Theme-based Research Scheme on Potentiating Host Immunity for HIV-1 Functional Cure

AIDS Institute, Dept of Microbiology

Seminar

Lipoarabinomannan-specific polycytotoxic T cells contribute to protection in human tuberculosis

11:00am, Thursday, October 18, 2018

Seminar Room 7, LG1/F, Laboratory Block, 21 Sassoon Road

Speaker: Professor Steffen Stenger

Institute for Medical Microbiology and Hygiene,
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Rationale: The development of host targeted, prophylactic and therapeutic interventions against tuberculosis requires a better understanding of the immune mechanisms that determine the outcome of infection with *Mycobacterium tuberculosis*.

Objectives: To identify and characterize T cell-dependent mechanisms that are protective in tuberculosis.

Main Results: In two independent study sites we found that bronchoalveolar lavage cells from protected donors limited the growth of virulent *Mycobacterium tuberculosis* more efficiently than patients that developed active disease. Unconventional, glycolipid-specific T cells contributed to antimicrobial activity because antibodies to CD1b partially neutralized this effect. Lipoarabinomannan was the most potent mycobacterial lipid antigen and activated CD1b-restricted T-cells with antimicrobial activity. A subset of IFN-γ-producing lipoarabinomannan-specific T cells co-expressed the cytotoxic molecules perforin, granulysin and granzyme B, which we termed "polycytotoxic T cells". Taking advantage of two well-defined, cohorts of subjects latently infected with *Mycobacterium tuberculosis* (protected phenotype) or patients that developed active disease after infection (susceptible phenotype), we found a correlation between the frequency of polycytotoxic T cells and the ability to control infection.

Conclusions: Our data define an unconventional CD8+ T cell subset, "polycytotoxic T cells", based on antigen recognition and function. The results link clinical and mechanistic evidence that glycolipid-specific, polycytotoxic T-cells contribute to protection against active tuberculosis.

ALL ARE WELCOME | FREE ADMISSION

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