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KnowledgeLab 2016

The New (Molecular) World Order: What New Technologies Offer the Microbiology Lab and its Stakeholders

CPTs Joshua Martinez and Amanda Roth

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Disclaimer

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Historically Speaking: Laboratory Medicine

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Historically Speaking: Origins of PCR

http://tribesports.com/

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Historically Speaking: PCR

http://dnature.co.nz/

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PCR Today




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NGS in the Clinical Laboratory

- Germline variant identification for inherited diseases
- Somatic variations in cancer
- Detection of circulating cell-free DNA subpopulations
- Metamicrobial genomes of human flora
- Viral and bacterial genome sequencing during infections

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NGS Challenges in the Clinical Laboratory

- Which platform is best?
- How do I fit it in my lab workflow?
- How much will it cost?
- Who do I need to hire?
- Where does all the data go?
- What do I report?

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So What?

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2003-2012: Origins of The Antibiotic Resistance Crisis in the Military Health System

- Complicated, slow healing wounds
- Patient to nurse transmission
- Co-location w/ host nation patients
- Rapid transfer to numerous facilities
- Frequent intra-hospital transfers
- Positive pressure irrigation
- Need for reconstructive surgeries
- Dry pipeline: “Bad bugs, no drugs”

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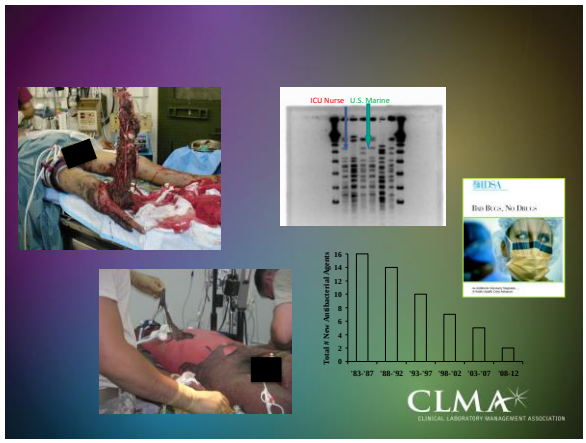
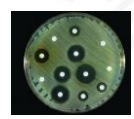


Standard Clinical Microbiology

- Bacterial Identification
- Antimicrobial susceptibility testing
- Screening assays for resistance
- Confirmatory tests for resistance



- Performed in-house?
- Sent out to reference lab?
- Turn-around time?

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Birth of the Multidrug-resistant organism Repository and Surveillance Network (MRSN)

- Still no novel ABX; AMR worsening
  - CDC, WHO, "Global threat" , Frontline – "Nightmare Bacteria"
- Resistance genes on the rise - best control strategies remain unknown
- Transformation by highly fragmented and damaged DNA - environmental cleaning implications
  - PNAS @www.pnas.org/cgi/doi10.1073
- Standard-of-care genotyping methods insufficient
  - Clin Infect Dis 2014:58:609-618
  - 2 MRSN reports Kuwait and CRE- SAMMC-WRNMMC
- Need WGS
- Sequencing not enough- need bioinformatics
- No integrated network: U.S. is 20yrs behind Europe
  - Clin Infect Dis 2013:56;1445

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Case in Point: the MRSN-ARMoR Program

- **MISSION:**
  - Conduct enterprise-wide epidemiologic surveillance of multidrug-resistant organisms (MDRO) to inform clinical practice, healthcare policy, and enhance infection control by collecting and characterizing MDRO across the Military Health System
  - Perform translational and applied research to improve surveillance and isolate characterization
- **BENEFITS & UNIQUENESS:**
  - Centralize and standardize the characterization and reporting of MDRO
  - Unburdens hospital labs of outbreak investigations
  - Collects isolates from unstable areas and war zones
  - Provides local and regional resistance data and trends
  - High resolution characterization of phenotypes of exceptional interest
  - Assist MHS with NHSN reporting of MDRO
  - Facilitates Joint Commission accreditation

