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Journal of Stem Cell Research & Therapy

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Research Interests

1. ***Effect of 2-Methoxyestradiol(2ME2), the final metabolite of estrogen metabolism on Angiotensin Type I Receptor(AT1R) Expression and Function***

2. ***2ME2 Mediated Cell Signaling Mechanism(s) for AT1R Downregulation***

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Pathophysiological Actions of AT1R

- **Hypertension**
- **Hypertrophy/hyperplasia**
- **Post-Myocardial infarction**
- **Heart Failure**
- **Breast cancer**
- **Atherosclerosis**
- **Liver fibrosis**

- *Angiotensin II/angiotensin II type I receptor (AT1R) signaling promotes MCF-7 breast cancer cells survival via PI3-kinase/Akt pathway.Zhao Y, ChenX et al.J Cell Physiol, 2010 Oct;225(1):168-73. doi: 10.1002/jcp.22209*
- *Molecular characterization of angiotensin II--induced hypertrophy of cardiac myocytes and hyperplasia of cardiac fibroblasts. Critical role of the AT1 receptor subtype.Sadoshima J and Izumo S.Circ Res, 1993 Sep;73(3):413-23*
- *Increased angiotensin II type 1 receptor expression in hypercholesterolemic atherosclerosis in rabbits.Yang BC, Phillips MI et al. Arterioscler Thromb Vasc Biol. 1998 Sep;18(9):1433-9.*
- *Mineralocorticoid and AT1 receptors in the paraventricular nucleus contribute to sympathetic hyperactivity and cardiac dysfunction in rats post myocardial infarct.Huang BS, Chen a et al. J Physiol. 2014 Jun 20. [Epub ahead of print]*
- *Angiotensin-II type 1 receptor interaction is a major regulator for liver fibrosis development in rats.Yoshiji H, Kuriyama S et al. Hepatology. 2001 Oct;34(4 Pt 1):745-50.*
- *The angiotensin II type 2 receptor in cardiovascular disease.Lemarie CA et al. J Renin Angiotensin Aldosterone Syst. 2010 Mar;11(1):19-31. doi: 10.1177/1470320309347785. Epub 2009 Oct 27*

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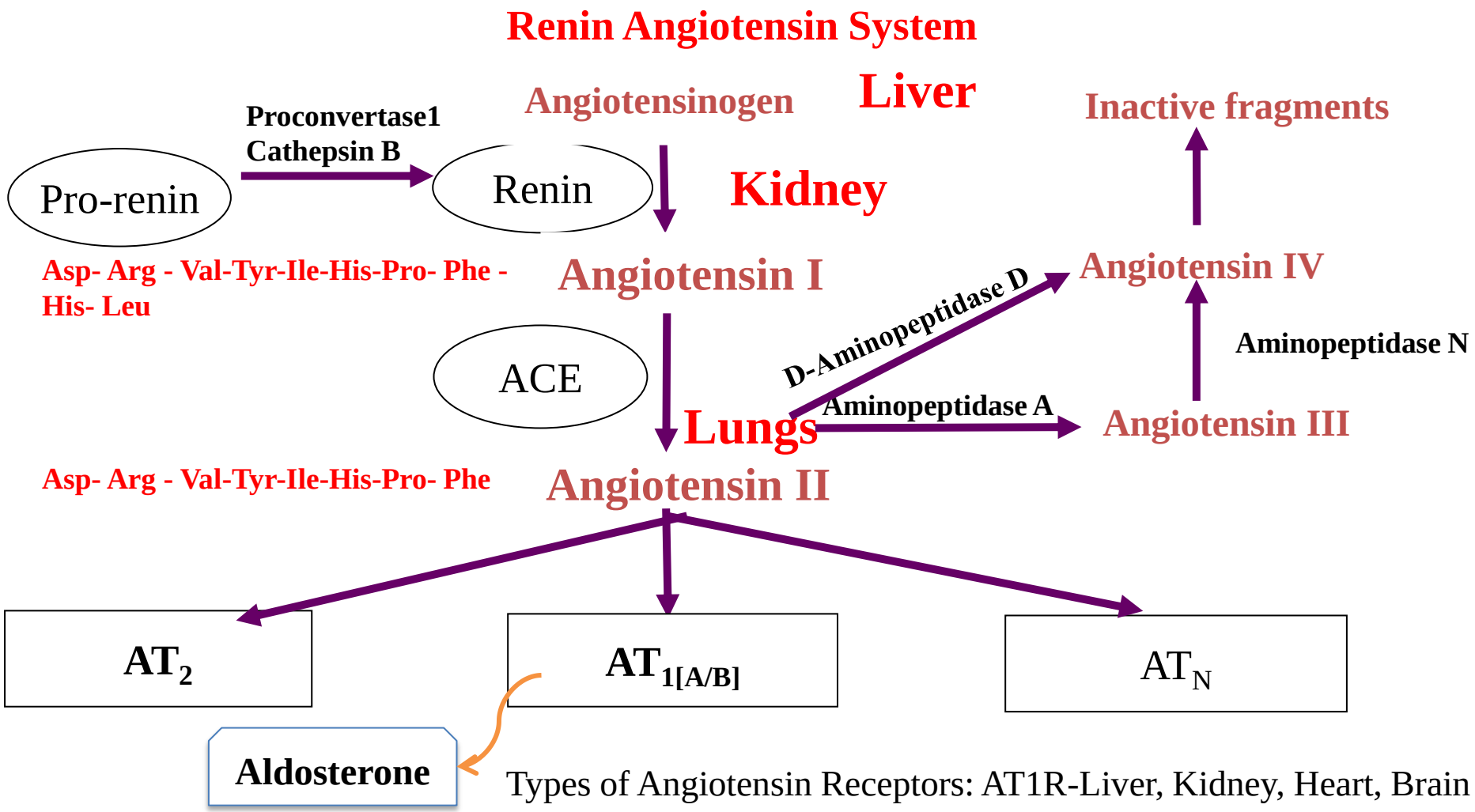

