophysiological understanding of the differences between sexual functions in reproductive steroidogenesis. In addition to classical biological matrices, such as blood serum and cell extracts, the dried blood spot will be also provided as non-invasive clinical samples in part of an overall plan of medical care.

Keywords
Cholesterol, Steroidogenesis, Reproductive Biology, Endocrinology, Mass Spectrometry

Symposium 9



Christine Des Rosiers Ph.D.

Organization

Montreal Heart Institute (MHI) & Department of Nutrition, Université de Montréal

Position & Title

Professor of Nutrition & Biochemistry

Director of MHI Metabolomics Laboratory & Platform

» Educational Background & Professional Experience

Year	Name of institution	Position
2015-2016	Department of Nutrition, Université de Montréal, Qc, Canada	Director of graduate studies
2009-	Montreal Heart Institute Research Center, Montreal, Qc, Canada	Director; Metabolomics Lab. & Platform
2004-	Montreal Heart Institute Research Center, Montreal, Qc, Canada	Researcher
2000-	Department of Nutrition, Université de Montréal, Qc, Canada	Full Professor
1989-2004	Centre hospitalier de l'Université de Montréal (CHUM), Montreal, Qc, Canada	Researcher
1995-2000/ 1989-1995	Department of Nutrition, Université de Montréal, Qc, Canada	Associate Professor Assistant Professor

» Research Interests

Metabolic & heart diseases; Biomarker discovery using metabolomics

» Publications

1. Ruiz, M, al., Des Rosiers C (2019) Lipidomics unveils lipid dyshomeostatis and low circulating plasmalogens as biomarkers in a monogenic mitrochondrial disorder. JCI-Insight, accepted for publication May 31sth, 2019.
2. Forest A, al., Des Rosiers C (2018) Comprehensive and reproducible untargeted lipidomic workflow using LC-QOTF validated for human plasma analysis. J Proteome Res 17: 3657.
3. Ruiz M, al., Des Rosiers C (2017) Circulating acylcarnitine profile in human heart failure: A surrogate of fatty acid metabolic dysregulation in mitochondria and beyond. Am J Physiol Heart & Circ Physiol, 313: H768.
4. Ruiz M, al., Des Rosiers C (2017) MK2 deletion prevents diabetes-induced perturbations in lipid metabolism and cardiac dysfunction. Diabetes 65: 381.
5. Taegtmeyer H, Young ME, Lopaschuk G, al., Des Rosiers C & al. (2016) American Heart Statement: Assessing cardiac metabolism, Circ Res 118: 1659.
6. Thompson Legault J, al., Des Rosiers C (2015) A metabolic signature of mitochondrial dysfunction revealed through a monogenic form of Leigh Syndrome. Cell Reports 13: 981.
7. Khairallah M, al., Des Rosiers C (2008) Sildenafil and cardiomyocyte-specific cGMP signaling prevent cardiomyopathic changes associated with dystrophin deficiency. Proc. Nat. Acad. Sci. 105: 7028.

Abstract

METABOLOMICS: HOW CAN WE USE IT FOR METABOLIC DISEASES - LESSONS FROM A MONOGENIC MITOCHONDRIAL DISORDER

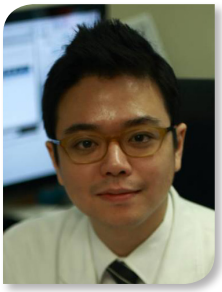
Christine DES ROSIERS[1,2]*, Matthieu RUIZ[1,3], Julie THOMPSON LEGAULT[1], John D. RIOUX[1,3], Yan BURELLE[4], LSFC CONSORTIUM[1]

[1] Montreal Heart Institute & Université de Montréal, Montreal, QC, Canada
[2] Department of Nutrition, Université de Montréal, Montreal, QC, Canada
[3] Department of Medicine, Université de Montréal, Montreal, QC, Canada
[4] Interdisciplinary School of Health Sciences, Faculty of Health Sciences; & Department of Cellular and Molecular Medicine, Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada
Christine.Des.Rosiers@umontral.ca

The use of recently emerging metabolomic technologies - which aim at systematically measure all low-molecular weight compounds within a biological system - has provided some valuable insight into the global metabolic perturbations prevailing in several metabolic diseases. This presentation will illustrate the value of lipidomics, a subset of metabolomics focusing on lipids, in deciphering the biochemical consequences ensuing from mitochondrial dysfunction, a condition that underlies many rare and common age-associated chronic diseases. The focus will be on recent results obtained through the application of comprehensive untargeted and targeted lipidomics to samples from patients with Leigh Syndrome French-Canadian variant (LSFC), a mitochondrial disorder caused by mutations in the nuclear gene leucine-rich pentatricopeptide repeat containing protein (LRPPRC), and mice harboring liver-specific inactivation of Lrpprc (H-*Lrpprc*$^{-/-}$). LSFC is characterized by a tissue-specific defect in the assembly of oxidative phosphorylation complexes, principally complex IV in brain and liver, and to a lesser extent in muscle. This study extends our previous work on LSFC (*Thompson Legault et al. Cell Reports 13: 981, 2015; Cuillerier et al. Hum Mol Genet 15: 186, 2017*) and takes advantage of our recently validated high-resolution LC-QTOF lipidomic workflow (*Forest et al. J. Prot. Res. 17: 3657, 2018*). Results show plasma and hepatic changes in plasmalogens, bile acid conjugates, as well as of very long chain and odd chain acylcarnitines, which are reminiscent albeit more subtle than those reported in primary peroxisomal disorders. Of potential broader relevance, they also include major lipid changes evocative of hepatic steatosis, which is consistent with previous findings in H-*Lrpprc*$^{-/-}$ mice and LSFC patients. Collectively, these results underscore the value of untargeted lipidomics to unveil unexpected mechanisms underlying lipid dyshomeostasis ensuing from mitochondrial dysfunction, herein implying peroxisomes, which likely contribute to the pathophysiology of LSFC, but also other rare and common chronic diseases with mitochondrial dysfunction.

Keywords
Lipidomics, Mitochondria, Peroxisomes, Plasmalogens, Acylcarnitines, Monogenic mitochondrial disorder, Liver steatosis

Symposium 9



Changhee Jung

Organization

Asan Medical Center, University of Ulsan College of Medicine

Position & Title

M.D., Ph.D.

Associate Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2017-Current	Asan Medical Center, University of Ulsan College of Medicine	Associate Professor
2018-Current	University of Virginia, Cardiovascular Research Center (CVRC)	Visiting Scholar
2013-2016	Asan Medical Center	Clinical Assistant Professor
2012-2013	Asan Medical Center	Post-fellowship Doctor
2010-2012	Asan Medical Center	Clinical Fellow
2014	University of Ulsan College of Medicine	Ph.D.
2012	University of Ulsan College of Medicine	M.S.
2002	Korea University	M.D.

» Research Interests

Obesity, Adipose Tissue Inflammation, Type 2 Diabetes

» Honors & Awards

· 2016 12th Young Investigator Award of Korean Diabetes Association (KDA)

» Publications

1. Implications of the dynamic nature of metabolic health status and obesity on risk of incident cardiovascular events and mortality: a Nationwide population-based cohort study. Cho YK, Kang YM, Yoo JH, Lee J, Park JY, Lee WJ, Kim YJ, **Jung CH**. *Metabolism*. 2019, Epub ahead of print
2. Effect of Sfrp5 (Secreted Frizzled-Related Protein 5) on the Wnt5a (Wingless-Type Family Member 5a)-Induced Endothelial Dysfunction and Its Relevance with Arterial Stiffness in Human Subjects. Cho YK, Kang YM, Lee SE, Lee Y, Seol SM, Lee WJ, Park JY, **Jung CH**. *Arterioscler Thromb Vasc Biol* 2018;38:1358-67
3. Efficacy and safety of combination therapy with SGLT2 and DPP4 inhibitors in the treatment of type 2 diabetes: A systematic review and meta-analysis. Cho YK, Kang YM, Lee SE, Lee J, Park JY, Lee WJ, Kim YJ, **Jung CH**. *Diabetes Metab* 2018;44:393-401.
4. Comparison between sodium-glucose cotransporter 2 inhibitors and pioglitazone as additions to insulin therapy in type 2 diabetes patients: A systematic review with an indirect comparison meta-analysis. Cho YK, Kim YJ, Kang YM, Lee SE, Park JY, Lee WJ, **Jung CH**. *J Diabetes Investig* 2018;9:882-892
5. Cardiovascular Diseases and Life Expectancy in Adults With Type 2 Diabetes: A Korean National Sample Cohort Study. Kang YM, Cho YK, Lee SE, Park JY, Lee WJ, Kim YJ, **Jung CH**. *J Clin Endocrinol Metab* 2017;102:3443-3451.

Abstract

CLONAL HEMATOPOIESIS; IS IT A NEW RISK FACTOR FOR METABOLIC DYSFUNCTION?

Changhee JUNG

Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Korea
chjung0204@gmail.com

The accumulation of somatic mutations in hematopoietic stem/progenitor cells (HSPCs) is known to be an inevitable consequence of the process of aging. Some of these random mutations confer a competitive advantage to the mutant cells, leading to clonal expansion. This phenomenon is called as age-related clonal hematopoiesis (CH). The genes that were most commonly mutated in CH were *DNMT3A*, *TET2* and *ASXL1*.

A number of studies have associated with CH with an increase in all-cause mortality. Although the presence of CH was associated with the increased risk of hematologic cancer, this only affected 0.5% to 1% of mutation carriers each year and did not explain the marked increase in all-cause mortality. Instead, the increased all-cause mortality was attributable to increased risk of cardiovascular disease (CVD). Based on these epidemiological data, several groups tried to elucidate the possible molecular mechanism underlying the presence of CH and CVD such as atherosclerosis, myocardial infarction and heart failure.

In addition to the causal link between CH and CVD, a modest and significant association between CH and type 2 diabetes was observed. In this talk, I'd like to introduce the possible causal link between the loss of function in *DNMT3A*, the most frequently mutated gene in CH, and metabolic dysfunction including adipose tissue inflammation in mouse.

Keywords
Clonal hematopoiesis, DNMT3A, Type 2 diabetes, Metabolic dysfunction, Adipose tissue inflammation

ICoLA 2019 by KSoLA

Symposium 10

Chairpersons

Sung Rae Kim | The Catholic University of Korea, Korea
Shun Ishibashi | Jichi Medical University, Japan

Date & Time: September 6 (Fri.), 14:00-15:30
Place: Room 4 (5F)

Symposium 10

Atsushi NOHARA

Organization

Ishikawa Prefectural Central Hospital

Position & Title

Director, Department of Clinical Genetics

(Dual role as Affiliated scientist of Kanazawa University Graduate School of Medical Sciences)

» Educational Background & Professional Experience

Year	Name of institution	Position
2019-	Department of Clinical Genetics, Ishikawa Prefectural Central Hospital, Japan	Director
2016-2019	Kanazawa University Health Service Center, Japan	Associate Professor
2017-2016	Department of Lipidology, Kanazawa University Graduate School of Medical Sciences, Japan	Associate Professor
2005-2016	Department of Lipidology, Kanazawa University Graduate School of Medical Sciences, Japan	Assistant Professor
2002-2004	Département d'athérosclérose, Institut Pasteur de Lille, France	Post-doctoral fellow
2001-2002	Molecular Genetics of Cardiovascular Disorders, Graduate School of Medical Science, Kanazawa University, Japan	Instructor

» Research Interests

Familial Hypercholesterolemia, Clinical Genetics in Lipidology

» Honors & Awards

· Japanese Atherosclerosis Society, 15th Young Investigator Encouragement Award

» Publications

1. Nohara A, et al. Statement for Appropriate Clinical Use of PCSK9 Inhibitors. *J Atheroscler Thromb*. 2018;25(8):747-750.
2. Nohara A, et al. Safety and Efficacy of Lomitapide in Japanese Patients with Homozygous Familial Hypercholesterolemia (HoFH): Results from the AEGR-733-301 Long-Term Extension Study. *J Atheroscler Thromb*. 2019 Apr 1;26(4):368-377
3. Harada-Shiba M, Nohara A, et al. Guidelines for Diagnosis and Treatment of Familial Hypercholesterolemia 2017. *J Atheroscler Thromb*. 2018;25(8):751-770.
4. Mabuchi H, Nohara A. PCSK9 inhibitors for treating familial hypercholesterolaemia. ***Nat Rev Endocrinol***. 2015;11(1):8-9.
5. Mabuchi H, Nohara A,et al. Genotypic and phenotypic features in homozygous familial hypercholesterolemia caused by proprotein convertase subtilisin/kexin type 9 (PCSK9) gain-of-function mutation. *Atherosclerosis*. 2014 Sep;236(1):54-61.
6. Mabuchi H, Nohara A, et al. Molecular genetic epidemiology of homozygous familial hypercholesterolemia in the Hokuriku district of Japan. *Atherosclerosis*, 2011 ;214(2):404-7.
7. Nohara A, et al. High frequency of a retinoid X receptor gamma gene variant in familial combined hyperlipidemia that associates with atherogenic dyslipidemia. *Arterioscler Thromb Vasc Biol*. 2007 Apr;27(4):923-8.

Abstract

PCSK9 INHIBITORS: IMPACT ON HIGH-RISK PATIENTS AND APPROPRIATE CLINICAL USE

Atsushi NOHARA[1,2,3]*

[1] Department of Clinical Genetics, Ishikawa Prefectural Central Hospital, Japan
[2] Department of Laboratory Sciences, Kanazawa University Graduate School of Medical Sciences, Japan
[3] Japan Atherosclerosis Society Working Group on Statement for Appropriate Use of PCSK9 Inhibitors
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•PCSK9 gene was identified as the third gene of familial hypercholesterolemia (FH) in 2003. Gain-of-function (GOF) mutations in PCSK9 gene cause autosomal-dominant hypercholesterolemia, and we have reported PCSK9 GOF mutation account for 5% of FH heterozygotes in Japan. Simultaneously, loss-of-function (LOF) mutations in PCSK9 gene were found to be common in the Western countries, and the lower LDL-C levels of PCSK9 LOF carriers were protective against cardiovascular disease in many cohorts.

•PCSK9 has become a promising target of cardiovascular disease, and monoclonal PCSK9 antibodies, evolocumab and alirocumab, have proved their cardiovascular risk reduction in addition to maximum tolerated dose of statins. Now PCSK9 siRNA drug, inclisiran, has been in clinical trial stage.

•Cardiovascular disease has been a great burden in many countries. Even though statins have saved many lives, big residual risk still exists. PCSK9 inhibitors propose one answer for this. “Further big reduction in LDL-C.”

•PCSK9 antibodies reduce LDL-C levels further 60% over maximum tolerated lipid-lowering drugs, and show less serious adverse events probably than statins. However, expensive cost of these drugs requires us appropriate use from the viewpoint of medical economics.

•Japan Atherosclerosis Society (JAS) Working Group reported statement for appropriate use of PCSK9 inhibitors. One of the best indications should be secondary prevention of heterozygous FH patients with particularly high risk and difficulties to achieve LDL-C less than 70mg/dL with maximum tolerated statin with ezetimibe. In secondary prevention of non-FH, if LDL-C levels cannot be achieved less than 70mg/dL with maximum drugs, the patient may be a FH. Also, PCSK9 inhibitors are useful for high-risk patients with statin intolerance. If PCSK9 inhibitor shows poor efficacy, this strongly suggests a possibility of homozygous FH, because PCSK9 inhibitor with statins is the best clinical test of LDL-receptor function.

•PCSK9 inhibitors should be used among patients still in very high-risk with maximum lipid-lowering drugs. These patients will be benefitted greatly from their use.

Keywords
PCSK9 inhibitor, familial hypercholesterolemia, statin intolerance, acute coronary syndrome

Symposium 10

Shun Ishibashi

Organization

Jichi Medical University

Position & Title

Professor and Chair of Division of Endocrinology and Metabolism, Department of internal medicine

» Educational Background & Professional Experience

Year	Name of institution	Position
2001-	Jichi Medical University, Japan	Professor
1994-2001	The University of Tokyo, Japan	Assistant Professor
1989-1994	University of Texas Southwestern Medical Center at Dallas, USA	Assistant instructor
1984-1989	The University of Tokyo, Japan	Attending physician
1982-1984	The University of Tokyo and Tokyo Hitachi Hospital, Japan	Intern
1976-1982	The University of Tokyo, Japan	Undergraduate student

» Research Interests

Atherosclerosis, Lipoprotein metabolism, Diabetes, Obesity

» Honors & Awards s

· Young investigator award, Japan Society of Diabetic Complications

» Publications

1. Sakai K et al. Myeloid HMG-CoA reductase determines atherosclerosis by modulating migration of macrophages. Arterioscler Thromb Vasc Biol 2018;38:2590-2600
2. Ishibashi S et al. Effects of K-877, a novel selective PPARα modulator (SPPARMα), in dyslipidaemic patients: A randomized, double blind, active- and placebo-controlled, phase 2 trial. Atherosclerosis. 2016;249:36-43
3. Sekiya M et al. Ablation of neutral cholesterol ester hydrolase 1 accelerates atherosclerosis. Cell Metab 2009; 10:219-28
4. Okazaki H et al. Identification of a novel member of the carboxylesterase family that hydrolizes triacylglycerol: a potential role in adipocyte lipolysis. Diabetes 2006;55:2091-7
5. Osuga J et al. Targeted disruption of hormone-sensitive lipase results in male sterility and adipocyte hypertrophy, but not in obesity. Proc Natl Acad Sci USA 2000;97:787-92
6. Ishibashi S et al. Disruption of cholesterol 7alpha-hydroxylase gene in mice. I. Postnatal lethality reversed by bile acid and vitamin supplementation. J Biol Chem 1996;271:18017-23
7. Ishibashi S et al. Hypercholesterolemia in low density lipoprotein receptor knockout mice and its reversal by adenovirus-mediated gene delivery. J Clin Invest 1993;92:883-93

Abstract

FIBRATES

Shun ISHIBASHI

Division of Endocrinology and Metabolism, Department of Internal Medicine, Jichi Medical University, Japan
ishibash@jichi.ac.jp

Epidemiological and genetic studies have shown that hypertriglyceridemia is an independent risk factor of ischemic heart disease and ischemic stroke. Clinical trials have shown that gemfibrozil significantly reduced CV events (Helsinki Heart Study and VA-HIT). However, gemfibrozil is not widely used because of the concern of adverse interaction with statins. Although fenofibrate can be safely used in combination with statins, it did not significantly reduce CV events when used on top of simvastatin (ACCORD-LIPID). Subgroup analysis showed significant reduction of CV events in patients with dyslipidemia (high TG and low HDL-C). The limitation of these classical fibrates can be ascribed to their adverse effects on plasma levels of creatinine and homocysteine, which are considered to be atherogenic. Fenofibrate also frequently increases liver enzymes. To circumvent the limitations, a new type of fibrate, pemafibrate, was developed. Since pemafibrate potently and selectively activates PPARα, it belongs to a novel category named as selective PPARα modulator (SPPARMα). Drug-drug interactions with any statins were negligible. Since pemafibrate was primarily excreted into bile, theoretically it can be safely used in patients with impaired kidney function, which is contraindication for other fibrates. Pemafibrate 0.2mg BID was more efficacious than fenofibrate 100mg QD in patients with dyslipidemia with remarkably low incidence of adverse effects. The increasing effects on plasma levels of creatinine and homocysteine were negligible. Moreover, pemafibrate significantly decreased liver enzymes such as ALT, gGT and ALP. Pemafibrate significantly decreased HOMA-R, while fenofibrate did not. Since the increasing effects of pemafibrate on plasma FGF21 levels were more pronounced than those of fenofibrate, FGF21 might mediate a part of the favorable metabolic effects of pemafibrate. Similar efficacy and safety were demonstrated in dyslipidemic patients with type 2 diabetes mellitus as well as in those taking various types of statins. Currently, the multinational outcome trial (PROMINENT) is underway.

Keywords
Triglyceride, dyslipidemia, HDL, PPAR, fibrates, pemafibrate, diabetes

Symposium 10

Hyekyung Yang

Organization

Sungkyunkwan University School of Medicine, Kangbuk Samsung Hospital

Position & Title

Research Professor (Research Fellow)

» Educational Background & Professional Experience

Year	Name of institution	Position
2016-Present	Sungkyunkwan University School of Medicine, Korea	Research Professor (Research Fellow)
2014-2016	Sungkyunkwan University School of Medicine, Korea	Research Professor
2012-2014	National Institute on Aging / National Institutes of Health, MD, U.S.A.	Visiting Fellow
2009-2012	University of Maryland, MD, U.S.A.	Post-Doctoral Fellow
2008-2009	Seoul National University, Korea	Post-Doctoral Fellow
2003-2008	Seoul National University, Korea	Ph.D. (Pharmacy)
2001-2003	Seoul National University, Korea	M.S. (Pharmacy)
1996-2000	Ewha Womans University, Korea	B.S. (Pharmacy)

» Research Interests

Nonalcoholic fatty liver disease, insulin resistance, lipid metabolism, metabolomics

» Publications

1. **Yang H**, Suh DH, Kim DH, Jung ES, Liu KH, Lee CH, Park CY. Metabolomic and lipidomic analysis of the effect of pioglitazone on hepatic steatosis in a rat model of obese Type 2 diabetes. Br J Pharmacol. 2018 Sep;175(17):3610-3625.
2. Chang E, Kim DH, **Yang H**, Lee DH, Bae SH, Park CY. CB1 receptor blockade ameliorates hepatic fat infiltration and inflammation and increases Nrf2-AMPK pathway in a rat model of severely uncontrolled diabetes. PLoS One. 2018 Oct 26;13(10):e0206152.
3. Doyle ME, Fiori JL, Gonzalez Mariscal I, Liu QR, Goodstein E, **Yang H**, Shin YK, Santa-Cruz Calvo S, Indig FE, Egan JM. Insulin Is Transcribed and Translated in Mammalian Taste Bud Cells. Endocrinology. 2018 Sep 1;159(9):3331-3339.
4. **Yang H**, Park CY. Glucose-Lowering Agents in the Management of Nonalcoholic Fatty Liver Disease. J Korean Diabetes. 2018 Jun;19(2):88-96.
5. **Yang H**, Park CY. Implications for Farnesoid X Receptor Signaling on Bile Acid Metabolism as a Potential Therapeutic Strategy for Nonalcoholic Fatty Liver Disease. Korean J Obes 2016; 25(4): 167-175.
6. **Yang H**, Cong WN, Yoon JS, Egan JM. Vismodegib, an antagonist of hedgehog signaling, directly alters taste molecular signaling in taste buds. Cancer Med. 2015 Feb;4(2):245-52.

Abstract

USEFULNESS OF EZETIMIBE IN THE MANAGEMENT OF DYSLIPIDEMIA AND NAFLD

Hyekyung YANG

Medical Research Institute, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul 03181, Republic of Korea
hyekyung.yang102@gmail.com

Ezetimibe, a lipid-lowering drug, selectively binds to the cholesterol transporter, Niemann-Pick C1 like 1 (NPC1L1), which is present in the intestinal membranes and within the liver, thereby inhibiting intestinal cholesterol absorption and lowering blood and tissue cholesterol levels. Ezetimibe, as monotherapy decreases LDL-C by about 10–18%. When added to statin, ezetimibe results in greater reductions in LDL-C levels than with statin alone. Recently, the IMPROVE-IT trial demonstrated that ezetimibe reduces the rate of cardiovascular events in high-risk patients. In patients who cannot achieve LDL-C targets despite treatment with the maximal tolerated dose of a potent statin, ezetimibe is recommended to be added on to statin therapy. In addition to its hypolipidemic effect, it has been reported that ezetimibe is effective in attenuating the aminotransferases, hepatic steatosis and serum cholesterol level in patients with nonalcoholic fatty liver disease (NAFLD), which is defined by massive triglyceride accumulation in the liver, ranging from simple fatty liver (steatosis) to nonalcoholic steatohepatitis (NASH) and shares many risk factors with cardiovascular disease including obesity, type 2 diabetes mellitus, insulin resistance, inflammation and oxidative stress. Here we will briefly review the current evidence base for the use of ezetimibe as drug option for the management of the residual risk through further lipid modification. In addition, we will present our current efforts to investigate the molecular mechanism of ezetimibe for treatment of dyslipidemia and NAFLD.

Keywords
Ezetimibe, residual risk, low-density lipoprotein cholesterol, dyslipidemia, nonalcoholic fatty liver disease.

Symposium 10

Soo LIM

Organization

Seoul National University Bundang Hospital

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2007-	Seoul National University Bundang Hospital	Assistant/Associate/Full time Professor
2011-2012	Harvard Medical School, MGH	Research Fellow
2006	Seoul National University College of Medicine	PHD
2002	Seoul National University School of Public Health	MPH
1990-1996	Seoul National University College of Medicine	MD

» Research Interests

Diabetes, Obesity, Atherosclerosis

» Honors & Awards

- 2018 Official commendation from the Minister of Public Health and Welfare, Korea
- 2013 Namgok Scientific Research Award from the Korean Endocrine Society
- 2016 Hamchoon Scientific Research Award from the Seoul National University College of Medicine

» Publications

1. **Lim S**, Taskinen MR, Borén J. Crosstalk between nonalcoholic fatty liver disease and cardiometabolic syndrome. **Obes Rev. 2019 Apr;20(4):599-611.**
2. Lee DH, Chun EJ, Oh TJ, Kim KM, Moon JH, Choi SH, Park KS, Jang HC, **Lim S**. Effect of cilostazol on coronary artery stenosis and plaque characteristics in patients with type 2 diabetes. **Diabetes Obes Metab. 2019 21(6):1409-1418**
3. **Lim S**. Effects of sodium-glucose cotransporter inhibitors on cardiorenal and metabolic systems. **Diabetes Obes Metab. 2019 Apr;21 Suppl 2:5-8**
4. Ahn CH, **Lim S**. Effects of Thiazolidinedione and New Antidiabetic Agents on Stroke. **Journal of Stroke 2019 May;21(2):139-150.**
5. **Lim S**, Kim KM, Nauck MA. Glucagon-like Peptide-1 Receptor Agonists and Cardiovascular Events. **Trends Endocrinol Metab. 2018 Apr;29(4):238-248.**
6. **Lim S**, Eckel RH, Koh KK. Clinical implications of current cardiovascular outcome trials with sodium glucose cotransporter-2 (SGLT2) inhibitors. **Atherosclerosis. 2018 Mar 8;272:33-40.**

Abstract

ROLE OF OMEGA-3 FATTY ACID IN CARDIOMETABOLIC RISK REDUCTION

Soo LIM

Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, South Korea
limsoo@snu.ac.kr

Evidence has supported cardiovascular effects of n-3 polyunsaturated fatty acid (PUFA) consumption, focusing on potential molecular pathways and bioactive metabolites. n-3 PUFA consumption lowers plasma triglycerides, resting heart rate, and blood pressure and might also improve myocardial filling and efficiency, lower inflammation, and improve vascular function. Experimental studies demonstrate direct antiarrhythmic effects, which have been challenging to document in humans. Except coronary heart disease mortality and sudden cardiac death, effects on other cardiovascular outcomes are less-well-established. Current data provide strong concordant evidence that n-3 PUFA are bioactive compounds that reduce risk of cardiac death. Many international guidelines have recommended to consume at least 250 mg/day of long-chain n-3 PUFA or at least 2 servings/week of oily fish.

Icosapent ethyl is a highly purified eicosapentaenoic acid ethyl ester. Recently, a multicenter, randomized, double-blind, placebo-controlled trial involving patients with established cardiovascular disease or with diabetes and other risk factors was performed. They had been receiving statin therapy and who had a fasting triglyceride level of 135 to 499 mg/dL and an LDL-cholesterol level of 41 to 100 mg/dL. The patients were randomly assigned to receive 2 g of icosapent ethyl twice daily (total daily dose, 4 g) or placebo. The primary end point was a composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina. A total of 8179 patients were enrolled (70.7% for secondary prevention of cardiovascular events) and were followed for a median of 4.9 years. A primary end-point event occurred in 17.2% of the patients in the icosapent ethyl group, as compared with 22.0% of the patients in the placebo group (hazard ratio, 0.75; 95% CI, 0.68-0.83; P<0.001). Serious bleeding events occurred in 2.7% of the patients in the icosapent ethyl group and in 2.1% in the placebo group (P = 0.06). In conclusion, among patients with high triglyceride levels, the risk of ischemic events, including cardiovascular death, was significantly lower among those who received 2 g of icosapent ethyl twice daily than among those who received placebo. These data suggest positive role of omega-3 fatty acid in cardiometabolic risk reduction.

