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LIVERPOOL SCHOOL
OF TROPICAL MEDICINE

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

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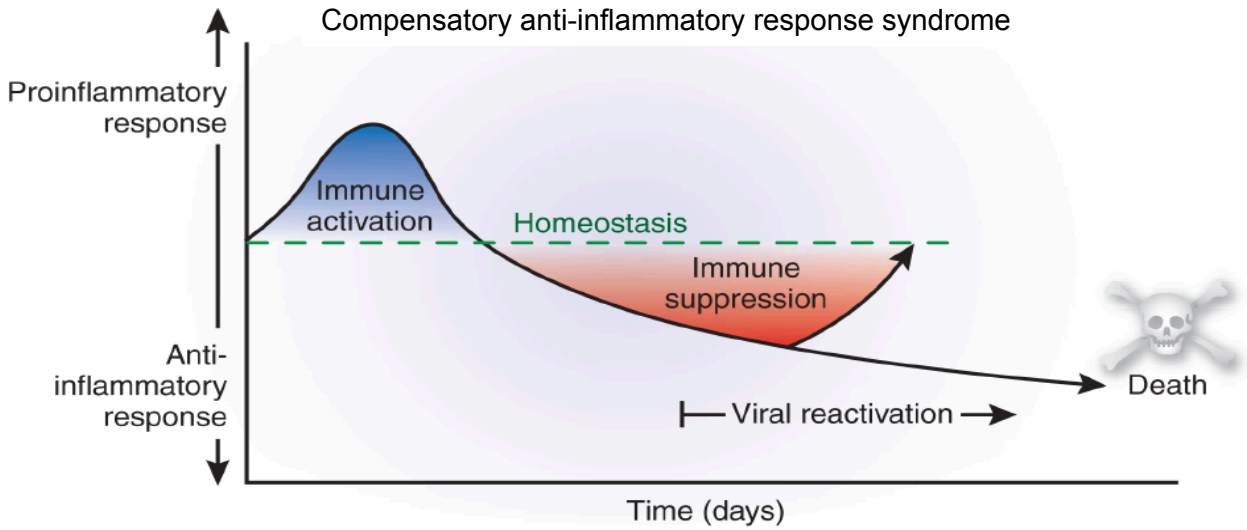
Outline

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

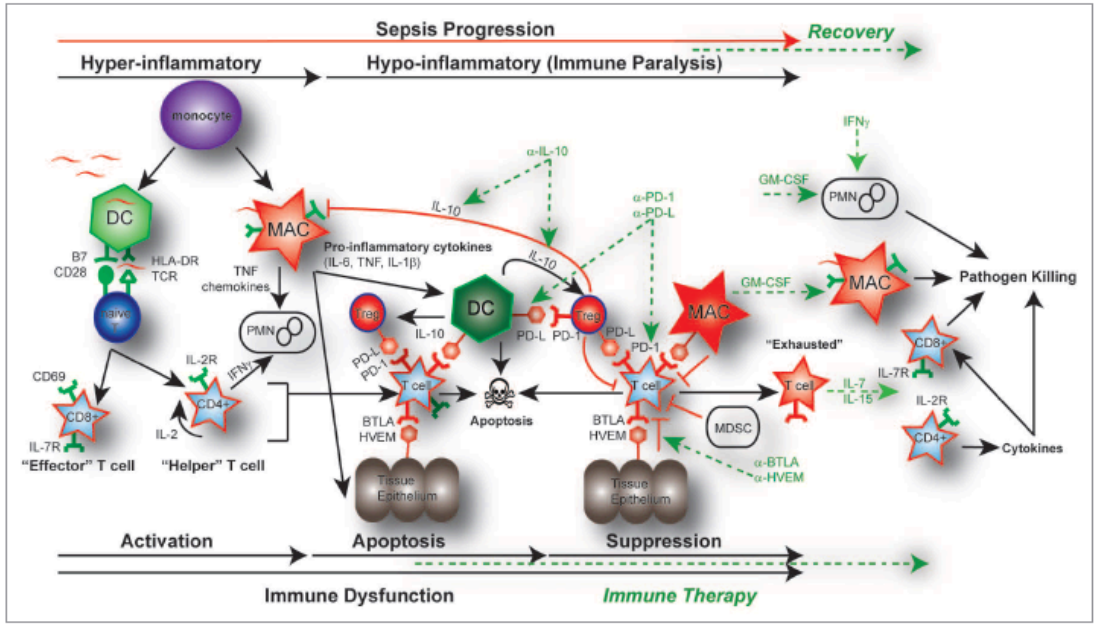
Background

- **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**

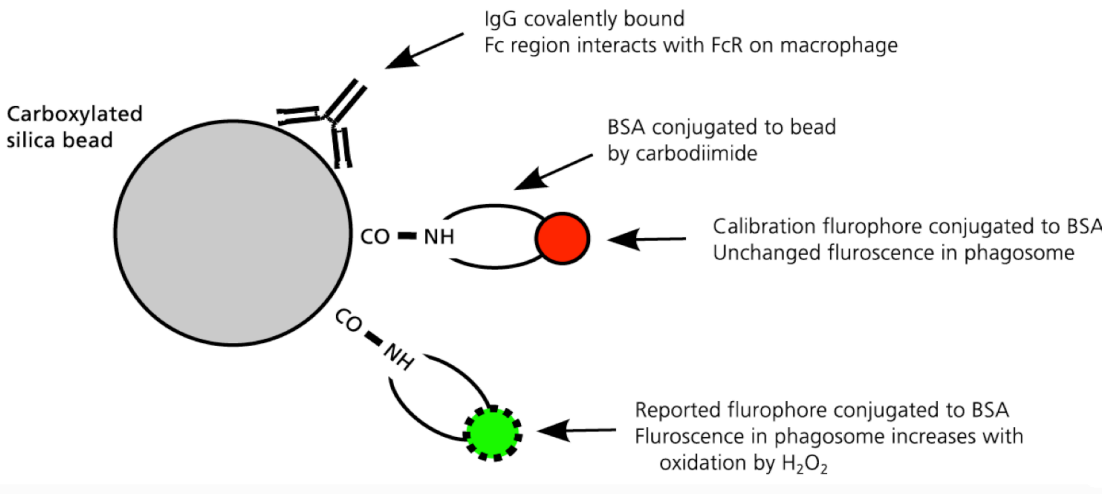


- **Our approach was to directly measure the activity of neutrophils, the key effector cells in response to infection**