Types of Angiotensin Receptors: AT1R-Liver, Kidney, Heart, Brain

Atlas, S. A. (2007) The renin-angiotensin aldosterone system: pathophysiological role and pharmacologic inhibition, Journal of managed care pharmacy : JMCP 13, 9-20.

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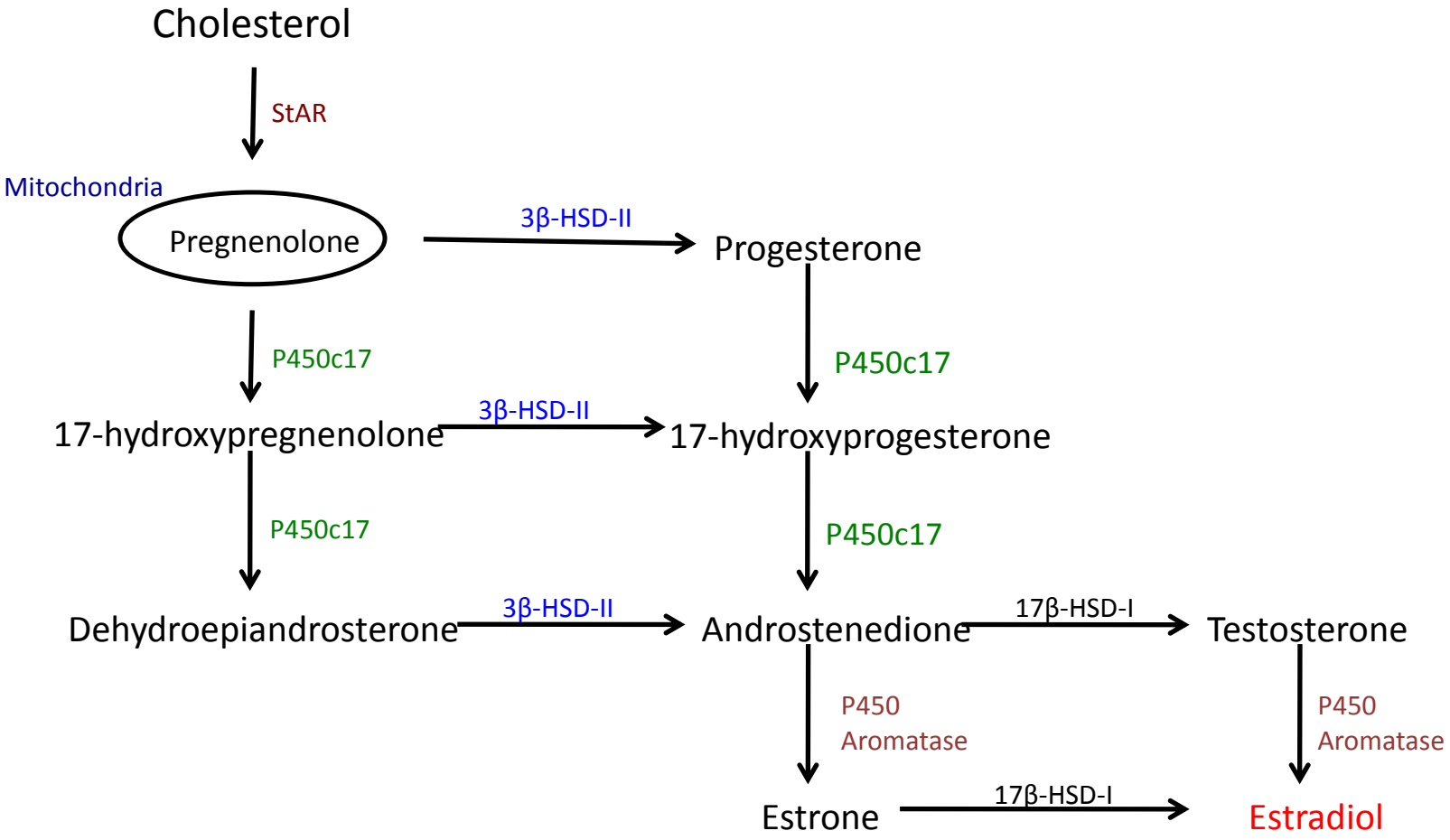
Estradiol Synthesis from Cholesterol



