Translational Immunology, Inflammation and Infection

Representative Case Study — Human Pulmonary Immunology.

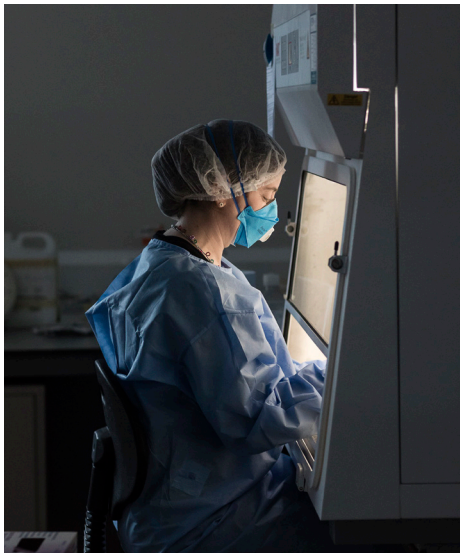
Prof. Joseph Keane

Clinical Need

So many lung diseases such as Chronic Obstructive Pulmonary Disease (COPD), lung cancer and tuberculosis occur in people's lungs because the local pulmonary immune system has been damaged by insults, such as cigarette smoking, yet the cellular mechanisms underlying these conditions are poorly understood due to limited direct access to human lung tissue. In recent years, investigators at TCD have started exploring how cellular metabolism is the master controller of how immune cells work. Such immune cells can either propagate or prevent important diseases, yet most work is done on animal models. Investigators at the TTMI were the first group to demonstrate the role of immuno-metabolism as a defence against tuberculosis in cells taken from human lungs*.

Partnership

Working closely with the clinical research facility (CRF) at St. James' Hospital, the Trinity based TB immunology research lab is uniquely placed to access human alveolar macrophages donated by volunteers at bronchoscopy on our hospital site. This is exploited to address important clinical questions locally and with international collaborators**.



Approach

In the TTMI, investigators use primary human material to interrogate the role of metabolism in directing the host response to infections (such as tuberculosis). Using high-throughput analysis, as well as a panel of cell biology assays to measure macrophage and cell mediated responses; our group is uniquely placed to map out the immune response of the human lung in health and disease.

Our track record in developing new paradigms of host defence has allowed us to screen numerous novel therapeutic approaches – with potential to drive innate and cell mediated responses to support diseased patients with immune defects and lung disease. Our collaboration with the RCSI has led to the development of novel inhaled micro-particle approaches to lung directed therapy.

** Gleeson LE, Sheedy FJ, Palsson-McDermott EM, Triglia D, O'Leary SM, O'Sullivan MP, O'Neill LA, Keane J, Cutting Edge: Mycobacterium tuberculosis Induces Aerobic Glycolysis in Human Alveolar Macrophages That Is Required for Control of Intracellular Bacillary Replication. Journal of Immunology, 2016 Mar 15;196(6):2444-9.*

*** Berg RD, Levitte S, O'Sullivan MP, O'Leary SM, Cambier CJ, Cameron J, Takaki KK, Moens CB, Tobin DM, Keane J, Ramakrishnan L Lysosomal Disorders Drive Susceptibility to Tuberculosis by Compromising Macrophage Migration.,*
Cell, 165, (1), 2016, p139-52

Collaborator/Funding Agencies

HRB Health Research Board
Science Foundation Ireland sfi For what's next
Royal City of Dublin Hospital
Wellcome Trust - HRB Clinical Research Facility at St. James's Hospital