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Impact of a long-term antibiotic prophylaxis on the bladder colonisation by E. coli in clean intermittent self-catheterisation patients

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Introduction & Objectives: The uropathogenic E.coli (UPEC) is responsible for causing between 60 to 80% of all UTI cases. The AnTIC study was a randomised, open-label, superiority trial which compared the antibiotic prophylaxis versus short term antibiotic treatment for recurrent UTI prevention in CISC patients. Our aim was to genetically define AnTIC UPEC isolates and correlate bacterial motility, a UTI virulence factor, and antibiotic use asking: 1) Does antibiotic treatment select specific genetic subgroupings? 2) What is the nature of multi-drug resistance (MDR) development? and 3) Does the genetics of motile strains aid our understanding of the observed clade structure and antibiotic use?

Materials & Methods: The AnTIC bio-bank of bacterial isolates generated during the RCT phase was the source of 96 random UPEC isolates that were genotyped. A phylogenetic tree was generated. Motility was assessed using motility agar assays and correlated to clade data. Finally, we exploited next-generation sequencing technology to sequence the whole genome of specific samples from our cohort, based on motility and antibiotic resistance profiles.

Results: AnTIC E.coli showed a bias toward clades B2 and D (Fig1),while B2 isolation is expected from rUTI, the incidence of clade D members was not. 44% of all isolates were non-motile, and if motile 63% exhibited an unexpected low motility phenotype (< or =1cm;p< 0.001) (Fig2) compared to commensal E.coli (average motile swarm: 3.3 cm). Analysis for MDR amongst UPEC isolates has led to ongoing whole genome sequencing of 50 more AnTIC isolates and all clade D strains.

Fig 1: Phylogenetic tree of 96 randomized AnTIC *E. coli* strains. McNally et al (2013) *E. coli* genomes were reference points for clade boundaries (defined by EHEC, EPEC, ETEC, Comm etc.). Phylogenetic data dissects the species *E. coli* in to 6 clades (A, B1, B2, D, E and F). Uropathogenic *E. coli* (UPEC) are predominantly grouped in clade B2.

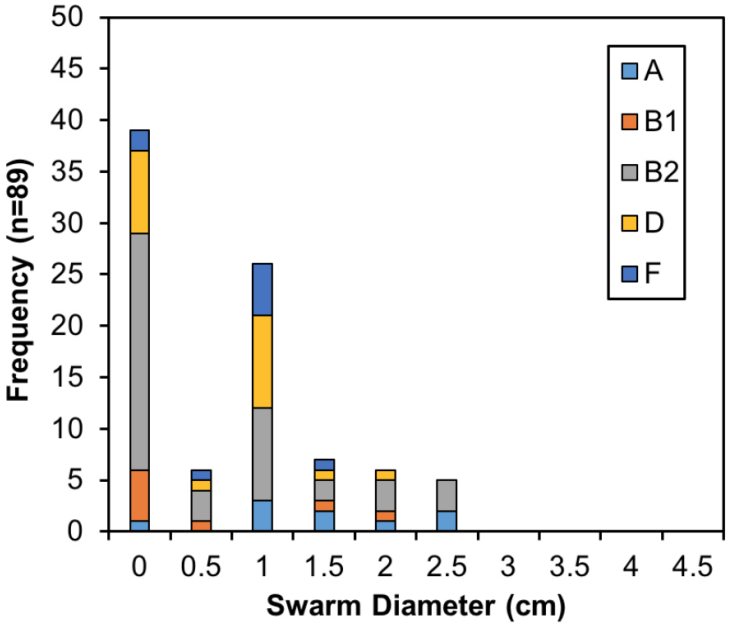

Fig 2: Swarm diameter of the 96 AnTIC *E. coli* strains showing the clade distribution in each grouping.

Conclusions: Our work provides a unique insight of UPEC isolated during a CISC based clinical trial. The greater frequency of clade D and reduced motility may reflect the source of the isolates. Whole genome sequence analysis will further improve our understanding of host-microbe interactions during CISC use.