Infectious Diseases Labs

ID LABS

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Friday, 21 April 2023
11:00am to 12:00pm (SGT)

Venue: Cistron A and B @ Matrix Level 5

Oxidised Cholesterols Drive Macrophage Infiltration into the Lung during Bacterial and Viral Respiratory Infections

Immune cell recruitment to the site of infection is an integral part of an effective immune response to both bacterial and viral pathogens. However, excessive immune cell infiltration in the lung can result in increased lung pathology and disease severity. We recently discovered a novel and previously unrecognised mechanism of immune cell recruitment to the infected lung, which can be targeted pharmacologically to improve respiratory infection outcomes. We showed that infection with M. tuberculosis (Mtb), influenza A virus (IAV) and SARS-CoV-2 leads to production of the oxidised cholesterols 25-hydroxycholesterol and 7α,25-dihydroxycholesterol in the lung through upregulation of the oxysterol-producing enzymes CH25H and CYP7B1. 7α,25-dihydroxycholesterol is the endogenous high affinity ligand for the oxysterol-sensing receptor GPR183, which is expressed on innate and adaptive immune cells. In a preclinical model of Mtb infection both CYP7B1 and GPR183 are required for rapid macrophage infiltration into the lung. Gpr183-/- mice and mice that were unable to upregulate CYP7B1 upon infection had delayed macrophage infiltration and higher mycobacterial burden during early infection. Similarly, in Gpr183-/- mice infected with either IAV or SARS-CoV-2 the infiltration of macrophages was delayed compared to control animals. This was associated with a reduction in inflammatory cytokines and beneficial infection outcomes. Furthermore, a GPR183 antagonist significantly reduced macrophage infiltration, reduced lung viral load and attenuated the severity of SARS-CoV-2 infection in mice. Together this study demonstrates that oxysterols drive macrophage infiltration and inflammation in the lung via GPR183. We provide the first preclinical evidence for therapeutic benefit of targeting GPR183 for respiratory infections.

Cheng Xiang Foo completed his undergraduate studies at the University of Queensland (UQ) where he graduated with a Bachelor of Science (Honours) degree with a major in immunology. Currently, Cheng is completing his PhD at Mater Research Institute, UQ under the supervision of Prof. Katharina Ronacher, Prof. Matt Sweet and A/Prof. Kirsty Short. His PhD project focuses on investigating the role of oxidized cholesterols in the host defence against respiratory pathogens.

Hosted by: Dr Amit Singhal

Seminar is open to all . No registration required

Questions? Contact us at **seminars@idlabs.a-star.edu.sg**