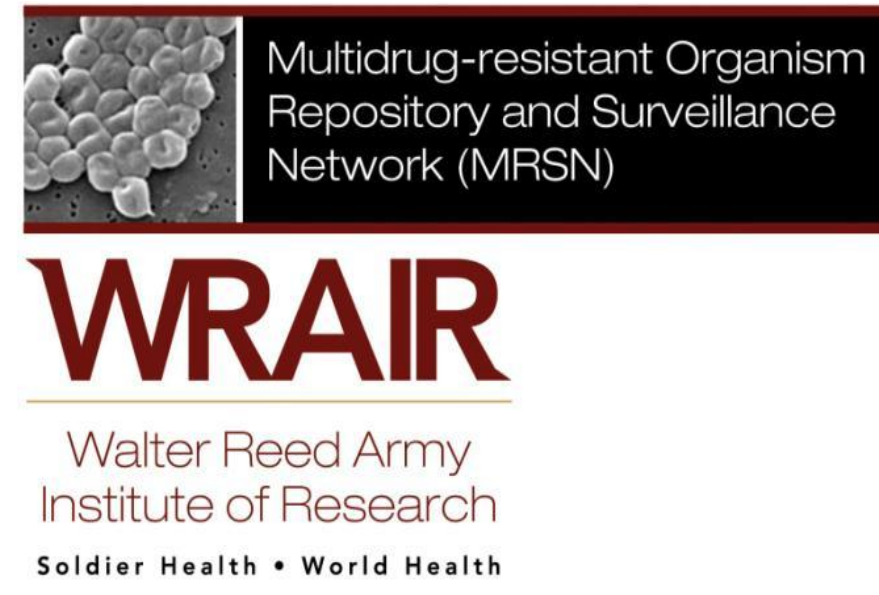


# The Multidrug-resistant Organism Repository and Surveillance Network: Program Announcement and Early Results



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## Background

Responding to an epidemic of nosocomial and wound infections with multidrug-resistant Gram-negative bacteria (MDRO), the Walter Reed Army Institute of Research (WRAIR) launched the Multidrug-resistant organism Repository and Surveillance Network (MRSN) in July 2009.

## Mission

The current mission of the MRSN is to conduct Army-wide epidemiologic surveillance of MDRO to inform clinical practice, healthcare policy, and enhance infection control by collecting and characterizing MDRO across the Army Medical Command.

## Objective

The ultimate goal of the MRSN is to expand to include all three services, and inform MDRO-related epidemiology across the MHS enterprise.

## Methods

Under a performance improvement mandate (MEDCOM Policy 09-050), US Army hospitals - including those in Iraq and Afghanistan - submit MDRO and methicillin-resistant *S. aureus* isolated from clinical infections and active surveillance programs along with the associated clinical-demographic information.

Navy and Air Force hospitals are invited and encouraged, but not required to participate.

At the repository in Maryland, isolates undergo the following:

- 1) confirmation of organism identification and drug susceptibility in triplicate
- 2) pulsed-field gel electrophoresis (PFGE) to determine strain relatedness
- 3) optical genome mapping to distinguish features not detectable by PFGE and to determine genomic markers of virulence, drug resistance, or organism evolution
- 4) real-time polymerase chain reaction (PCR) for genes that confer extreme drug resistance (New Delhi Metallo-beta-lactamase) or antiseptic resistance (qacA/B)
- 5) DNA sequencing
- 6) archival cryopreservation with linkage to a relational database

