

**THE IMPACT OF  
RAPID DETECTION OF  
ANTIMICROBIAL RESISTANT  
PATHOGENS**

**CIRAR Pilot Study**

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# CIRAR PILOT STUDY

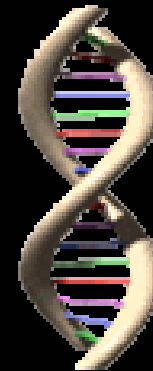
- **Principle:** Antimicrobial resistance presents a growing threat that may be best addressed through an interdisciplinary collaborative research approach.
- **Objective:** Demonstrate how molecular diagnostic tools can improve the rapid detection of drug resistant pathogens and be integrated into a larger interdisciplinary approach that translates molecular data into improved health outcomes
- **Long-term Goal:** Reduce and control antimicrobial resistance

# THE INTERDISCIPLINARY TEAM

- **CLINICAL MICROBIOLOGY**
  - ✓ Dr. Phyllis Della-Latta
- **PEDIATRICS**
  - ✓ Dr. Lisa Saiman
- **PHARMACY**
  - ✓ Dr. Christine Kubin
- **OB/GYN + EPIDEMIOLOGY**
  - ✓ Dr. Katherine Chen

# WHY MOLECULAR?

- **Faster time to results**
  - ✓ 2 hr vs. 48-72 hrs
- **Expedited institution of Infection Control precautions**
- **Reduction**
  - ✓ Nosocomial infection rates
  - ✓ Hospital length of stay
  - ✓ Spread of resistance into the environment/community
  - ✓ Healthcare costs
- **Improved clinical outcomes**



# THE CIRAR PILOT STUDY

- **Goal 1:** Develop rapid molecular ID methods for nontuberculous mycobacteria (NTM).
- **Goal 2:** Evaluate the impact of early reporting of NTM species identity.
- **Goal 3:** Develop rapid molecular methods to identify community- associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA).
- **Goal 4:** Determine the carriage of CA-MRSA in a cohort of pregnant women from our local community.

# PROGRESS NTM-RELATED GOALS

- **Important points:**
  - 1.** Antimicrobial resistance is not only acquired through mutation or by exchange of genetic elements carrying resistance determinants but can be intrinsic in nature.
  - 2.** In these cases, rapid pathogen identification can predict species specific drug resistance patterns in advance of drug susceptibility testing → inform the choice of empiric therapy.
  - 3.** Many NTM → differential patterns of intrinsic drug resistance → NTM species ID is important.

# GOAL 1

Develop rapid molecular ID methods for NTM.

- **Test strategy is to identify each NTM by way of unique DNA sequences:**
  1. Amplify portions of the DNA that are common to all NTM by PCR (e.g. *16S rRNA* ).
  2. Perform DNA sequence analysis (automated).
  3. Use that data to identify the NTM by the species-specific “bar-code” within its DNA .
- **Progress**
  1. Evaluating the protocol performance with clinical isolates of known identity.
  2. Building a database of accurate sequences.
  3. Utilizing the protocol to identify NTMs in the lab.
    - ✓ >40 isolates – later found to be accurately identified
    - ✓ 3 new NTM species found
    - ✓ One segment of the protocol works for all bacteria

# GOAL 2

Evaluate the impact of early reporting of NTM species.

- **Interdisciplinary Component:**
  - ✓ Chart reviews of relevant parameters that may be impacted by rapid molecular diagnostics prior to the institution of these protocols for NTM ID.
    - e.g. time to positive ID, changes in therapy following positive ID (appropriate?), response to treatment/outcome – understand the baseline
  - ✓ Hope to launch a prospective component to begin to see how these parameters change once molecular ID of NTM is initiated routinely.

# PROGRESS MRSA-RELATED GOALS

- **Important points:**
  - 1. Almost 60% of all healthcare-associated *S. aureus* infections are due to MRSA.**
  - 2. High morbidity and mortality and excess hospitalization costs are associated with MRSA infections.**
  - 3. MRSA colonization of persons in the hospital and the community acts as a reservoir for continued dissemination.**

- **Healthcare-associated (HA)-MRSA:**
  1.  $\beta$ -lactam resistance is conferred by the *mecA* gene carried on a Staphylococcal Chromosomal Cassette (*SCCmec*) element
  2. HA-MRSA, that carry *SCCmec* types I-III, are **resistant** to many classes of drugs
  3. Choice for empiric therapy is vancomycin

- **CA-MRSA:**

1. CA-MRSA carry *SCCmec* types IV or V and are generally **sensitive** to many non- $\beta$ -lactam classes of drugs.
2. Endemic in the community, reentering the healthcare system.
3. *SCCmec*-type of an isolate is usually not established and so the default choice for empiric therapy for any MRSA remains vancomycin.