Keywords
omega-3 fatty acid, cardiovascular disease, triglyceride

ICoLA 2019 by KSoLA

Symposium 11

Chairpersons

Sin-Gon Kim | Korea University, Korea
Kausik Ray | Imperial College London, UK

Date & Time: September 6 (Fri.), 16:30-18:00
Place: Room 1 (3F)

Symposium 11

Chi Young Shim

Organization

Yonsei University College of Medicine

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2019-Present	Yonsei University College of Medicine	Professor
2014-2018	Yonsei University College of Medicine	Associate Professor
2012-2014	Oregon Health and Science University	Postdoctoral Fellow
2008-2013	Yonsei University College of Medicine	Assistant Professor

» Research Interests

1. Echocardiography and Cardiovascular Imaging
2. Heart Failure and Myocardial Function
3. Valvular Heart Disease

» Honors & Awards

- 2014 The American Society of Echocardiography, Arthur E. Weyman Young Investigator's Award Competition Winner
- 2012 Department of Internal Medicine, Yonsei University College of Medicine, The Best First Author's Award
- 2012 Department of Internal Medicine, Yonsei University College of Medicine, Woo-Hyun Research Award

» Publications

1. **Chi Young Shim***, Jong-Won Ha, Sungha Park, Eui-Young Choi, Donghoon Choi, Se-Joong Rim, Namsik Chung. Exaggerated blood pressure response to exercise is associated with augmented rise of angiotensin II during exercise. J Am Coll Cardiol. 2008; 52:287-292.
2. **Chi Young Shim***, Sungha Park, Donghoon Choi, Woo-In Yang, In-Jeong Cho, Eui-Young Choi, Namsik Chung, Jong-Won Ha. Sex differences in central hemodynamics and their relationship to left ventricular diastolic function. J Am Coll Cardiol 2011; 57:1226-1233.
3. **Chi Young Shim***, Ya Ni Liu, Tamara Atkinson, Aris Xie, Ted Foster, Brian P. Davidson, Mackenzie Treible, Yue Qi, Jose A. Lopez, Adam Munday, Zaverio Ruggeri, Jonathan R. Lindner. Molecular imaging of platelet-endothelial interactions and endothelial von willebrand factor in early and mid-stage atherosclerosis. Circulation Cardiovascular Imaging 2015; 8:e002765.
4. **Chi Young Shim***, Sajeevani Kim, Scott Chadderdon, Melinda Wu, Yue Qi, Aris Xie, Nabil Alkayed, Brian P. Davison, Jonathan R. Lindner. Epoxyeicosatrienoic acids mediate insulin-mediated augmentation in skeletal muscle perfusion and blood volume. Am J Physiol Endocrinol Metab. 2014; 302:E1097-104.
5. **Chi Young Shim***, Sung-Ai Kim, Donghoon Choi, Woo-In Yang, Jin-Mi Kim, Sun-Ha Moon, Hyun-Jin Lee, Sungha Park, Eui-Young Choi, Namsik Chung, Jong-Won Ha. Clinical outcomes of exercise-induced pulmonary hypertension in subjects with preserved left ventricular ejection fraction: implication of an increase in left ventricular filling pressure during exercise. Heart 2011; 97:1417-24
6. **Chi Young Shim***, Darae Kim, Sungha Park, Chan Joo Lee, Jong-Won Ha, Yang-Je Cho, Geu-Ru Hong. Effect of continuous positive airway pressure therapy on left ventricular diastolic function: a randomised, sham-controlled clinical trial. Eur Respir J. 2018; Jan 31; 51(2).

Abstract

DIABETES AND THE HEART

Chi Young Shim

Division of Cardiology, Severance Cardiovascular Hospital, Yonsei University College of Medicine, Korea
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Diabetes mellitus is an important risk factor of heart failure, not only for heart failure with reduced ejection fraction but also for heart failure with preserved ejection fraction. Recently, the association between diabetes mellitus and heart failure has been focused because of different cardiovascular effects of oral hypoglycemic agents. Diastolic dysfunction, microvascular disease, cardiac fibrosis are important features of diabetic cardiomyopathy. Beyond the structural and functional changes that characterize diabetic cardiomyopathy, a complex underlying, and interrelated pathophysiology exists. The aim of this lecture is to provide a contemporary view of the pathophysiology of heart failure in patients with diabetes mellitus. Moreover, we will discuss about risk stratification and early detection of vulnerable patients for heart failure.

Keywords
Diabetes mellitus; Heart failure; Diastolic dysfunction

Symposium 11

Vincent Woo
MD FRCP

Organization

University of Manitoba

Position & Title

Section of Endocrinology and Metabolism

Health Sciences Centre

Head – Diabetes Research Group

John Buhler Research Centre

» Educational Background & Professional Experience

Year	Name of institution	Position
Present	Endocrinology and Metabolism University of Manitoba	Associate Professor

» Honors & Awards

- Gerald S Wong Award – Canadian Diabetes Association
- Best Banting Award – Diabetes Canada

» Publications

1. Diabetes Canada Clinical Practice Guidelines
2. Canadian Hypertension Guidelines
3. Sustain - 6

Abstract

CARDIOVASCULAR EFFECTS OF GLP-1 AGONISTS

Vincent Woo MD FRCPC

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• The GLP-1 receptor agonists are antihyperglycemic agents that lower glucose levels as well as if not superior to most other antihyperglycemic agents including basal insulin. They are given subcutaneously (although oral GLP-1 agonists are being developed) and have low rates of hypoglycemia, are associated with significant weight loss and lower systolic blood pressure. In 2008 the Food and Drug Administration mandated that all new antihyperglycemic agents undergo cardiovascular safety studies and it is from these studies that many of the cardiovascular outcomes have been gleamed. These studies are powered for safety and not superiority and the populations studied are different and therefore head-to-head comparisons should not be made. If safety has been proven statistically in these cardiovascular safety outcome trials then superiority can be assessed.

Of the eight GLP-1 cardiovascular safety trials reported at least initially, all have been shown to demonstrate cardiovascular safety. However, a number of trials showed cardiovascular benefit. The LEADER study comparing liraglutide to placebo demonstrated a statistically significant reduction in 3-point MACE (Major Adverse Cardiac Events) which was the primary endpoint. Secondary analysis also demonstrated a reduction in CV death and all-cause mortality. SUSTAIN-6 which assessed semaglutide compared to placebo revealed a significant reduction in 3-point MACE. Albiglutide as well showed a significant reduction in 3-point MACE. Dulaglutide will report this year and an initial press release has stated there is a clinical benefit. Therefore now GLP-1 agonists should not only be thought of as antihyperglycemic agents but as medications that can prevent important cardiovascular events.

Keywords
GLP-1 agonist, cardiovascular, liraglutide, semaglutide, dulaglutide, albigltide, safety

Symposium 11

Subodh Verma

Organization

St. Michael's Hospital, University of Toronto

Position & Title

Cardiac Surgeon

Professor of Surgery

Professor of Pharmacology & Therapeutics

» Educational Background & Professional Experience

Year	Name of institution	Position
2014-	University of Toronto	Professor
2015-	St. Michael's Hospital	Chair, CardioLink Clinical Trials
2018-	University of Toronto	Tier 1 Canada Research Chair in Cardiovascular Surgery
2006-	St. Michael's Hospital	Cardiac Surgeon
2017-	University of Toronto	Member, Banting & Best Diabetes Centre
2007-2014	University of Toronto	Associate Professor

» Research Interests

Novel mediators of cardiovascular and cardiometabolic disease

» Honors & Awards

- Howard Morgan Award, International Academy of Cardiovascular Sciences
- Young Investigator Award, American College of Cardiology, United States
- Young Investigator Award, American College of Cardiology, United States

» Publications

1. Lancet. 2019 Jan 5;393(10166):31-39
2. Lancet. 2019 Jan 5;393(10166):3-5
3. Circulation. 2019 May 28;139(22):2516-2527
4. Circulation. 2019 May 28;139(22):2528-2536
5. Circulation. 2019 May 28;139(22):2537-2541
6. Cell Metab. 2018 Dec 4;28(6):813-815
7. Eur J Heart Fail. 2019 May;21(5):665-675

Abstract

CARDIOVASCULAR EFFECTS OF SGLT2 INHIBITORS

Subodh Verma

University of Toronto, Canada

Although sodium-glucose transport protein 2 inhibitors (SGLT2is) were originally developed to manage type 2 diabetes, the serendipitous discovery that the SGLT2is exert cardioprotective effects independent of their influence on glycemia status has led to the notion that SGLT2i should be re-classified as "cardiac drugs".

SGLT2i were consistently demonstrated in three cardiovascular outcome trials to lower the rates of hospitalizations for heart failure, reduce cardiovascular mortality and decrease the risk for major adverse cardiac events. The underlying mechanisms for these positive cardiovascular outcomes remain to be fully dissected although recently published data suggest that SGLT2i may reduce ventricular remodelling, alter cardiac autophagy and mitophagy, promote angiogenesis, elevate the population of regenerative cardiac stem cells and modulate cardiac energy metabolism.

Symposium 11

Seung-Hyun Ko

Organization

St. Vincent's Hospital, The Catholic University of Korea

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2015-	The Catholic University of Korea, Korea	Professor
2010-2015	The Catholic University of Korea, Korea	Associate Professor
2005-2010	The Catholic University of Korea, Korea	Assistant Professor
2008-2009	University of Virginia, USA	Visiting Professor

» Research Interests

Type 2 diabetes, Diabetic complication, Pancreatic beta-cell

» Publications

1. Han K, Ko SH et al. Development and validation of a risk prediction model for severe hypoglycemia in adult patients with type 2 diabetes: a nationwide population-based cohort study. Clin Epidemiol. 2018;10:1545-1559.
2. Yun JS, Ko SH et al. Progression of cardiovascular autonomic neuropathy and cardiovascular disease in type 2 diabetes. Cardiovasc Diabetol. 2018;17(1):109
3. Cha SA, Ko SH et al. Time- and frequency-domain measures of heart rate variability predict cardiovascular outcome in patients with type 2 diabetes. Diabetes Res Clin Pract. 2018;143:159-169
4. Ko SH et al. Severe hypoglycemia is a risk factor for atrial fibrillation in type 2 diabetes mellitus: Nationwide population-based cohort study. J Diabetes Complications. 2018;32(2):157-163
5. Cha SA, Ko SH et al. Baseline-Corrected QT (QTc) Interval Is Associated with Prolongation of QTc during Severe Hypoglycemia in Patients with Type 2 Diabetes Mellitus. Diabetes Metab J. 2016;40(6):463-472
6. Cha SA, Ko SH et al. Severe Hypoglycemia and Cardiovascular or All-Cause Mortality in Patients with Type 2 Diabetes. Diabetes Metab J. 2016;40(3):202-10
7. Yun JS, Ko SH et al. Cardiovascular autonomic dysfunction predicts severe hypoglycemia in patients with type 2 diabetes: a 10-year follow-up study. Diabetes Care. 2014;37(1):235-41

Abstract

HYPOGLYCEMIA AND CARDIOVASCULAR DISEASE IN TYPE 2 DIABETES

Seung-Hyun Ko

Department of Internal Medicine, St. Vincent's Hospital, The Catholic University of Korea, Korea
kosh@catholic.ac.kr

Severe hypoglycemia (SH), which is defined as a hypoglycemic episode requiring assistance to treat, is associated with a wide range of adverse outcomes in patients with diabetes. SH can be fatal; many previous studies have demonstrated that SH was associated with increased mortality in patients with type 1 and type 2 diabetes. SH usually occurs in advanced type 2 diabetes, and patients who experienced SH tend to have a higher cardiovascular risk. Therefore, it is considered that the association of SH with cardiovascular disease (CVD) would be related to reverse causation by the confounding factors rather than direct causality. It is difficult to clearly distinguish whether there is direct causality between SH and CVD. Our study demonstrated the relationship between prior SH and increased risk of CVD and CVD-related mortality, which exhibited a dose-response relationship, wherein subjects who experienced more SH events had a higher risk of mortality and CVD than those who experienced one SH event or those without an SH event using National Health Insurance Service Database in Korea. This study highlights the prognostic importance of prior history of SH on CV events and mortality. SH was strongly and positively associated with and exhibited a dose-dependent and temporal relationship with subsequent macrovascular morbidity and all-cause mortality. In patients who experienced SH, preventing the risk of CVD and mortality should be carefully considered in patients who are at a greater risk of hypoglycemia. In addition, the study illustrates the need for careful management and frequent monitoring of all individuals with type 2 diabetes to minimize the risk of hypoglycemia. Intensive, individualized diabetic education should be performed in these high risk patients for SH.

Keywords
Hypoglycemia, Severe hypoglycemia, Type 2 diabetes, cardiovascular disease

ICoLA 2019 by KSoLA

Symposium 12

Chairpersons

Wook Bum Pyun | Ewha Womans University, Korea
Anselm K. Gitt | Klinikum Ludwigshafen, Germany

Date & Time: September 6 (Fri.), 16:30-18:00
Place: Room 2 (3F)

Symposium 12

Jinho SHIN

Organization

Hanyang University College of Medicine

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2013-	Department of Internal Medicine, Hanyang University College of Medicine	Professor
2006-2013	Division of Cardiology, Department of Internal Medicine, Hanyang University College of Medicine	Associate Professor
2003-2006	Division of Cardiology, Department of Internal Medicine, Hanyang University College of Medicine	Assistant Professor
2002-2003	Weil Cornell Medical College, New York, USA	Clinical Fellow
2000-2002	Eulji Medical School, Daejon, Korea	Fulltime instructor

Abstract

TARGET BLOOD PRESSURES IN RECENT HYPERTENSION GUIDELINES, UPDATED REASONS AND CLINICAL IMPLICATIONS

Jinho Shin

Division of Cardiology, Department of Internal Medicine, Hanyang University Seoul Hospital, Seoul, Korea
jhs2003@hanyang.ac.kr

In recent hypertension guidelines published after SPRINT (Systolic Blood Pressure Intervention Trial), target blood pressure was lowered around or below 130/80 mmHg. Because there are many controversies related to the target blood pressure level in SPRINT, clinical implications of new target blood pressure needs to be clarified in terms of patient safety and potential clinical benefit.

There are two clinical pathways for patients taking antihypertensive medication. In addition to non-complicated patient who start antihypertensive medication when BP is 140/90 mmHg or higher, all other hypertensive patients combined or complicated clinical CVD or renal disease should be started with ACE inhibitor, beta blocker, calcium channel blocker, and/or diuretics. Some patients need maximal tolerable dose of specific drug if BP, heart rate and side effects are acceptable. In this case, the target BP indicates the maximal BP allowed during the titration of those drugs.

Most guidelines are based on or influenced by the randomized clinical trials or meta-analyses. In some meta-analyses, the study including patients with complications already taking antihypertensive medication was included for analyses, and the others are not. Another issue regarding the meta analyses of hypertension treatment is how to interpret the influence of SPRINT. Because the corresponding clinic BP level to 120 mmHg by automated out-of-office BP (AOBP) is speculated to be, at least, above 130 mmHg, it seems to be safe not to include SPRINT as it is.

When further lowering target BP, as shown in SPRINT and Action to Control Cardiovascular Risk in Diabetes (ACCORD) trail, harmful side effects should be considered. In the recent meta-analyses excluding the study for complicated patient but including SPRINT and ACCORD trial, relative risk reduction by BP lowering below therapy below 130 mmHg could be statistically significant only when SRINT was included. At the same time, absolute risk reduction per standardized BP reduction of 10/5 mmHg in systolic/diastolic BPs, decreased down to a half according to the level of initial BP levels when it was 150 mmHg versus 130 mmHg.

In conclusion, in achieving target blood pressure below < 130/80 mmHg, clinician should be more careful not to do harm patient than the target blood pressures in the previous guidelines.

Keywords
Guidelines, Target blood pressure, Hypertension, Stroke, Myocardial infarction, Metaanalysis

Symposium 12

Hideki ISHII

Organization

Department of Cardiology, Nagoya University

Position & Title

Associated Professor

M.D., PhD, FAHA, FESC, FJCS, FJCC

» Educational Background & Professional Experience

Year	Name of institution	Position
1995.4-1996.3	Yokkaichi Municipal Hospital, Japan	Intern
1996.4-2004.3	Yokkaichi Municipal Hospital, Japan	Resident
2004.4-2007.3	Nagoya University Graduate School of Medicine	MD
2007.4-	Nagoya University Graduate School of Medicine	Associated Professor

» Research Interests

Interventional cardiology, Reperfusion injury: Myocardial ischemia reperfusion, Coronary artery disease in chronic kidney disease

» Honors & Awards

- 2006 Japanese Society of Interventional Cardiology, Intervention Research Award
- 2011 Top scoring abstracts by council (Peripheral Vascular Disease), American Heart Association Scientific Sessions
- 2008, 2011, 2012, 2015-2018 The Best Reviewers of the Circulation Journal

» Publications

1. Numasawa Y, Inohara T, Ishii H, Yamaji K, Kohsaka S, Sawano M, Kodaira M, Uemura S, Kadota K, Amano T, Nakamura M. Comparison of outcomes after percutaneous coronary intervention in elderly patients including 10,628 nonagenarians: insights from a Japanese nationwide registry (J-PCI Registry). J Am Heart Assoc. 2019 Mar 5;8(5):e011183. doi: 10.1161/JAHA.118.011017.
2. Negishi Y, Tanaka A, Ishii H, Takagi K, Inoue Y, Uemura Y, Umemoto N, Yoshioka N, Morishima I, Asano H, Watarai M, Shibata N, Suzuki S, Murohara T. Contrast-induced nephropathy and long-term clinical outcomes following percutaneous coronary intervention in patients with advanced renal dysfunction (estimated glomerular filtration rate < 30 mL/min/1.73 m2) Am J Cardiol. 2019 Feb 1;123(3):361-367.
3. Kitagawa K, Amano T, Uetani T, Ishii H, Okumura T, Suzuki S, Takashima H, Kurita A, Ando H, Matsubara T, Murohara T. Association between plaque characteristics and the amount of debris captured by a filter-type distal protection device in patients with acute coronary syndrome. Atherosclerosis. 2017;258:72-78.
4. Ishii H, Kobayashi M, Kurebayashi N, Yoshikawa D, Suzuki S, Ichimiya S, Kanashiro M, Sone T, Tsuboi H, Amano T, Uetani T, Harada K, Marui N, Murohara T. Impact of Angiotensin II Receptor Blocker Therapy (Olmesartan or Valsartan) on Coronary Atherosclerotic Plaque Volume Measured by Intravascular Ultrasound in Patients with Stable Angina Pectoris Am J Cardiol 2013;112:363-368.
5. Miyagi M, Ishii H, Murakami R, Isobe S, Hayashi M, Amano T, Arai K, Yoshikawa D, Ohashi T, Uetani T, Yasuda Y, Matsuo S, Matsubara T, Murohara T. Impact of renal function on coronary plaque composition. Nephrol Dialysis Transplantation 2010;25:175-181.
6. Ishii H, Amano T, Matsubara T, Murohara T. Pharmacological intervention for prevention of left ventricular remodeling and improving prognosis in myocardial infarction. Circulation 2008:118:2710-2718.
7. Ishii H, Ichimiya S, Kanashiro M, Amano T, Imai K, Murohara T, Matsubara T. Impact of a Single Intravenous Administration of Nicorandil Before Reperfusion in Patients With ST-Segment-Elevation Myocardial Infarction. Circulation. 2005; 112: 1284-1288.

Abstract

EFFECTS OF PHARMACOLOGICAL THERAPIES ON REGRESSION OF CORONARY PLAQUE IN PATIENTS WITH ISCHEMIC HEART DISEASE

Hideki ISHII[1]*, Akihito TANAKA[1], and Toyoaki MUROHARA[1]

[1] Department of Cardiology, Nagoya University, Japan
hkishii@med.nagoya-u.ac.jp

Progression of coronary plaque volume is associated with higher incidence of cardiac adverse events. In contrast, it is considered that coronary plaque volume regression reduces incidence of adverse events.

New modalities can clearly show not only coronary plaque volume but coronary plaque components. Recent intravascular ultrasound (IVUS) systems such as vertical histology (VH)-IVUS, integrated backscatter (IB)-IVUS and near infrared spectroscopy (NIRS)-IVUS can be also a sensitive tool to detect coronary vulnerable plaques. Prior studies using those imaging have suggested that there is a close relationship among lifestyle diseases including diabetes, dyslipidemia, hypertension and chronic kidney disease and coronary plaque volume. Moreover, lipid rich and vulnerable coronary plaques are more frequently seen in patients with lifestyle diseases. The finding might explain why such subjects have an increasing risk of cardiovascular disease.

It is well known that lipid-lowering therapy, anti-hypertensive therapy, and some specified antidiabetic therapies improve the clinical outcome in patients with coronary artery disease. Some mechanisms can be explained for the phenomena. One possible mechanism may be that coronary plaques can be reduced in volume and be stabilized by such therapies. Stabilizing coronary plaque may inhibit onset of acute coronary syndrome. In many studies, treatments with statins have been associated with reduction in both coronary total plaque volume and lipid volume. In addition, some antihypertensive medications such as RAS inhibitors significantly reduce coronary plaque volume.

In my presentation, I'd like to show our IB-IVUS data on relationships between coronary plaque composition and lifestyle diseases. Also, effects of pharmacological therapy on reducing and stabilizing coronary plaque will be discussed.

Keywords
coronary plaque, vulnerable plaque, lifestyle diseases, pharmacology, intravascular ultrasound

Symposium 12

Hye Jin Yoo

Organization

Korea University Guro Hospital

Position & Title

Associate Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2016-2017	University of California, San Diego Endocrinology Department	Visiting Scholar
2015-	Korea University Guro Hospital Endocrinology Department	Associate Professor
2010-2014	Korea University Guro Hospital Endocrinology Department	Assistant Professor
2008-2009	Korea University Guro Hospital Endocrinology Department	Clinical Instructor
2005-2008	The Korea University, Medical Science/Internal Medicine	The degree of Doctor
2003-2005	The Korea University, Medical Science/Internal Medicine	The degree of Master
1995-2001	The Korea University, Medical science	The degree of Bachelor

» Research Interests

Obesity and atherosclerosis

» Honors & Awards

- 2014 Seoul International Congress of Endocrinology and Metabolism; Superior Presentation Winner
- 2014 International Conference on Diabetes and Metabolism; Superior Presentation Winner
- 2016 The Best Young Researcher in Medical Field Awarded by the Joongang-Newspaper

» Publications

1. Proportion and Characteristics of the Subjects with Low Muscle Mass and Abdominal Obesity among the Newly Diagnosed and Drug-Naïve Type 2 Diabetes Mellitus Patients Kim JA, Hwang SY, Chung HS, Kim NH, Seo JA, Kim SG, Kim NH, Choi KM, Baik SH, **Yoo HJ**. Diabetes Metab J. 2019 Feb;43(1):105-113
2. Protectin DX prevents H2O2-mediated oxidative stress in vascular endothelial cells via an AMPK-dependent mechanism. Hwang HJ, Jung TW, Kim JW, Kim JA, Lee YB, Hong SH, Roh E, Choi KM, Baik SH, **Yoo HJ**. Cell Signal. 2019 Jan;53:14-21
3. Knockdown of Sestrin2 Increases Lipopolysaccharide-Induced Oxidative Stress, Apoptosis, and Fibrotic Reactions in H9c2 Cells and Heart Tissues of Mice via an AMPK-Dependent Mechanism Hwang HJ, Kim JW, Chung HS, Seo JA, Kim SG, Kim NH, Choi KM, Baik SH, **Yoo HJ**. Mediators Inflamm. 2018 Jul 5;2018:6209140.
4. Association of serum Sestrin2 level with metabolic risk factors in newly diagnosed drug-naïve type 2 diabetes Chung HS, Hwang HJ, Hwang SY, Kim NH, Seo JA, Kim SG, Kim NH, Baik SH, Choi KM, **Yoo HJ** Diabetes Res Clin Pract. 2018 Oct;144:34-41.
5. Differential relationship between waist circumference and mortality according to age, sex, and body mass index in Korean with age of 30-90 years; a nationwide health insurance database study Cho GJ, **Yoo HJ (co-1st author)** Hwang SY, Choi J, Lee KM, Choi KM, Baik SH, Han SW, Kim T. BMC Med. 2018 Aug 10;16(1):131.
6. Association of leukocyte cell-derived chemotaxin 2 (LECT2) with NAFLD, metabolic syndrome, and atherosclerosis. **Yoo HJ**, Hwang SY, Choi JH, Lee HJ, Chung HS, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM. PLoS One. 2017 Apr 4;12(4):e0174717.
7. Knockdown of sestrin2 increases pro-inflammatory reactions and ER stress in the endothelium via an AMPK dependent mechanism. Hwang HJ, Jung TW, Choi JH, Lee HJ, Chung HS, Seo JA, Kim SG, Kim NH, Choi KM, Choi DS, Baik SH, **Yoo HJ**. Biochim Biophys Acta. 2017 Jun;1863(6):1436-1444.

Abstract

MANAGEMENT OF BLOOD PRESSURE AND HYPERLIPIDEMIA IN PATIENTS WITH ATHEROSCLEROSIS

Hye Jin Yoo

Division of Endocrinology and Metabolism, Department of Internal Medicine, Korea University College of Medicine, Seoul, Republic of Korea
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Atherosclerosis is a very long lasting and preceding condition before ischemic cardiovascular diseases. Because hypertension and hyperglycemia, family history, obesity, and smoking are important risk factors for the progression of arteriosclerosis, it is well known that controlling these risk factors will help prevent cardiovascular diseases. As most representative methods that can be used for early screening of arteriosclerosis progression, there are carotid intima media thickness, measurement of coronary calcium score through non-enhance computed tomography, and measurement of ankle brachial index. These tests are used to stratify the risk of cardiovascular disease, and in accordance to determine the control goals and timing of medications of hyperlipidemia and hypertension management which are major risk factors affecting the progression of arteriosclerosis. Today, I will summarize about the criteria for the management of hypertension and dyslipidemia are in patients with arteriosclerosis identified by several other means of testing, which are based on the recent updated guidelines.

Keywords
Atherosclerosis, Hypertension, Dyslipidemia

Symposium 12

Manlio Vinciguerra

Organization

International Clinical Research Center (FNUSA-ICRC), Brno, Czech Republic

Position & Title

Principal Investigator

» Educational Background & Professional Experience

Year	Name of institution	Position
2016-	International Clinical Research Center (FNUSA-ICRC), Brno, Czech Republic	Principal Investigator
2012-2016	Division of Medicine, University College London (UCL), London, United Kingdom	Principal Research Associate (Senior Lecturer)
2008-2011	European Molecular Biology Laboratory (EMBL), Heidelberg, Germany	Post-doctoral fellow
2005-2008	Faculty of Medicine, University of Geneva, Geneva, Switzerland	Post-doctoral fellow
2000-2004	Faculty of Medicine, University of Geneva, Geneva, Switzerland	Ph.D.
1994-1999	Bachelor in Science, University of Catania, Catania, Italy	B.Sc.

