

# A\*STAR Infectious Diseases Labs

Virtual Seminar hosted by Prof Laurent Renia

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**16 February 2021 | Tuesday | 10.00 am – 11.00 am**

**Join Zoom Meeting: [LINK](#)  
Meeting ID: 922 5256 5887  
Passcode: 071339**

Seminar is open for all to attend.  
Registration is not required.

## Host-pathogen interactions in non-tuberculous mycobacterial infections and tuberculosis

This seminar will cover three major themes in mycobacterial infections that my research program has addressed with zebrafish models and additional opportunities for the development of host-directed therapies for infectious diseases.

Firstly, I have used adult zebrafish to create the first model of persistent *Mycobacterium abscessus* infection in an animal with fully functional immune system. I identified fundamental differences in the interaction between host immune system components and rough or smooth variant *M. abscessus* strains that cannot be investigated using conventional mouse models. These findings demonstrate the adult zebrafish is a much-needed platform to study the host-pathogen interactions of persistent *M. abscessus* infection.

Secondly, we have used the genetic and small molecule tools to map a druggable pathway connecting modulation of cellular potassium flux to control of intracellular bacterial infection via potentiating inflammasome activation. We have validated this pathway in human macrophages and zebrafish embryos suggest this pathway could be targeted to provide broadly acting therapy against a range of infections.

Finally, I have examined the development and consequences of vascular dysfunction of the tuberculous granuloma in the zebrafish-*M. marinum* infection model and illustrated a bidirectional interaction between granuloma formation and vascular dysfunction. Inhibiting angiogenesis with VEGFR-targeting drugs, vascular permeability via disruption of the ANG-2/TIE-2 signalling pathway, and thrombocyte activation with anti-platelet drugs are potential host directed therapies that reduce infection burden and protect the host from mycobacterial infection. Clinical data supports further efforts to repurpose existing medications for the treatment of TB and other infectious diseases including cryptococcal meningitis.