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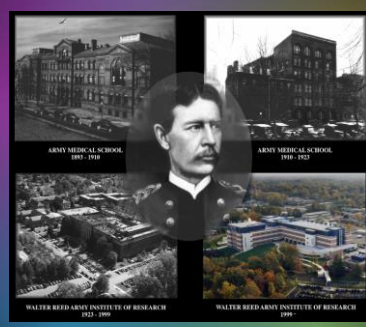
MRSN at the Walter Reed Army Inst. of Research



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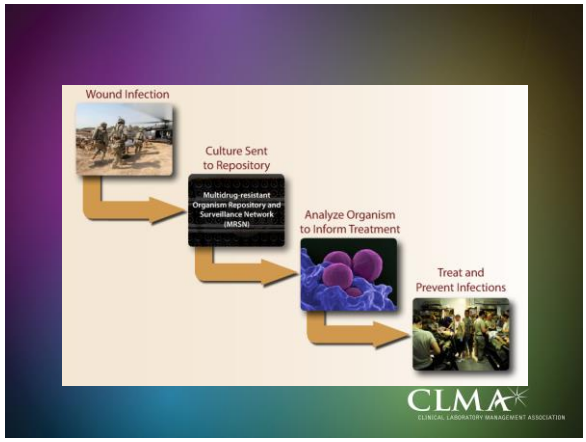

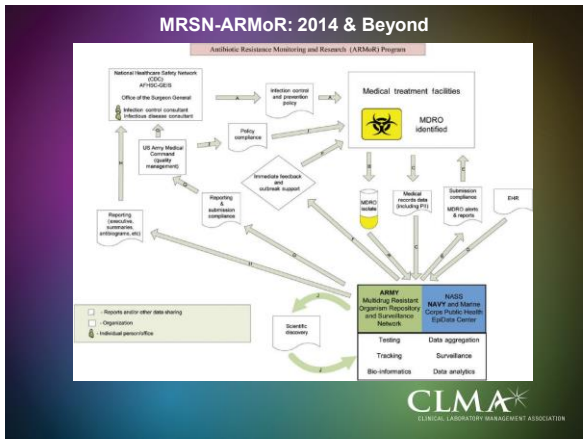

MRSN Capabilities

- Phenotypic Microbiology
  - Phoenix
  - Microscan
  - Vitek
  - MALDI-TOF
  - Sensititre
  - E-tests
- Sequencing
  - Next-Seq
  - Mi-Seq
  - PacBio
  - Automated Liquid Handlers
- Bioinformatics analysis
- ARMoR-Database

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MRSN Challenges

- Lack of standardized QC metrics
- "Non-agile" contract and acquisition process
- Technology limits

Lessons Learned and Solutions

- Maximize sequencing capacity!
- Minimize TAT!
- Pursuing CAP-accreditation of NGS (Mi-Seq), participation in GMI 2016 Proficiency Test
- Be vigilant of the NGS market and have vendors provide notification of new products
- Be business-minded – know how to get your purchases through!
- Be ready to hurry up and wait for IT assistance/approval
- Support and participate in standardization and accreditation organizations

MRSN-ARMoR Impact

- Hospitals currently enrolled: 288 (Iraq and Afghanistan included)
- Total isolates collected: ~26,000; total characterized: 5,000
- Assists w/ outbreak investigations: 25
  - USNS Comfort post earthquake Haiti
  - Fatal MRSA in NICU (policy influenced; illness and death probably averted)
  - HAP/VAP in Afghanistan (bronchoscope)
  - Colistin resistant *Acinetobacter* (antibiotic restriction)
  - VRE
- Monthly reports and special bulletins generated as needed: 11
  - First report of bla_{NDM-1} gene in MHS
  - First report of *qac*A/B gene in U.S. patient cohort
- Infection Prevention support to military working dogs (MRSA analog)
- Developed and validated RT-PCR assays for 'ESKAPE' pathogens

Making an Impact?