» Research Interests

Cardiovascular epidemiology, epigenetics, metabolic health

» Honors & Awards

- 2016-2022 European Regional Development Fund (ERFD) – PI project MAGNET (€6.5M)
- 2012-2015 AIRC Young Investigator Award (Italy) (€240K)
- 2008-2011 EMBL Interdisciplinary POst-Doctoral (EIPOD) fellowship

» Publications

1. Association between eating time interval and frequency with ideal cardiovascular health: Results from a random sample Czech urban population. Maugeri A, Kunzova S, Medina-Inojosa JR, Agodi A, Barchitta M, Homolka M, Kiacova N, Bauerova H, Sochor O, Lopez-Jimenez F, **Vinciguerra M**. **Nutr Metab Cardiovasc Dis**. 2018 Apr 18. pii: S0939-4753(18)30123-6.
2. Kardiovize Brno 2030, a prospective cardiovascular health study in Central Europe: Methods, baseline findings and future directions. Movsisyan NK, **Vinciguerra M**, Lopez-Jimenez F, Kunzová Š, Homolka M, Jaresova J, Cífková R, Sochor O. **Eur J Prev Cardiol**. 2018 Jan;25(1):54-64.
3. Fasting regulates EGR1 and protects from glucose- and dexamethasone-dependent sensitization to chemotherapy. Di Biase S, Shim HS, Kim KH, **Vinciguerra M**, Rappa F, Wei M, Brandhorst S, Cappello F, Mirzaei H, Lee C, Longo VD. **PLoS Biol**. 2017 Mar 30;15(3):e2001951
4. A Periodic Diet that Mimics Fasting Promotes Multi-System Regeneration, Enhanced Cognitive Performance, and Healthspan. Brandhorst S, Choi IY, Wei M, Cheng CW, Sedrakyan S, Navarrete G, Dubeau L, Yap LP, Park R, **Vinciguerra M**, Di Biase S, Mirzaei H, Mirisola MG, Childress P, Ji L, Groshen S, Penna F, Odetti P, Perin L, Conti PS, Ikeno Y, Kennedy BK, Cohen P, Morgan TE, Dorff TB, Longo VD. **Cell Metab**. 2015 Jul 7;22(1):86-99.
5. Fibroblast growth factor 21 protects against cardiac hypertrophy in mice. Planavila A, Redondo I, Hondares E, **Vinciguerra M**, Munts C, Iglesias R, Gabrielli LA, Sitges M, Giralt M, van Bilsen M, Villarroya F. **Nat Commun**. 2013;4:2019.
6. mIGF-1/JNK1/SirT1 signaling confers protection against oxidative stress in the heart. **Vinciguerra M**, Santini MP, Martinez C, Pazienza V, Claycomb WC, Giuliani A, Rosenthal N. **Aging Cell**. 2012 Feb;11(1):139-49
7. MicroRNA-29 in aortic dilation: implications for aneurysm formation. Boon RA, Seeger T, Heydt S, Fischer A, Hergenreider E, Horrevoets AJ, **Vinciguerra M**, Rosenthal N, Sciacca S, Pilato M, van Heijningen P, Essers J, Brandes RP, Zeiher AM, Dimmeler S. **Circ Res**. 2011 Oct 28;109(10):1115-9.

Abstract

ANTI-HYPERTENSIVE EFFECTS OF FMD (FASTING MIMICKING DIET) AND CARDIOVASCULAR DISEASE

Manlio VINCIGUERRA[1]*, Valter D. LONGO[2,3]

[1] International Clinical Research Center (FNUSA-ICRC), Brno, Czech Republic
[2] Longevity Institute, Davis School of Gerontology, University of Southern California, Los Angeles, CA, US
[3] Institute of Molecular Oncology, Italian Foundation for Cancer Research, Milan, Italy
manlio.vinciguerra@fnusa.cz

Cardiovascular disease (CVD) is the leading cause of death in many developed countries and remains one of the major diseases strongly affected by the diet. Nutrition can affect CVD directly by contributing to the accumulation of vascular plaques and also indirectly by regulating the rate of aging. In this talk I will summarize research on nutrition and CVD incidence based on a multipillar system that includes basic research focused on aging, epidemiological studies, clinical studies, and studies of centenarians. The relevant research linking nutrition and CVD with focus on macronutrients and aging will be highlighted. I will review some of the most relevant studies on nutrition and CVD treatment, also focusing on interventions known to delay aging. I will discuss both everyday dietary compositions, as well as intermittent and periodic fasting interventions with the potential to prevent and treat CVD. Caveats to almost all of these diets are the required lifestyle changes and need for the continuous implementation into daily routines. One way to address some of these concerns is the development of a periodic dietary intervention that can be integrated into daily routines. The fasting-mimicking diet (FMD) is a periodic, short-term, low-calorie, and low-protein dietary intervention designed to promote benefits while reducing side effects and the burden of chronic dieting. I will finally present the results of our randomized crossover clinical trial that included 100 generally healthy participants, consuming the FMD for 5 days per month during 3 consecutive months, displaying – among other beneficial effects - a significant reduction in blood pressure.

Keywords
Cardiovascular diseases, aging, nutrition, fasting mimicking diet, blood pressure, epidemiology, animal studies

ICoLA 2019 by KSoLA

Symposium 13

Chairpersons

In-Kyu Lee | Kyungpook National University, Korea
Terje S. Larsen | The Arctic University of Norway, Norway

Date & Time: September 6 (Fri.), 16:30-18:00
Place: Room 3 (3F)

Symposium 13

Veronique ANGELI

Organization

National University of Singapore

Position & Title

Associate Professor, leader of Immunology Programme

» Educational Background & Professional Experience

Year	Name of institution	Position
2014-Present	National University of Singapore, Singapore	Associate Professor
2006-2014	National University of Singapore, Singapore	Assistant Professor
2005-2006	Mount Sinai School of Medicine, NYC, USA	Instructor
2002-2005	Mount Sinai School of Medicine, NYC, USA	Post-doctoral fellow

» Research Interests

Macrophage and lymphatic biology and function & cardiovascular disease

» Honors & Awards

- 2015 National University Health System-Mochtar Riady Pinnacle Young Achiever Award, Singapore
- 2011 Faculty Young Researcher Award National University Health System, Singapore

» Publications

1. Tay MHD, Lim SYJ, Leong YFI, Thiam CH, Tan KW, Torta FT, Narayanaswamy P, Wenk M, **Angeli V**. Halted Lymphocyte Egress via Efferent Lymph Contributes to Lymph Node Hypertrophy During Hypercholesterolemia. Front Immunol. 2019 Mar 27;10:575. doi: 10.3389/fimmu.2019.00575. eCollection 2019.
2. Chakarov S, Lim HY, Tan L, Lim SY, See P, Lum J, Zhang XM, Foo S, Nakamizo S, Duan K, Kong WT, Gentek R, Balachander A, Carbajo D, Bleriot C, Malleret B, Tam JKC, Baig S, Shabeer M, Toh SES, Schlitzer A, Larbi A, Marichal T, Malissen B, Chen J, Poidinger M, Kabashima K, Bajenoff M, Ng LG, **Angeli V**, Ginhoux F. Two distinct interstitial macrophage populations coexist across tissues in specific subtissular niches. Science. 2019 Mar 15;363(6432). pii: eaau0964. doi: 10.1126/science.aau0964.
3. Lim HY, Lim SY, Tan CK, Thiam CH, Goh CC, Carbajo D, Chew SHS, See P, Chakarov S, Wang XN, Lim LH, Johnson LA, Lum J, Fong CY, Bongso A, Biswas A, Goh C, Evrard M, Yeo KP, Basu R, Wang JK, Tan Y, Jain R, Tikoo S, Choong C, Weninger W, Poidinger M, Stanley ER, Collin M, Tan NS, Ng LG, Jackson DG, Ginhoux F, **Angeli V**. Hyaluronan Receptor LYVE-1-Expressing Macrophages Maintain Arterial Tone through Hyaluronan-Mediated Regulation of Smooth Muscle Cell Collagen. Immunity. 2018 Aug 21;49(2):326-341.e7. doi: 10.1016/j.immuni.2018.06.008. Epub 2018 Jul 24.
4. Lim HY, Thiam CH, Yeo KP, Bisoendial R, Hii CS, McGrath KC, Tan KW, Heather A, Alexander JS, **Angeli V** Lymphatic vessels are essential for the removal of cholesterol from peripheral tissues by SR-BI-mediated transport of HDL. Cell Metab. 2013 May 7;17(5):671-84. doi: 10.1016/j.cmet.2013.04.002.
5. Tan KW, Chong SZ, Wong FH, Evrard M, Tan SM, Keeble J, Kemeny DM, Ng LG, Abastado JP, **Angeli V**. Neutrophils contribute to inflammatory lymphangiogenesis by increasing VEGF-A bioavailability and secreting VEGF-D. Blood. 2013 Nov 21;122(22):3666-77. doi: 10.1182/blood-2012-11-466532.
6. Tan KW, Yeo KP, Wong FH, Lim HY, Khoo KL, Abastado JP, **Angeli V**. Expansion of cortical and medullary sinuses restrains lymph node hypertrophy during prolonged inflammation. J Immunol. 2012 Apr 15;188(8):4065-80. doi: 10.4049/jimmunol.
7. Lim HY, Rutkowski JM, Helft J, Reddy ST, Swartz MA, Randolph GJ, **Angeli V**. Hypercholesterolemic mice exhibit lymphatic vessel dysfunction and degeneration. Am J Pathol. 2009 Sep;175(3):1328-37. doi: 10.2353/ajpath.2009.080963. Epub 2009 Aug 13.

Abstract

THE ROLE OF LYVE-1+ MACROPHAGES IN ATHEROSCLEROSIS

Veronique ANGELI[1]*, Hwee Ying LIM[1], Sheau-Yng LIM[1], Gregory JONES[2], Lai-Guan NG[3] and Florent GINHOUX[3]

[1] Department of Microbiology & Immunology, National University of Singapore, Singapore
[2] Department of Surgical Sciences, University of Otago, New-Zealand
[3] Singapore Immunology Network, A*STAR, Singapore
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Tissue resident macrophages can exert beyond their established immune functions additional activities to support tissue homeostasis and function. Although tissue resident macrophages were identified in healthy arteries whether they have a homeostatic function in this tissue remains an open question. Recently, we unveiled a hitherto unknown homeostatic contribution of arterial LYVE-1 expressing macrophages through the control of collagen production by smooth muscle cells utilizing a mouse model lacking specifically LYVE-1$^+$ macrophages. In my talk, I would share new findings supporting the contribution of these resident arterial macrophages in the arteria remodelling associated with human and experimental atherosclerosis.

Keywords
Macrophage, atherosclerosis, extracellular matrix

Symposium 13

Ekaterina Koltsova

Organization

Fox Chase Cancer Center

Position & Title

Associate Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2019-	Fox Chase Cancer Center, Philadelphia, PA	Associate Professor
2016-2019	Fox Chase Cancer Center, Philadelphia, PA	Assistant Professor
2014-2016	Fox Chase Cancer Center, Philadelphia, PA	Assistant Research Professor
2012-2014	La Jolla Institute for Allergy and Immunology, San Diego, CA	Instructor
2009-2012	La Jolla Institute for Allergy and Immunology, San Diego, CA	Postdoctoral Fellow
2007	Fox Chase Cancer Center/Institute of peoples friendship, Russia	PhD

» Research Interests

Immunology, cardiovascular diseases, microbiota, metabolism, liver cancer

» Honors & Awards

- 2012 AAI Young Investigator Award, La Jolla Immunology Conference
- 2013 Irvine H. Page Young Investigator Research Award Finalist
- 2013 Arteriosclerosis Thrombosis and Vascular Biology Conference

» Publications

1. Fatkhullina AR, Peshkova I.O, Dzutsev A, Aghayev T, McCulloch J.A., Thovarai V., Badger J.H., Vats R., Sundd P., Tang H-Y, Kossenkov A.V., Hazen SL, Trinchieri, G, Grivennikov SI, Koltsova EK. An interleukin-23- interleukin-22 axis regulates intestinal microbial homeostasis to protect from diet-induced atherosclerosis. *Immunity. 49, 1-15.*
2. Peshkova I.O., Fatkhullina A.R, Mikulski Z, Ley K and Koltsova EK. IL-27R signaling controls myeloid cells accumulation and antigen-presentation in atherosclerosis. *Scientific Reports.* 2017 May 23;7(1):2255
3. Koltsova E.K., Sundd P, Zarpellon A., Ouyang H., Mikulski Z., Zampolli A, Ruggeri Z, Ley K. Genetic deletion of platelet Glycoprotein Ib alpha but not its extracellular domain protects from atherosclerosis. *Thrombosis Hemostasis*. 2014 Dec;112(6):1252-63.
4. Koltsova E.K., Garcia Z., Chodaczek G., Landau M., McArdle S., Scott S.R., von Vietinghoff S., Galkina E., Miller Y.I., Acton S.T., Ley K. Dynamic T cell-APC interactions sustain chronic inflammation in atherosclerosis. *J. Clin. Invest*. 2012; 122:3114-26.
5. Koltsova E.K., Kim G., Lloyd K.M., Saris C.J.M, von Vietinghoff, S, Kronenberg M., Ley K. IL-27 receptor limits atherosclerosis in $Ldlr^{-/-}$ mice. *Circ. Res*. 2012; 111:1274-85.
6. Sundd P., Gutierrez E., Koltsova E.K., Kuwano Y., Fukuda S., Pospieszalska M.K., Groisman A., Ley K. 'Slings' enable neutrophil rolling at high shear. *Nature* 2012; 488:399-403.

Abstract

CYTOKINE MEDIATED CONTROL OF MICROBIOTA AND INFLAMMATION IN ATHEROSCLEROSIS

Ekaterina K. Koltsova*[1], Iuliia Peshkova[1], Amiran Dzutsev[2], Turan Aghayaev[1], Giorgio Trinchieri[2] and Aliia Fatkhullina[1]

[1] Blood Cell Development and Function Program, Fox Chase Cancer Center, Philadelphia, PA, USA
[2] Cancer and Inflammation Program, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA
Ekaterina.Koltsova@fccc.edu

Atherosclerosis is lipid-driven, chronic inflammatory disease of the arterial wall. While commensal microbiota is involved in the distal regulation of systemic immune responses, how this distant connection influences the development of atherosclerosis and what are the underlying mechanisms remains largely unknown. In a mouse model of atherosclerosis, we found that disease was augmented when expression of the otherwise inflammatory cytokine IL23 was ablated. IL23 and its immediate downstream target IL22 restrict atherosclerosis by preventing outgrowth of microbiota, as inactivation of IL23/IL22 signaling led to dysbiosis and expansion of bacteria with pro-atherogenic properties, due to defective production of antimicrobial peptides in the intestine. These pro-atherogenic bacteria contributed to elevated serum levels of several pro-atherogenic metabolites, which in turn induced osteopontin (OPN) expression by subsets of myeloid cells including aortic macrophages. Microbiota transfer from IL23 deficient mice accelerated atherosclerosis, while microbial depletion or IL22 administration reduced aortic osteopontin expression and ameliorated the disease. Overall, our work uncovers the innate inflammatory IL23-IL22 cytokine signaling axis as a key regulator of atherosclerosis that controls diet-induced expansion of pro-atherogenic microbiota, and argues for informed usage of cytokine blockers with regard to cardiovascular side effects driven by microbiota and inflammation.

Keywords
Atherosclerosis, cytokines, inflammation, microbiota, myeloid cells

Symposium 13

Gary Sweeney

Organization

York University

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2001-Present	York university, canada	Professor
1996-2001	The Hospital for Sick Children, Toronto	Fellow

» Research Interests

Diabetes, obesity, cardiovascular disease

» Honors & Awards

- Tier 1 Research Chair in Mechanisms of Cardiometabolic Diseases, York University
- Heart & Stroke Foundation of Canada Career Investigator Award
- Canadian Diabetes Association Scholar

» Publications

1. Jahng JWS, Alsaadi RM, Rengasamy P, Song E, Hipolito VEB, Sung HK, Botelho RJ, Russell, RC & Sweeney G. Iron overload inhibits late stage autophagy flux leading to insulin resistance. EMBO Reports (2019 in press)
2. Sung HK, Song E, Jahng JWS, Pantopoulos, K. & Sweeney G. Iron induces insulin resistance in cardiomyocytes via regulation of oxidative stress. Scientific Reports (2019) 15;9(1):4668.
3. Yoon, N, Dadson, K. Sung, KH. Chu, T. Grant, J. McKee, T. Peterson, J, Kelly, SP. & Sweeney G. Tracking adiponectin biodistribution via fluorescence molecular tomography indicates increased vascular permeability after streptozotocin-induced diabetes. ***American Journal of Physiology (2019 in press)***
4. Song E, Ramos SV, Huang X, Liu Y, Botta A, Sung HK, Turnbull PC, Wheeler MB, Berger T, Wilson DJ, Perry CGR, Mak TW, Sweeney G.Holo-lipocalin 2-derived siderophores increase mitochondrial ROS and impair oxidative phosphorylation in rat cardiomyocytes. Proc Natl Acad Sci U S A. 2018 115(7):1576-1581
5. Song E. Jahng JWS. Chong L. Sung HK. Han M. Luo C, Wu D, Boo S, Hinz B, Berger T, Mak TW, George I, Schulze PC, Wang Y. Xu A & Sweeney G. Lipocalin-2 deficiency attenuates pressure overload induced heart failure in mice via reduced HMGB-1 induced TLR-4 signaling. American Journal of Translational Research (2017) 9(6):2723-2735
6. Liu Y, Palanivel R, Rai E, Park M, Gabor T, Scheid M, Xu A & Sweeney G. Adiponectin stimulates autophagy and reduces oxidative stress to enhance insulin sensitivity during high-fat diet feeding in mice. Diabetes (2015) 64(1):36-48
7. Liu Y, Sen S, Wannaiampikul S, Rengasamy P, Hoo RIC, Isserlin R, Bader G, Tungtrongchitr R, Deshaies Y, Xu A & Sweeney G. Metabolomic profiling in liver uncovers lysophospholipid metabolism as an important target of adiponectin action. Biochemical Journal (2015) 469(1):71-82

Abstract

A LIPOCALIN-2 (NGAL)-IRON AXIS INTEGRATES INNATE IMMUNITY, MICROBIOME AND CARDIOMETABOLIC DISEASE

Gary Sweeney

Department of Biology, York University, Toronto, Canad
gsweeney@yorku.ca

Lipocalin-2 (Lcn2), a critical component of the innate immune response which binds siderophores and limits bacterial iron acquisition, can elicit spillover adverse proinflammatory effects. We have shown that holo-Lcn2 (Lcn2-siderophore-iron, 1:3:1) increases mitochondrial reactive oxygen species (ROS) generation and attenuates mitochondrial oxidative phosphorylation in adult rat primary cardiomyocytes in a manner blocked by the mitochondria-specific antioxidant SkQ1. We further demonstrate using siderophores 2,3-DHBA (2,3-dihydroxybenzoic acid) and 2,5-DHBA that increased ROS and reduction in oxidative phosphorylation are direct effects of the siderophore component of holo-Lcn2 and not due to iron or apo-Lcn2 alone. At high concentrations such as in iron overload, iron can directly impact mitochondrial function via stimulating ROS production and via inhibiting autophagy flux. The latter is characterized by accumulation of dysfunctional autolysosomes and loss of free lysosomes and leads to decreased insulin stimulated metabolism. This occurs via a mechanism of decreased Akt-mediated repression of tuberous sclerosis complex (TSC2) and Rheb-mediated mTORC1 activation on autolysosomes, thereby inhibiting autophagic lysosomal regeneration. Constitutive activation of mTORC1 or iron withdrawal replenishes lysosomal pools via increased mTORC1-UVRAG signaling, which restores insulin sensitivity. Preliminary data will be presented which indicate that in addition to direct effects on metabolic tissues, iron overload can reshape the microbiome and lead to metabolic dysfunction in the host.

Keywords
Lipocalin-2, iron, autophagy, insulin sensitivity, mitochondria, metabolism

Symposium 13

Xu Aimin

Organization

The University of Hong Kong

Position & Title

Chair Professor, Director

» Educational Background & Professional Experience

Year	Name of institution	Position
2018-	University of Hong Kong	Chair Professor
2011-2018	University of Hong Kong	Professor
2013-	State Key Laboratory of Pharmaceutical Biotechnology, University of Hong Kong	Director
2008-	Antibody and Immunoassay Centre, University of Hong Kong	Director

» Research Interests

Obesity and its related medical complications; adipokines, biomarkers, antibody-based biotechnology

» Honors & Awards

· Croucher Senior Research Fellow award by Croucher Foundation

» Publications

1. Y, Hui XY, Hoo RL, Ye D, Chan CY, Feng T, Wang Y, Lam KS, **Xu A***. Adipocyte-secreted exosomal miR-34a inhibits M2 macrophage polarization to promote obesity-induced adipose inflammation. **Journal of Clinical Investigation**, 2019 Feb 1;129(2):834-849.
2. Huang Z, Zhong L, Wang Y, Wong CM and **Xu A***. The FGF21-CCL11 Axis Mediates Beiging of White Adipose Tissues by Coupling Sympathetic Nervous System to Type 2 Immunity. **Cell Metabolism**. 2017 Sep 5;26(3):493-508,
3. Li J, Lin S, Vanhoutte PM, Woo CW, **Xu A***. Akkermansia Muciniphila Protects Against Atherosclerosis by Preventing Metabolic Endotoxemia-Induced Inflammation in Apoe-/- Mice. **Circulation**. 2016 Jun 14;133(24):2434-46.
4. Hui X, Gu P, Zhang J, Nie T, Pan Y, Wu D, Feng T, Zhong C, Wang Y, Lam KS, **Xu A***, Adiponectin Enhances Cold-Induced Browning of Subcutaneous Adipose Tissue via Promoting M2 Macrophage Proliferation. **Cell Metabolism**. 2015 Aug 4;22(2):279-90
5. Lin Z, Pan X, Wu F, Ye D, Zhang Y, Wang Y, Jin L, Lian Q, Huang Y, Ding H, Triggle C, Wang K, Li X, **Xu A***. Fibroblast Growth Factor 21 Prevents Atherosclerosis by Suppression of Hepatic Sterol Regulatory Element-Binding Protein-2 and Induction of Adiponectin in Mice. **Circulation**, 2015 May 26;131(21):1861-71
6. Ye D, Wang Y, Li H, Jia W, Man K, Lo CM, Wang Y, Lam KSL, **Xu A***. Fibroblast growth factor 21 protects against acetaminophen-induced hepatotoxicity by potentiating peroxisome proliferator-activated receptor coactivator protein-1α-mediated antioxidant capacity in mice. **Hepatology**. 2014 Sep;60(3):977-989

Abstract

PERIVASCULAR ADIPOSE TISSUES AND ATHEROSCLEROSIS

Aimin Xu

State Key Laboratory of Pharmaceutical Biotechnology, the University of Hong Kong
amxu@hku.hk

There is a close anatomical and functional relationship between adipose tissue and blood vessels. The crosstalk between these two organs is vital to both metabolic and vascular homeostasis. Almost all blood vessels are surrounded by perivascular adipose tissue (PVAT), which regulates vascular function by producing a large number of "vasocrine" molecules. Notably, PVAT exhibits striking similarity to brown adipocytes with high expression of uncoupling protein-1 (UCP1), a mitochondrial inner membrane protein which dissipates energy into heat. We found that obesity-induced endothelial dysfunction and vascular inflammation are associated with reduced browning of PVAT, but are revered by cold exposure-induced conversion of white to brown phenotype of PVAT. Likewise, UCP1 deficiency renders apoE$^{-/-}$ mice more susceptible to dietary fat-induced endothelial damage and atherosclerosis, without obvious effects on glucose, lipid metabolism and adiposity. Mechanistically, UCP1 exerts anti-oxidant and anti-inflammatory activities by reducing mitochondrial membrane potential (MMP) in PVAT, independent of its thermogenic activities. Treatment with a chemical uncoupler is sufficient to reduce reactive oxygen species and reverse atherosclerosis in UCP1 and apoE double deficient mice. Thus, the brown phenotype of PVAT is protective against vascular disease through a mechanism independent of thermogenesis. (Acknowledgement: supported by Hong Kong Research Grant Council C7030-17G)

Keywords
Perivascular fat; atherosclerosis; inflammation; cytokines; brown fat, mitochondria

ICoLA 2019 by KSoLA

Symposium 14

Chairpersons

Moon-Kyu Lee | Sungkyunkwan University, Korea
Brian Tomlinson | The Chinese University of Hong Kong, Hong Kong

Date & Time: September 6 (Fri.), 16:30-18:00
Place: Room 4 (5F)

Symposium 14

Brian Tomlinson

Organization

The Chinese University of Hong Kong

Position & Title

Adjunct Professor

Department of Medicine and Therapeutics

» Educational Background & Professional Experience

Year	Name of institution	Position
2015-2019	The Chinese University of Hong Kong	Adjunct Professor
2007-2015	The Chinese University of Hong Kong	Chair Professor of Medicine and Therapeutics
1990-2007	The Chinese University of Hong Kong	Senior Lecturer/Professor I in Clinical Pharmacology
1980-1990	University College London, UK.	Clinical Lecturer in Clinical Pharmacology & Medicine.
1993	University of London, UK	MD Degree
1973	University of London, UK	MBBS Degree

» Research Interests

Hyperlipidaemia, hypertension, pharmacogenetics, cardiovascular pharmacology

» Honors & Awards

- 1994 Fellow of the Royal College of Physicians, FRCP (Lond)
- 1994 Fellow of the Royal College of Physicians of Edinburgh, FRCP (Edin)
- 1993 Fellow of the Hong Kong Academy of Medicine, FHKAM (Medicine)

» Publications

1. Flannick J, et al. Exome sequencing of 20,791 cases of type 2 diabetes and 24,440 controls. Nature 2019;570:71-6.
2. Liu J, et al. Endothelial Foxp1 Regulates Pathological Cardiac Remodeling Through TGF-beta1-Endothelin-1 Signal Pathway. Circulation 2019.
3. Tomlinson B, et al. Current status of familial hypercholesterolemia in Chinese populations. Curr Opin Lipid 2019;30:94-100.
4. Wang Y, et al. Is lipid goal one-size-fits-all: A review of evidence for recommended low-density lipoprotein treatment targets in Asian patients. Eur J Prev Cardiol 2019:2047487319843077.
5. Ma Y-B, et al. Evaluating the efficacy and safety of atorvastatin + ezetimibe in a fixed-dose combination for the treatment of hypercholesterolemia. Expert Opin Pharmacother 2019;20:917-28.
6. Chan P, et al. An evaluation of pitavastatin for the treatment of hypercholesterolemia. Expert Opin Pharmacother 2019;20:103-13.
7. Jiang G, et al. Progression of diabetic kidney disease and trajectory of kidney function decline in Chinese patients with Type 2 diabetes. Kid Int 2019;95:178-87.

Abstract

EPIDEMIOLOGY AND GENETIC STUDIES SHOWING AN ASSOCIATION OF LP(A) WITH ELEVATED CARDIOVASCULAR RISK AND AORTIC VALVE DISEASE

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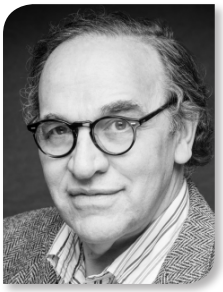
Lipoprotein(a) [Lp(a)] has been demonstrated to be an independent risk factor for cardiovascular disease (CVD) in observational, genetic and large Mendelian randomization studies and it is likely to be a causal risk factor. It is also one of the determinants of residual risk in patients on statin therapy. In fact, statin therapy appears to increase levels of Lp(a), despite reducing overall levels of low-density lipoprotein-cholesterol (LDL-C), which include the cholesterol carried in Lp(a) particles. Plasma levels of Lp(a) are about 80%–90% genetically determined with the main genetic determinant being the LPA gene. Lp(a) levels are inversely associated with smaller isoforms of apolipoprotein(a) which can be synthesized more rapidly by hepatocytes. The distribution of Lp(a) levels varies in different ethnic groups and Lp(a) levels may also increase with inflammation.

Valvular aortic stenosis (VAS) has several risk factors in common with atherosclerotic CVD and oxidized phospholipids carried by Lp(a) may provide a mechanistic link in the pathological processes. This is supported by genetic studies. Prospective population-based studies show that individuals with Lp(a) in the top 5th percentile (≥120 mg/dL) compared with those in the lower 20th percentile (<5 mg/dL) have 3- to 4-fold increased risk of myocardial infarction and 3-fold increased risk of VAS. Genomewide association studies in large case-control consortia have generally found that genetic variation in the human genome related to high Lp(a) levels confers the highest risk of atherosclerotic CVD and VAS of all the variants tested. Measurement of Lp(a) levels may be particularly useful to refine risk assessment for atherosclerotic CVD in selected subjects and to identify those at risk for progressive VAS. Currently available therapies have limited effects on Lp(a) levels and it remains to be seen whether newer treatments that can lower Lp(a) levels more substantially can reduce the risk of atherosclerotic CVD and VAS in those with higher levels.

Keywords
Cardiovascular disease, lipoprotein(a), valvular aortic stenosis

Symposium 14



Gerald F Watts DSc PhD MD FRACP FRCP (London)

Organization

Royal Perth Hospital, University of Western Australia, Perth, Western Australia

Position & Title

Winthrop of Professor of Cardiometabolic Medicine, Department of Cardiology and Internal Medicine, Royal Perth Hospital, University of Western Australia.

