Disease modelling

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Disease Modelling: A New Facility in CLS

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Why Has CLS Established The Facility?

Aim: To maximise scientific output and to minimise adverse welfare to the animals during regulated procedures.

- Facility will provide skilled assistance in the design, execution, analysis and reporting of experimental studies involving regulated procedures.
- This will reduce the number of personal licence holders to ensure only experienced, skilled workers are performing regulated procedures to maintain the welfare of the animals.
- Having a disease modelling facility in-house rather than outsourcing enables flexibility.

Role of Facility

- To establish new models of disease or use currently available models to meet scientific aims.
- To supply protocols and advice for planning regulated procedures regarding animal model, techniques, concentrations and time points.
- To consult project licences and/or assist in writing and/or amending project licences and study plans to enable experimentation.
- To teach techniques and encourage confidence in animal handling if required.

Model Systems Currently Available

Staphylococcus aureus-induced pneumonia

- *S. aureus* is a gram positive bacterium commonly found in the airways of patients with lung disease.
- Model of lung infection characterised by neutrophilic inflammation and dissemination of bacteria to spleen and liver (James Chalmers, MMB).
- Experimental readouts:
  - Effects on cell recruitment and cytokine responses in response to *S.aureus*.
  - Comparison of bacterial counts in infected organs to test virulence factors using GM bacteria.
  - Whole cell immunisation studies as a potential therapeutic.

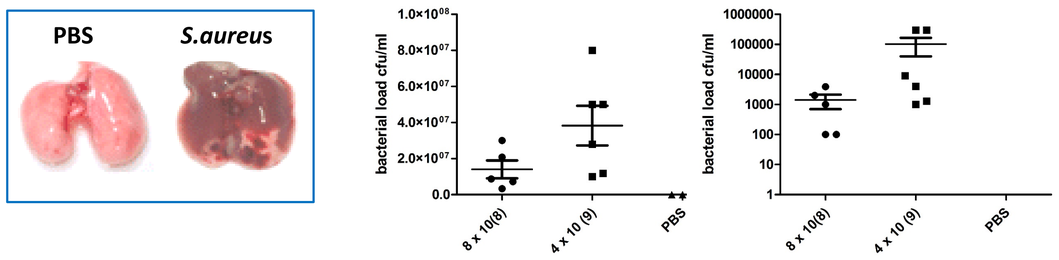

Figure 1. (A) Comparison of mouse lungs 24h following infection with *S.aureus* or PBS control. (B) CFU counts in the mouse lung and liver following infection with *S.aureus*.

Listeriosis

- *Listeria monocytogenes,* a gram positive bacterium that is a common cause of food poisoning.
- Establishing a model of infection with Mahima Swamy, CSI to study the pathogenesis of gut epithelium infection and with Nicola Stanley-Wall, MMB to study the impact virulence factors on the course of infection.

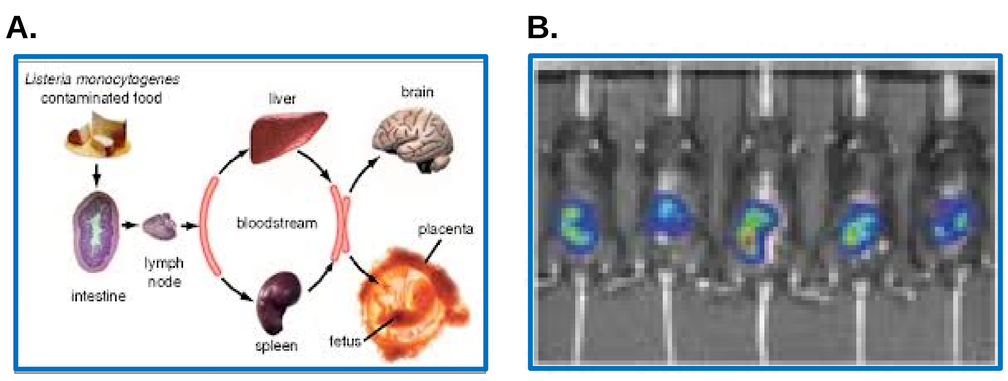

Figure 3. (A) Schematic of the course of listeria infection after eating contaminated food. (B) Example of model system where C57Bl6/J mice can be bioimaged (IVIS) following administration of 5x10^9 CFU *Listeria monocytogenes*-EGDe-InA-mur-lux. Data shows significant bacterial load in the intestines at 1h post infection (Bergmann *et al*, BMC Microbiology 2013, 13:90).