# GOAL 3

Develop rapid molecular methods to identify CA-MRSA.

- **Progress:**

- ✓ For *SCCmec*-typing, two previously described multiplex PCR platforms were adopted.\*
- ✓ Combined, these protocols differentiate the main *SCCmec* types and subtypes of HA-MRSA and CA-MRSA.
- ✓ Currently applying the PCR strategies to clinical isolates and control strains.

\* Oliveira and de Lencastre (AAC46:2155-61); Zhang et al. (JCM43:5026)

# GOAL 4

Determine the carriage of CA-MRSA in a cohort of pregnant women from our local community.

- **Interdisciplinary Component:**
  - ✓ Prospective surveillance study for methicillin-sensitive *S. aureus* (MSSA) and MRSA in prenatal group B *Streptococcus* (GBS) screening cultures.
  - ✓ Standard-of-care protocols for GBS screening.
  - ✓ Finalized cultures then evaluated for *S. aureus* by looking for growth on solid culture media.
  - ✓ Identified strains were further characterized – routine microbiology and molecular techniques.

# GOAL 4

Determine the carriage of CA-MRSA in a cohort of pregnant women from our local community.

- **Overall,**
  - ✓ 2963 vaginal/rectal GBS screening cultures
  - ✓ 508 *S. aureus* (17.1%)
  - ✓ 14 MRSA (0.5%)
- **SCC*mec*-typing**
  - ✓ 1 HA-MRSA (SCC*mec* type II).
  - ✓ 13 CA-MRSA (SCC*mec* type IV and type V).

# GOAL 4

- **Relevance:**
  - ✓ First to estimate the vaginal/rectal carriage of MSSA in pregnant women using prenatal GBS screening cultures.
  - ✓ First study to find vaginal/rectal MRSA colonization in women (pregnant or otherwise).
- **Future questions to address:**
  - ✓ Not known if vaginal/rectal MRSA carriage is associated with any risks to the mother or the neonate.
  - ✓ MRSA in the NICU is a big worry – should we be screening the mothers for vaginal/rectal MRSA? What to do if MRSA colonization is found?

# SUMMARY

- **Achievements:**
  - ✓ Developed a protocol to rapidly characterize difficult to ID bacterial pathogens.
  - ✓ Instituted and applied a method to identify CA-MRSA strains by SCC*mec*-typing.
- **How to broaden these molecular diagnostic-related projects and make them more interdisciplinary?**

Rapid  
Molecular  
Dx

Treatment + Outcomes

Epidemiology

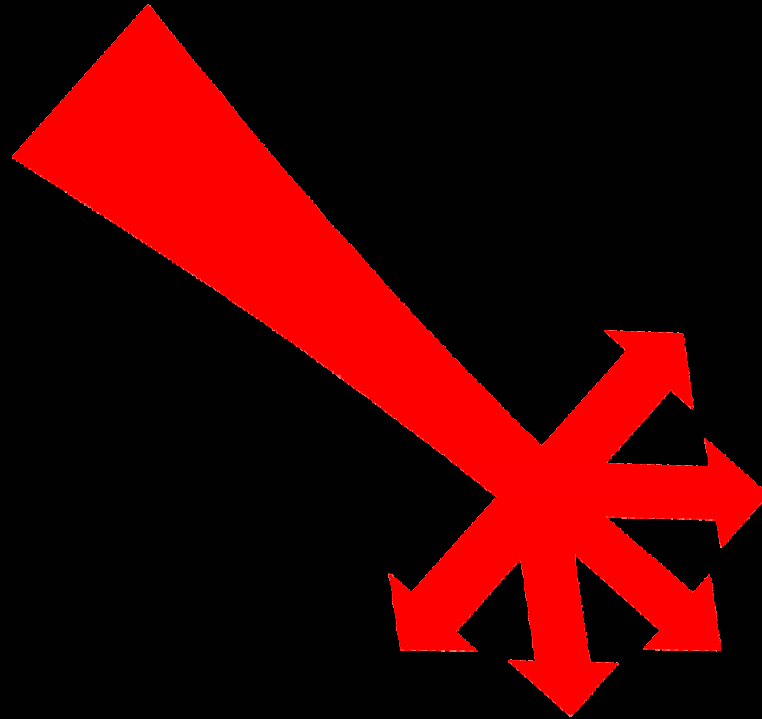
Surveillance +  
Infection Control

Routine Screening

Policy

Cost Analyses

Physician Education +  
Notification



**THANKS**