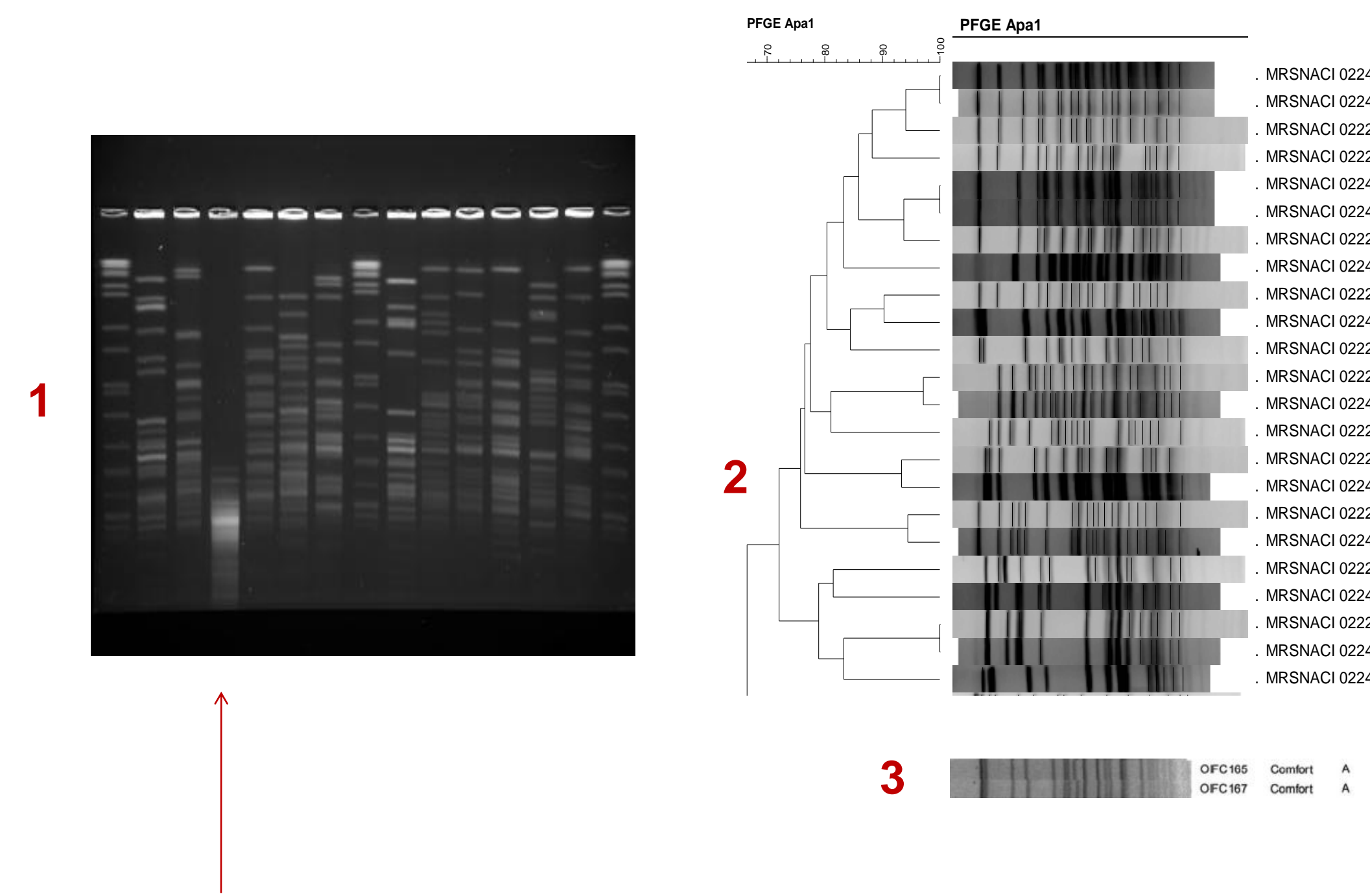
Repository personnel provide epidemiologic and microbiologic reports and infection control information to hospitals and policy makers, and conduct site assistance visits.

The MRSN collaborates with the Navy and Marine Corps Public Health Center, the Army Public Health Command, the Tri-Services Infection Prevention and Control Panel, the Army Veterinary Corps, and the Centers for Disease Control and Prevention (CDC).

