A novel approach to the development of a murine model of cystic fibrosis associated chronic pulmonary bacterial infection

A. Monahan1, P. McGunnaghan2, R. McMullan2, J. S. Elborn3, R. Ingrain1. 1QBRCentre for Infection and Immunity, Belfast, United Kingdom; 2Royal Victoria Hospital, Department of Medical Microbiology, Belfast, United Kingdom

Research into the immunopathogenesis of chronic bacterial colonisation of cystic fibrosis (CF) patients has been hampered by lack of a suitable animal model. Whilst models of chronic infection have been described, they rely on the use of artificial embedding material to prevent rapid clearance of the bacteria. We hypothesised that careful selection of the bacterial isolate, mouse strain and infection regime, will result in a clinically relevant murine model of chronic S. aureus (SA) and P. aeruginosa (PA) infection without the need for embedding materials. Previously published models have largely used PA01 and lab attenuated SA strains. We have screened several hundred clinical isolates of SA and PA and selected 5 strains each for murine infection experiments, based on genotype and phenotype. The selected SA isolates include haemolytic strains from CF and non-CF sputum. The PA isolates originated from CF or ICU patients and were selected based on phenotype including ability to form biofilm in vitro. Significant differences in the in vivo virulence of these strains have been shown. Equally essential is mouse strain. C57BL6 mice are used almost exclusively, however this strain are inherently resistant to bacterial infection. We have compared the survival and colonisation of C57BL6, A/J, BALBc, Biozzi, FVB/N, NIH, SJL, CD1, MF1 and NMRI female mice with PA and SA. Identifying a combination of mouse and bacterial strain resulting in the prolonged survival of the animal whilst maintaining chronic pulmonary infection, will allow investigation of the intricate immunological and physiological disease processes involved during chronic pulmonary infection of CF patients.

Investigation of immunogenic outer membrane proteins of Burkholderia cepacia complex using serum from cystic fibrosis patients

M Shinoy1, K. Schaffer2, M. Callaghan1, S. McClean1. 1Institute of Technology Tallaght Dublin, Centre of Microbial Host Interactions, Dublin, Ireland; 2St. Vincent's University Hospital, Elm Park, Dublin, Ireland; 3Institute of Technology Tallaght Dublin, Centre of Applied Science for Health, Dublin, Ireland

Burkholderia multivorans and B. cenocepacia are the two most frequently acquired species of Burkholderia cepacia complex (Bcc) in CF patients. This pathogen is transmissible and very difficult treat due to its antimicrobial resistance.

Objective: To identify the immunogenic outer membrane proteins (OMP) of B. multivorans and B. cenocepacia using CF patient serum in order to aid the design of prophylactic therapies.

Methods: The OMPs were isolated individually from two B. cenocepacia strains and two B. multivorans strains, separated by 2-D electrophoresis and blotted onto PVDF membranes. Immunogenic OMPs were detected by probing blots with serum from CF patients colonised with Bcc followed by chemiluminescent detection. Proteins spots were matched to corresponding spots on a Coomasie blue stained gel, excised and subsequently identified by MALDI-TOF/MS.

Conclusion: Among the 140 immunogenic proteins identified from the four Bcc strains, six of them were common to all strains, twelve were identified in both B. multivorans strains and seven of them were identified in both B. cenocepacia strains. The OMP Porin, OprM and chaperonin GroEL were all identified as being considerably immunogenic in all strains.

Funding: HEA PRTLI Cycle 4.