The whole blood phagocytosis assay: a near patient test to promote a personalised approach to immunomodulatory therapy.

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Outline

• Background
• Preliminary work
• Project aims
• Current status
• Future direction
Background

- Urgent need to develop new therapies for severe infection
- Currently there are no licensed immunomodulatory therapies
- Personalised approach essential to measure immune function and effectively target therapies
Background

- Search for useful biomarkers has proven elusive

- Our approach was to directly measure the activity of neutrophils, the key effector cells in response to infection
Background

“Whole blood phagocytosis assay”

• Functional assay to measure neutrophil activity
• Minimise pre-processing with aim to mimic *in vivo* conditions
• Rapid turnaround – results less than 4 hours from blood sampling
• Reproducibility

Preparatory work

- CiC funded project – “Targeting the patient with most to gain from P4”
- Patients admitted to critical care with severe infection (n=44)
- Whole blood incubated with intraphagosomes reporter beads
- Detect association and oxidation as a kinetic assay
Preparatory work

- Clinical factors associate with neutrophil–bead binding
  Mechanical ventilation, Charlson index, white cell count, platelet count

- Increased oxidation in response to P4 peptide was associated with 28-day survival
Project Aims

1. Standardisation and refinement of the whole blood phagocytosis assay

2. Validation of optimized assay in patients with moderate and severe infections and age-matched controls.

3. Plan NIHR i4i application to fund a large-scale clinical evaluation trial for the assay.
Current Status

- Ethical approval granted: 15/NW/0869
- CRN portfolio status approved
- Work package 1 (assay refinement) underway
  - Bead manufacture and stability
  - Healthy volunteer work to commence 22nd February
- Work package 2 (assay validation) to commence May 2016
Future Direction

- **Paediatric population**
  - Small blood volumes mandated: use refined assay in critically ill children to measure immune function.

- **Oncological population**
  - Can this assay be used to predict neutropenic sepsis in patients who require chemotherapy? Stratify patients to prophylactic antibiotics.

- **Planned for use in phase 1 clinical trials with P4 peptide**
  - Test phagocyte function *ex vivo* after administration

- **NIHR i4i application to fund multi-site evaluation study**
Questions

Collaborators

• Dr Jamie Rylance
• Dr Daniela Ferreira
• Dr Jesus Reine
• Dr Robert Parker
• Dr Ingeborg Welters
• Prof Stephen Gordon

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