Cystic Fibrosis

- *Pseudomonas aeruginosa* is a gram negative bacterium found in abundance in the lungs of cystic fibrosis patients.
- Model of lung infection with associated neutrophil infiltration (Robert Ryan, MMB).
- Experimental readouts:
  - Effects on cell recruitment & mediators in response to *Pseudomonas aeruginosa*.
  - Comparison of bacterial counts in infected organs to test virulence factors using GM bacteria and in cystic fibrosis-KO mice.
  - Assess the rate of clearance of different bacterial strains.

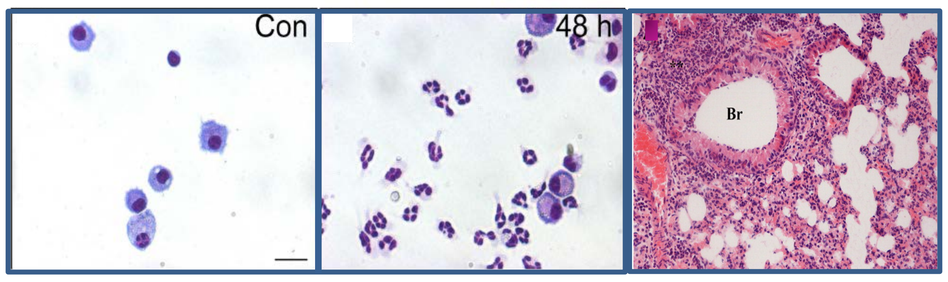

Figure 2 shows the cellular differences in cytospins prepared from bronchoalveolar lavage (BAL) from control PBS mice and mice treated with intranasal *Pseudomonas aeruginosa* (strain PA14) at 48h. The last panel shows an example of an infected mouse lung with peribronchiolar (Br = bronchiole) and alveolar bed infiltration of inflammatory cells 48h post infection.

Characterisation of Immune & Inflammatory Responses

- Are there differences in B and T cell responses in your genetically modified mice? Test using immunisation studies and measurement of serum immunoglobulins.
- Are there effects on cell recruitment? Innate and adaptive immune responses to stimuli.
- Generation of bone marrow chimeric mice.
  - Technically demanding requiring accurate injection of cells.
  - Skilled technical expertise available to ensure minimal adverse welfare to the animal.

Models of infection in the pipeline

- Lung infection model of influenza (H1N1). E.g. to study the role of macrophage receptors on recognition of the virus (Paul Crocker, CSI).
- *Serratia marcescens*, a gram negative bacterium is a common cause of hospital-acquired infections. Establish a model of infection to study virulence factors using GM bacteria (Sarah Coulthurst, MMB).

How To Approach The Facility

- E-mail a brief proposal or arrange an informal meeting to discuss the overall scientific aim(s).
- Enquires to: s.j.mcmillan@dundee.ac.uk or internal telephone 85778.
- Followed by:
  - ➢Consultation of project licence (PPL) and/or advice on writing a PPL and/or amendment.
  - ➢Assistance with associated paperwork e.g. animal orders, writing study plans, use of resource unit computer software.
  - ➢Calculation of full costings for each experiment.
  - ➢Agreement on contribution of service on experimental days.
- Cost: There is no charge for the service at present however, all animal and consumable costs will apply. The position is funded by the Wellcome Trust until Sept 2016. If applying for new funding please enquire about costings for this service from 2016.
- Location: Cell Signalling & Immunology, PRC lab, WTB2 South.

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