

3rd International Conference and Exhibition on Clinical & Cellular Immunology

September 29-October 01, 2014 DoubleTree by Hilton Baltimore-BWI Airport, USA

Protracted protection against malaria is maintained by memory T cells

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Immunologic memory is one of the cardinal features of adoptive immune responses and is inextricably linked to lasting protection against infections. While many re-infections are prevented by memory T and B cells, malaria re-infections occur frequently and the reasons for the absence of lasting protection in endemic areas remain poorly understood. By contrast, exposures of humans and laboratory rodents to radiation-attenuated *Plasmodium* sporozoites (γ -spz) induce sterile and durable protection against experimental sporozoite challenge. The presence of memory CD4 T cells has been shown to be associated with lasting protection in humans exposed *P. falciparum* (Pf) γ -spz. Studies focusing on durable protection induced in mice with *P. yoelii* and *P. berghei* γ -spz have, instead, implicated memory CD8 T cells as crucial features of lasting protection. We observed that in the P γ -spz model, MHC class I-dependent liver-stage (LS) Ag-specific memory CD8 T cells are indispensable for the maintenance of protection. We hypothesize that long-term protection to malaria, whether mediated by CD8 or CD4 T cells, can be induced and maintained. As such, it requires the formation and persistence of memory T cells with a reservoir of central memory cells maintained in part by LS Ag-depot, IL-15 and possibly IL-4 and other cytokines that promote constriction of IFN- γ producing effector/effector memory CD8 T cells during re-infections.

Biography

Urszula Krzych received her PhD degree from Rutgers University and subsequently as a Postdoctoral fellow studied with the late Eli Sercarz at UCLA. She currently heads the Department of Cellular Immunology at WRAIR, where she has been conducting research on the various aspects of malaria, most notably investigating immune mechanisms of protection induced by malaria vaccines in humans and mice. She is also affiliated with the George Washington University, Washington, DC.

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Autophagy supports influenza A replication in the distal respiratory epithelium

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Autophagy (macroautophagy) is a highly conserved catabolic pathway in eukaryotes which supports cellular homeostasis through recycling of metabolites and clearance of cytotoxic agents and damaged organelles from the intracellular space. Impaired autophagy has been linked to disease pathogenesis in multiple organ systems, with recent studies hinting at the existence of cell or tissue-specific requirements for autophagic function. To date, the requirement for autophagy in lung epithelial homeostasis has been poorly defined. Similarly, while a growing body of evidence suggests a role for autophagy in influenza A pathogenesis, a relative lack of in vivo study obfuscates the clinical relevance of this connection. The present study aimed to address these knowledge gaps through the generation and analyses of transgenic mouse models for targeted deletion of the Atg5 in the distal lung epithelium. Partial inhibition of autophagy, by recombination in up to 50% of targeted lung epithelial cells, was associated with significantly decreased morbidity and mortality, preservation of lung structure/function, and reduced levels of cellular apoptosis and viral replication following infection with influenza A/H3N2 virus. Importantly, a 50% reduction of autophagy in the lung epithelium was both stable and well tolerated throughout the lifespan of the mouse. In contrast, a model with >90% loss of Atg5 in the lung epithelium developed progressive lung pathology beyond one year of age and fared poorly with viral challenge, suggesting that at least some autophagy is needed. Taken together, these findings support the concept of targeting autophagy inhibition to lung epithelia as an adjunct to current therapies.

Biography

David R Hahn, PhD completed his Doctoral studies in Molecular and Developmental Biology at the Cincinnati Children's Hospital Medical Center and the University of Cincinnati College of Medicine. Presently, he is pursuing his Postdoctoral studies in the Department of Clinical Pharmacology at Cincinnati Children's Hospital with research interests in pharmacogenomic studies and pharmacological targeting of pathogen-host molecular interactions.

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