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SIgN Immunology Seminar



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Molecular Targeting of Key Pathogenic Effects on Host Defense Mechanisms, Focusing on Tuberculosis

Host
Dr Amit Singhal
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Date
Wednesday
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Time
10am – 11am

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

Discovering novel host-directed therapies (HDTs) for infectious diseases requires an improved understanding of how pathogens disrupt the master regulatory signaling networks controlling basic functions of infected cells. Dysregulation of these pathways, and particularly for the links between metabolism and immune function, will be discussed along with innovative new drug therapies in cancer and other diseases that are based on correction of dysregulation. The lack of new classes of anti-microbial drugs in development for tuberculosis has provided an impetus for discovery of adjunctive HDTs. Several promising HDT candidates are being evaluated, but major advancement will require **new research to understand how pathogens affect core regulatory signaling pathways of cells**. Very little research has addressed the role of these core signaling pathways in tuberculosis. Master regulators include poly(ADP-Ribose) polymerases, sirtuins, and AMP-activated protein kinase, and mTOR. Interactions among them and with the pathways already known to be influenced by M.tb control several key cell metabolic, inflammatory, and immune functions.

Both general cell functions and the specific immune responses to infections are governed by these essential regulatory mechanisms that have been conserved in almost all eukaryotic cells throughout the course of evolution. Therefore, "precision medicine" drug interventions now in clinical use for other diseases caused by dysregulation may be re-purposed for reversing the immune cell dysfunctions caused by the pathogenic mechanisms of microbes. Many new pathway modulating agents are well tolerated, and only short-term (8-12 weeks) use may be needed for adjunctive TB treatment. **Appropriately designed screening of drugs approved or in clinical trials for these other diseases** is needed to identify those that may be effective for targeted molecular therapy of infections. If only a small percentage of new classes of HDT drugs in development for other diseases are found to be useful for TB, the number of candidates in the therapeutic pipeline will be greatly expanded. A wide spectrum of new knowledge, research tools, and candidate therapies await adaption to advance innovative and powerful precision medicine approaches to fundamentally transform infectious diseases therapy.