## Results

### MRSN Activity Summary July 2009- March 2011

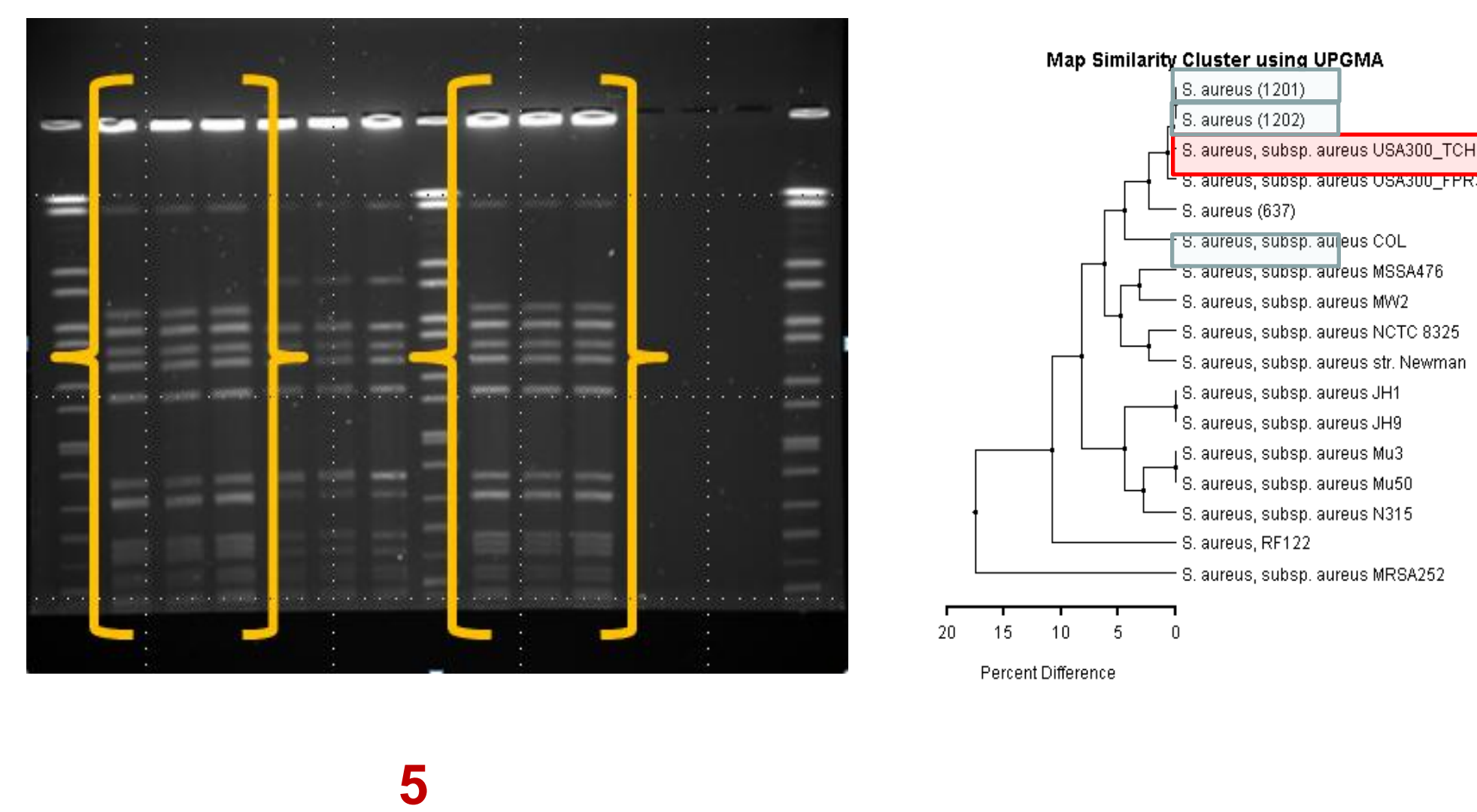
Hospitals currently enrolled: 2 deployed / 7 fixed  
 Assists w/ outbreak investigations: 8 requests from 4 different MTFs  
 Total isolates collected: ~3,000; total characterized: 1,500  
 Monthly reports and special bulletins generated as needed: 5  
 First report of NDM1 gene in MHS: 2/840  
 First report of qacA/B gene in U.S.: 8/ 230  
 Infection Prevention support to military working dogs (MRSA analog)  
 Use and Value of MRSN published in Lancet ID, Jan 2011



Figures 1, 2 and 3

Gel image (1) and dendrogram (2) of Haitian isolates showing lack of a predominant strain and absence of relationship and similarity to previous outbreak isolates (3)

Red arrow indicates a lane with *Klebsiella* originally misidentified as *Acinetobacter*, demonstrating importance of re-confirmation by MRSN laboratory



Figures 5 and 6

Gel image of MRSA isolates demonstrating that isolates are indistinguishable using PFGE (5), but contain potentially important difference in genomic content based on optical genome mapping, demonstrating the discriminatory power of that technology (6)

