Reviewer's report

**Title:** Antibiotic perturbation of mixed-strain Pseudomonas aeruginosa infection in patients with cystic fibrosis

**Version:** 0  **Date:** 05 Jul 2017

**Reviewer:** Craig Winstanley

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Although others have looked at sets of multiple isolates from CF patient sputum samples in order to study populations of P. aeruginosa, this study is interesting because some of the findings are different. For example, whereas with the Liverpool Epidemic Strain (LES), no mixed strain infections are evident in chronically infected patients, even when large numbers of isolates are examined, here AUST-02, another transmissible strain, co-exists with other strains. In addition, whereas infection with the LES is associated with greater morbidity but is a single "strain" infection, here there is some evidence for more severe disease in multi-strain infections. Although the evidence is fairly weak because of the small numbers of patients in each group, the findings are worth reporting because they will help in the design of better studies to specifically address that question.

Page 4 - the authors could also refer to a recent paper by Hilliam et al. in ERJ (currently on-line) where genome sequence data was used to show that there are often multi-strain P.aeruginosa lung infections in bronchiectasis patients.

Page 9 - it is notable that from two of the patients included in the study and identified as chronically infected with the AUST-02, no AUST-02 isolates were obtained. The patient were initially positive using PCR of sweeps. Is this the method used routinely in the clinic to define these patients, or are single colonies tested? Are the authors saying that PCR assays of sweeps were negative for subsequent samples (or just that AUST-02 was not identified amongst the colonies selected)? Please clarify.

It is interesting that overall resistance was greater amongst AUST-02 colonies yet AUST-06 seems to prosper during the exacerbation periods. The authors do discuss the limitations of in vitro antimicrobial susceptibility. There could also be other factors involved favouring AUST-06 during these periods, such as other species of microorganisms or host responses.
The Discussion perhaps focuses a little too much on the issue of more severe disease in the mixed infection patients. It would be interesting to see some discussion about the obvious contrast between this transmissible strain and the LES.

Page 13, sentence beginning "These findings contrast…" I wasn't convinced that they do contrast. These other studies were not addressing changes in the relative abundance of lineages (or sub-lineages) within P.aeruginosa populations over short periods of time.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

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