



Infectious  
Diseases Labs

ID LABS



## Dr Prashant Rai

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NIEHS, NIH, United States



**Monday, 19 June 2023**

10:00am to 11:00am (SGT)

**Join Zoom Meeting [here](#)**

Meeting ID: 939 7175 6599

Passcode: 418770

### Chronic type I interferon disrupts tissue macrophage homeostasis and induces bacterial susceptibility

Type I interferon (IFN) plays a central role in the pathogenesis of common autoimmune disorders. We have reported that mice deficient in the interferon- $\gamma$ -inducible immunity-related GTPase - *Irgm1*, which regulates autophagy and also localizes to mitochondria, have an autoimmune exocrinopathy accompanied by increased autoantibodies and spontaneous induction of IFN-stimulated genes in several organs. Here, we show that genetic deletion of the type I interferon receptor rescues the autoimmune tissue pathology and excess autoantibody levels in *Irgm1*-null animals, demonstrating the pathogenicity of type I interferon in these animals. Abnormal induction of type I interferon in *Irgm1*-null fibroblasts is associated with simultaneous dysfunction in mitochondria and lysosomes, resulting in soiling of the cytosol with mtDNA, which activates the double stranded DNA sensor - cGAMP synthase (cGAS) to drive type I interferon production. In vivo, we found that the cGAS pathway underlies the exocrinopathy of salivary glands, autoantibodies as well as inflammatory cytokine production in *Irgm1*-null mice. Most recently, we have learned from our ongoing (unpublished) work in *Irgm1*-null mice model, that chronic type I interferon can perturb tissue macrophage homeostasis, and this could be partly responsible in compromising host defense against intracellular bacteria.

**Dr Prashant Rai** earned his PhD in Microbiology from Department of Microbiology and Immunology, NUS via Singapore-MIT Alliance for Research & Technology program. Currently, he is a Staff Scientist in Michael Fessler's lab at National Institute of Health (NIH/NIEHS), where he has been working on understanding mechanisms of production of the cytokine 'type I interferon', its role in modulating macrophage fate and function and its overall impact on bacterial pathogenesis. His long-term research interest is to investigate mechanisms by which type I interferon induces susceptibility to intracellular bacteria by using animal models.

**Host: Prof Lisa Ng**

Webinar is open to all. No registration required

Questions? Contact us at [seminars@idlabs.a-star.edu.sg](mailto:seminars@idlabs.a-star.edu.sg)

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