

## Targeting intracellular *Burkholderia* by antibody and antibiotic combination therapies

ATaylor<sup>1,2</sup>, DJenner<sup>1</sup>, GJBancroft<sup>2</sup>, CA Rowland<sup>1</sup>, J Prior<sup>1</sup>

### Introduction

The ability of *Burkholderiapseudomallei* to survive intracellularly, avoiding traditional antibiotic therapy, highlights the importance of investigating novel anti-microbial therapies. This project aims to target *B. pseudomallei* intracellularly with an antibody-antibiotic conjugate. Antibody-antibiotic conjugates as therapies have the ability to target bacteria directly, localising the delivery and functionality of antibiotics. The antibiotic is only functional once cleaved from the antibody at the target site of infection; this has the potential to reduce current antibiotic treatment doses and duration of therapy.

### Methods

We are currently developing and utilising in vitro macrophage infection assays with *Burkholderiathailandensis* and *B. pseudomallei* to investigate antibody opsonisation and the effect of antibodies on bacterial fate. Antibiotics will be assessed in these assays in combination with free antibodies, this will be compared with an antibody-antibiotic conjugate which is being developed to deliver antibiotic intracellularly to the site of infection. We are using imaging flow cytometry and confocal microscopy to visualise and quantify bacterial infection within macrophages with *Burkholderia* strains expressing green and red fluorescent protein.

### Results

Results from macrophage infection assays show that monoclonal antibodies directed against the capsule of *Burkholderia* can significantly increase bacterial uptake by macrophages ( $P < 0.0001$ ), a greater than 1 log increase in colony forming units was observed when bacteria were opsonised with anti-capsule antibody compared to control antibody. Multi-spectral imaging flow cytometry confirmed this result with an increase in intracellular *B. thailandensis* from a control level of 15% up to 40% when opsonised.

### Discussion and Conclusion

In conclusion, a *Burkholderia* macrophage infection assay has been created in which bacterial infection can be assessed in vitro. Monoclonal antibodies specific against *B. pseudomallei* capsule polysaccharide have demonstrated significant opsonisation ability in vitro. This data in combination with in vivo protection studies will be used to down select antibodies for conjugation to antibiotics. This represents the first steps towards developing a novel treatment for *Burkholderia* infection.

---

<sup>1</sup>DSTL Porton Down, Salisbury, Wiltshire SP4 0JQ, UK.

<sup>2</sup>Dept of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, UK

Address for correspondence: Mr Adam Taylor, Department of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, UK. +44 1980 953689 Email: [ataylor1@dstl.gov.uk](mailto:ataylor1@dstl.gov.uk)

 <https://orcid.org/0000-0002-5098-6993>