» Educational Background & Professional Experience

Year	Name of institution	Position
1984-1994	Kings College, University of London	Lecturer
1994-2000	Royal Perth Hospital, University of Western Australia	Associate Professor
2000-2009	Royal Perth Hospital, University of Western Australia	Full Professor of Medicine
2009-Present	Royal Perth Hospital, University of Western Australia	Winthrop Professor

» Research Interests

Lipidology, Cardiovascular Medicine, Inherited Heart Disease

» Honors & Awards

- 2003 Doctor of Science (Imperial College, University of London)
- 2006 GlaxoSmithKline Research Innovation Award, Australia
- 2014 Excellence in the Primary Care of FH, Government of WA

» Publications (top 5, 2014-17)

1. **Watts GF**, Gidding S, Wierzbicki AS, et al. Integrated Guidance on the Care of Familial Hypercholesterolaemia from the International FH Foundation. **Int J Cardiol 2014**;171:309-325.
2. **Watts GF**, Chan DC, Dent R, Somaratne R, Wasserman SM, Scott R, Burrows S, R Barrett PH. Factorial Effects of evolocumab and atorvastatin on lipoprotein metabolism. **Circulation** 2017; 135:338-351.
3. Perez de Isla L, Alonso R, **Watts GF**, et al. Attainment of LDL-Cholesterol Treatment Goals in Patients With Familial Hypercholesterolemia: 5-Year SAFEHEART Registry Follow-Up. **J Am Coll Cardiol** 2016;67:1278-1285.
4. Gidding SS, Champagne M, de Ferranti SD, Defesche J, Ito MK,Knowles JW, McCrindle B, Raal F, Rader D, Santos RD, Lopes-Virella M, **Watts GF**, Wierzbicki AS. The Agenda for Familial Hypercholesterolemia: A Scientific Statement From the American Heart Association. **Circulation** 2015;132:2167-2192.
5. Benn M, **Watts GF**, Tybjærg-Hansen A, Nordestgaard BG. Mutations causative of familial hypercholesterolaemia: screening of 98 098 individuals from the Copenhagen General Population Study estimated a prevalence of 1 in 217. **Eur Heart J** 2016; ;37:1384-1394.

Professor Watts has over 600 published works to his credit, including scientific articles, reviews and editorials, book chapters (15) and monographs (3), mostly as senior author. H-index of 73 on Web of Science, May 2019.

Abstract

ROLE OF LP(A) AS AN ASCVD RISK FACTOR AND ITS HERITABILITY IN FAMILIAL HYPERCHOLESTEROLEMIA: IMPLICATIONS FOR CASCADE TESTING PROGRAMS

Gerald F WATTS

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Background: Lipoprotein (a) [Lp(a)] is an LDL-like particle covalently bound to a glycoprotein, called apolipoprotein (a) [apo(a)], that is under unique genetic control and has potent athero-thrombotic and pro-inflammatory properties. Plasma concentrations of Lp(a) are positively skewed, highly heritable, inversely correlated with apo(a) isoform size, and vary markedly among ethnic groups. One in four people have plasma Lp(a) levels that are associated with increased risk of atherosclerotic cardiovascular disease (ASCVD). New evidence supports a causal role for Lp(a) in ASCVD and calcific aortic valve disease (CAVD); risk may be particularly higher in South Asians and Latin Americans. Individuals with elevated Lp(a) have a high life-time burden of ASCVD and this is important for coronary prevention, particularly in high risk conditions, such as familial hypercholesterolaemia (FH).

Investigation: An novel investigation was carried out to assess whether testing for Lp(a) was effective in detecting and risk stratifying individuals participating in FH cascade screening programs. Family members from index cases enrolled in the SAFEHEART and FHWA cohorts were tested for genetic FH and elevated Lp(a) based an established screening protocols. Elevated Lp(a) was defined as a plasma level ≥50 mg/dL. The prevalence and yield of new cases of high Lp(a) in relatives of FH probands both with and without high Lp(a) were estimated, and in the Spanish cohort the association was assessed between elevated Lp(a) and incident ASCVD events.

Findings: Systematic screening from index cases with both FH and elevated Lp(a) identified one new case of elevated Lp(a) for every 2.4 screened. Opportunistic screening from index cases with FH but without elevated Lp(a) identified one individual for 5.8 screened. Over 5-years follow-up, FH (HR=2.47; P=0.036) and elevated Lp(a) (HR=3.17; P=0.024) alone were associated with a significantly increased risk of a new ASCVD event or death compared with individuals with neither disorder; the greatest risk was observed in relatives with both FH and elevated Lp(a) (HR=4.40; P<0.001), independent of conventional risk factors.

Conclusions and Future Perspective: Systematic testing for elevated Lp(a) during cascade screening for FH is highly effective in identifying new cases of high Lp(a). Opportunistic testing has a lower yield but may be a useful approach for detecting probands, with subsequent testing of relatives being more effective employing a systematic approach. The detection of new cases of elevated Lp(a) is important because these individuals are at increased risk of ASCVD, particularly with coexistent FH. Hence, cascade screening programs for FH should incorporate both systematic and opportunistic testing for elevated plasma Lp(a). Our findings also suggest that beyond FH there may be value in systematically screening for elevated Lp(a), but this requires further investigation. The practicabilities, organization and cost-effectiveness of screening strategies for high Lp(a) remain to be demonstrated. This is critical in an era of novel RNA-based therapies that can selectively and potently lower plasma Lp(a) concentrations and potentially mitigate risk of ASCVD and CAVD.

Keywords
Lipoprotein(a), Familial Hypercholesterolaemia, Screening, Inheritance, Risk of ASCVD

Symposium 14

Sang-Hyun Kim

Organization

Seoul Boramae Hospital, Seoul National University College of Medicine

Position & Title

Professor, MD.PhD

» Educational Background & Professional Experience

Year	Name of institution	Position
2012–Present	Seoul Boramae Hospital, Seoul National University College of Medicine	Professor
2017–2012	Seoul Boramae Hospital, Seoul National University College of Medicine	Associate Professor
2002–2017	Seoul Boramae Hospital, Seoul National University College of Medicine	Assistant Professor
1999–2000	Seoul National University Hospital, Seoul National University College of Medicine	Fellow

» Research Interests

1. Atherosclerosis
2. Dyslipidemia
3. Quality of Care

» Publications

1. Rhee TM, Kim HL, Lim WH, Seo JB, Kim SH, Zo JH1, Kim MA. Association between epicardial adipose tissue thickness and parameters of target organ damage in patients undergoing coronary angiography. Hypertens Res. 2019 Apr;42(4):549-557
2. Kim HL, Lee JP, Lim WH, Seo JB, Zo JH, Kim MA, Kim SH. Association between the level of serum soluble ST2 and invasively measured aortic pulse pressure in patients undergoing coronary angiography. Medicine. 2019;98:8
3. Kang J, Kim HL, Lim WH, Kim MA, Kim SH. Relationship between brachial-ankle pulse wave velocity and invasively measured aortic pulse pressure. J Clin Hypertens 2018;20:462-468.
4. Rhee TM, Lee JM, Shin ES, Park KW, Kim SH, Kim HS. Impact of Optimized Procedure-Related Factors in Drug-Eluting Balloon Angioplasty for Treatment of In-Stent Restenosis. J Am Coll Cardiol Intv 2018;11:969–78
5. Lee H, Kim HL, Lim WH, Kim SH, Kim MA. Interaction of Metabolic Health and Obesity on Subclinical Target Organ Damage. Metab Syndr Relat Disord 2018;16(1):46-53
6. Kim HL, Lee JP, Lim WH, Kim MA, Kim SH. Soluble Tumor Necrosis Factor Receptors and Arterial Stiffness in Patients With Coronary Atherosclerosis. Am J Hypertens. 2017;30(3):313-318
7. Im MS, Kim HL, Lim WH, Kim MA, Park KW, Kim SH, Kim HS. Different prognostic factors according to left ventricular systolic function in patients with acute myocardial infarction. Int J Cardiol. 2016;221:90-96

Abstract

STRATEGIES FOR LOWERING LP(A) LEVELS

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The most important management strategy for people with high levels of Lp(a) is to treat all risk factors, in particular LDL cholesterol. The current treatment strategy for Lp(a) is to reduce the cholesterol burden of the particle with a statin. New injectable treatment with an anti-sense therapy which stops Lp(a) is currently under clinical research trials and has shown this treatment can reduce LP(a) levels by up to 90%. Other treatments lowering Lp(a) levels include PCSK9 inhibitors (reduce levels by 25%), niacin (reduce levels by 20-30%), and lipoprotein apheresis, (reduce levels by up to 75%). Further research is required to ascertain whether lowering LP(a) levels reduce cardiovascular disease and how to reduce Lp(a) levels.

Keywords
Lipoprotein, Lp(a), Treatment

Symposium 14

Eun-Jung Rhee

Organization

Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
1991-1997	Graduated from Ewha Women's University School of Medicine	
2003-2007	Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine	Fellowship and instructor in
2002-2007	The Catholic University School of Medicine	Master's and Ph degree
2010-2011	Cardiovascular Division, Brigham and Women's Hospital, Harvard University, Boston, MA, USA	Visiting professor
2017-Present	Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine	Professor

» Research Interests

Diabetes vascular complications, Vascular calcification, prediabetes, Pharmaceutical management of diabetes, metabolic syndrome, non-alcoholic fatty liver disease, coronary artery calcium score

» Honors & Awards

- 2015 Winter Best Research Achievement Award for 2015 from Sungkyunkwan University School of Medicine
- 2016 Spring Best Research Paper Award from Korean Federation of Science and Technology Societies
- 2017 Spring Young Investigator Award from Korean Diabetes Association

» Publications

1. Rhee EJ, Cho JH, Kwon H, Park SE, Jung JH, Han KD, Park YG, Kim YH, Lee WY. Relation between Baseline Height and New Diabetes Development: A Nationwide Population-Based Study. Diabetes Metab J. 2019 Mar 22. doi: 10.4093/dmj.2018.0184. [Epub ahead of print]
2. Lee YH, Cho Y, Lee BW, Park CY, Lee DH, Cha BS, Rhee EJ. Nonalcoholic Fatty Liver Disease in Diabetes. Part I: Epidemiology and Diagnosis. Diabetes Metab J. 2019 Feb;43(1):31-45
3. Kwon H, Chang Y, Cho A, Ahn J, Park SE, Park CY, Lee WY, Oh KW, Park SW, Shin H, Ryu S, Rhee EJ. Metabolic Obesity Phenotypes and Thyroid Cancer Risk: A Cohort Study. Thyroid. 2019 Mar;29(3):349-358.
4. Cho JH, Rhee EJ, Park SE, Kwon H, Jung JH, Han KD, Park YG, Yoo SJ, Kim YH, Lee WY; Taskforce Team of the Obesity Fact Sheet of the Korean Society for the Study of Obesity. Maintenance of body weight is an important determinant for the risk of ischemic stroke: A nationwide population-based cohort study. PLoS One. 2019 Jan 3;14(1):e0210153.
5. Cho JH, Rhee EJ, Park SE, Kwon H, Jung JH, Han KD, Park YG, Park HS, Kim YH, Yoo SJ, Lee WY; Taskforce Team of the Obesity Fact Sheet of the Korean Society for the Study of Obesity. The Risk of Myocardial Infarction and Ischemic Stroke According to Waist Circumference in 21,749,261 Korean Adults: A Nationwide Population-Based Study. Diabetes Metab J. 2019 Apr;43(2):206-221.
6. Rhee EJ, Cho JH, Kwon H, Park SE, Jung JH, Han KD, Park YG, Park HS, Kim YH, Yoo SJ, Lee WY; Taskforce Team of the Obesity Fact Sheet of the Korean Society for the Study of Obesity. Association between abdominal obesity and increased risk for the development of hypertension regardless of physical activity: A nationwide population-based study. J Clin Hypertens (Greenwich). 2018 Oct;20(10):1417-1426.
7. Lee DAY, Rhee EJ, Cho JH, Kwon H, Park SEE, Kim YH, Han K, Park YK, Yoo SJ, Lee WY. Appropriate Amount of Regular Exercise Is Associated with a Reduced Mortality Risk. Med Sci Sports Exerc. 2018 Dec;50(12):2451-2458.

Abstract

THE IMPLICATION OF LIPOPROTEIN(A) IN METABOLIC DISEASES

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Lipoprotein(a) [Lp(a)] is produced mainly by the liver and is a low-density lipoprotein (LDL)-like particle, consisting of a apolipoprotein(a) moiety covalently attached to one molecule of apoB100 via a disulfide bond. High serum level of Lp(a) is known to be associated with increased risk of cardiovascular disease (CVD). Given that Lp(a) is known to be able to enter the intima of blood vessels in humans and animals, where it may contribute to intimal inflammation, thrombosis, and foam cell formation, it is plausible that Lp(a) may contribute to atherosclerosis.

Recent studies suggest the association between hyperlipidemia and diabetes development. In animal studies, high intracellular concentration of cholesterol is known to affect insulin secretory process, and hypercholesterolemia impairs insulin secretion in LDL receptor knockout mice. In a human study, increased serum level of total cholesterol was related with decreased insulin secretory function assessed by homeostasis model assessment for beta cell. Risk of development of type 2 diabetes is reported to significantly increase as the ratio of TC to high-density lipoprotein cholesterol (HDL-C) increases.

Apart from known evidence of association between Lp(a) and CVD, there are not many evidences on its association with metabolic diseases. In this talk, I would like to review recent works and evidences on association between Lp(a) and metabolic diseases.

Keywords
Lipoprotein(a), diabetes, metabolic diseases, cardiovascular diseases, insulin resistance

ICoLA 2019 by KSoLA

Symposium 15

Chairpersons

Soon Jib Yoo | The Catholic University of Korea, Korea
Stefano Del Prato | University of Pisa, Italy

Date & Time: September 7 (Sat.), 09:40-11:10
Place: Room 1 (3F)

Symposium 15

Anselm K. Gitt

Organization

Heart Center Ludwigshafen, Dep. of Cardiology, Germany

Position & Title

Senior Interventional Cardiologist

MD, FESC, FACC

» Educational Background & Professional Experience

Year	Name of institution	Position
2018-	Heart Center Ludwigshafen, Germany	Head of CV Imaging
2000-2018	Heart Center Ludwigshafen, Germany	Senior Cardiology Consultant Interventional Cardiology
1994-1999	Heart Center Ludwigshafen, Germany	Resident
1992-1994	University of Cologne, Cardiology, Germany	Resident
1991	UCLA Los Angeles, Harbor UCLA Medical Center	Intern
1985-1991	Medical Study University of Cologne UCLA Los Angeles, USA	Student

» Research Interests

Acute Coronary Syndromes, Secondary Prevention, Lipid Lowering Therapy, Diabetes

» Honors & Awards

- Silver Medal of the European Society of Cardiology (ESC)
- Fellow of the European Society of Cardiology (FESC)
- Fellow of the American College of Cardiology (FACC)

» Publications

1. Liberopoulos E, Rallidis L, Spanoudi F, Xixi E, Gitt A, Horack M, Ashton V, Brudi P, Lautsch D, Ambegaonkar B, Elisaf M. Attainment of cholesterol target values in Greece: results from the Dyslipidemia International Study II. Arch Med Sci. 2019 Jul;15(4):821-831
2. Schwaab B, Zeymer U, Jannowitz C, Pittrow D, Gitt A. [Improvement of LDL-C target value achievement through cardiac rehabilitation in patients with acute coronary syndrome: PATIENT-CARE registry]. MMW Fortschr Med. 2019 Jul;161(Suppl 5):21-24.
3. Liosis S, Hochadel M, Darius H, Behrens S, Mudra H, Lauer B, Elsässer A, Gitt AK, Zahn R, Zeymer U; ALKK study group. Effect of renal insufficiency and diabetes mellitus on in-hospital mortality after acute coronary syndromes treated with primary PCI. Results from the ALKK PCI Registry. Int J Cardiol. 2019 Oct 1;292:43-49.
4. Buddhari W, Uerojanaungkul P, Sriratanasathavorn C, Sukonthasarn A, Ambegaonkar B, Brudi P, Horack M, Lautsch D, Vyas A, Gitt AK. Low-Density Lipoprotein Cholesterol Target Attainment in Patients Surviving an Acute Coronary Syndrome in Thailand: Results From the Dyslipidemia International Study (DYSIS) II. Heart Lung Circ. 2019 Mar 28. pii: S1443-9506(19)30294-X.
5. Chuang LH, Gumbs P, van Hout B, Agnelli G, Kroep S, Monreal M, Bauersachs R, Willich SN, Gitt A, Mismetti P, Cohen A, Jimenez D. Health-related quality of life and mortality in patients with pulmonary embolism: a prospective cohort study in seven European countries. Qual Life Res. 2019 Aug;28(8):2111-2124.
6. Poh KK, Chin CT, Tong KL, Tan JKB, Lim JS, Yu W, Horack M, Vyas A, Lautsch D, Ambegaonkar B, Brudi P, Gitt AK. Cholesterol goal achievement and lipid-lowering therapy in patients with stable or acute coronary heart disease in Singapore: results from the Dyslipidemia International Study II. Singapore Med J. 2019 Feb 18. doi: 10.11622/smedj.2019021
7. Weipert KF, Bauer T, Nef HM, Hochadel M, Weidinger F, Gitt AK, Zeymer U, Hamm CW. Incidence and outcome of peri-procedural cardiogenic shock: results from the international Euro Heart Survey PCI registry. Eur Heart J Acute Cardiovasc Care. 2019 Jan 8:2048872618822460. doi: 10.1177/2048872618822460

Abstract

ONE SIZE DOESN'T FIT ALL: ETHNIC DIFFERENCE OF CV RISK EXAMPLE EUROPE VS ASIA

Anselm K. Gitt, MD, FESC, FACC

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Background: Chronic statin treatment is well established for patients with dyslipidemia and high risk for subsequent cardiovascular events and its use is widespread in clinical practice. Little is known about differences in patient characteristics and target achievements between Europe and China.

Methods: The cross sectional, observational study DYSIS examined lipid goal attainment among statin-treated very high cardiovascular risk (defined as per 2011 EAS/ESC guidelines, including patients suffering from coronary heart disease, diabetes, chronic kidney disease or peripheral atherosclerotic disease) patients in Canada, Europe, Middle East countries and China. Data were collected under real life conditions in physicians' offices and hospital outpatient wards between 2008-2012. We compared the level of LDL-C goal achievement in Europe and China.

Results: Of a total of 57,090 patients, 25,317 were enrolled in China and 31,773 in Europe. There are substantial differences in the prevalence of cardio-vascular risk factors between China and Europe. Chinese patients less often were smokers and less often suffered from obesity, diabetes and hypertension, sedentary lifestyle as compared to European patients, but more often had prior cerebro-vascular events. In both regions, two thirds of patients did not reach the recommended LDL-Chol target <70mg/dl. Chinese patients more often had combined dyslipidemia with low HDL-Chol as well as high triglycerides.

Conclusion: Patients treated with statins for secondary prevention in China have a substantially different cardiovascular risk profile as compared to European patients. Despite statin treatment, two thirds of patients in China and Europe do not reach the recommended LDL-Chol target value of < 70mg/dl in clinical practice.

Keywords
Lipid Lowering Treatment, Statins, Target Achievement, Europe, China

Symposium 15

Kyung Woo Park

Organization

Seoul National University Hospital

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2019-current	Seoul National University Hospital	Chief Innovation and Quality Officer
2018-current	Seoul National University Hospital, Department of Internal Medicine, Cardiovascular Center	Professor
2014-2016	The Wharton School, University of Pennsylvania	MBA
2005-2008	Seoul National University Graduate School of Medicine	PhD
1992-1998	Seoul National University College of Medicine	MD

» Research Interests

Atherosclerosis, Antiplatelet and antithrombotic therapy, Clinical trial design

» Honors & Awards

- 23rd Wunsch Medical Award, Young Scientist Prize
- Astra Zeneca Research Award, Korean Society of Cardiology
- Minister's Award, Ministry of Education & Human Resources Development

» Publications

1. Kang J, Park KW (corresponding author), Ki YJ, Park J, Rhee T, Kim CH, Han JK, Yang HM, Kang HJ, Koo BK, Nakamura M, Hamasaki T, Yokoi H, Cohen D, Kim HS. Development and Validation of an Ischemic and Bleeding Risk Evaluation Tool in East Asian Patients Receiving Percutaneous Coronary Intervention. Thromb Haemost. 2019 May 12
2. Kang J, Park KW (corresponding author), Palmerini T, Stone GW, Lee MS, Colombo A, Chieffo A, Feres F, Abizaid A, Bhatt DL, Valgimigli M, Hong MK, Jang Y, Gilard M, Morice MC, Park DW, Park SJ, Jeong YH, Park J, Koo BK, Kim HS. Racial Differences in Ischaemia/Bleeding Risk Trade-Off during Anti-Platelet Therapy: Individual Patient Level Landmark Meta-Analysis from Seven RCTs. Thromb Haemost. 2019 Jan;119(1):149-162
3. Rhee TM, Park KW (corresponding author), Kim CH, Kang J, Han JK, Yang HM, Kang HJ, Koo BK, Kim HS. Dual Antiplatelet Therapy Duration Determines Outcome After 2- But Not 1-Stent Strategy in Left Main Bifurcation Percutaneous Coronary Intervention. JACC Cardiovasc Interv. 2018 Dec 24;11(24):2453-2463
4. Palmerini T, Bacchi Reggiani L, Della Riva D, Romanello M, Feres F, Abizaid A, Gilard M, Morice MC, Valgimigli M, Hong MK, Kim BK, Jang Y, Kim HS, Park KW, Colombo A, Chieffo A, Ahn JM, Park SJ, Schüpke S, Kastrati A, Montalescot G, Steg PG, Diallo A, Vicaut E, Helft G, Biondi-Zoccai G, Xu B, Han Y, Genereux P, Bhatt DL, Stone GW. Bleeding-Related Deaths in Relation to the Duration of Dual-Antiplatelet Therapy After Coronary Stenting. J Am Coll Cardiol. 2017 Apr 25;69(16):2011-2022
5. Palmerini T, Benedetto U, Bacchi-Reggiani L, Della Riva D, Biondi-Zoccai G, Feres F, Abizaid A, Hong MK, Kim BK, Jang Y, Kim HS, Park KW, Genereux P, Bhatt DL, Orlandi C, De Servi S, Petrou M, Rapezzi C, Stone GW. Mortality in patients treated with extended duration dual antiplatelet therapy after drug-eluting stent implantation: a pairwise and Bayesian network meta-analysis of randomised trials. Lancet. 2015 Jun 13;385(9985):2371-82
6. Kang SH, Park KW [co-first author], Kang DY, Lim WH, Park KT, Han JK, Kang HJ, Koo BK, Oh BH, Park YB, Kandzari DE, Cohen DJ, Hwang SS, Kim HS. Biodegradable-polymer drug-eluting stents vs. bare metal stents vs. durable-polymer drug-eluting stents: a systematic review and Bayesian approach network meta-analysis. Eur Heart J. 2014 May;35(17):1147-58
7. Park KW, Lee JM, Kang SH, Ahn HS, Yang HM, Lee HY, Kang HJ, Koo BK, Cho J, Gwon HC, Lee SY, Chae IH, Youn TJ, Chae JK, Han KR, Yu CW, Kim HS. Safety and efficacy of second-generation everolimus-eluting Xience V stents versus zotarolimus-eluting resolute stents in real-world practice: patient-related and stent-related outcomes from the multicenter prospective EXCELLENT and RESOLUTE-Korea registries. J Am Coll Cardiol. 2013 Feb 5;61(5):536-44

Abstract

STATIN IS A PANACEA?

Kyung Woo Park, MD, PhD, MBA

Professor, Seoul National University Hospital, Seoul, Korea

Statin therapy is the standard for management of dyslipidemia in patients with established cardiovascular disease and those at elevated risk. It is very effective in both the prevention and treatment of cardiovascular events and is one of the few drugs that have shown to improve clinical outcomes in patients with cardiovascular disease. Further high dose high intensity statin therapy has been shown to improve outcome when compared to lower doses of the same statin or moderate intensity statins. However, patients at high risk still have significant residual risk despite high intensity statin therapy and we need to target other pathways to inhibit atherosclerosis, inflammation, and further lower LDL-C. Also, although statins are generally well tolerated, certain patients experience adverse events such as myalgia, myopathy, rhabdomyolysis, and liver enzyme elevation that prohibit its use. Therefore, it is my opinion that statins cannot be a panacea and we need to focus on other methods of reducing residual risk.

In patients with partial intolerance to statins or those do not reach target goals, we may consider the addition of ezetimibe, a NPC1L1 inhibitor. Another option could be the addition of PCSK-9 inhbitors. PCSK-9 inhibitors such as evolucumab and alirocumab can reduce LDL-C very effectively, and have been shown in randomized trials to further improve clinical outcomes in those with residual risk after statin therapy. There are other targets that we need to consider such as the inflammatory process, since one of the major mechanisms of atherosclerosis progression is inflammation. Recently, canakinumab, a monoclonal antibody targeted at interleukin-1 beta, was shown to improve outcomes in post-MI patients with persistent elevation of hs-CRP, in the CANTOS trial. Finally, since the final mechanism of an adverse event from atherosclerosis involves thrombosis, hence the term 'atherothrombosis', antithrombotic agents may have the possibility to improve outcomes in those with chronic atherosclerosis, as was shown in the COMPASS randomized trial.

In summary, statin therapy is very effective in lowering LDL-C levels, inhibiting atherosclerotic progression, and lowering the risk for atherosclerosis-associated acute cardiovascular events. It definitely should be and is the first-line treatment for patients with atherosclerosis. However, because these patients still have significant residual risk, it is difficult to conclude that statin therapy is the panacea of atherosclerosis. There are other adjunctive therapies on top of statin therapy that may be of significant benefit for these patients.

Symposium 15

Kausik Ray

Organization

Imperial College London

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2007	University of Cambridge	MPhil
2007	Harvard Medical School	Postdoctoral Fellowship
2004	University of Sheffield	MD
1991	University of Birmingham Medical School	MB,ChB

» Research Interests

The prevention of coronary disease with a focus on lipids, diabetes, biomarkers and risk prediction

» Publications

1. Pérez de Isla L, Ray KK, Watts GF, et al., 2019, Potential utility of the SAFEHEART risk equation for rationalising the use of PCSK9 monoclonal antibodies in adults with heterozygous familial hypercholesterolemia, Atherosclerosis, Vol:286, ISSN:0021-9150, Pages:40-45
2. Müller-Wieland D, Rader DJ, Moriarty PM, Bergeron J, Langslet G, Ray KK, Manvelian G, Thompson D, Bujas-Bobanovic M, Roth EMet al., 2019, Efficacy and safety of alirocumab 300 mg every 4 weeks in individuals with type 2 diabetes on maximally tolerated statin, *Journal of Clinical Endocrinology and Metabolism*, ISSN: 0021-972X
3. Fruchart J-C, Santos RD, Aguilar-Salinas C, Aikawa M, Al Rasadi K, Amarenco P, Barter PJ, Ceska R, Corsini A, Després J-P, Duriez P, Eckel RH, Ezhov MV, Farnier M, Ginsberg HN, Hermans MP, Ishibashi S, Karpe F, Kodama T, Koenig W, Krempf M, Lim S, Lorenzatti AJ, McPherson R, Nuñez-Cortes JM, Nordestgaard BG, Ogawa H, Packard CJ, Plutzky J, Ponte-Negretti CI, Pradhan A, Ray KK, Reiner Ž, Ridker PM, Ruscica M, Sadikot S, Shimano H, Sritara P, Stock JK, Su T-C, Susekov AV, Tartar A, Taskinen M-R, Tenenbaum A, Tokgözoğlu LS, Tomlinson B, Tybjærg-Hansen A, Valensi P, Vrablík M, Wahli W, Watts GF, Yamashita S, Yokote K, Zambon A, Libby Pet al., 2019, The selective peroxisome proliferator-activated receptor alpha modulator (SPPARMα) paradigm: Conceptual framework and therapeutic potential: A consensus statement from the International Atherosclerosis Society (IAS) and the Residual Risk Reduction Initiative (R3i) Foundation, *Cardiovascular Diabetology*, Vol: 18, ISSN: 1475-2840
4. Ray K, Morales-Villegas EC, 2019, PCSK9 Inhibition with Evolocumab Reaching Physiologic LDL-C Levels for Reducing Atherosclerotic Burden and Cardiovascular Disease-The Full Landscape, Frontiers in Cardiovascular Drug Discovery Vol. 4, Pages: 148-185, ISBN: 978-1-68108-400-8
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6. Ference BA, Ray KK, Catapano AL, Ference TB, Burgess S, Neff DR, Oliver-Williams C, Wood AM, Butterworth AS, Di Angelantonio E, Danesh J, Kastelein JJP, Nicholls SJet al., 2019, Mendelian Randomization Study of ACLY and Cardiovascular Disease, *NEW ENGLAND JOURNAL OF MEDICINE*, Vol: 380, Pages: 1033-1042, ISSN: 0028-4793
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Abstract

EXTREMELY LOW LDL CHOLESTEROL, FRIEND OR FOE?