## Results cont'd

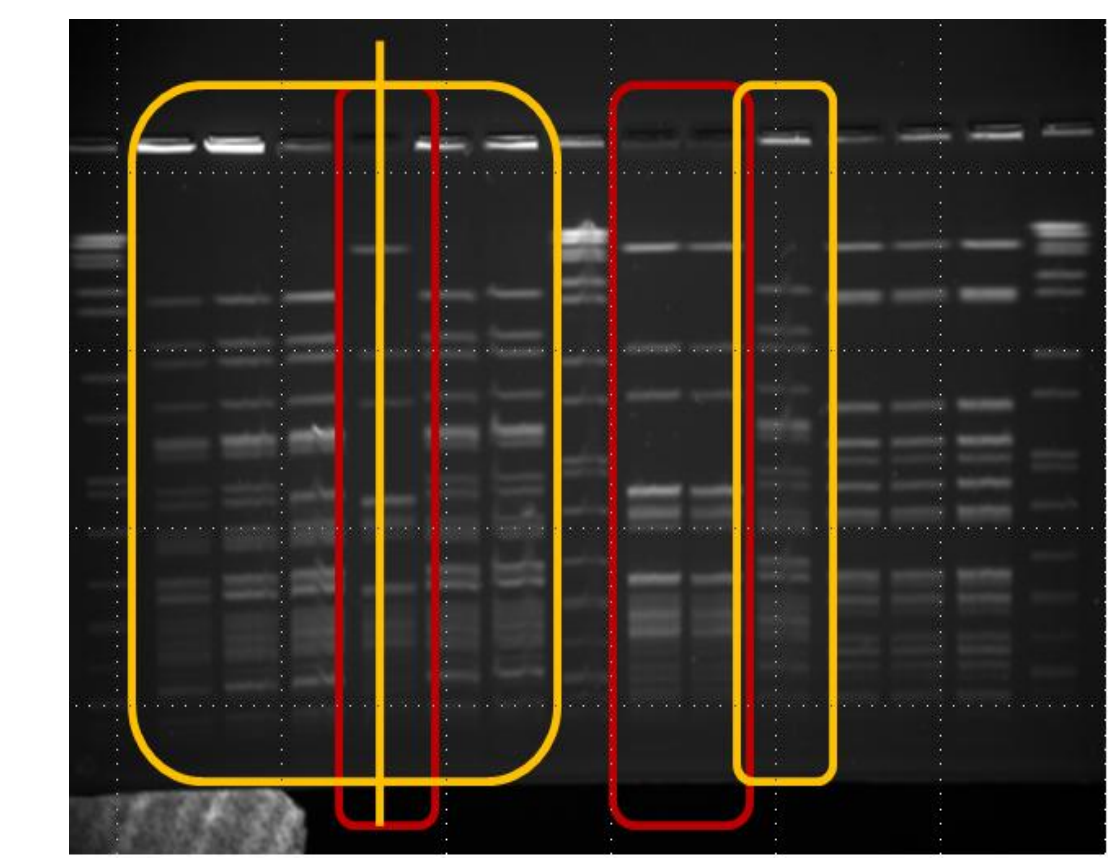


Figure 7

Gel image demonstrating 2 different indistinguishable *Acinetobacter* isolates from 2 patients and also demonstrating the importance of collecting every isolate from each patient. Collection approach allows for identification of shared multiple strains.

## Discussion

From July 2009 to January 2011, 1965 isolates were collected.

Assistance with outbreak investigation or isolate characterization was requested from four facilities on eight occasions.

Three antibiograms were produced, which highlight the alarmingly high frequency of multidrug resistance. For example, only 16% of *Acinetobacter* isolates remain susceptible to carbapenem antibacterials (the therapeutic mainstays.)

Turn-around time from requesting assistance from the MRSN followed by shipping, characterization of isolates by the MRSN, and feedback of actionable information to the healthcare facility was 2 weeks for overseas hospitals (USNS Comfort in Haiti) to 3.5 days for hospitals in the eastern U.S. Requests to provide isolates for isolates for basic research or assay and drug development occurred frequently.

Although nascent, the MRSN has demonstrated its impact and usefulness by providing actionable information in near real time to MTFs in Iraq, Haiti, Maryland, and the District of Columbia; and by unburdening clinical labs of outbreak investigation regardless of location.

The MRSN was also awarded the 2010 Surgeon General's Excalibur Award.

As the program matures, turn around time is expected to decrease and the surveillance network will increase.

Currently the MRSN is providing support to the Veterinary Command by performing active surveillance for important pathogens affecting military working dogs (multidrug-resistant *Staphylococcus aureus*, *S. pseudintermedius*, and *S. schleiferi*).

As was recently briefed to the House Armed Services Committee Oversight and Investigations Subcommittee, the program should be expanded to include all three Services.

The views expressed here are solely those of the authors and do not reflect the official policy of the Department of the Army, Department of Defense or U.S. Government.