Bulun, S. E., Lin, Z., et al. (2005) Regulation of aromatase expression in estrogen-responsive breast and uterine disease: from bench to treatment, Pharmacological reviews 57, 359-383.

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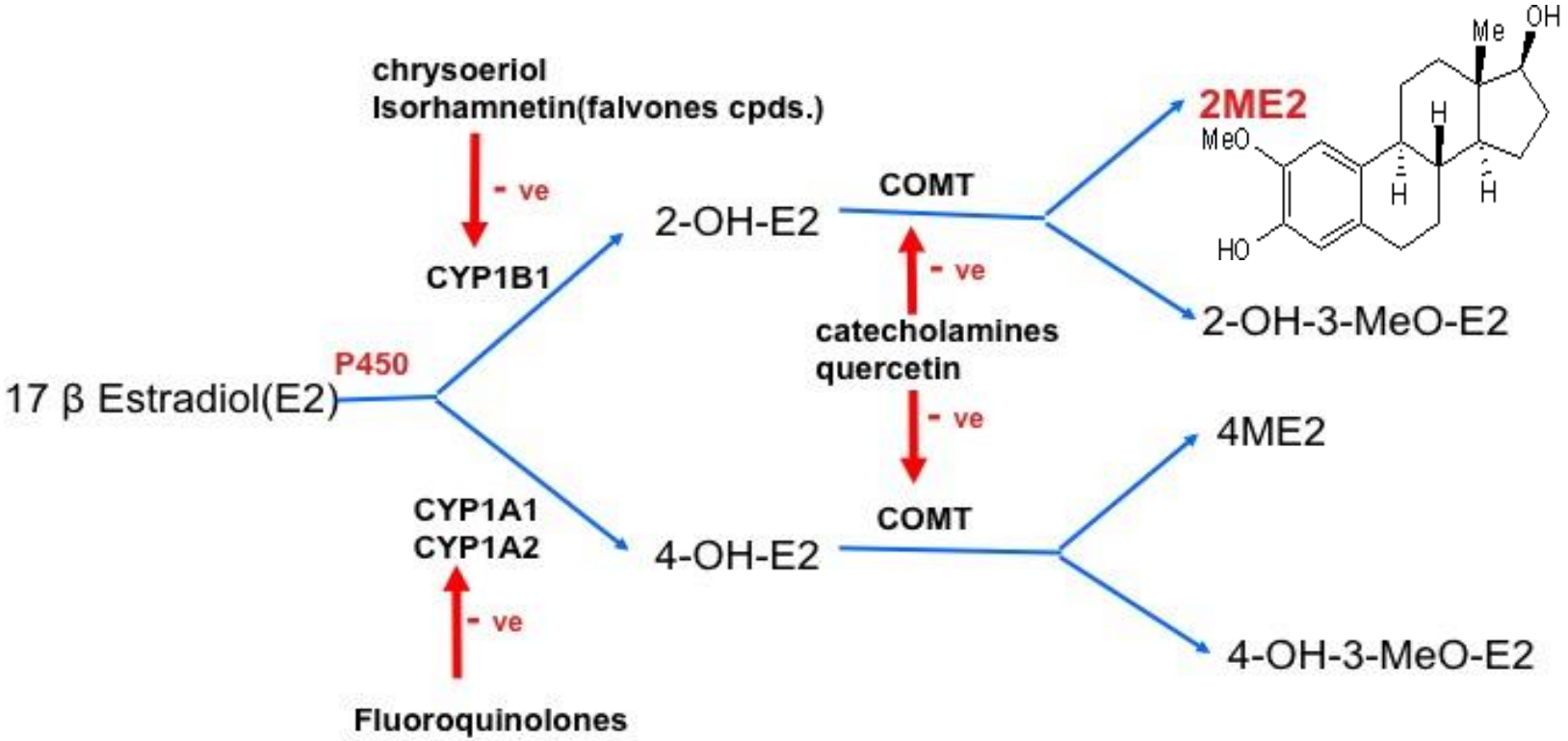
Metabolism of Estradiol to 2-Methoxyestradiol