Prof Kausik K Ray

Imperial Centre for Cardiovascular Disease Prevention, Department of Primary Care and Public Health, Imperial College London, London, UK
k.ray@imperial.ac.uk

LDL-C is causal and cumulative. Genetic and epidemiological studies show a log linear relationship between cardiovascular risk and absolute differences in LDL-C. Trials of lipid lowering therapies show a similar log linear relationship between risk and LDL-C difference.

In nature among those with PCSK9 gene mutations or abetalipoproteinaemia risk of CAD is extremely low.

Trials of statins, ezetimibe, and PCSK9 have not shown any relationship between reductions in LDL-C and adverse cardiovascular outcomes in particular stroke risk is lower. In observational studies from trials lower appperes to be safe and beneficial from a cardiovascular standpoint when all is safe.

Keywords
LDL-C, genetics, statins, ezetimibe, PCSK9, safety, efficacy

ICoLA 2019 by KSoLA

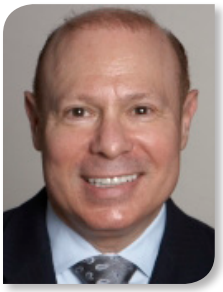
Symposium 16

Chairpersons

Myeong Chan Cho | Chungbuk National University, Korea
Gerald F Watts | The University of Western Australia, Australia

Date & Time: September 7 (Sat.), 09:40-11:10
Place: Room 2 (3F)

Symposium 16



Robert S. Rosenson, MD

Organization

Icahn School of Medicine at Mount Sinai

Position & Title

Director of Cardiometabolics

Professor of Medicine (Cardiology)

» Educational Background & Professional Experience

Year	Name of institution	Position
2010	Icahn School of Medicine at Mount Sinai	Professor
2006-2009	University of Michigan	Professor
2000-2006	Northwestern University	Associate Professor, Professor
1990-2000	Rush University	Assistant Professor, Associate Professor
1986-1990	University of Chicago	Fellow in Cardiovascular Medicine, Research Associate
1983-1986	Brigham and Women's Hospital	Resident in Internal Medicine

» Research Interests

HDL biology, Inflammation, Lipoprotein Disorders

» Honors & Awards

- Clinician/Educator Award for continued excellence in clinical care of patients with lipid disorders and excellence in the field of clinical lipidology, National Lipid Association, 2019
- Jan J. Kellerman Memorial Award for distinguished contribution in the field of cardiovascular prevention, International Academy of Cardiology
- Simon Dack Award for outstanding scholarship, Journal of the American College of Cardiology, 2015, 2016, 2017 and 2019

» Publications

1. Rosenson RS, Baker S, Banach M, Braun LT, Bruckert E, Brunham LR, Catapano AL, Elam MB, Mancini GBJ, Morris PB, Munter P, Ray KK, Stroes ES, Taylor BA, Taylor VH, Watts GF, Thompson P. Optimizing cholesterol treatment in patients with muscle complaints. J Am Coll Cardiol. 2017;70:1290-1301.
2. Kent ST, Rosenson RS, Avery CL, Chen YI, Correa A, Cummings SR, Cupples LA, Cushman M, Evans DS, Gudnason V, Harris TB, Howard G, Irvin MR, Judd SE, Jukema JW, Lange L, Levitan EB, Li X, Liu Y, Post WS, Postmus I, Psaty BM, Rotter JI, Safford MM, Sitlani CM, Smith AV, Stewart JD, Trompet S, Sun F, Vasan RS, Woolley JM, Whitsel EA, Wiggins KL, Wilson JG, Muntner P. PCSK9 loss of function variants, low-density lipoprotein cholesterol, and risk of coronary heart disease and stroke: Data from 9 studies of blacks and whites. Circ Cardiovasc Genet. 2017; Aug 10:e001632. doi: 10.1161/CIRCGENETICS.116.001632.
3. Serban MC, Muntner P, Rosenson RS. Reply: Statin intolerance and risk of recurrent myocardial infarction, coronary heart disease events, and all-cause mortality. J Am Coll Cardiol. 2017;70:685-686.
4. Rosenson RS, Brewer HB Jr, Ansell B, Barter P, Chapman MJ, Heinecke JW, Kontush A, Tall AR, Webb NR. Translation of high-density lipoprotein function into clinical practice: current prospects and future challenges. Circulation.2013;128:1256-1267.
5. Rosenson RS, Brewer HB Jr., Ansell B, Barter P, Chapman MJ, Heinecke J, Kontush A, Tall AR, Webb NR. Dysfunctional HDL in atherosclerotic cardiovascular disease. Nat Cardiol 2016;13:48-60.
6. Rosenson RS, Brewer HB, Barter P, Bjorkegren J, Chapman J, Gaudet D, Kim DS, Niesor E, Rye K-A, Sacks F, Tardif J-C, Hegele RA. High-density lipoproteins and atherosclerotic cardiovascular disease: Genetic insights on complex biology. Nat Rev Cardiol. 2018;15:9-19.
7. Rosenson RS, Tangney CC. Anti-atherothrombotic properties of statins: implications for cardiovascular event reduction. JAMA 1998;279:1643-1650.

Abstract

DYSFUNCTIONAL HDL - BENCH TO CLINIC

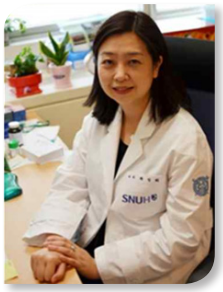
Robert S. Rosenson

Cardiometabolics Unit, Mount Sinai Heart, Icahn School of Medicine at Mount Sinai, USA
robert.rosenson@mssm.edu

High-density lipoproteins (HDLs) protect against atherosclerosis through multiple salutary mechanisms. Factors that impair the availability of functional apolipoproteins or the activities of macrophage cholesterol efflux pathways could markedly influence atherogenesis. HDL also inhibits lipid oxidation, restores endothelial function, exerts anti-inflammatory and antiapoptotic actions, and exerts anti-inflammatory actions in animal models. Such properties could contribute considerably to the capacity of HDL to inhibit atherosclerosis. Systemic and vascular inflammation has been proposed to convert HDL to a dysfunctional form that has impaired antiatherogenic effects. A loss of anti-inflammatory and antioxidative proteins, perhaps in combination with a gain of proinflammatory proteins, might be another important component in rendering HDL dysfunctional. The proinflammatory enzyme myeloperoxidase renders HDL dysfunction by inducing both oxidative modification and nitrosylation of specific residues on plasma and arterial apolipoprotein A-I to render HDL dysfunctional, which results in impaired ABCA1 macrophage transport, the activation of inflammatory pathways, and an increased risk of coronary artery disease. Understanding the features of dysfunctional HDL or apolipoprotein A-I in clinical practice might lead to new diagnostic and therapeutic approaches to atherosclerosis.

Keywords
HDL function, HDL dysfunction, HDL proteome, HDL lipidome, macrophage cholesterol efflux, proinflammatory HDL

Symposium 16



Sung Hee Choi

Organization

Seoul National University, College of Medicine Bundang SNUH

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2017-present	Seoul National University, College of Medicine, Bundang Hospital	Professor
2004-2017	Seoul National University, College of Medicine, Bundang Hospital	Assistant & Associate Professor
1998 & 2006	Yonsei University, Severance Hospital	MSc & MD, PhD
1991-1997	Yonsei University, College of Medicine	MD

» Research Interests

Diabetes Mellitus, Cardiovascular complications, Biomarkers, Adipose tissue biology and multiomics, adipokines

» Honors & Awards

- 2015 Korean Endocrinology Society, Research Award
- 2009 Seoul National University, Excellent research award

» Publications

1. Lee JE, Oh TJ, Moon JH, Park KS, Jang HC, **Choi SH**. Serum neopterin concentration and impaired glucose metabolism: relationships with beta cell function and insulin resistance. Front. Endocrinol. Feb 29th, 2019
2. Kim BR, Lee GY, Yu H, Maeng HJ, Oh TJ, Kim KM, Moon JH, Lim S, Jang HC, **Choi SH**. Suppression of Nrf2 attenuates adipogenesis and decreases FGF21 expression through PPAR gamma in 3T3-L1 cells. Biochem Biophys Res Commun 2018 Mar 18:497(4) 1149-1153
3. Kim JH, Lim S, Park KS, Jang HC, **Choi SH**. Total and differential WBC counts are related with coronary artery atherosclerosis and increase the risk for cardiovascular disease in Koreans. PLoS One 2017 July 28:12(7)
4. Oh TJ, Ahn CH, Kim BR, Kim KM, Moon JH, Lim S, Park KS, Lim C, Jang HC, **Choi SH**. Circulating sortilin level as potential biomarker for coronary atherosclerosis and diabetes mellitus. Cardiovasc Diabetol 2017 16 (1):92
5. Moon JH, Roh E, Oh TJ, Kim KM, Moon JH, Lim S, Jang HC, **Choi SH**. Increased risk of metabolic disorders in healthy young adults with family history of diabetes from the Korea National Health and Nutrition Survey. Diabetes Metab Syndr 2017 Mar 1:9:16
6. Khang AR, Song YS, Kim KM, Moon JH, Lim S, Park KS, Jang HC, **Choi SH**. Comparison of different statin therapy to change LDL cholesterol and HDL cholesterol in Korean patietns with and without diabetes, J Clin Lipidol 2016. May 10(3):528-537
7. Hong ES, Lim C, Choi HY, Ku EJ, Kim KM, Moon JH, Lim S, Park KS, Jang HC, **Choi SH**. The amount of C1q-adiponectin complex is higher in the serum and the complex localizes to perivascular areas of fat tissues and the intimal-medial layer of blood vessels of coronary artery disease patients. Cardiovasc Diabetol. 2015 May: 14:50.

Abstract

CURRENT STATUS OF DRUGS FOR RAISING HDL-CHOLESTEROL

SUNG HEE CHOI

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Many attempts have been made to enhance HDL levels based on the belief that raising HDLcholesterol would have beneficial effect on decreasing atherosclerotic cardiovascular diseases. However, there seems a big gap between ideal theory and realtiy regarding to HDL-cholesterol and many drug trials could not result in fancy results.

In this talk, I want to discuss the past and current drugs targeting HDL-cholesterol, its mechanisms and results of CVD outcome trials.

Keywords
HDL-cholesterol, Apo A1, CETP inhibitor

Symposium 16

Hayato Tada

Organization

Kanazawa University

Position & Title

Assistant Professor, Department of Cardiology, Kanazawa University Graduate School of Medicine

» Educational Background & Professional Experience

Year	Name of institution	Position
2014-	Kanazawa University, Japan	Assistant Professor
2012-2014	Massachusetts General Hospital, USA	Research Scholar
2011-	Kanazawa University, Japan	Assistant Professor
2003-	Kanazawa University, Japan	Medical Staff

» Research Interests

Cardiovascular Genetics, Lipid Metabolism

» Honors & Awards

- Japanese Circulation Society Young Investigator's Award (1st Prize)
- 2017 Japanese College of Cardiology Young Investigator's Award (2nd Prize)
- 2018 Kanazawa Medical Association, Kanazawa Memorial Award

» Publications

1. Peloso GM, Tada H, et al. Rare Protein-Truncating Variants in APOB, Lower Low-Density Lipoprotein Cholesterol, and Protection Against Coronary Heart Disease. Circ Genom Precis Med. 2019 May;12(5):e002376
2. Tada H, et al. Oligogenic familial hypercholesterolemia, LDL cholesterol, and coronary artery disease. J Clin Lipidol. 2018 Nov - Dec;12(6):1436-1444
3. Turcot V, Tada H, et al. Protein-altering variants associated with body mass index implicate pathways that control energy intake and expenditure in obesity. Nat Genet. 2018 Jan;50(1):26-41
4. Liu DJ, Tada H, et al. Exome-wide association study of plasma lipids in >300,000 individuals. Nat Genet. 2017 Dec;49(12):1758-1766
5. Tada H, et al. Impact of clinical signs and genetic diagnosis of familial hypercholesterolaemia on the prevalence of coronary artery disease in patients with severe hypercholesterolaemia. Eur Heart J. 2017 May 21;38(20):1573-1579
6. Tada H, et al. Risk prediction by genetic risk scores for coronary heart disease is independent of self-reported family history. Eur Heart J. 2016 Feb 7;37(6):561-7
7. Tada H, et al. Twelve-single nucleotide polymorphism genetic risk score identifies individuals at increased risk for future atrial fibrillation and stroke. Stroke. 2014 Oct;45(10):2856-2862

Abstract

DEBATES IN THE CAUSAL ASSOCIATION BETWEEN HDL CHOLESTROL AND CV RISK: VIEW POINT FROM RCT AND GENETIC STUDIES

Hayato Tada[1]*, Akihiro Nomura[1], Masayuki Takamura[1] and Masa-aki Kawashiri[1]

[1] Department of Cardiology, Kanazawa University Graduate School of Medicine, Kanazawa, Japan
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We have long believed that HDL cholesterol is “good” cholesterol. However, failures in recent randomized controlled trials aimed to raise HDL cholesterol as well as findings from Mendelian randomization studies have cast a doubt on its “goodness”. Our group has been investigating the associations between blood lipids and cardiovascular (CV) risk among the patients with Mendelian genetic lipid disorders, including familial hypercholesterolemia (FH), sitosterolemia (STL), autosomal recessive hypercholesterolemia (ARH), familial hypobetalipoproteinemia (FHBL), abetalipoproteinemia (ABL), familial hyperchylomicronemia, such as lipoprotein lipase (LPL) deficiency, cholesteryl ester transfer protein (CETP) deficiency, and Tangier disease. Our group has also contributed to Mendelian randomization studies aimed to see the causal association between lipids and CV risk. Those studies have consistently showed us several important facts. 1) genetic variants and diseases associated with LDL cholesterol were associated with CV risk. 2) genetic variants and diseases associated with triglycerides were associated with CV risk. 3) genetic variants and diseases associated with HDL cholesterol were NOT associated with CV risk. On the other hand, we have found that extremely low HDL cholesterol level was significantly associated with several types of fatal situations, including malignancy, and bleeding, not necessarily with CV death. Those observations could lead us to rethink HDL cholesterol as a pure biomarker, not as a causal factor, which we want to increase or decrease. However, functions in HDL particle, such as cholesterol efflux seems to be causally associated with CV risk. Accordingly, we may also need to establish an universal measurement not to quantify, but to qualify our HDL particle.

Keywords
HDL cholesterol; LDL cholesterol; Triglycerides; Cardiovascular genetics

ICoLA 2019 by KSoLA

Symposium 17

Chairpersons

Hyojee Joung | Seoul National University, Korea
Kazumasa Yamagishi | University of Tsukuba, Japan

Date & Time: September 7 (Sat.), 09:40-11:10
Place: Room 3 (3F)

Symposium 17

Eunmi Park

Organization

Department of Food and Nutrition, Hannam University

Position & Title

Associate professor & Ph.D.

» Educational Background & Professional Experience

Year	Name of institution	Position
2017-Present	Hannam University, Korea	Associate Professor
2014-2016	Hannam University, Korea	Assistant Professor
2008-2014	Harvard Medical School, USA	Postdoc Fellow
2002-2008	University of Texas at Austin, USA	Ph.D
1998-2000	Seoul National University, Korea	M.S.
1993-1997	Yong-In University, Korea	B.S.

» Research Interests

A field of Vitamin D and DNA repair pathway in metabolic syndrome

» Honors & Awards

- 2010 Susan G. Komen Breast Cancer Foundation – Postdoc Fellowship, USA
- 2013 Claudia Adams Barr Award, USA
- 2016 Korean Nutrition Society, Academic Award, Korea

» Publications

1. Multivitamin and mineral supplementation containing phytonutrients scavenges reactive oxygen species in healthy subjects: a randomized, double-blinded, placebo-controlled trial(S. Kang et al, Nutrients, 2019)
2. Curcumin enhances poly (ADP-ribose) polymerase inhibitor sensitivity to chemotherapy in breast cancer cells (Y. Choi and E. Park, JNB, 2015)
3. FANCD2 activates transcription of TAp63 and suppresses tumorigenesis (E. Park et al., Mol Cell, 2013)
4. MicroRNAs down-regulate homologous recombination in the G1 phase of cycling cells to maintain genomic stability (Y. Choi et al.,E-life, 2014).
5. Inactivation of UAF1 causes homologous recombination defects and early embryonic lethality in mice (E. Park et al., MCB, 2013)
6. IKKalpha is required to maintain skin homeostasis and prevent skin cancer(B. Liu et al., Cancer Cell, 2008)
7. Reduction in I kappa B kinase alpha expression promotes the development of skin papillomas and carcinomas(E. Park et al., Cancer Research 2007)

Abstract

BRIDGING A ROLE OF VITAMIN D AND METABOLOMICS IN DYSLIPIDEMIA

Eunmi PARK

Department of Food and Nutrition, Hannam University, Korea
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Lack of DNA repair pathway is characterized by an increased susceptibility to metabolic syndrome and cancers. Recently, several studies reported that obese person have a mutation or polymorphism of DNA repair gene in cell signal pathway. Interestingly, 25(OH)D levels of vitamin D are typically lower in obese individuals who are more likely to develop diabetes mellitus and metabolic syndrome. How DNA repair pathway prevents metabolic disease and a regulation of the vitamin D level affects to obesity are still unknown. Our laboratory mainly focuses on finding a new role of vitamin D regarding to metabolic syndrome using a vitamin D knock-out mouse system and clinical human study. In this presentation, we report Korean submariners study in obese group (≥25.0kg/m²) and normal group (18.5~22.9kg/m²) with an intake of vitamin D supplementation or placebo on a double-blind study. Subjects of each group were fifteen people and sixteen, respectively. The study was to collect and analysis data of Korean submariner's plasma vitamin D levels, metabolic syndrome status, metabolomics. We assessed the plasma vitamin D levels of subjects in collected their blood lipid profiling, dietary record, physical activity and metabolomics data in two group. We hope this study provides some basis evidence of a role of vitamin D on obesity and metabolic syndrome.

Keywords
Vitamin D, Dyslipidemia, Obesity, DNA repair pathway, Metabolomics

Symposium 17

Manohar Garg

Organization

University of Newcastle

Position & Title

Professor & Director, Nutraceuticals Research Program

» Educational Background & Professional Experience

Year	Name of institution	Position
2007-Present	University of Newcastle, Australia	Professor
2001-2007	University of Newcastle, Australia	Associate Professor
1995-2001	University of Newcastle, Australia	Senior Lecturer
1993-1995	University of Newcastle, Australia	Lecturer
1988-1993	University of Alberta, Canada	Assistant Professor

» Research Interests

Dietary supplements, functional foods, nutraceuticals, dyslipidaemias, inflammation, cardiovascular health, type 2 diabetes, dietary fats

» Honors & Awards

- 2007-2013 President of the Nutrition Society of Australia (NSA)
- 2014 Excellence in Innovation Award by the Newcastle Innovation Pty Ltd
- 2012 ISH Professor Austin Doyle Medal for Research Excellence in prevention of Cardiovascular Complications

» Publications

1. J.J.A. Ferguson, A. Wolskab, A.T. Remaley, E. Stojanovskic, L. MacDonald-Wicks and **M.L. Garg** (2019) Bread enriched with phytosterols with or without curcumin modulates lipoprotein profile in hypercholesterolaemic individuals. A randomised controlled trial. Food & Function 10, 2515 - 2527.
2. N. Panth, C.B. Dias, K. Wynne, H. Singh, **M.L. Garg** (2019) Medium-chain fatty acids lower postprandial lipemia: a randomized crossover trial. Clinical Nutrition https://doi.org/10.1016/j.clnu.2019.02.008.
3. N.A. Kalagi, K.A. Abbott, K.A. Alburikan, H.A. Alkofide, E. Stojanovsky and **M.L. Garg** (2019) Modulation of circulating trimethylamine N-oxide concentrations by dietary supplements and pharmacological agents: A systematic review. Advances in Nutrition nmz012, https://doi.org/10.1093/advances/nmz012.
4. C.B. Dias, X. Zhu, A.K. Thompson, H. Singh and **M.L. Garg** (2019) Effect of food form and structure on lipid digestion and postprandial lipaemic response. Food & Function 10, 112-124.
5. R.N. Thota, C.B. Dias K.A. Abbott, S.H. Acharya and **M.L. Garg** (2018) Curcumin alleviates postprandial glycaemic response in healthy subjects: A cross-over RCT. Scientific Reports 8:13679, DOI:10.1038/s41598-018-32032-x.
6. N. Panth, K.A. Abbott, C.B. Dias, K. Wynne and **M.L. Garg** (2018) Differential effects of medium and long-chain saturated fatty acids on blood lipid profile: a systematic review and meta-analysis. American Journal of Clinical Nutrition 108, 675-687.
7. J.J. Ferguson, E. Stojanovski, L. MacDonald-Wicks and **M.L. Garg** (2018) Curcumin potentiates cholesterol-lowering effects of phytosterols in hypercholesterolaemic individuals. A randomised controlled trial. Metabolism: Clinical & Experimental 82, 22-35.

Abstract

ANTI-INFLAMMTAORY AND LIPID-LOWERING DIETARY SUPPLEMENTS FOR REDUCING THE RISK OF CARDIOVASCULAR DISEASE

Manohar GARG

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manohar.garg@newcastle.edu.au

For the past 3-4 decades, the focus of public health strategies for reducing the risk of cardiovascular disease (CVD) have been aimed at lowering blood cholesterol levels. However recent findings have highlighted that not only cholesterol but also circulating triglycerides are a risk factor for CVD. In addition, elevated inflammation has emerged to be a major risk factor for the development of coronary heart disease. A suite of diet and lifestyle changes are used for the management of dyslipidaemia and have been shown to modestly lower LDL-C. Long-term compliance, complexity of adopted diet/lifestyle changes, poor motivation, lack of clinical follow-up and food aversions can impede the ability to achieve and sustain target blood lipid levels. Subsequently, pharmacological interventions are often indicated, however, cost, adverse health effects and intolerance, lack of effectiveness, patient perceived concern of long-term side effects and complex drug regimens are barriers for long-term compliance. Consequently, nutraceuticals such as phytosterols, soluble fibres and other bioactives have been recognised as adjunct and/or alternative lipid-modulating therapies for optimising dyslipidaemia. Dietary strategies to reduce not only circulating lipid levels, but also those lowering inflammation and/or increasing resolution of inflammation are desirable and are currently being sought, which may be able to offer long-term safe and efficacious comparable with effective drug treatments. Human intervention studies involving a combination of lipid-lowering and anti-inflammatory nutraceuticals have provided evidence for favourable health outcomes and is paving way for the development of functional foods fortified with healthful bioactive compounds.

Keywords
Dietary supplements, functional foods, nutraceuticals, dyslipidaemia, inflammation, cardiovascular health

Symposium 17

Hyunjung Lim

Organization

Department of Medical Nutrition, Kyung Hee University

Position & Title

Associate Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2017-Present	Department of Medical Nutrition, Kyung Hee University, Korea	Associate Professor
2013-2017	Department of Medical Nutrition, Kyung Hee University, Korea	Assistant Professor
2016-2018	The Korean Society of Clinical Nutrition, Korea	General directorate
2015-Present	Research Institute of Medical Nutrition Kyung Hee University, Korea	Director
2010-2013	Johns Hopkins University, USA	Post-doctoral fellow
2002-2009	Medical Nutrition, Kyung Hee University, Korea	MS., Ph.D.
1998-2002	Food and Nutrition, Kyung Hee University, Korea	BS

» Research Interests

- Relationship among nutritional status, dietary quality, and quality of life in patients with chronic or degenerative diseases
- Effect of medical nutrition therapy for diet-related disease patients

» Honors & Awards

· 2018 27th Academic grand award. The Korean Dietetic Association
· 2018 Best Presentation Award, The Korean Nutrition Society

» Publications

1. **Lim H**, Lee HJ, Wang Y, Choue R. Trends in fast-food and sugar-sweetened beverage consumption and their association with social environmental status in South Korea. J Acad Nutr Diet 2018;118:1228-1236.
2. Seo YG, Kim JH, Kim Y, **Lim H**, Ju YS, Kang MJ, Lee K, Lee HJ, Jang HB, Park SI, Park KH. Validation of body composition using bioelectrical impedance analysis in children according to the degree of obesity. Scand J Med Sci Sports 2018; doi: 10.1111/sms.13248.
3. Min J, Kim G, **Lim H**, Carvajal NA, Lloyd CW, Wang Y. A kindergarten-based child health promotion program: the Adapted National Aeronautics and Space Administration (NASA) Mission X for improving physical fitness in South Korea. Glob Health Promot 2018; doi: 10.1177/1757975918760517.
4. Kim DY, Kim SH, **Lim H**. Association between Dietary Carbohydrate Quality and Prevalence of Obesity and Hypertension. J Hum Nutr Diet 2018:31(5):587-596.
5. Kim DY, Kim CO, **Lim H**. Associations of diet quality and physical performance with inflammatory markers in community-dwelling frail, elderly people. Nutrition 2017;38:48–53.
6. Kwon HN, **Lim H**. Relationship between Serum Vitamin D Status and Metabolic Risk Factors among Korean Adults with Prediabetes. PLoS One 2016:26;11(10):e0165324.
7. Lee H, Kim H, Choue R, **Lim H**. Evaluation of the Effects of Pinus koraiensis Needle Extracts on Serum Lipid and Oxidative Stress in Adults with Borderline Dyslipidemia: A Randomized, Double-Blind, and Placebo-Controlled Clinical Trial. Evid Based Complement Alternat Med 2016:9594251.

Abstract

DIETARY SUPPLEMENTS FOR PREVENTING CARDIOMETABOLIC RISK IN KOREAN

Hyunjung LIM

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In South Korea, the mortality rate from cardiovascular/cardiometabolic disease has continuously increased from 2.3 persons in 1983 to 16.2 persons in 1998 and reached to 25.1 persons in 2012 per 10 million person. The cardiometabolic risk describes a person's chances of damaging heart and blood vessels when one or more risk factors are present. Therefore, efforts continue to be made to prevent the development of the disease by reducing the associated risk factors such as high blood lipids, high blood pressure, hyperglycemia, and others. Although cadiometabolic disease and diet/nutrition are closely connected, dietary modification for prevention and management of chronic disease is not easy. So, dietary supplements or functional foods are widely used for preventing cardiometabolic risks. However, the effectiveness on metabolic and cardiovascular effects are still controversial. These controversial results in experimental studies with animal model can be explained by handling with different methods of preparation and extraction, dose, and materials. In addition, it is hard to find clinical efficacy trials in human and besides it has seldom been examined the effect of dietary supplements depending on sex, age, underlying medical conditions, ethnicity and others. In South Korea, many researchers, institute, or company have been conducted clinical trials to prove the effect of reducing body fat, lowering blood sugar, lowering blood pressure, improving blood lipids, improving blood circulation, antioxidant. This phase is essential to be approved as a health functional food by the Ministry of Food and Drug Safety in Korea. First of all, healthy and well-balanced diet should be prioritized. Dietary supplements should take appropriately with proven safe and effective materials based on well-designed clinical studies. This seminar will introduce and discuss some previous clinical trials of the effects of dietary supplements applied to Koreans to prevent cardiometabolic risks.