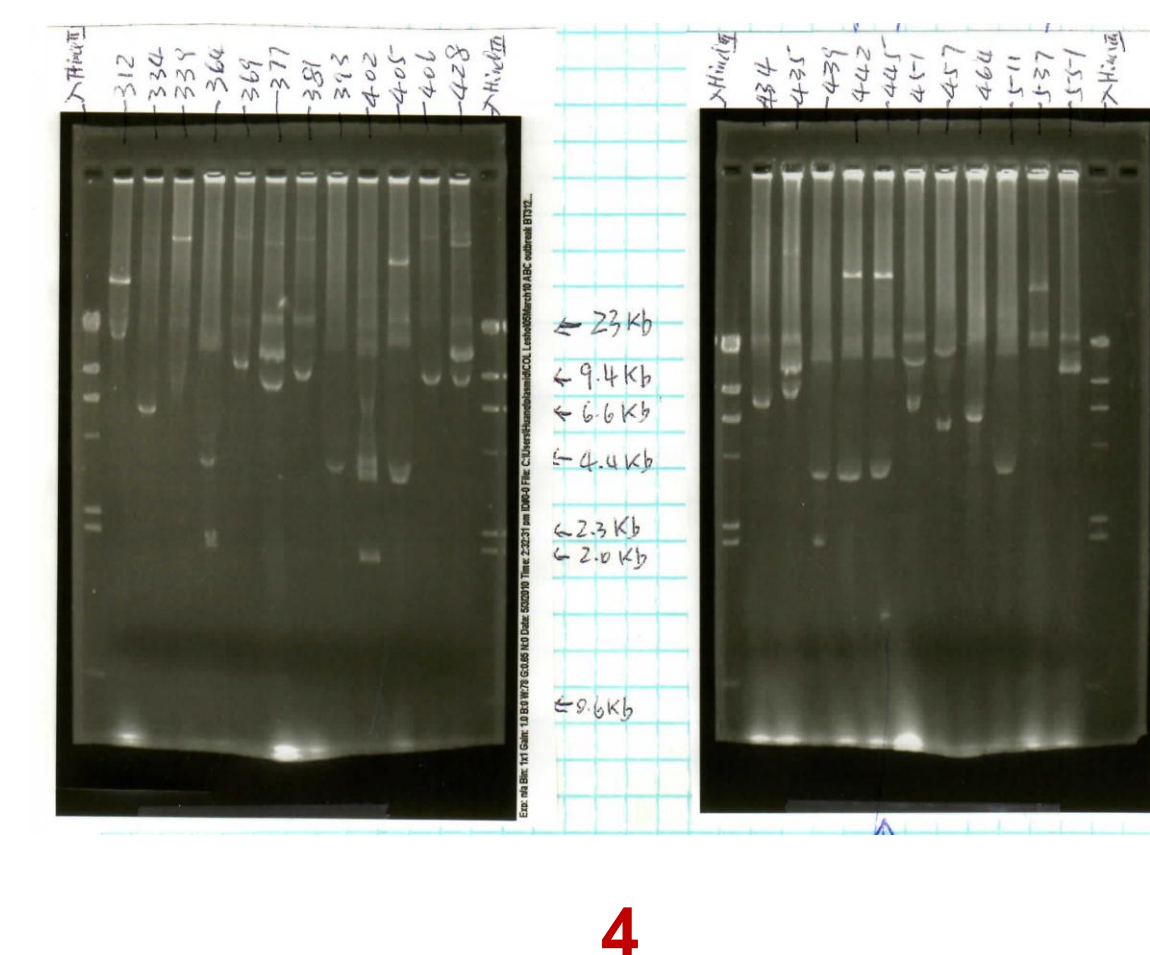
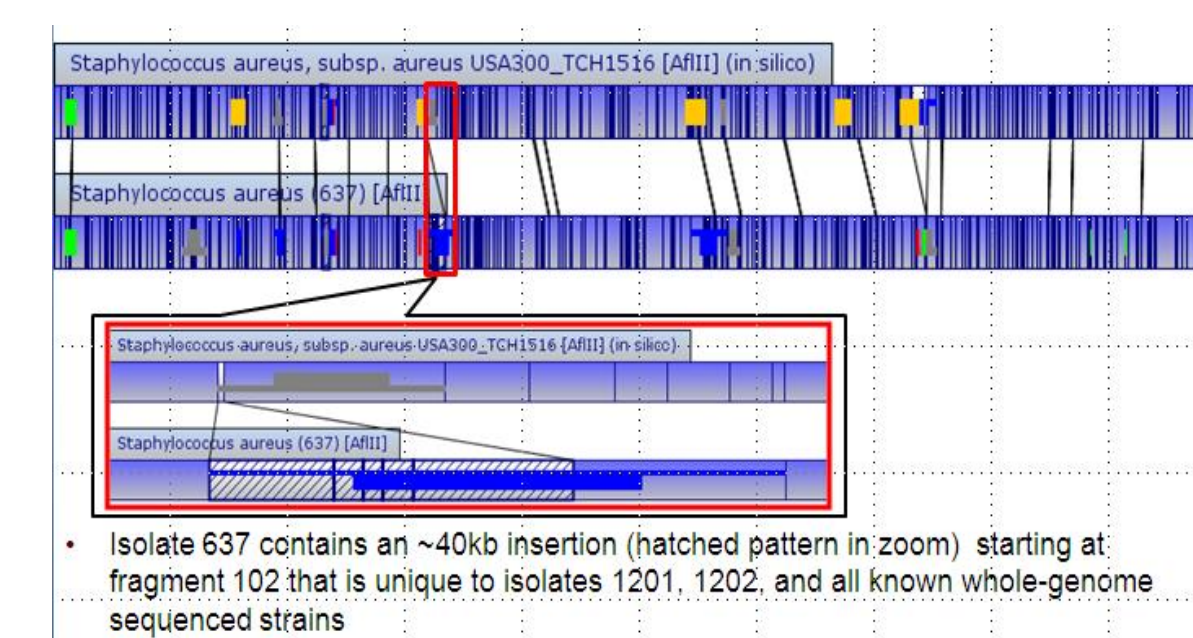
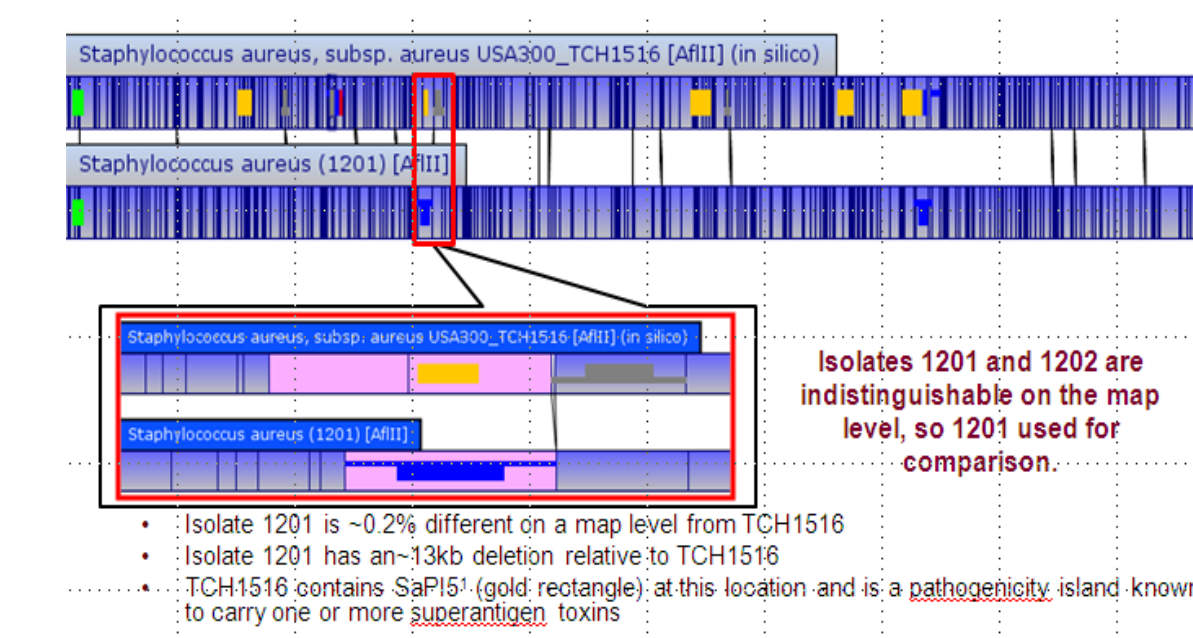


Figure 4

Gel image of plasmid profiles of same Haitian isolates showing absence of shared plasmid and overall concordance with PFGE profile



6a



6b

Isolate 637 contains an ~40kb insertion (hatched pattern in zoom) starting at fragment 102 that is unique to isolates 1201, 1202, and all known whole-genome sequenced strains

Isolate 1201 is ~0.2% different on a map level from TCH1516

TCH1516 contains SAPH (gold rectangle) at this location and is a pathogenicity island known to carry one or more superantigen toxins

Isolates 1201 and 1202 are indistinguishable on the map level, so 1201 used for comparison