- *Is 2-Methoxyestradiol an Endogenous Estrogen Metabolite That Inhibits Mammary Carcinogenesis? Bao Ting Zhu and Allan H. Conney;Cancer research 58, 2269-2277,1998*
- *Methoxyestradiols Mediate the Antimitogenic Effects of Estradiol on Vascular Smooth Muscle Cells Via Estrogen Receptor-Independent Mechanisms. Dubey, R. K., D. G. Gillespie, L. C. et al.. Biochem Biophys Res Commun 278, 27-33, 2000*

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Research Study

Cell Models:

1. A continuously passaged (normal) rat liver epithelial cells (WB)

The WB cells were maintained in Richter's Improved Minimum Essential Medium containing 10% fetal bovine serum (FBS), at 37^0C in 5% CO_2 under 100% humidity

2. Rat primary aortic smooth muscle cells(VSMC)

VSMC were maintained in Richter's Improved Minimum Essential Medium containing 20% fetal bovine serum (FBS) at 37^0C in 5% CO_2 under 100% humidity

Cells were grown to 75-80% confluence, and treatments were initiated in fresh medium

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Conclusions

- **Our study shows for the first time that 2ME2 mediates AT1R down-regulation through G-protein coupled receptor 30 tethering with epidermal growth factor receptor (EGFR) by activating matrix metalloproteinases inducing ERK1/2 activation.**

- **2ME2 mediated changes in AT1R expression may provide beneficial effects to the cardiovascular disorders such as hypertension**

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PUBLICATIONS & PRESENTATIONS

Sivaramakrishna, Koganti, Russell Snyder, Thomas Thekkumkara," Pharmacologic Effects of 2-Methoxyestradiol on Angiotensin Type 1 Receptor Down-regulation in Rat Liver Epithelial and Aortic Smooth Muscle Cells" *Gender Medicine*, 2012, Pubmed ID: 22366193.

Sivaramakrishna Koganti, Russell Snyder, Upendra Gumaste, Vardan Karamyan, Thomas Thekkumkara, "2-Methoxyestradiol binding of GPR30 down-regulates angiotensin AT_1 receptor" *The European Journal of Pharmacology*, 2013, Pubmed ID: 24262995.

Sivaramakrishna Koganti, Thomas Thekkumkara. *Experimental Biology, Anaheim, CA.* 4/2010.2-Methoxy Estradiol Mediated Downregulation of Angiotensin Type 1 Receptor Expression.

Stem Cells Research & Therapy Related Journals

- Single Cell Biology
- Cell & Developmental Biology
- Journal of Cell Science & Therapy

Stem Cell Research & Therapy
Related Conferences

- 4th International Conference and Exhibition on Cell & Gene Therapy
- 5th World Congress on Cell Science & Stem Cell Research
- 4th World Congress on Cell Science & Stem Cell Research

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