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 4hours from blood sampling
- Reproducibility

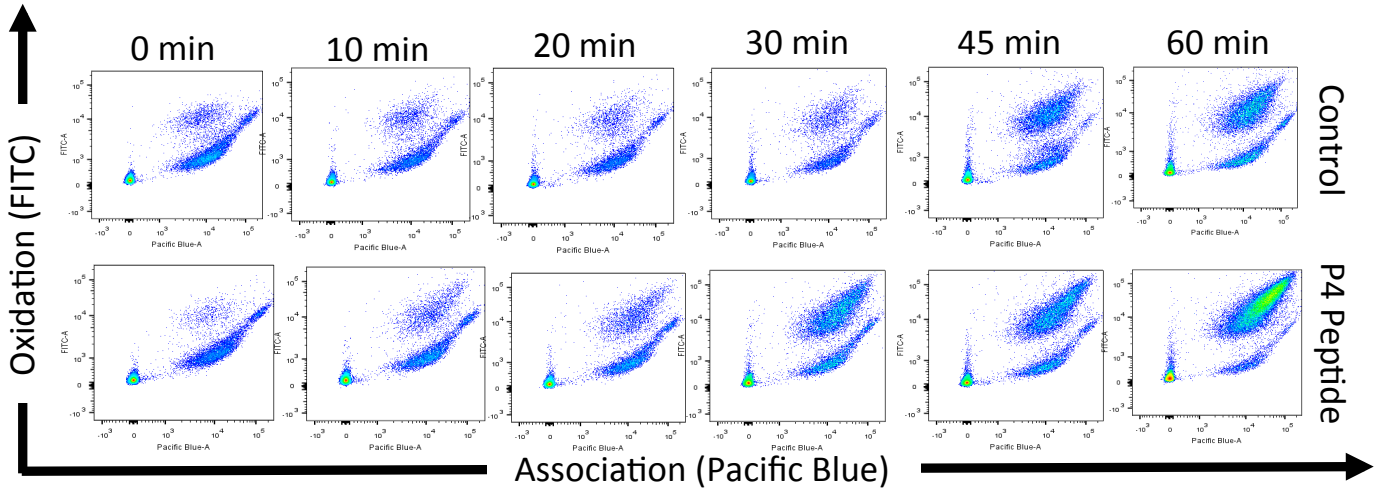


VanderVen B. Traffic . 2009 April ; 10(4): 372–378.

Preparatory work

- CiC funded project – “Targeting the patient with most to gain from P4”

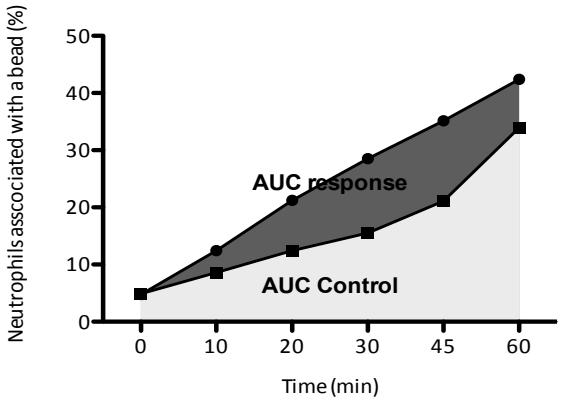
- Patients admitted to critical care with severe infection (n=44)
- Whole blood incubated with intraphagosomal reporter beads
- Detect association and oxidation as a kinetic assay

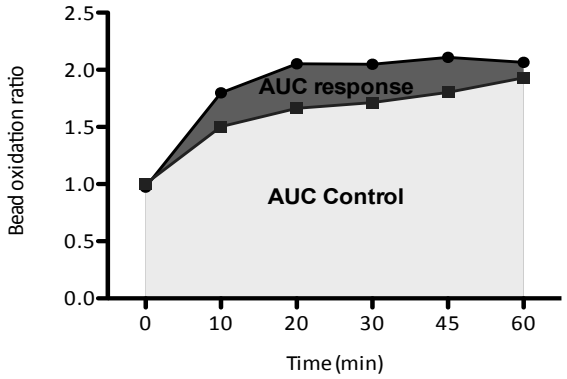


Preparatory work

- 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





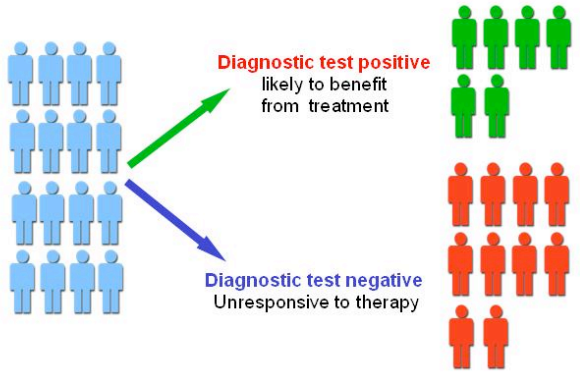
Project Aims

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.**

Personalised medicine: future vision



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

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Collaborators

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

Funding