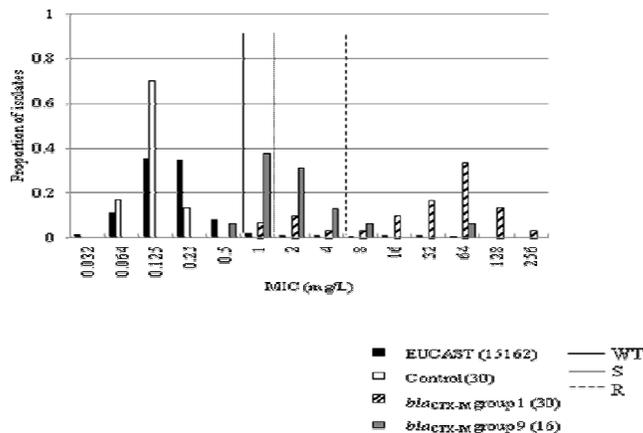


## AGAR proposal

Jon Iredell 2015

Antibiotic resistance in the Enterobacteriaceae is dominated by transmissible resistance (R) with variable phenotype. Much of the more recently troublesome phenotypes such as carbapenem resistance, is usually “silently” transmitted. The MIC for a given R gene in an organism such as *E coli* is normally distributed (Fig 1), and can be predicted on genotype<sup>1</sup>.



The distribution of R genes among plasmids and host strains is being studied in a collection of isolates from UK (Woodford N/ Livermore D), US (Kaul K/Tang YW/ Peterson L), China (Ai X), Singapore (Lin R/ Tamyah P), Ghana (Agyekum A), Bangladesh (Kamruzzaman/ Mohsin), and other sites in order to test the predictive power of the genotype-phenotype relationship as this is essential for effective planning of screening and diagnostic tool development.

We propose to test a range of *E coli* and *K pn* with CTX MIC>1 and GEN >8 and compare these with those that are “sensitive” from the same geographical regions (see listed countries above). Initially we would test for the presence of the important beta-lactam and aminoglycoside and associated mobile quinolone resistance genes. A high-throughput assay for AbR targets in multiplex based on a Sequenom platform but suitable for a range of others will be used. The results will be sent to AGAR for further consideration but is likely to be of sufficient interest to be publishable in some form, even if just on the AGAR website.

Target genes include CTX-M major types and subsets; SHV-5/12, TEM-1; VEB, GES, OXA including -10, -30, -48/181, AIM, KPC, IMP major types and subsets, NDMs, major pAmpCs incl DHA-1, CMY-2, major qnrs (A,B,S), qep, aadB, aac3(II), acc6II subtypes (aacA4 including amikacin and qr variants), rmtA, B, C, armA

Source isolates up to 100 *E coli* CTX>1 and 100 GEN>8 (accepting that overlap is expected in more than half, but selection done on single phenotype alone so that it is random) and a matching set of at least 50 that are S to “everything”. These are the criteria used for all other sets above. These are also being applied to *K pn* but numbers are slower to obtain and may need to be 50/50/20 rather than 100/100/50.

Funding requested: nil.

Labour: we can provide experienced personnel to streak out strains and package for transport.

Expected outcomes: all data will be sent back to AGAR to determine disposition

Opportunities exist to further examine relationships between isolates, plasmids and genes and can be discussed after initial analysis.

<sup>i</sup> Ginn, A., Zong, Z., Wiklendt, A., Thomas, L., Merlino, J., Gottlieb, T., van Hal, S., Harkness, J., Macleod, C., Bell, S., Partridge, S., Iredell, J. (2013). Limited diversity in the gene pool allows prediction of third-generation cephalosporin and aminoglycoside resistance in *Escherichia coli* and *Klebsiella pneumoniae*. *International Journal of Antimicrobial Agents*, 42(1), 19-26