Towards an integrated approach to the problem of antimicrobial resistance in Australia

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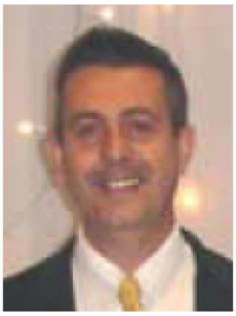

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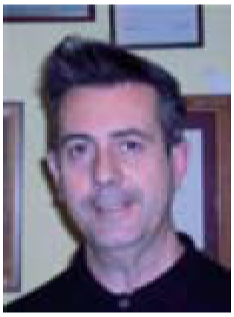
Molecular science of antimicrobial resistance



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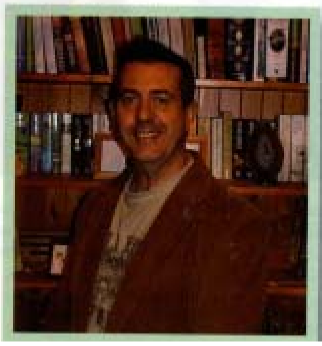
Making sense of resistance genes

New technology in defining phenotypic and molecular methods in detecting and understanding bacterial resistance

In recent years, a wide variety of new technology has been introduced in the laboratory for detecting resistance markers. This has helped the scientific and medical community in detecting and understanding antimicrobial resistance. One thing that we have learned from this new technology is that both phenotypic standardised methods and molecular techniques are needed to understand the complex evolution of resistance. Table 1 shows organisms with unusual bacterial resistances that need reference laboratory confirmation[1].



bacteria may include one or several factors such as modified penicillin-binding proteins (PBP) sites, exclusion by porin down-regulation, efflux systems and inner membrane transporters, membrane fusion proteins and efflux-associated outer membrane protein. Figures 1-5 illustrate some of these physiological resistance mechanisms[5-8].

In GNB, the ability to regulate access to the cell through a hydrophobic outer membrane, coupled with the ability to acquire genetic material under

Global changes

Bacterial populations, environmental pressures and the future of predicting antimicrobial resistance and pathogenicity

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Robert Koch quickly recognised that there was no universal environmental condition which would support the growth of all bacteria. Bacterial cells within clonal populations can show phenotypic variation due to internal stochastic processes. Variation between individual cells can be beneficial as well as detrimental to the survival of a population exposed to stress such as change in environmental conditions and many other variables such as selective antibiotic pressure. Variation in the level of proteins relevant for growth or survival among individual cells in a population is likely to play a role in drug resistance and disease. Cells reproduce by incorporating metabolite molecules and die at rates dependent on their gene expression and environmental states [1,2].

Fitness costs of antimicrobial resistance associated with chromosomal mutations and plasmid-borne resistance genes have been demonstrated in many studies in both Gram-negative (ESBL as shown in Figure 1, MBL and plasmid-mediated AmpC) and Gram-positive resistant (MRSA and VRE) bacteria [3]. The best example of this is the current global distribution of a staphylococcal bacterial strain, called USA300; this was first isolated in September 2000 and has been implicated in outbreaks of skin and soft tissue infections in healthy individuals in 21 US states, Canada, Europe and recently from travellers to Australia [4]. USA300 is associated with unusually invasive disease and is also sometimes resistant to multiple antibiotics.

Françoise Perdreau-Remington, Binh Diep [5] (University of California, San Francisco, CA, USA), and colleagues worked out the genetic sequence of USA300 and compared it to other strains of *S. aureus* to identify the genes responsible for its distinctive virulence properties. They found that USA300

Workshops ASM National Meetings:

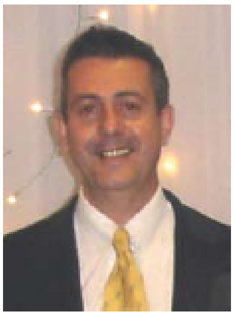
ASM members listen attentively to the lecturer

Professor Tom Riley from the University of WA

Stephen Teistram from the University of Tasmania

Dr. John Merlino (left) Chair/Convenor and Dr. Peter Taylor South Eastern Area Laboratory Services, Sydney

Improved methods in the identification and screening for antimicrobial resistance: chromogenic screening for *Staphylococcus aureus* and methicillin resistance



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New enzyme specific synthetic chromogenic substrates offer an advance in the laboratory screening and detection of *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA), with increased efficiency, reduced labour costs and decreased turn around times, especially when incorporated into existing laboratory workflows, to support current methods of microbial identification and the detection of resistance.

incorporated readily into existing laboratory workflows to support current methods of microbial identification (Figure 1).

The development of a new class of synthetic chromogen compounds, the indolyl compounds, which are linked to pyranoside or other substrates targeting specific constitutive enzymes, offers an alternative and specific approach to the detection of *S. aureus* and MRSA. The advantage of the halogenated indolyl derivatives is that they produce finer precipitates that are less likely to diffuse from the site of formation, making them especially useful for detecting enzymatic activity in bacterial cells. The use of new synthetic chromogenic substrates such as 5-bromo-4-chloro-3-Indolyl-beta-D- and 5-bromo-6-chloro-3-Indolyl-beta-D- compounds in primary isolation media allows the recovery and early visual presumptive identification *S. aureus* or specifically MRSA if an inhibitory antibiotic such as cefoxitin is introduced in the media [11].

In traditionally described chromogenic reactions, an organism is usually detected indirectly by noting a biochemical change in the substrate in relation to the organism. This detection usually takes place extracellularly and is perceived by an indicator change in response to a pH change, or by the addition of chemicals

First clinical case of a locally acquired carbapenem-resistant VIM-1 metallo-β-lactamase in *Pseudomonas aeruginosa* in Australia

John Merlino, Harold W Stokes, Elaine Y-L Cheong and Thomas Gottlieb

MJA 2009; 191 (5): 28

Recognition of USA300 isolates of community-acquired methicillin-resistant *Staphylococcus aureus* in Australia

Thomas Gottlieb, Wei-Yuen Su, John Merlino and Elaine Y-L Cheong

MJA 2008; 189 (3): 179-180

Tn*6060*, a Transposon from a Genomic Island in a *Pseudomonas aeruginosa* Clinical Isolate That Includes Two Class 1 Integrons▽

Piklu Roy Chowdhury,[1] John Merlino,[2] Maurizio Labbate,[1] Elaine Y.-L. Cheong,[2] Thomas Gottlieb,[2] and H. W. Stokes[1*]

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