Keywords
Cardiometabolic risk, dietary supplement, clinical trial, functional food, Korean

ICoLA 2019 by KSoLA

Symposium 18

Chairpersons

Jaetaek Kim | Chung-Ang University, Korea
Gary Sweeney | York University, Canada

Date & Time: September 7 (Sat.), 09:40-11:10
Place: Room 4 (5F)

Symposium 18

Scott Summers

Organization

University of Utah

Position & Title

Professor and Chair of Nutrition & Integrative Physiology

» Educational Background & Professional Experience

Year	Name of institution	Position
2004-2008 2016-Present	University of Utah, Salt Lake City, UT	· Professor and Chair · Co-Director · Associate Investigator, · Adjunct Faculty Member · Associate Professor
2015-2016	Baker IDI Heart and Diabetes Institute, Melbourne, Australia	· Head, Translational Metabolic Health Laboratory, 2/1/15-8/1/16 · Head, Metabolism and Inflammation Program, 2/1/15-8/1/16
2008-2015	Duke University, Durham, NC and the Duke-NUS Graduate Medical School, Singapore	· Associate Professor, Program in Cardiovascular and Metabolic Diseases, Duke-NUS, 11/1/08-9/30/14 · Associate Professor, Department of Medicine, Duke University, 11/1/08-6/30/15
1999-2004	Colorado State University, Fort Collins, CO	· Associate Professor, Department of Biochemistry and Molecular Biology, 7/1/04-7/30/04 · Assistant Professor, Department of Biochemistry and Molecular Biology, 7/99-6/30/03
1995-1999	University of Pennsylvania, Philadelphia, PA	· Post-Doctoral Research Associate, Howard Hughes Medical Institute, 8/95-6/99

» Research Interests

Investigating the Therapeutic Potential of Ceramide-Reduction Interventions

Our early work utilized cultured cell systems to probe the mechanisms through which ectopic fats influence insulin sensitivity. Using various strategies to modulate rates of sphingolipid synthesis or degradation in cultured cells, we demonstrated that ceramide was a key intermediate linking saturated fatty acids to the antagonism of insulin action. We later demonstrated that inhibition of ceramide biosynthesis improved insulin sensitivity and prevented diabetes in rodent models of the condition. This work, which has been cited over 800 times, defined a paradigm that has been repeated by us and others in studies on cardiomyopathy, hepatic steatosis, vascular dysfunction, etc. The relevance of ceramide was later evaluated using various drug candidates, confirming the potential of ceramide reduction intervention as a therapeutic strategy.

» Publications

1. Targeting a Ceramide Double Bond Improves Insulin Resistance and Hepatic Steatosis. Science 2019
2. Conditional deletion of Des1 in the mouse retina does not impair the visual cycle in cones. FASEB J. 33(4), 5782-5792 2019
3. Ablation of autophagy machinery in mature adipocytes induces insulin resistance and reveals new roles for lipid peroxides and Nrf2 signaling in adipose-liver crosstalk. Cell Reports 25(7), 1708-1717 2018
4. Plasma Ceramides as Prognostic Biomarkers and Their Arterial and Myocardial Tissue Correlates in Acute Myocardial Infarction. JACC Basic and Translational Science 3(2), 163-175 2018
5. The Ceramide Ratio: A Predictor of Cardiometabolic Risk. Journal of Lipid Research 59(9), 1549-1550 2018
6. Strong Heart, Low Ceramides. Diabetes 67(8), 1457-1460 2018

Abstract

TARGETING A DOUBLE BOND IN CERAMIDES TO TREAT METABOLIC DISEASE

Scott A. Summers

Department of Nutrition and Integrative Physiology, University of Utah, Salt Lake City, UT USA
Scott.a.Summers@healt.utah.edu

Overnutrition and physical inactivity promote the accumulation of fat-derived molecules in tissues not suited for lipid storage, leading to tissue dysfunction that underlies diabetes and cardiovascular disease. Of the myriad of lipids that accumulate, sphingolipids such as ceramides may be amongst the most deleterious, as they antagonize insulin-stimulated glucose disposal and mitochondrial lipid oxidation. Inhibition of ceramide biosynthesis in rodents ameliorates insulin resistance, hypertriglyceridemia, type 2 diabetes, cardiomyopathy, atherosclerosis, and steatohepatitis. Owing to a strong association of certain serum ceramides with insulin resistance and major adverse cardiovascular events, the Mayo Clinic is now marketing tests to measure circulating ceramides as markers of cardiovascular mortality resulting from metabolic disease. The author will discuss the development of a new therapeutic strategy to lower ceramides and combat these metabolic disorders.

Symposium 18

Toshiro Okazaki

Organization

Ishikawa Prefectural University

Position & Title

Professor

Research Institute for Bioresources and Biotechnology

Ishikawa Prefectural University

» Educational Background & Professional Experience

Year	Name of institution	Position
1983-1987	Department of Hematology/Oncology, Graduate School of Medicine, Kyoto University, Kyoto, Japan	Graduate student
1997-2004	Department of Hematology/Oncology, Kyoto University, Kyoto, Japan	Assistant Professor and Associate Professor
2005-2011	Department of Hematology/Oncology, Tottori University, Yonago, Japan	Professor
2011-2019	Department of Hematology/Immunology, Kanazawa Medical University, Kanazawa, Japan	Professor
2019-	Research Institute for Bioresources and Biotechnology, Ishikawa Prefectural University	Professor

» Research Interests

Role of sphingolipids in diseases

» Honors & Awards

- 2006 Leukemia Research foundation Award
- 2007 Research Fellowship, Uehara Memorial Foundation
- 2012-16 Takeda Special Research Fund

» Publications

1. Takuji Nakamura, Tomomi Satoh-Nakamura, Akio Nakajima, Takafumi Kawanami, Tomoyuki Sakai, Yoshimasa Fujita, Haruka Iwao, Miyuki Miki, Yasufumi Masaki, Toshiro Okazaki, Yasuhito Ishigaki, Mitsuhiro Kawano, Kazunori Yamada, Shoko Matsui, Takako Saeki, Terumi Kamisawa, Motohisa Yamamoto, Hideaki Hamano, Tomoki Origuchi, Shintaro Hirata, Yoshiya Tanaka, Hiroto Tsuboi, Takayuki Sumida, Kazuichi Okazaki, Masao Tanaka, Tsutomu Chiba, Tsuneyo Mimori & Hisanori Umehara Impaired expression of innate immunity-related genes in IgG4-related disease: A possible mechanism in the pathogenesis of IgG4-RD. MODERN RHEUMATOLOGY https://doi.org/10.1080/14397595.2019.1621475
2. Takuji Nakamura, Tomomi Satoh-Nakamura, Akio Nakajima, Takafumi Kawanami, Tomoyuki Sakai, Yoshimasa Fujita, Haruka Iwao, Miyuki Miki, Yasufumi Masaki, Toshiro Okazaki, Yasuhito Ishigaki, Mitsuhiro Kawano, Kazunori Yamada, Shoko Matsui, Takako Saeki, Terumi Kamisawa, Motohisa Yamamoto, Hideaki Hamano, Tomoki Origuchi, Shintaro Hirata, Yoshiya Tanaka, Hiroto Tsuboi, Takayuki Sumida, Kazuichi Okazaki, Masao Tanaka, Tsutomu Chiba, Tsuneyo Mimori & Hisanori Umehara Impaired expression of innate immunity-related genes in IgG4-related disease: A possible mechanism in the pathogenesis of IgG4-RD. MODERN RHEUMATOLOGY https://doi.org/10.1080/14397595.2019.1621475
3. Kaoru Toshima, Masakazu Nagafuku, Toshiro Okazaki, Toshihide Kobayashi and Jin-ichi Inokuchi Plasma membrane sphingomyelin modulates thymocyte development by inhibiting TCR-induced apoptosis International Immunology doi:10.1093/intimm/dxy082, 2019
4. Hisatoshi Hanamatsu, Susumu Mitsutake, Shota Sakai, **Toshiro Okazaki**, Ken Watanabe, Yasuyuki Igarashi and Kohei Yuyama. Multiple roles of Sms2 in white and brown adipose tissues from diet-induced obese mice. ***Journal of Metabolic Syndrome*** OI:10.4172/2167-0943.1000241, 2018
5. Go Matsumoto, **Toshiro Okazaki** et al. The important roles played by the Sphingomyelin Synthases in osteoblast differentiation and bone development. ***JBMR Plus*** in submit, 2018
6. Hisatoshi Hanamatsu, Susumu Mitsutake, Shota Sakai, Toshiro Okazaki, Ken Watanabe, Yasuyuki Igarashi and Kohei Yuyama. Multiple roles of Sms2 in white and brown adipose tissues from diet-induced obese mice. Journal of Metabolic Syndrome OI:10.4172/2167-0943.1000241, 2018
7. Go Matsumoto, Toshiro Okazaki et al. The important roles played by the Sphingomyelin Synthases in osteoblast differentiation and bone development. JBMR Plus in submit, 2018

Abstract

INHIBITION OF INFLAMMATION AND TUMOR PROGRESSION IN MOUSE MODEL BY SMS2 DEFICIENCY

Toshiro Okazaki[1]*, Makoto Taniguchi[2] and Chieko Hashizume[2]

[1] Ishikawa Prefectural University
[2] Kanazawa Medical University
t_okazaki@ishikawa-pu.ac.jp

Sphingomyelin (SM) synthase is a key enzyme to generate SM and diacylglycerol by converting phosphocholine of phosphatidylcholine to ceramide. SM synthase (SMS) genes consist of three homologs, SMS1, SMS2 and SMSr. SMS1 acts as a homeostatic enzyme to maintain the level of SM in the membrane, whereas SMS2 seems to work when the SM level in the membrane was changed by a diverse stresses such as inductions of apoptosis and autophagy-related cell death. We established SMS2-deficient mouse embryonic fibroblasts (MEF) and conventional SMS2-KO mouse. SMS1-deficient MEF did not grow well, but SMS2-deficient MEF can grow similar to wild type MEF. SMS1 increases SM content, and SMS2 also increases SM but the level is lower than SMS1 does. In addition interestingly SMS2 can increase glucosylceramide content in MEFs. As compared to SMS1-KO mouse SMS2-KO mouse looks normal in terms of ordinary phenotypes.

Dextran sodium sulfate (DSS)-induced mouse acute colitis model has been used to investigate the mechanism of inflammation in colon and by addition of azoxymethane (AOM) adenomatous colon tumor is produced in mice. In SMS2-KO mice DSS-induced colitis was inhibited by increasing of ceramide/SM balance, which suppressed the expression of inflammatory cytokines such as IL-6 and TNFα and the recruitment of T lymphocytes to the inflammatory lesions. In addition DSS/AOM-induced polypoid tumors was also inhibited in SMS2-KO mice. Next we examined the effect of SMS2-deficiency in progression of T lymphoma (EL4)-xenograft model. EL4 cell growth was inhibited and overall survival time was prolonged in SMS2-KO mice. Then we investigated the mechanism of tumor inhibition by SMS2-deficient condition and found that the infiltration of host T cells into tumor-microenvironment was suppressed because of increase of ceramide in TIL (tumor-infiltrating lymphocytes) and decrease of SM.

Keywords
Sphingolipids, sphingomyelin synthase, inflammation and cancer

Symposium 18

Mee-Sup Yoon

Organization

College of Medicine, Gachon University

Position & Title

Assistant Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2014.9-	College of Medicine, Gachon University	Assistant Professor
2014.1-2014.8	Department of Cell and Developmental Biology, University of Illinois at Urbana-Champaign, USA	Research Assistant Professor
2011-2013	Department of Cell and Developmental Biology, University of Illinois at Urbana-Champaign, USA	Research scientist
2006-2011	Department of Cell and Developmental Biology, University of Illinois at Urbana-Champaign, USA	Post-doctoral researcher
2004-2006	College of Medicine, Hanyang University, Korea	Post-doctoral researcher
2001-2004	College of Medicine, Hanyang University, Korea	Ph.D

» Research Interests

The role of phosphatidic acid in mTOR signaling

» Publications

1. Kook S, You JS, **Yoon MS**, Dai C, Kim JH, Khanna N, Banerjee A, Martinis S, Han GH, Han JM, Kim SH, Chen J (2019) Nontranslational function of leucyl-tRNA synthetase regulates myogenic differentiation and skeletal muscle regeneration, The Journal of Clinical Investigation 10.1172/JCI122560
2. Baek MO, Song HI, Han JS, **Yoon MS** (2018) Differential regulation of mTORC1 and mTORC2 is critical for 8-Br-cAMP-induced decidualization. Exp Mol Med 50:141.
3. Kim IJ, Lee J, Oh SJ, **Yoon MS**, Jang SS, Holland RL, Reno ML, Hamad MN, Maeda T, Chung HJ, Chen J, Blanke, SR (2018) Helicobacter pylori infection modulates host cell metabolism through VacA-dependent inhibition of mTORC1, Cell Host & Microbe, 2018 May 9;23(5):583-593
4. Hur JH, Park SY, Dall'Armi C, Lee JS, Di Paolo G, Lee HY, **Yoon MS***, Min DS*, Choi CS*(2016) Phospholipase D1 deficiency in mice causes nonalcoholic fatty liver disease via an autophagy defect. Scientific reports 6: 39170 (*Co-corresponding author)
5. Song HI, **Yoon MS** (2016) PLD1 regulates adipogenic differentiation through mTOR - IRS-1 phosphorylation at serine 636/639. Scientific reports 6: 36968
6. Lee SY, Lee YY, Choi JS, **Yoon MS***, Han JS*(2016) Phosphatidic acid induces decidualization by stimulating Akt-PP2A binding in human endometrial stromal cells. FEBS Journal 283: 4163–4175. doi:10.1111/febs.13914 (*Co-corresponding author)
7. **Yoon MS***, Son K, Arauz E, Han JM, Kim SH, Chen J * (2016) Leucyl-tRNA synthetase activates Vps34 in amino acid-sensing mTORC1 signaling. Cell Reports 16, 1510–1517 (*Co-corresponding author)
8. **Yoon MS***, Rosenberger C, Wu C, Truong N, Sweedler JV, Chen J* (2015) Rapid Mitogenic Regulation of the mTORC1 Inhibitor, DEPTOR, by Phosphatidic Acid. Molecular Cell, 58, 549–556 **(*Co-corresponding author; selected for the cover image and the author in "meet the author"; recommended in F1000Prime as being of special significance in its field**

Abstract

THE ROLE OF PHOSPHOLIPASE D1/PHOSPHATIDIC ACID IN AMINO ACID-SENSING MTORC1 SIGNALING

Mee-Sup Yoon

Department of Molecular Medicine, School of Medicine, Gachon University, Republic of Korea
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Phospholipase D1 catalyzes the hydrolysis of phosphatidylcholine (PC) to phosphatidic acid (PA), which serves as a second messenger to regulate a range of signaling proteins. PLD1-produced PA binds with high affinity to the FKBP12 rapamycin binding domain (FRB) domain of the mammalian target of rapamycin (mTOR), a master regulator of cell growth. We identified a role for PLD1 in amino acid sensing pathway. Amino acid availability activates signaling by mTORC1. The class III PI-3-kinase Vps34 mediates amino acid signaling to mTORC1 by regulating lysosomal translocation and activation of the phospholipase PLD1. In addition, leucyl-tRNA synthetase (LRS) as a leucine sensor for the activation of Vps34-PLD1 upstream of mTORC1. LRS physically interacts with Vps34 in amino acid-stimulatable non-autophagic complexes. The UNE-L domain of LRS c-terminal is required for the non-canonical function of LRS in activating Vps34-PLD-mTORC1 signaling. Collectively, our findings provide compelling evidence that PLD/PA plays a in amino acid activation of mTORC1 via a non-canonical mechanism of LRS.

Keywords
Phosphatidic acid, Phospholipase D1, mTOR, amino acids

Symposium 18

Seyun Kim

Organization

KAIST

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2018-Present	KAIST	Associate Professor
2012-2017	KAIST	Assistant Professor
2007-2011	Johns Hopkins University, School of Medicine	Postdoctoral Fellow
2000-2001	Seoul National University	Research Fellow

» Research Interests

1. Dissecting signaling actions of inositol polyphosphate multikinase & IP metabolism
2. Identifying novel mechanisms of how inositol pyrophosphates regulates cellular signaling
3. Elucidating the biological significance of metabolite-protein interactions

» Honors & Awards

- Harold M. Weintraub Award (Fred Hutchinson Cancer Research Center, USA)
- Martin & Carol Macht Award (2007 Johns Hopkins Young Investigators'
- Award, Johns Hopkins University, School of Medicine, USA)
- Predoctoral Travel Award (American Society for Cell Biology, USA)

» Publications

1. Park, J., Park, S.J., Kim, S. Inositol polyphosphate multikinase deficiency leads to aberrant induction of synaptotagmin-2 in the forebrain. Molecular Brain(accepted)
2. Park, J., Longo, F., Park, S.J., Lee, S., Bae, M., Tyagi, R., Han, J.H., **Kim, S.**[+], Santini, E.[+], Klann, E.+, Snyder, S.H.[+] Inositol polyphosphate multikinase mediates extinction of fear memory. **Proc. Natl. Acad. Sci. USA**. 116(7):2707-2712. (+co-corresponding authors)
3. Park, S.J., Lee, S., Park, S.E., Kim, S. (2018) Inositol pyrophosphates as multifaceted metabolites in the regulation of mammalian signaling networks. Animal Cells and Systems 22(1)1-6. (invited review article)
4. Kim, E., Beon, J., Lee, S., Park, S.J., Ahn, H., Kim, M.G., Park, J.E., Kim, W., Yuk, J.M., Kang, S.J., Lee, S.H., Jo, E.K., Seong, R.H.*, **Kim, S.*** (2017) Inositol polyphosphate multikinase promotes Toll-like receptor-stabilizing TRAF6. **Science Advances** 3(4) e1602296. (*co-corresponding authors)
5. Kim, E., Ahn, H., Kim, M.G., Lee, H., **Kim, S.** (2017) The expanding significance of inositol hub. **Molecules and Cells** 40(5):315-321. (invited review article)
6. Kim, D.E*., Jang, M.J.*, Kim, Y.R.*, Lee, J.Y., Cho, E.B., Kim, E., Kim, Y., Kim, M.Y., Jeong, W.I., Kim. S.[+], Han, Y.M.[+], Lee, S.H.[+] (2017) Prediction of drug-induced immune-mediated hepatotoxicity using hepatocyte-like cells derived from human embryonic stem cells. Toxicology 387:1-9. (*equally contributed to this work, +co-corresponding authors)
7. Ramazzotti, G., Billi, A.M., Manzoli, L., Mazzetti, C., Ruggeri, A., Erneux, C., Kim, S., Suh, P.G., Cocco, L., Faenza, I. (2016) IPMK and β-catenin mediate PLC-β1-dependent signaling in myogenic 7(51):84118-84127.

Abstract

REGULATORY ACTION OF INOSITOL PYROPHOSPHATE METABOLISM IN THE CONTROL OF SYNAPTIC VESICLE MEMBRANE CYCLING

Seyun Kim, Ph.D.

Dept. Biological Sciences, KAIST

Inositol is a naturally occurring glucose isomer and a key nutrient of the human diet. When levels of inositol are extremely low, disturbances such as diabetic changes, anxiety disorders, and hypercholesterolemia ensue. Inositol-derived metabolites (e.g., phosphoinositides and inositol polyphosphates) are key second messengers that are essential for controlling a wide range of cellular events such as growth and metabolic homeostasis. Inositol pyrophosphates such as 5-IP_7 (5-diphosphoinositol pentakisphosphate) are highly energetic inositol polyphosphates harboring phosphoanhydride bonds. While inositol pyrophosphates are known to regulate various physiologic events, including growth, the detailed modes of actions in cellular signaling networks have remained unclear. I will discuss our recent work demonstrating that 5-IP_7 acts through Synaptotagmin-1 (Syt1) binding to interfere with the fusogenic activity of Ca^{2+} in the control of vesicle membrane fusion. The data reveal a role of 5-IP_7 as a potent inhibitor of Syt1 in regulating the synaptic exocytotic pathway and expand our view on the signaling mechanisms of neuronal inositol pyrophosphates.

ICoLA 2019 by KSoLA

Symposium 19

Chairpersons

Duk-Kyung Kim | Sungkyunkwan University, Korea
Gerald F Watts | The University of Western Australia, Australia

Date & Time: September 7 (Sat.), 15:20-16:50
Place: Room 1 (3F)

Symposium 19

Brian A. Ference

Organization

University of Cambridge, UK

Position & Title

Professor

Abstract

SAFETY OF EXTREME LOW LDL FROM AN ANALYSIS OF FOURIER, SPIRE, AND THE CHOLESTEROL TREATMENT TRIALISTS COLLABORATION

Brian A. Ference

University of Cambridge, UK

Symposium 19

Dae Ho LEE

Organization

Gachon University Gil Medical Center

Position & Title

Professor

Research Planning Director

Clinical & Medical Research Center, Director

» Educational Background & Professional Experience

Year	Name of institution	Position
1984-1999	Chonnam National University Medical School	MD, PhD
1998-2000	Chonnam National University Hospital	Clinical & Research Fellow
2003-2013	Jeju National University Hospital	Associate Professor
2013-2016	Wonkwang University Hospital	Professor
2007-2009	Harvard Medical School, Division of Endocrinology & Metabolism	Visiting Scholar
2016-	Gachon University Gil Medical Center	Professor

» Research Interests

Diabetes, Insulin Resistance, NAFLD, Lipid metabolism

» Publications

1. Lee KY et al. Characterization of variable presentations of diabetic ketoacidosis based on blood ketone levels and major society diagnostic criteria: a new view point on the assessment of diabetic ketoacidosis. Diabetes Metab Syndr Obes (in press).
2. Park SJ et al. Urinary and Blood microRNA-126 and -770 are Potential Noninvasive Biomarker Candidates for Diabetic Nephropathy: A Meta-analysis. Cellular Physiology and Biochemistry 2018;46(4):1331-1340
3. Choi IS, et al. Angiotensin-Converting Enzyme Inhibitors Provide Better Long-Term Survival Benefits to Patients With AMI Than Angiotensin II Receptor Blockers After Survival Hospital Discharge. Journal of Cardiovascular Pharmacology and Therapeutics 2019; 24(2) 120-129
4. Cho JL, et al. Statin has more protective effects in AMI patients with higher plasma BNP or NT-proBNP level, but not with lower left ventricular ejection fraction. Journal of Cardiology 71 (2018) 375–381
5. Shin DS et al., Factors influencing insulin sensitivity during hyperinsulinemic-euglycemic clamp in healthy Korean male subjects. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2019, 12:469-476
6. Leem SS et al., SPARTA: Super-fast Permutation AppRoach To Approximate extremely low p-values. International Journal of Data Mining and Bioinformatics, 2018; 21(4), 352-364
7. Lamichhane S et al., ROS production and ERK activity are involved in the effects of D-beta-hydroxybutyrate and metformin in a glucose deficient condition. International Journal of Molecular Sciences. Int J Mol Sci. 2017 Mar 21;18(3).

Abstract

CHARACTERISTICS OF SUBJECTS WITH VERY LOW SERUM LOW-DENSITY LIPOPROTEIN CHOLESTEROL AND THE RISK FOR INTRACEREBRAL HEMORRHAGE

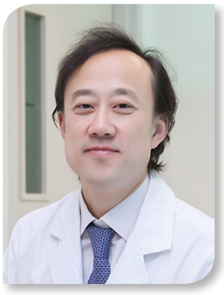
Dae Ho Lee

Department of Internal Medicine, Gachon University Gil Medical Center, Republic of Korea
drhormone@naver.com

Some clinical studies and meta-analyses including CTT have shown increased risk of intracerebral hemorrhage (ICH) with statin therapy. The Stroke Prevention with Aggressive Reductions in Cholesterol Levels (SPARCL) trial was a prospective, double-blind, RCT which showed that treatment with a high dose of atorvastatin (80 mg per day) resulted in a 16% reduction in the combined risk of fatal and nonfatal stroke in patients with a recent stroke or TIA and no known coronary heart disease, with unadjusted HR for hemorrhagic stroke was 1.68, 95% CI 1.09 to 2.59). Post hoc analysis of data from patients with prior cerebrovascular disease enrolled in the Heart Protection Study found a non-significant increase in hemorrhagic stroke in those treated with simvastatin 40 mg per day vs placebo. It is yet not clear why there is an increased risk of ICH in those who receive high dose of statins. Although some epidemiologic studies have found an association between low cholesterol levels and an increased risk of ICH, such a relationship has not been found in more recent clinical trials of statins given for CAD patients with a strategy of intensive reductions in LDL cholesterol. Elderly male patients with previous history of hemorrhagic stroke and patients with hypertension are at increased risk of ICH. Also an increased risk of hemorrhagic strokes was also observed in subjects with an investigator-designated small-vessel distribution stroke at entry, which requires further studies about this association. Currently, various modes of therapies are possible to lower LDL cholesterol level to a very low level than ever. This review aimed to discuss about whether very low LDL cholesterol level is associated an increased risk of ICH, under various clinical conditions and different modes of cholesterol-lowering therapies.

Keywords
Statin, Low-Density Lipoprotein Cholesterol, Intracerebral Hemorrhage

Symposium 19



Ki Hoon Han

Organization

University of Ulsan, Korea

Position & Title

Professor

Abstract

HYPERTRIGLYCERIDEMIA AND LOW LDL-C

Ki Hoon Han

University of Ulsan, Korea

Symposium 19

In-Kyung Jeong

Organization

Kyung Hee University
School of Medicine

Position & Title

Professor,
Department of
Endocrinology and
Metabolism
Kyung Hee University
Hospital at Gangdong

» Educational Background & Professional Experience

Year	Name of institution	Position
2015-Present	Kyung Hee University, Korea	Professor
2010-2014	Kyung Hee University, Korea	Associate Professor
2008-2009	Harvard University, Joslin Diabetes Center	Visiting Researcher
2006-2009	Kyung Hee University, Korea	Assistant professor
2002-2005	Hallym University College of Medicine	Assistant Professor
1999-2002	Samsung Medical Center, Korea	Fellowship
1997-1999	Kyung Hee University, Korea	PhD
1995-1997	Kyung Hee University, Korea	MS
1988-1994	Kyung Hee University, Korea	M.D

» Research Interests

Energy Metabolism, Vascular biology, Islet biology, NAFLD

» Honors & Awards

- 2012 Best Teaching Professor Award (Kyung Hee University)
- 2013.5 Award of excellent presentation in Korean Endocrinology Society

» Publications

1. Rhee EJ, Kim HC, Kim JH, Lee EY, Kim BJ, Kim EM, Song Y, Lim JH, Kim HJ, Choi S, Moon MK, Na JO, Park KY, Oh MS, Han SY, Noh J, Yi KH, Lee SH, Hong SC, **Jeong IK**. 2018 Guidelines for the management of dyslipidemia. Korean J Intern Med. 2019 Jul;34(4):723-771.
2. Jun JE, Cho IJ, Han K, **Jeong IK**, Ahn KJ, Chung HY, Hwang YC. Statins for primary prevention in adults aged 75 years and older: A nationwide population-based case-control study. Atherosclerosis. 2019 Feb 2;283:28-34.
3. Jun JE, **Jeong IK**, et al. Efficacy and Safety of Omega-3 Fatty Acids in Patients Treated with Statins for Residual Hypertriglyceridemia: A Randomized, Double-Blind, placebo- Controlled Clinical Trial. Diabetes Metab J. 2019 Jun 20.
4. Hwang YC, Jun JE, **Jeong IK**, Ahn KJ, Chung HY. Comparison of the Efficacy of Rosuvastatin Monotherapy 20 mg with Rosuvastatin 5 mg and Ezetimibe 10 mg Combination Therapy on Lipid Parameters in Patients with Type 2 Diabetes Mellitus. Diabetes Metab J. 2019 Jan 16.
5. Yoo J, Cho IJ, **Jeong IK**, Ahn KJ, Chung HY, Hwang YC. Exendin-4, a glucagon-like peptide-1 receptor agonist, reduces hepatic steatosis and endoplasmic reticulum stress by inducing nuclear factor erythroid-derived 2-related factor 2 nuclear translocation. Toxicol Appl Pharmacol. 2018 Dec 1;360:18-29.
6. Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJL, Charytan DM, Edwards R, Agarwal R, Bakris G, Bull S, Cannon CP, Capuano G, Chu PL, de Zeeuw D, Greene T, Levin A, Pollock C, Wheeler DC, Yavin Y, Zhang H, Zinman B, Meininger G, Brenner BM, Mahaffey KW; **CREDENCE Trial Investigators**. Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy. N Engl J Med. 2019 Jun 13;380(24):2295-2306.
7. Hwang YC, Cho IJ, **Jeong IK**, Ahn KJ, Chung HY. Factors associated with regression from prediabetes to normal glucose tolerance in a Korean general population: A community-based 10-year prospective cohort study. Diabet Med. 2018 Nov;35(11):1544-1551.