- First Place 2010 Surgeon General's Excalibur Award
- 2013 MHS Health Innovations Readiness Award
- 2015 MHSRS Outstanding Research Award – Military Team
- $10M funding for FY16

Summary

- Implementing a large scale NGS surveillance program is hard!
- Contracting and acquisitions in a bureaucracy is hard!
- Consider potential hurdles to avoid/mitigate risk
  - Data generation
  - Data analysis
  - Data sharing
  - Data storage
- Leverage experience of others

Acknowledgments

MRSN

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  - COL Stephen Thomas
  - COL Pitzer
  - COL Dana Renta
- COL Dana Renta

Questions?

Thank you for your attention!

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Carbapenemase Producers in the MHS

Carbapenemase Encoding Gene	Species	# of Isolates Found In	# of Patients Found In	Infection by species	Surveillance by species	Facilities Found At
bla_{KPC}	*K. pneumoniae*	110	70	86	24	A, B, C, E, F, K, L, N, Q, R
	E. coli	11	6	11	0	B, G N
	E. cloacae	3	3	3	0	B, D, N
bla_{NDM}	*K. pneumoniae*	6 (3*)	4	2	4	H, M, N, P
	E. cloacae	3*	3	3	0	I, M, H
	A. baumannii	27 (3*)	24	27	0	F, I
	A. schindleri	1	1	0	1	N
	P. stuartii	2	1	2	0	H
	E. coli	2	2	1	1	H
bla_{VIM}	*P. aeruginosa*	1*	1	1	0	J
	A. hemolyticus	1*	1	1	0	J
	A. junii	2*	2	2	0	J
	A. nosocomialis	1*	1	0	1	J
	A. baumannii	1*	1	1	0	J
bla_{OXA}	*C. freundii*	2	2	1	1	B, E
	P aeruginosa	3	3	2	1	H, O, U
	P. sneseudii	1	1	1	0	E
	E. cloacae	1	1	0	1	N

Carbapenemase Encoding Gene	Infection n (%)	Surveillance n (%)	Total
bla_{KPC}	100 (81%)	24 (19%)	124
bla_{NDM}	35 (85%)	6 (15%)	41
bla_{OXA}	5 (83%)	1 (17%)	6
bla_{VIM}	4 (57%)	3 (43%)	7

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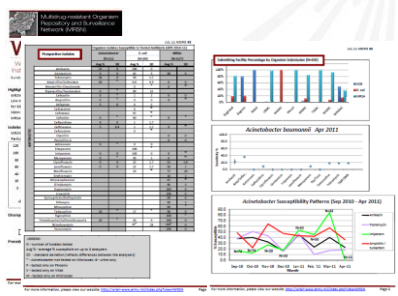
MRSN Deliverables: Monthly Reports



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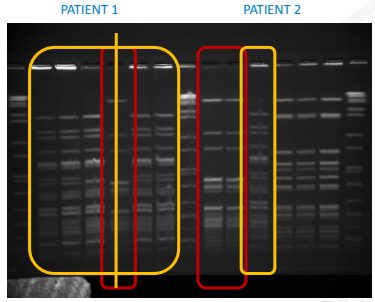
MRSN Deliverables: Outbreak Reports



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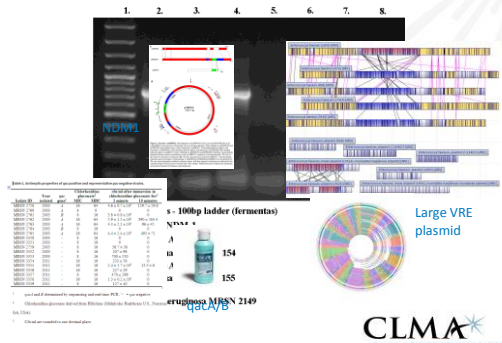
MRSN Deliverables: Emerging Pathogens



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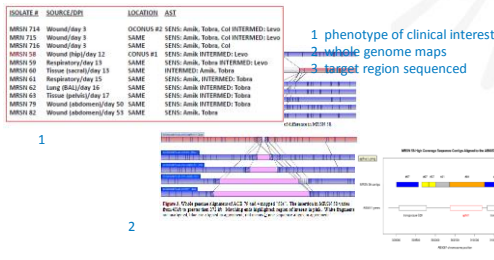
MRSN Deliverables: Comparative Genomics



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