

PROGRAMME 1: GENETIC FACTORS CONTRIBUTING TO THE SUCCESS OF CF ‘SUPERBUGS’ IN THE UNITED KINGDOM

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Summary of research

Lung infections due to the bacterium *Pseudomonas aeruginosa* are the major cause of morbidity and mortality in patients with cystic fibrosis (CF), but not all “strains” of *P. aeruginosa* are the same. We have been studying a particular strain called the “Liverpool Epidemic Strain (LES)” which can be called a “CF superbug” because of its unusual properties. It is very resistant to antibiotics, is associated with more severe disease, has caused unusual non-CF infections and, most importantly, can be transmitted from one CF patient to another. Hence LES-infected patients must be recognised and segregated from infection-free patients. Furthermore, this strain is the most common amongst CF patients in the UK. In our project, we sought to (1) identify factors that make this strain so successful as a pathogen of CF patients and (2) develop tests to enable better identification of the strain in a clinical setting. We have identified a novel “phenotype” associated with the LES. This involves the over-production of toxins. Secondly, we obtained the whole genome sequence of the bacterium and identified genes that are important in establishing a lung infection. Thirdly, we developed an improved diagnostic tests for this and other UK epidemic strains, which is now being used in laboratories processing CF patient samples. In addition, we studied the genetic variation that occurs within populations of the LES. These variations (mutations / loss of genes) make it difficult to develop diagnostic tests that are 100% effective. Hence, there will be a need for continuing vigilance to make sure that we can identify this and future emerging epidemic strains.

Publications arising from research

Winstanley C & Fothergill JL (2009). The role of quorum sensing in chronic cystic fibrosis *Pseudomonas aeruginosa* infections. *FEMS Microbiol. Lett.* 290(1), 1-9.

Winstanley C, Langille MGI, Fothergill JL, Kukavica-Ibrulj I, Paradis-Bleau C, Sanschagrin F, Thompson NR, Winsor GL, Thornhill J, Parkhill J, Hancock REW, Brinkman FSL & Levesque RC (2009). Newly introduced genomic prophage islands are critical determinants of *in vivo* competitiveness in the Liverpool Epidemic Strain of *Pseudomonas aeruginosa*. *Genome Research* 19(1), 12-23.

Mohan K, Fothergill JL, Storrar J, Ledson MJ, Winstanley C, & Walshaw MJ (2008). Transmission of a *Pseudomonas aeruginosa* epidemic strain from a cystic fibrosis patient to a pet cat. *Thorax* **63**, 839-840.

Fothergill JL, Upton AL, Pitt TL, Hart CA, & Winstanley C (2008) Diagnostic multiplex PCR assay for the identification of the Liverpool, Midlands-1 and Manchester CF epidemic strains of *Pseudomonas aeruginosa*. *J. Cyst. Fibros.* **7**, 258-261

Fothergill JL, Panagea S, Hart CA, Walshaw MJ, Pitt TL, & Winstanley C (2007) Widespread pyocyanin over-production among isolates of a cystic fibrosis epidemic strain. *BMC Microbiol.* **7**, 45.

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