Abstract

GENETIC AND ACQUIRED LOW LDL CHOLESTEROL

In-Kyung JEONG

Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine, Seoul, Korea
Jik1016@khu.ac.kr

The strong evidence that reduction in LDL-C levels provides significant CV beneficial effects has been demonstrated by large clinical trials and is recommended by many guidelines for management of dyslipidemia. However, there are concerns for the optimal lower limit in which LDL-C can prevent the cardiovascular event without causing adverse events. Low LDL-C has been accused of potentially increased risk of neurocognitive function disorder, depression, hemorrhagic stroke, cataract, steroid hormone synthesis, diabetes mellitus, infections, and cancer. This lecture is to present available data for the safety of low LDL-C in genetic and acquired situation as it comes from studies of lipid-lowering drugs.

Keywords
Low LDL cholesterol, Cardiovascular disease, Safety, Depression, Hemorrhagic stroke, Cancer

ICoLA 2019 by KSoLA

Symposium 20

Chairpersons

Jeong Hyun Park | Inje University, Korea
Manlio Vinciguerra | St'Anne University, Czech Republic

Date & Time: September 7 (Sat.), 15:20-16:50
Place: Room 2 (3F)

Symposium 20

Sanjay Rajagopalan

Organization

University Hospitals Harrington Heart and Vascular Institute, Case Western Reserve School of Medicine, Cleveland OH

Position & Title

Herman Hellerstein Chair of Cardiovascular Research

Chief, Cardiovascular Medicine, University Hospitals

Director Case Cardiovascular Research Institute

» Educational Background & Professional Experience

Year	Name of institution	Position
1994-1998	Fellow Cardiovascular Medicine Emory University	Fellow
1998-2003	University of Michigan, Ann Arbor	Assistant Professor
2003-2006	Mount Sinai School of Medicine, New York, NY	Associate Professor
2006-2013	The Ohio State University, Ross Heart Institute	John W. Wolfe Professor of Cardiovascular Research
2013-2016	University of Maryland School of Medicine, Baltimore, MD	Mel Sharoky Chair of Cardiology, Chief of Cardiology
2016-Present	University Hospitals, Case Western Research School of Medicine	

» Honors & Awards

- 2014 Melvin Sharoky Professorship in Cardiovascular Medicine
- 2013 Charles Overstreet Chair in Cardiovascular Medicine, Ohio State University (offered but not accepted)
- 2007 John A. Wolfe Professorship in Cardiovascular Research, The Ohio State University

» Publications

1. Air Pollution and Cardiovascular Disease: JACC State-of-the-Art Review. Rajagopalan S, Al-Kindi SG, Brook RD. J Am Coll Cardiol. 2018 Oct 23;72(17):2054-2070
2. Air Pollution and Cardiometabolic Disease: An Update and Call for Clinical Trials. Brook RD, Newby DE, Rajagopalan S. Am J Hypertens. 2017 Dec 8;31(1):1-10.
3. Environmental stressors and cardio-metabolic disease: part I-epidemiologic evidence supporting a role for noise and air pollution and effects of mitigation strategies. Münzel T, Sørensen M, Gori T, Schmidt FP, Rao X, Brook J, Chen LC, Brook RD, Rajagopalan S. Eur Heart J. 2017 Feb 21;38(8):550-556
4. Environmental stressors and cardio-metabolic disease: part II-mechanistic insights. Münzel T, Sørensen M, Gori T, Schmidt FP, Rao X, Brook FR, Chen LC, Brook RD, Rajagopalan S. Eur Heart J. 2017 Feb 21;38(8):557-564
5. Incretin-Based Therapy for Diabetes: What a Cardiologist Needs to Know. Waldrop G, Zhong J, Peters M, Rajagopalan S. J Am Coll Cardiol. 2016 Mar 29;67(12):1488-1496. doi:
6. Noncontrast Magnetic Resonance Angiography for the Diagnosis of Peripheral Vascular Disease. Cavallo AU, Koktzoglou I, Edelman RR, Gilkeson R, Mihai G, Shin T, Rajagopalan S. Circ Cardiovasc Imaging. 2019 May;12(5):e008844

Abstract

THE ENVIRONMENT AND CARDIOVASCULAR DISEASE: A NEW FRONTIER FOR SUSTAINABLE GLOBAL HEALTH

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The Environment is increasingly recognized to play an outsize effect on cardiovascular health. Fine particulate matter <2.5 μm (PM2.5) air pollution is the most important environmental risk factor contributing to global cardiovascular (CV) mortality and disability. While short-term elevations in PM2.5 increase the relative risk of acute CV events longer-term exposures over several years increase this risk by a larger magnitude (~10%), which is partially attributable to the development of cardiometabolic conditions (e.g., hypertension and diabetes mellitus). In this talk, an overview of the mechanistic underpinnings and impact of air pollution exposure with a focus on systemic pathways of signal transduction and integration of air pollution effects on the cardiovascular system. Particular emphasis will be placed on currently understood pathways of translocation, particle sensing, vascular and cardiac effects and central nervous system pathways that may lead to potentiation of risk factors such as hypertension and insulin resistance. A brief overview of interaction between air pollution and global warming related health effects will be touched on. Finally, the impact of mitigation measures will be discussed.

Symposium 20

Duk-Hee Lee

Organization

Department of Preventive Medicine, School of Medicine, Kyungpook National University

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2003-Present	Department of Preventive Medicine, School of Medicine, Kyungpook National University	Associate Professor/Professor
1993-2002	Department of Preventive Medicine, School of Medicine, Kosin University	Instructor/Assistant Professor
1992-1995	School of Medicine, Kyungpook National University	Ph.D.
1989-1990	School of Medicine, Kyungpook National University	Master
1983-1989	School of Medicine, Kyungpook National University	M.D.

» Research Interests

Health effects of chronic exposure to low dose persistent organic pollutants in humans

» Publications

1. Lee DH, Jacobs DR Jr.New approaches to cope with possible harms of low-dose environmental chemicals. J Epidemiol Community Health. 2019;73:193-7
2. Lee DH, Jacobs DR Jr.Firm human evidence on harms of endocrine-disrupting chemicals was unlikely to be obtainable for methodological reasons. J Clin Epidemiol. 2019;107:107-15.
3. Kim SA, Lee YM, Choi JY, Jacobs DR Jr, Lee DH. Evolutionarily adapted hormesis-inducing stressors can be a practical solution to mitigate harmful effects of chronic exposure to low dose chemical mixtures. Environ Pollut. 2018;233:725-34.
4. Lee DH, Porta M, Lind L, Lind PM, Jacobs DR Jr. Neurotoxic chemicals in adipose tissue: A role in puzzling findings on obesity and dementia. Neurology. 2018;90:176-82
5. Lee YM, Ha CM, Kim SA, Thoudam T, Yoon YR, Kim DJ, Kim HC, Moon HB, Park S, Lee IK, Lee DH. Low-Dose Persistent Organic Pollutants Impair Insulin Secretory Function of Pancreatic β-Cells: Human and In Vitro Evidence. Diabetes. 2017;66:2669-80.
6. Lee YM, Kim KS, Jacobs DR Jr, Lee DH. Persistent organic pollutants in adipose tissue should be considered in obesity research. Obes Rev. 2017;18:129-39
7. Lee DH, Porta M, Jacobs DR Jr, Vandenberg LN. Chlorinated Persistent Organic Pollutants, Obesity, and Type 2 Diabetes. Endocr Rev. 2014;35(4):557-601

Abstract

PERSISTENT ORGANIC POLLUTANTS AND CVD

Duk-Hee Lee

Department of Preventive Medicine, School of Medicine, Kyungpook National University, Deagu, Republic of Korea
lee_dh@knu.ac.kr

Chronic exposure to environmental chemicals has been linked to many chronic diseases including cardiovascular diseases (CVD) through multiple mechanisms at low doses. As humans are continuously and simultaneously exposed to a tremendous number of environmental chemicals through food, air, water, and consumer products, this issue requires a much broader viewpoint than current prevailing individual chemical- or exposure source-based approaches. In fact, outdoor air pollution should be considered as one example of environmental chemical mixtures. Another common example of chemical mixture is persistent organic pollutants (POPs). As strong lipophilic chemical mixtures, when individual compounds belonging to POPs enter into our body from various exposure sources, they are mainly stored in adipose tissue and released to circulation through controlled and uncontrolled lipolysis. Therefore, there are multidimensional interrelationships between POPs and adipose tissue. In particular, chronic exposure to low dose POPs can play a more fundamental role in the development of obesity-related metabolic dysfunction rather than obesity itself. For example, POPs are involved in key mechanisms linking obesity and obesity-related diseases, such as chronic inflammation of adipose tissue and lipotoxicity with ectopic fat accumulation. Also, POPs can explain puzzling human findings which suggest benefits of obesity such as obesity paradox because healthy adipose tissue can be protective by reducing the amount of POPs reaching other organs. Besides obesity and obesity-related metabolic diseases, POPs are closely related to common CVD risk factors such as physical inactivity and unhealthy diet. Although POPs are well-known endocrine disrupting chemicals (EDCs), mitochondrial dysfunction would be a more plausible mechanism due to unpredictability of EDC mixtures. As adipose tissue plays a role as an internal exposure source of POPs, how to manage POPs inside us would be essential to protect against harms of POPs.

Keywords
Cardiovascular diseases; Chemical mixture; Diabetes; EDCs; Obesity; Persistent Organic Pollutants

Symposium 20

Byoung Geol Choi

Organization

Computer Software Engineering, Hanyang University

Position & Title

Post-Doc

» Educational Background & Professional Experience

Year	Name of institution	Position
2019.7-	Computer Software Engineering, Hanyang University	Post-Doc
2018.3-2019.6	Research Institute of Health Sciences, Korea University	Research Professor
2011.9-2018.2	Graduate School of Korea University	The degree of Doctor of Philosophy in Medicine

» Research Interests

Cardiology, Clinical research, BigData, Machine learning

» Honors & Awards

- "Academic Award" of Korea University Graduate School (2016 & 2018)
- "Best Abstract Award" at Asia-Pacific CardioMetabolic Syndrome CONGRESS 2018
- "Best Poster Abstract Award" at Angioplasty Summit-TCTAP 2012

» Publications

1. The association of chronic air pollutants with coronary artery spasm, vasospastic angina, and endothelial dysfunction. Coronary Artery Disease 2018;29:336-343
2. Air pollution and short-term clinical outcomes of patients with acute myocardial infarction. Clinical and experimental pharmacology & physiology 2017;44:631-638
3. Five-year clinical outcomes in patients with significant coronary artery spasm: A propensity score-matched analysis. International journal of cardiology 2015;184:533-539
4. Impact of Renin-Angiotensin System Inhibitors on Long-Term Clinical Outcomes of Patients With Coronary Artery Spasm. Journal of the American Heart Association 2016;5
5. Association of Major Adverse Cardiac Events up to 5 Years in Patients With Chest Pain Without Significant Coronary Artery Disease in the Korean Population. J Am Heart Assoc 2019;8:e010541
6. Hyperuricaemia and development of type 2 diabetes mellitus in Asian population. Clinical and experimental pharmacology & physiology 2017;46: 499-506
7. Machine Learning for the Prediction of New-Onset Diabetes Mellitus during 5-Year Follow-up in Non-Diabetic Patients with Cardiovascular Risks. Yonsei medical journal 2019;60:191-199.

Abstract

THE ASSOCIATION OF CHRONIC AIR POLLUTANTS WITH CORONARY ARTERY SPASM, VASOSPASTIC ANGINA AND ENDOTHELIAL DYSFUNCTION

Byoung Geol Choi[1]* and Seung-Woon Rha[2]

[1] Post-Doc, Computer Software Engineering, Hanyang University, Seoul, South Korea
[2] Cardiovascular Center, Korea University Guro Hospital, Seoul, Korea
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Background: We evaluated the effect of chronic exposure to air pollutants (APs) on coronary endothelial function and significant coronary artery spasm (CAS) as assessed by intracoronary acetylcholine (ACH) provocation test.

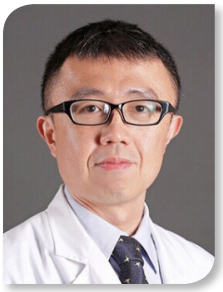
Method: A total 6,430 patients with typical or atypical chest pain underwent intracoronary ACH provocation test were enrolled. We obtained data on APs from the Korean National Institute of Environmental Research (NIER; http://www.nier.go.kr/). APs are largely divided into two types: Particulate matter with aerodynamic diameter of less than or equal to 10 μm in size (PM10) and gaseous pollutants such as nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO) and ozone (O_3). The primary endpoint is the incidence of significant CAS and its associated parameters during ACH provocation test.

Result: The incidence of CAS was positively correlated with an exposure duration of PM10, while SO_2, NO_2, CO, and O_3 were shown to be unrelated to CAS. During the ACH provocation test, as PM10 increased, the frequency of CAS was increased and the incidence of transient ST-segment elevation was also increased. There was a trend toward higher incidence of spontaneous spasm as PM10 increased. The mean exposure level of PM10 was 51.3 ± 25.4 $\mu g/m^3$. The CAS risk increased by 4 % when a level of PM10 increased by 20 $\mu g/m^3$ by an adjusted Cox-regression analysis.

Conclusion: CAS incidence is closely related to exposure to particulate matters but not to gaseous pollutants. Particularly, higher exposure concentrations and longer exposure duration of PM10 increased the risk of CAS. These important findings provide a plausible mechanism that links air pollution to vasospastic angina patients and provide new insights into environmental factors.

Keywords
air pollution, angina, coronary artery disease, coronary artery spasm, endothelial dysfunction

Symposium 20



Li-Wei Lo

Organization

Taipei Veterans General Hospital

Position & Title

Attending Physicians

» Educational Background & Professional Experience

Year	Name of institution	Position
2017-Present	National Yang-Ming University	Associate Professor
2008-Present	Taipei Veterans General Hospital	Attending Physician
2006-2008	Taipei Veterans General Hospital	Fellowship

» Research Interests

Arrhythmias, Cardiology, Electrophysiology

» Honors & Awards

- 2019 First Prize, Doctor JCS, Asian Championship, the 83rd Annual Scientific Meeting of the Japanese Circulation Society, JCS
- 2014 Best paper award, Basic science, 44th Taiwan Society of Cardiology Annual Scientific Meeting
- 2010 Best poster award, Basic section, 3rd Asian Pacific Heart Rhythm Society

» Publications

1. Cheng WH, **Lo LW***, Lin YJ, Chang SL, Hu YF, Hung Y, Chung FP, Liao JN, Tuan TC, Chao TF, Tsai TY, Liu SH, Chen SA. Ten-year ablation outcomes of patients with paroxysmal atrial fibrillation receiving pulmonary vein isolation. Heart Rhythm. 2019; In press.
2. Vicera JJB, **Lo LW***, Shinya Y, Chou YH, Lin YJ, Lo MT, Lin WL, Liu SH, Cheng WH, Tsai TY, Chen SA. Ultra-rapid high-density mapping system with the phase singularity technique is feasible in identifying rotors and focal sources and predicting AF termination. J Cardiovasc Electrophysiol. 2019; In press. (SCI 3.097)
3. Tsai TY, **Lo LW***, Liu SH, Cheng WH, Chou YH, Lin WL, Yamada S, Lin YJ, Chang SL, Hu YF, Chung FP, Liao JN, Chou TF, Tuan TC, Chen SA. Ambient fine particulate matter (PM2.5) exposure is associated with idiopathic ventricular premature complexes burden: A cohort study with consecutive Holter recordings. J Cardiovasc Electrophysiol 2019; 30(4):487-492. (SCI 3.097)
4. Lin WL, Chen YR, Lai CT, Yamada S, Liu SH, Chou YH, Fu YC, Yang CCH, Kuo TBJ, **Lo LW***, Chen SA. Neural mechanism of angiotensin-converting enzyme inhibitors in improving heart rate variability and sleep disturbance after myocardial infarction. Sleep Med. 2018; 48:61-69. (SCI 3.395)
5. Te ALD, **Lo LW***, Lin YJ, Chang SL, Hu YF, Chung FP, Tuan TC, Chao TF, Liao JN, Chang YT, Lin CY, Yamada S, Chang TY, Salim S, Hoang MQ, Huang TC, Chen SA. Vasovagal responses during cryoballoon pulmonary vein isolation in paroxysmal atrial fibrillation predict favorable mid-term outcomes. Int J Cardiol. 2018; 258:115-120. (SCI 4.034).
6. Yamada S, **Lo LW**, Chou YH, Lin WL, Chang SL, Lin YJ, Chen SA*. Renal denervation regulates the atrial arrhythmogenic substrates through reverse structural remodeling in heart failure rabbit model. Int J Cardiol. 2017; 235:105-113. (SCI 4.034).
7. Yamada S, **Lo LW***, Chou YH, Lin WL, Chang SL, Lin YJ, Chen WH, Tsai TY, Chen SA*. Beneficial effect of renal denervation on ventricular premature complex induced cardiomyopathy. J Am Heart Assoc 2017;5: e004479 doi10.1161/JAHA.116.004479 (SCI 4.450)
8. Allamsetty S, **Lo LW**, Lin YJ, Chang SL, Chung FP, Hu YF, Lin CY, Chang YT, Chiang CH, Huang HK, Chan CC, Bun Dan DV, Lin CH, Raharjo S, Jhuo SJ, Walia R, Chen SA*. Impact of Aortic Encroachment to Left Atrium on Non-Pulmonary Vein Triggers of Atrial Fibrillation. Int J Cardiol 2017; 227:650-655. (SCI 4.034).

Abstract

PM 2.5-INDUCED ARRHYTHMIA

Li-Wei Lo MD., PhD., Tsung-Ying Tsai MD., Wen-Han Cheng MD., Yu-Hui Chou MS., Wei-Lun Lin MS., Shih-Ann Chen MD.

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Epidemiological evidence has shown association between ambient fine particulate matter (PM 2.5) exposure and cardiovascular mortality. The association between an increased risk of arrhythmia admissions and a PM2.5 exposure has also been established. It is known that PM2.5 particles can travel deep into alveolar and enter systemic circulation, which leads to: Increasing systemic inflammation and vasculoactive mediators, directly affecting local vasoconstriction and/or platelet aggregation through translocation, and altering the systemic and cardiac autonomic nervous system.

Reduced heart rate variability (HRV) has been associated with higher cardiovascular events and arrhythmias, is a marker of autonomic dysfunction and sympathetic hyperactivity. In our recent researches, we found that LH/HF ratios of the HRV are associated with a diurnal PM2.5 exposure. A PM2.5 exposure may have a stronger impact on the cardiac autonomics with a reduced HRV and sympathetic hyperactivity during the daytime. In addition, we also observed that a diurnal change in the PM2.5 exposure and diurnal change in the HRV. The atrial arrhythmia burdens are not different among different levels of PM2.5 exposure. But the ventricular premature contraction (VPC) burdens are significantly higher under high PM2.5 exposure than that under low PM2.5 exposure. Those increases are significantly observed in the daytime, not at night time.

Our findings suggest that exposure to PM2.5 will cause sympathetic hyperactivity and are associated with increased VPC burdens, even in the patients without structural heart disease. The PM2.5 has a stronger impact on ventricular arrhythmogenesis during daytime than at nighttime.

Keywords
Air pollution, arrhythmia, diurnal, PM2.5, ventricular arrhythmia.

ICoLA 2019 by KSoLA

Symposium 21

Chairpersons

Jin Han | Inje University, Korea
Christine Des Rosiers | Universite de Montreal, Canada

Date & Time: September 7 (Sat.), 15:20-16:50
Place: Room 3 (3F)

Symposium 21

Kyu-Tae Kang

Organization

College of Pharmacy, Duksung Innovative Drug Center, Duksung Women's University

Position & Title

Associate Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2019-Present	Duksung Women's University, Korea	Associate Professor
2013-2018	Duksung Women's University, Korea	Assistant Professor
2008-2013	Boston Children's Hospital /Harvard Medical School, United States	Postdoctoral Research Fellow
2002-2007	Medical College of Georgia, United States	Ph.D. student (Biomedical Science)
1999-2001	College of Pharmacy, Seoul National University, Korea	M.S. student (Pharmacy)
1995-1999	College of Pharmacy, Chung-Ang University, Korea	B.S. student (Pharmacy)

» Research Interests

Development of angiogenesis modulators

» Honors & Awards

· 2013 Cardiovascular Section Research Recognition Award (The American Physiological Society)

» Publications

1. Shah S, Lee H, Park YH, Jeon EK, Chung HK, Lee ES, Shim JH, **Kang KT***. 3-dimentional angiogenesis assay system using two-cell spheroids formed by endothelial colony forming cells and mesenchymal stem cells. Journal of Visualized Experiments (accepted)
2. Lim HK, Lee H, Moon A, **Kang KT***, Jung J*. Exploring protocol for breast cancer xenograft model using endothelial colony-forming cells. Translational Cancer Research 7(5): 1228-1234, 2018
3. Shah S and **Kang KT***. Two-Cell Spheroid Angiogenesis Assay System Using Both Endothelial Colony Forming Cells and Mesenchymal Stem Cells. Biomol Ther (seoul). 26(5):474-480, 2018
4. **Kang KT**, Lin RZ, Kuppermann D, Melero-Martin JM, Bischoff J*. Endothelial colony forming cells and mesenchymal progenitor cells form blood vessels and increase blood flow in ischemic muscle. Scientific reports. 7: DOI:10.1038/s41598-017-00809-1, 2017
5. Boscolo E, Limaye N, Huang L, **Kang KT**, Soblet J, Uebelhoer M, Mendola A, Natynki M, Seront E, Dupont S, Hammer J, Legrand C, Brugnara C, Eklund L, Vikkula M*, Bischoff J*, Boon LM*. Rapamycin improves TIE2-mutated venous malformation in murine model and human subjects. Journal of Clinical Investigation. 125(9):3491-3504, 2015

Abstract

DEVELOPMENT OF A NOVEL ANGIOGENESIS ASSAY FOR VASCULAR DISEASES

Sajita SHAH[1,2], Hyunsook LEE[1,2], Kyu-Tae KANG[1,2]*

[1] College of Pharmacy, Duksung Women's University, Seoul, Republic of Korea
[2] Duksung Innovative Drug Center, Duksung Women's University, Seoul, Republic of Korea
ktkang@duksung.ac.kr

Angiogenesis have been an aggressively-growing research field in the last few decades with the recognition that angiogenesis is a hallmark of more than 50 different pathological conditions, such as rheumatoid arthritis, oculopathy, cardiovascular diseases, and tumor metastasis. During angiogenesis modulator development, it is crucial to use in vitro assay systems with appropriate cell types and proper conditions to reflect the physiologic angiogenesis process. To overcome limitations of current in vitro angiogenesis assay systems using mainly endothelial cells, we developed a 3-dimensional (3D) co-culture spheroid sprouting assay system. Co-culture spheroids were produced by two human vascular cell precursors, endothelial colony forming cells (ECFCs) and mesenchymal stem cells (MSCs). ECFCs+MSCs spheroids were embedded into type I collagen matrix to mimic the in vivo extracellular environment. A real-time cell recorder was utilized to continuously monitor the progression of angiogenic sprouting from spheroids for 24 hours. Live cell fluorescent labeling technique was also applied to tract the localization of each cell type during sprout formation. Angiogenic potential was quantified by counting the number of sprouts and measuring the cumulative length of sprouts generated from the individual spheroids. Comparison experiments demonstrated that ECFCs+MSCs spheroids showed greater sprout number and cumulative sprout length compared with ECFCs-only spheroids. Bevacizumab, an FDA-approved angiogenesis inhibitor, was tested with the newly-developed co-culture spheroid assay system to verify its potential to screen anti-angiogenic drugs. The IC50 value for ECFCs+MSCs spheroids compared to the ECFCs-only spheroids was closer to the effective plasma concentration of bevacizumab obtained from the xenograft tumor mouse model. The present study suggests that 3D ECFCs+MSCs spheroid angiogenesis assay system is relevant to physiological angiogenesis, and can predict an effective plasma concentration of drug candidates in advance of animal experiments.

Keywords
angiogenesis, co-culture spheroid, endothelial colony forming cells, mesenchymal stem cells, type I collagen gel, bevacizumab

Symposium 21

JAN F.C. GLATZ

Organization

MAASTRICHT UNIVERSITY, MAASTRICHT, THE NETHERLANDS

Position & Title

PROFESSOR OF CARDIAC METABOLISM

CHAIR, DEPT. OF GENETICS & CELL BIOLOGY

DEPUTY CHAIR, DEPT. OF CLINICAL GENETICS

» Educational Background & Professional Experience

Year	Name of institution	Position
2014-Present	Maastricht University Hospital	Deputy Chair, Dept. of Clinical Genetics
2013-Present	Maastricht University	Chair, Dept. Genetics & Cell Biology
2003-Present	Maastricht University	Professor of Cardiac Metabolism
2007-2013	Maastricht University	Director of Education, Biomedical Sciences program
1986-2003	Maastricht University	Assistant/Associate Professor
1979-1986	Radboud University Nijmegen	PhD Candidate and Post-Doc

» Research Interests

Investigations are directed at disclosing the mechanisms underlying the process of metabolic (mal)adaptation and its relation to cardiac (dys)function in pathophysiological conditions such as cardiac hypertrophy/ cardiac failure, and diabetic cardiomyopathy. Our previous studies have indicated that fatty acid uptake (i) is a rate-limiting step in cardiac fatty acid utilization, and (ii) is mediated by both membrane-associated and cytoplasmic fatty acid-binding proteins. Subsequently, we discovered that fatty acid uptake is (acutely) regulated by translocation of putative fatty acid translocase (CD36) from intracellular stores to the sarcolemma. Therefore, at present our research focuses on disturbances in the regulation of cardiac substrate uptake, in particular the signal transduction and trafficking pathways involved in recycling of membrane fatty acid transporters as well as glucose transporters (GLUT) in cardiac myocytes, and the intracellular transport and targeting of substrates to sites of metabolism and of modulatory action (e.g. gene expression). This research includes the use of substrate transporters as target for metabolic modulation therapy.

» Honors & Awards

· 1990-1995 Established Investigator, Netherlands Heart Foundation

» Publications

1. Geraets IME, **Glatz JFC**, Luiken, JJFP, Nabben M. Pivotal role of membrane substrate transporters on the metabolic alterations in the pressure-overloaded heart. *Cardiovasc Res* 115: 1000-1012, 2019
2. **Glatz JFC**, Luiken JJFP. Dynamic role of the transmembrane glycoprotein CD36 (SR-B2) in cellular fatty acid uptake and utilization. *J Lipid Res* 59: 1084-1093, 2018
3. Abdurrachim D, Nabben M, Hör V, Kuhlmann MT, Bovenkamp P, Ciapaite J, Geraets IME, Coumans WA, Luiken JJFP, **Glatz JFC**, Schäfers M, Nicolay K, Faber C, Hermann S, Prompers JJ. Diabetic db/db mice do not develop heart failure upon pressure overload: a longitudinal in vivo PET, MRI, and MRS study on cardiac metabolic, structural, and functional adaptations. *Cardiovasc Res* 113: 1148-1160, 2017
4. **Glatz JFC**, Luiken JJFP. From fat to FAT (CD36/SR-B2): Understanding the role of cellular fatty acid uptake. *Biochimie* 136: 21-26, 2017
5. Liu Y, Steinbusch LKM, Nabben M, Kapsokalyvas D, van Zandvoort M, Schönleitner P, Antoons G, Simons PJ, Coumans WA, Geomini A, Chanda D, **Glatz JFC**, Neumann D, Luiken JJFP. Palmitate-induced vacuolar-type H^+-ATPase inhibition feeds forward into insulin resistance and contractile dysfunction. *Diabetes* 66: 1521-1534, 2017
6. Mansor LS, da Luz Sousa Fialho M, Yea G, Coumans WA, West JA, Kerr M, Carr CA, Luiken JJFP, **Glatz JFC**, Evans RD, Griffin JL, Tyler DJ, Clarke K, Heather LC. Inhibition of sarcolemmal FAT/CD36 by sulfo-N-succinimidyl oleate rapidly corrects metabolism and restores function in the diabetic heart following hypoxia/reoxygenation. *Cardiovasc Res* 113: 737-748, 2017
7. **Glatz JFC**, Luiken JJFP, Bonen A. Membrane fatty acid transporters as regulators of lipid metabolism: Implications for metabolic disease. (Invited Review). *Physiol Rev* 90: 367-417, 2010

Abstract

DYNAMIC ROLE OF TRANSMEMBRANE PROTEIN CD36/SR-B2 IN MYOCARDIAL LIPID SENSING AND UTILIZATION

JAN F.C. GLATZ and JOOST J.F.P. LUIKEN

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The widely expressed transmembrane glycoprotein CD36, a scavenger receptor class B protein (SR-B2), serves many functions in lipid metabolism and signaling. In the heart, CD36 is the main sarcolemmal lipid transporter and presents a rate-limiting step in cardiac lipid utilization. The cellular fatty acid uptake rate is governed primarily by the presence of CD36 at the cell surface, which is regulated by the subcellular vesicular recycling of CD36 from endosomes to the plasma membrane. CD36 has been implicated in dysregulated fatty acid and lipid metabolism in pathophysiological conditions, particularly in high-fat diet-induced insulin resistance and diabetic cardiomyopathy. Thus, under chronic lipid overload conditions, CD36 is increasingly being expelled to the cell surface, setting the heart on a route towards increased lipid uptake, excessive myocardial lipid accumulation, insulin resistance and eventually contractile dysfunction. Insight into the subcellular trafficking machinery of CD36 is expected to provide novel targets to treat the lipid-overloaded heart. A recent systematic screen for CD36-dedicated trafficking proteins yielded, amongst others, vacuolar type H^+-ATPase (v-ATPase) and specific vesicle-associated membrane proteins (VAMPs) to be uniquely involved in CD36 recycling. Preliminary data suggest that these latter proteins may offer clues to manipulate myocardial lipid uptake and utilization, and thus be promising targets for metabolic intervention therapy to treat the failing heart.

Keywords
CD36, SR-B2, cardiac fatty acid uptake, diabetic cardiomyopathy, metabolic intervention

Symposium 21

Tae-Sik Park

Organization

Dept. of Life Science, Gachon University

Position & Title

Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
2007-Present	Dept. of Life Science, Gachon University	Professor
2005-2007	Dept. of Medicine, Columbia University, New York, USA.	Associate Research Scientist
2002-2005	Cardiovascular Pharmacology, Pfizer. Ann Arbor, MI, USA	Postdoctoral Scientist

» Research Interests

Sphingolipid metabolism, Metabolisc dysfunction, NAFLD.

» Publications

1. Tran NKS, Kim GT, Lee DY, Kim YJ, Park HJ, Park DK, Park TS*. Fermented Cordyceps militaris Extract Ameliorates Hepatosteatosis via Activation of Fatty Acid Oxidation. J Med Food. 2019. 22(4):325-336
2. Botta A, Liu Y, Wannaiampikul S, Tungtrongchitr R, Dadson K, Park TS, Sweeney G. An adiponectin-S1P axis protects against lipid induced insulin resistance and cardiomyocyte cell death via reduction of oxidative stress. Nutr Metab (Lond). 2019. 16:14.
3. Song YJ, Kim A, Kim GT, Yu HY, Lee ES, Park MJ, Kim YJ, Shim SM, Park TS*. Inhibition of lactate dehydrogenase A suppresses inflammatory response in RAW 264.7 macrophages. Mol Med Rep. 2019. 19(1):629-637
4. Lee SY, Lee HY, Song JH, Kim GT, Jeon S, Song YJ, Lee JS, Hur JH, Oh HH, Park SY, Shim SM, Yoo HJ, Lee BC, Jiang XC, Choi CS, *Park TS. Adipocyte-Specific Deficiency of De Novo Sphingolipid Biosynthesis Leads to Lipodystrophy and Insulin Resistance. Diabetes. 2017. 66(10):2596-2609.
5. Lee SY, Hong IK, Kim BR, Shim SM, Sung Lee J, Lee HY, Choi CS, Kim BK, *Park TS. Activation of sphingosine kinase 2 by endoplasmic reticulum stress ameliorates hepatic steatosis and insulin resistance in mice. Hepatology. 2015. 62(1):135-46.

Abstract

REGULATION OF KERATINOCYTE DIFFERENTIATION BY SPHINGOSINE 1-PHOSPHATE

Tae-Sik Park

Department of Life Science, Gachon University, Sungnam, Republic of Korea
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Sphingosine 1-phosphate (S1P) lyase is an intracellular enzyme that catalyzes the irreversible degradation of S1P and has been suggested as a therapeutic target for the treatment of psoriasis vulgaris. Here, we demonstrated that S1P lyase inhibition reduced cell proliferation and induced differentiation of keratinocytes. To identify the physiological functions, we inhibited S1P lyase by S1P lyase-specific inhibitor (SLI) or SGPL1-specifc small interference RNA (siSGPL1). Treatment with SLI caused G1 arrest by upregulation of p21, p27 and induced keratin 1, an early differentiation marker, in human epidermal keratinocytes, neonatal (HEKn). Similar to the pharmacological effects, genetic suppression by siSGPL1 arrested cell cycle at G1 phase and differentiation was activated. In addition, suppression by siSGPL1 upregulated keratin 1 as well as late differentiation markers including involucrin and loricrin. When hyperproliferation of HEKn cells was induced by interleukin-17 (IL-17) and interleukin-22 (IL-22), pharmacological inhibition of S1P lyase by SLI decreased proliferation and activated differentiation of HEKn cells simultaneously. In addition, SLI ameliorated imiquimod-induced psoriatic symptoms including erythema, scaling, and epidermal thickness in vivo. Collectively, these findings suggest that S1P lyase is a modulating factor for proliferation and differentiation, and could be a therapeutic target for psoriasis in human keratinocytes.

Keywords
sphingosine 1-phosphate, keratinocytes, differentiation, sphingosine 1-phosphate lyase, cell cycle, psoriasis.

Symposium 21

Terje Steinar Larsen

Organization

UiT the Arctic University of Norway

Position & Title

Professor

Chairman of the Cardiovascular Research Group

» Educational Background & Professional Experience

Year	Name of institution	Position
2017-Present	Department of Medical Biology, UiT	Professor/Chairman of the Cardiovascular research Group,
2009-2017	UiT	Professor, Chairman of the Department of Medical Biology
2005-2009	Institute of Medical Biology, UiT	Professor/Chairman of the Department of Medical Physiology
1998-2005	UiT	Professor, Chairman of the Institute of Medical Biology
1997-1998	Institute of Medical Biology, UiT	Professor
1992-1996	Institute of Medical Biology, UiT	Professor/Chairman of the Department of Medical Physiology

» Research Interests

Diabetes and lipid metabolism and their cardiovascular complications

» Publications

1. Kirsten M. Jansen, Sonia Moreno, Pablo M. Garcia-Roves, Terje S. Larsen Dietary Calanus oil recovers metabolic flexibility and rescues post-ischemic cardiac function in obese female mice. In press, Am J Physiol
2. Angel Moldes-Anaya, Thomas Sæther, Silvio Uhlig, Hilde I. Nebb, Terje Larsen, Hans C. Eilertsen and Steinar M. Paulsen. Two Isomeric C16 Oxo-Fatty Acids from the Diatom Chaetoceros karianus Show Dual Agonist Activity towards Human Peroxisome ProliferatorActivated Receptors (PPARs). Mar. Drugs 2017, 15, 148; doi:10.3390/md15060148.
3. Cook CM, Larsen TS, Derrig LD, Kelly KM, Tande KS.Wax-ester rich oil from the marine crustacean, Calanus finmarchicus, is a bioavailable source of EPA and DHA for human consumption. Lipids. 2016; 51(10):1137-44, Epub 2016 Sep 7
4. Salma W, Franekova V, Lund T, Höper A, Ludvigsen S, Lund J, Aasum E, Ytrehus K, Belke DD, Larsen TS. Dietary Calanus oil antagonizes angiotensin II-induced hypertension and tissue wasting in diet-induced obese mice. Prostaglandins Leukot Essent Fatty Acids. 2016;108:13-21
5. Larsen T. Historical Perspectives, in The Scientist's Guide to Cardiac Metabolism, 1st Edition, 2015 (eds. Michael Schwarzer and Torsten Doenst), Chapter 15 (page 207-218). ISBN-9780128023945
6. Bakkehaug JP, Kildal AB, Engstad ET, Boardman N, Næsheim T, Rønning L, Aasum E, Larsen TS, Myrmel T, How OJ. Response to Letter Regarding Article, "Myosin Activator Omecamtiv Mecarbil Increases Myocardial Oxygen Consumption and Impairs Cardiac Efficiency Mediated by Resting Myosin ATPase Activity". Circ Heart Fail. 2015 Nov;8(6):1142Am J Physiol Heart Circ Physiol. 2015; 308(8):H823-9.
7. Lund J, Hafstad AD, Boardman NT, Rossvoll L, Rolim NP, Ahmed MS, Florholmen G, Attramadal H, Wisløff U, Larsen TS, Aasum E. Exercise training promotes cardioprotection through oxygen-sparing action in high fat-fed mice. Am J Physiol Heart Circ Physiol. 2015 Apr 15;308(8):H823-9

Abstract

ANTI-OBESOGENIC TREATMENT MODIFIES CARDIAC ENERGY METABOLISM

Terje S. Larsen

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Diet-induced obesity in mice is associated with insulin resistance and a switch in fuel selection by the heart towards fatty acids at the expense of carbohydrates. We have previously reported, however, that dietary supplementation with Calanus oil (a novel marine oil extracted from the crustacean, Calanus finmarchicus) attenuates abdominal obesity and adipose tissue low-grade inflammation in mice during high-fat feeding. Here, utilizing female high fat diet-fed C57bl/6J mice, we show that dietary Calanus oil and infusion of the incretin mimetic exenatide (used for the treatment of type 2 diabetic patients) were able to antagonize obesity-induced alterations in myocardial energy metabolism. In contrast to exenatide, Calanus oil supplementation also protected the heart towards ischemic stress, based on recordings of left ventricular functional parameters during the post-ischemic recovery phase.

Keywords
Ischemia-reperfusion; Myocardial fatty acid oxidation; Myocardial glucose oxidation; Obesity; Ventricular function

ICoLA 2019 by KSoLA

Symposium 22

Chairpersons

Sang Hong Baek | The Catholic University of Korea, Korea
Alberico L. Catapano | University of Milan, Italy

Date & Time: September 7 (Sat.), 15:20-16:50
Place: Room 4 (5F)

Symposium 22

Christoph J. Binder, MD, PhD

Organization

Medical University of Vienna & Research Center for Molecular Medicine of the Austrian Academy of Sciences

Position & Title

Professor of Atherosclerosis Research

CeMM Principal Investigator

» Educational Background & Professional Experience

Year	Name of institution	Position
2019-	Dept. of Laboratory Medicine, Medical University of Vienna, Austria	Vice Chair
2009-	Medical University of Vienna	Professor of Atherosclerosis Research
2006-	CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences	Principal Investigator
2005-2012	Dept. of Medicine, University of California San Diego, USA	Adjunct Assistant Professor of Medicine
2005-2009	Dept. of Laboratory Medicine, Medical University of Vienna, Austria	Resident and Assistant Professor in Laboratory Medicine (Clinical Pathology)
2002-2005	Dept. of Medicine, University of California San Diego, USA	Postdoctoral fellow
1997-2002	University of California San Diego, USA	PhD student
1991-1997	Medical faculty of the University of Vienna, Austria	Medical student

» Research Interests

Inflammation and cardiovascular disease, immune mechanisms of atherosclerosis, lipid-peroxidation derived structures as targets of innate immunity, natural antibodies in health and disease, microvesicles.

» Honors & Awards

- 2003 Young Investigator Award, XIIIth Intl. Symposium on Atherosclerosis, Kyoto, Japan
- 2003 Postdoctoral Fellowship, American Heart Association
- 1997 Fulbright Scholarship, Austrian J.W. Fulbright Commission

» Publications

1. Tsiantoulas D, Sage AP, Göderle L, Ozsvar-Kozma M, Murphy D, Porsch F, Pasterkamp G, Menche J, Schneider P, Mallat Z, Binder CJ. B Cell-Activating Factor Neutralization Aggravates Atherosclerosis. Circulation. 2018 Nov 13;138(20):2263-2273.
2. Gruber S, Hendrikx T, Tsiantoulas D, Ozsvar-Kozma M, Göderle L, Mallat Z, Witztum JL, Shiri-Sverdlov R, Nitschke L, Binder CJ. Sialic Acid-Binding Immunoglobulin-like Lectin G Promotes Atherosclerosis and Liver Inflammation by Suppressing the Protective Functions of B-1 Cells. Cell Rep. 2016 Mar 15;14(10):2348-61.
3. Cardilo-Reis L, et al. Interleukin-13 protects from atherosclerosis and modulates plaque composition by skewing the macrophage phenotype. EMBO Mol Med. 2012 Oct;4(10):1072-86.
4. Weismann D, et al. Complement factor H binds malondialdehyde epitopes and protects from oxidative stress. Nature. 2011 Oct 5;478(7367):76-81.
5. Chou MY, et al. Oxidation-specific epitopes are dominant targets of innate natural antibodies in mice and humans. J Clin Invest. 2009 May;119(5):1335-49.
6. Binder CJ, et al. Pneumococcal vaccination decreases atherosclerotic lesion formation: molecular mimicry between Streptococcus pneumoniae and oxidized LDL. Nat Med. 2003 Jun;9(6):736-43.
7. Binder CJ, et al. Innate and acquired immunity in atherogenesis. Nat Med. 2002 Nov;8(11):1218-26.

Abstract

LIPOPROTEIN METABOLIC DERANGEMENTS IN FH

Christoph J. Binder[1,2]

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[2] Research Center for Molecular Medicine, Austrian Academy of Sciences, Vienna, Austria
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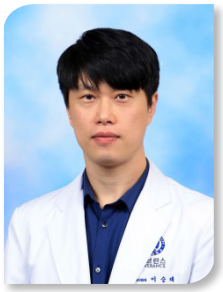
Familial hypercholesterolemia (FH) results from delayed clearance of LDL from the plasma, resulting in hypercholesterolemia, physical signs and premature atherosclerotic cardiovascular disease (ASCVD). Elevated levels of LDL have multiple negative effects on vascular function, including impairement of the normal arterial response to vasodilatory stimuli, promotion of vascular inflammation, and pathological uptake by arteyl wall macrophages when LDL particles become oxidized, leading to the formation of foam cells – hallmark cells of atherosclerotic lesions. The majority of plasma cholesterol is transported within LDL particles, which are primarily cleared by cellular uptake via LDL receptors on hepatocytes. The increased LDL-C levels in FH result from impaired LDL-receptor activity, which is often caused by different classes of mutations that directly affect the receptor or receptor-mediated clearance. In most cases FH is an autosomal co-dominant disorder. Heterozygous FH (HeFH) is the most common inherited metabolic disorder causing ASCVD, affecting 1:200-250 individuals, while homozygous FH (HoFH) is thought to affect about 1:160,000 - 300,000 people. Most individuals with genetically confirmed HeFH and HoFH have one and two mutant alleles of the LDLR gene, respectively, conferring either defective or null LDL receptor functionality. More than 2,300 unique FH-causing mutations have been reported in the LDLR gene. Heterozygous mutations in other genes, including APOB and PCSK9 explain <10% of HeFH cases, and two mutant alleles of these genes and of LDLRAP1 also called ARH (autosomal recessive hypercholesterolaemia) produce a phenotype resembling HoFH. Notably, at least 20% of patients referred to a lipid clinic with suspected HeFH do not have a single gene mutation, but instead carry polygenic susceptibility to high LDL-C. Diagnosis of FH is commonly based on scores that include lipid values (total cholesterol and/or LDL-C levels); the presence of physical stigmata considered pathognomonic for FH, such as tendon xanthomas, xanthelasmas, or arcus cornealis; the family history of premature CVD; and the presence of pathogenic DNA variants. Two clinical scoring systems are in general use: the Simon Broome Register (SBR) and the Dutch Lipid Clinic Network (DLCN) criteria. The basic metabolic alterations in FH, the functional and genetic basis for it, as well as the diagnosis and clinical implications will be discussed.

Keywords
Familial hypercholesterolemia, atherosclerosis, LDL-C, LDL receptor, diagnostic criteria

Symposium 22



Seung-Tae Lee

Organization

Yonsei University College of Medicine

Position & Title

Associate Professor

» Educational Background & Professional Experience

Year	Name of institution	Position
1993-1999	Yonsei University College of Medicine	M.D.
2007-2009	Sungkyunkwan University School of Medicine	Ph.D.
2004-2015	Samsung Medical Center	Redidency, Fellowship, Clinical Assisant/Associate Professor
2011-2012	University of California, San Francisco	Visiting Professor
2015-	Yonsei University College of Medicine	Associate Professor

» Research Interests

Genomics

» Publications

1. Lee ST, Wiemels JL. Genome-wide CpG island methylation and intergenic demethylation propensities vary among different tumor sites. Nucleic acids research 2016; 44(3): 1105-17.
2. Hwang IS, Shin S, Min YH, Lee ST, Choi JR. NOTCH2 missplicing can occur in relation to apoptosis. Blood 2015; 126(14): 1731-2.
3. Lee ST, Muench MO, Fomin ME, et al. Epigenetic remodeling in B-cell acute lymphoblastic leukemia occurs in two tracks and employs embryonic stem cell-like signatures. Nucleic acids research 2015; 43(5): 2590-602.
4. Lee ST, Xiao Y, Muench MO, et al. A global DNA methylation and gene expression analysis of early human B-cell development reveals a demethylation signature and transcription factor network. Nucleic acids research 2012; 40(22): 11339-51.
5. Kim DH, Lee ST, Won HH, et al. A genome-wide association study identifies novel loci associated with susceptibility to chronic myeloid leukemia. Blood 2011; 117(25): 6906-11.

Abstract

GENETIC DIAGNOSIS OF FH: WHAT IS NEW AND WHAT IS OPTIMAL?

Seung-Tae Lee

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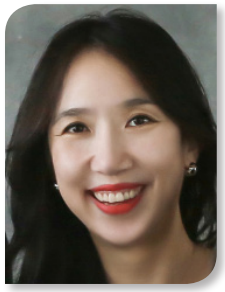
Familial hypercholesterolemia (FH) is a common hereditary lipid disorder inherited as an autosomal co-dominant condition in that heterozygotes are not as severely affected as homozygotes. Affected patients have high lifetime LDL levels leading to premature vascular disease and especially coronary artery disease (CAD). Genetic defects are found mainly in the LDL receptor gene (LDLR 90%), Apo-Lipoprotein B gene (APOB 5–10%) and the proprotein convertase subtilisin kexin type 9 (PCSK9 1–2%). Rare mutations have also been found in other genes including APOE, STAP1 and LDLRAP1. Treatment for high LDL using lipid-lowering drugs is effective, and has been shown to reduce the risk of premature CAD and early mortality in the condition. It could be emphasized that early diagnosis of FH is essential for an efficient patient management plan and the WHO, NICE and the European Atherosclerosis Society all recommend that molecular testing is the best approach for early detection of FH especially using cascade testing of families. It is important to use a combination of clinical scoring criteria in concert with molecular mutation screening to establish a diagnosis of FH.

Conventional genetic testing of FH has been DNA sequence analysis by Sanger sequencing and capillary electrophoresis, and MLPA for detection of larger deletions/duplications. Recently, NGS technologies have become more cost-efficient for smaller laboratories, and have now been adopted by many diagnostic laboratories. This allows for increased numbers of patients to be tested, and the potential investigation of larger numbers of genes involved in each disease, albeit with the increased analysis and interpretation which accompanies that. Although this detection level was lower than might be expected using accepted clinical criteria, it demonstrated that primary-care screening via NGS analysis of a limited number of target genes could be a viable approach to patient-finding.

Keywords
Genetics, Familial Hypercholesterolemia, Next-generation Sequencing

Symposium 22



Hae Sun Suh

Organization

Pusan National University

Position & Title

Associate Professor

Ph.D., M.Pharm., M.A.

» Educational Background & Professional Experience

Year	Name of institution	Position
2018-	Pusan National University, Korea	Associate Professor
2014-2018	Pusan National University, Korea	Assistant Professor
2013-2014	Health Insurance Review & Assessment Service, Korea	Associate Research Fellow
2011-2013	Yonsei University, Korea	Research Professor
2009-2011	National Evidence-based Healthcare Collaborating Agency, Korea	Principal Researcher
2004-2009	University of Southern California, USA	PhD in Pharmaceutical Economics and Policy
2004-2006	University of Southern California, USA	MA in Economics
2001-2004	MSD Inc., Korea	Medical Service Specialist
1999-2001	Ewha Womans University, Korea	MPharm in Pharmacy
1995-1999	Ewha Womans University, Korea	BPharm in Pharmacy

» Research Interests

Health Economics, Health Policy, Pharmacoepidemiology

» Honors & Awards

- Best Research Award in the area of Claims Database Analysis, National Health Insurance Service (Korea)
- Best New Investigator Podium Research Presentation Award, International Society for Pharmacoeconomics and Outcomes Research 15th Annual Conference (USA)
- Best Student Podium Research Presentation Award, International Society for Pharmacoeconomics and Outcomes Research 14th Annual Conference (USA)

» Publications

1. Kim S, Cheon SM, and Suh HS. Association Between Drug Exposure and Occurrence of Parkinsonism in Korea: A Population-Based Case-Control Study. Annals of Pharmacotherapy. 2019 Jun 19:1060028019859543.
2. Han S, Park KS, Lee H, Zhu X, Lee JM, Suh HS. Transcutaneous electrical nerve stimulation (TENS) for pain control in women with primary dysmenorrhoea. Cochrane Database of Systematic Reviews. 2019, Issue 5.
3. Han S, Kim S, Kim H, and Suh HS. Cost-utility analysis of reslizumab for patients with severe eosinophilic asthma inadequately controlled with high-dose inhaled corticosteroids and long-acting β2-agonists in South Korea. Current Medical Research and Opinion. 2019 Apr 9:1-9.
4. Han S, Kim H, and Suh HS. The treatment pattern and adherence to direct oral anticoagulants in patients with atrial fibrillation aged over 65. PLOS ONE. 2019;14(4):e0214666.
5. Jung SY, Suh HS, and Kwon JW. Drug Holiday Patterns and Bisphosphonate-Related Osteonecrosis of the Jaw. Oral Diseases. 2019;25(2):471-480.
6. Kim S, Kim H, Kim E, Han S, Rane PP, Fox KM, Zhao Z, Qian Yi, and Suh HS. Utilization Patterns of Lipid-lowering Therapies in Patients with Atherosclerotic Cardiovascular Disease or Diabetes: A Population-based Study in South Korea. Clinical Therapeutics. 2018;40(6):940-951.
7. Suh HS, Kim JA, and Lee IH. Effects of a price cut reform on the cost and utilization of antidiabetic drugs in Korea: a national health insurance database study. BMC Health Services Research. 2018;18:429-439.

Abstract

COST-EFFECTIVENESS OF PHARMACOLOGIC TREATMENT OF FAMILIAL HYPERCHOLESTEROLEMIA

Hae Sun SUH[1]*, Hyungtae KIM[1], Siin KIM[1], and Sola Han[1]

[1] Pharmaceutical Economics, Outcomes Research and Policy, College of Pharmacy, Republic of Korea
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Familial hypercholesterolemia (FH) is a common genetic disorder and getting more attention nowadays. Patients with FH are experiencing a life time burden of increased low density lipoprotein cholesterol and elevated cardiovascular risk. To alleviate these burden, new therapies have been developed for the treatment of familial hypercholesterolemia. Assessing the clinical efficacy and effectiveness of new therapies is important in determining the role of new intervention. However, in general, new interventions are effective at a higher cost. Thus, economic evaluation of new intervention is getting more attention, which assesses whether the added benefit of a certain intervention is worth the added cost of that intervention. Healthcare costs are rapidly increasing and we need to understand how limited healthcare resources (budget) can be used most efficiently. The concept and types of economic evaluation will be introduced followed by an empirical cost-effectiveness analysis (cost-utility analysis) of a new treatment of familial hypercholesterolemia.

Keywords
Economic Evaluation, Cost-Effectiveness Analysis, Cost-Utility Analysis, Familial Hypercholesterolemia

Symposium 22

Alberico L.Catapano

Organization

University of Milan-Department of pharmacological and Biomolecular Sciences

Position & Title

Full Professor of Pharmacology

» Educational Background & Professional Experience

Year	Name of institution	Position
1979	University of Milan	Ph.D. in Clinical Pharmacology in the School of Pharmacology, University of Milan.
1977-1978	Hospital,Houston, TX, USA-Director Prof. A.M. Gotto	Hospital,Houston, TX, USA- Director Prof. A.M. Gotto
1975	University of Milan	Degree in CTF
2000 to date	University of Milan	· Full Professor of Pharmacology Chair of Pharmacology · Director of the Laboratory of Lipoprotein · Metabolism at the Department of Pharmacological Sciences University of Milan · The Director of Center of Epidemiology and Preventive Pharmacology of the University of Milano (SEFAP) · Director of the Center for the Study of Atherosclerosis · President of the Italian Society of Clinical and Sperimental Therapy(SITeCS) and General Director of the SISA Foundation · Director of the Center for the Study, Prevention and Therapy of Atherosclerosis of the University of Milan, at the Bassini Hospital · Head of Cardiovascular Research Line at Multimedica IRCCS- Sesto San Giovanni (Mi)

Alberico L. Catapano has been involved from 1972 in the field of Atherosclerosis, Lipids, Lipoproteins and genetic dislypidaemias. From the scientific standpoint Prof. Catapano has made landmark observations regarding the role of HSP's and of Petranxins in Atherogenesis and on the role of HDL in the modulation of the immune response. Alberico Catapano is Full Professor of Pharmacology at the University of Milano, Director of the Laboratory for the study of Lipoproteins and Atherosclerosis and of the Center for the Study of Atherosclerosis of the Italian Society of Atherosclerosis (S.I.S.A.) at the "Bassini" Hospital. He is also the Director of Center of Epidemiology and Preventive Pharmacology of the University of Milano (SEFAP). Professor Catapano is Past President of the European Atherosclerosis Society (EAS) and the Chairman of the EAS/ESC guidelines for the treatment of dyslipoproteinemias. He holds board positions in several learned Scientific Societies including the Italian Society for the Study of Atherosclerosis ; he is also President of the Italian Society of Clinical and Experimental Therapy (SITeCS)and General Director of the SISA Foundation.

He has authored more than 423 scientific papers in peer-reviewed journals and several books in the area of the atherosclerosis, lipoproteins and lipid metabolism. He is Editor of Atherosclerosis Supplements and also Co-editor of Atherosclerosis and Associate Editor of other scientific journals. According to Google Scholar, his H-index is 74 and the last 5 years has received more than 19,000 citations.

Abstract

THE FHSC COLLABORATION: CURRENT STATUS AND FUTURE DEVELOPEMENT

Alberico L CATAPANO

Department of Pharmacological and Biomolecular Sciences – University of Milan
Professor of Pharmacology - Director Center of Epidemiology and Preventive Pharmacology
Director Laboratory of Lipoproteins, Immunity and Atherosclerosis Director Center for the Study of Atherosclerosis at Bassini Hospital –Italy

BACKGROUND AND AIMS: Management of familial hypercholesterolaemia (FH) may vary across different settings due to factors related to population characteristics, practice, resources and/or policies. We conducted a survey among the worldwide network of EAS FHSC Lead Investigators to provide an overview of FH status in different countries.

METHODS: Lead Investigators from countries formally involved in the EAS FHSC by mid-May 2018 were invited to provide a brief report on FH status in their countries, including available information, programmes, initiatives, and management.

RESULTS: 63 countries provided reports. I will report the data on the principal activities and therapies offered as well as on the current status of FH detection rate

CONCLUSIONS: FH is a recognised public health concern. Management varies widely across countries, with overall suboptimal identification and under-treatment. Efforts and initiatives to improve FH knowledge and management are underway, including development of national registries, but support, particularly from health authorities, and better funding are greatly needed.

Keywords
FHSC; Familial hypercholesterolaemia; Primary dyslipidaemia