



Rajatava Basu

University of Alabama at Birmingham, USA

All disease begins in the gut: A story of the warrior T helper cells and the invading microbes of the gut

A human body can harbour 5-10 times more microbes than the total number of cells and 90% of all these microbes enter our body through the intestine. Intestine contains the largest compartment of our entire immune system. CD4 T helper cells, arguably the most important cells in our immune system are required to protect the intestine against daily invasion of millions of microbes. Besides combating pathogens, CD4 T helper cells also play a critical role in various inflammation, autoimmune disorders and allergic diseases. While, a class of CD4 T helper cell, known as regulatory T cells (iTreg), encourages infection while suppressing autoimmune responses; another class of T helper cells, known as T helper 17 (Th17), fights infection while promoting autoimmune response. Interestingly, the intestinal immune system doesn't react to commensal microbes due to production of a Vitamin A metabolite- retinoic acid. This 'Vitamin A' metabolite helps to maintain homeostasis in gut as it promotes differentiation of iTreg cells, which in turn promote tolerance so that the intestinal immune cells don't react to commensal bacteria unnecessarily. During invasion of pathogenic microbes, the homeostasis is broken and other classes of CD4 T cells differentiate to take over the role of the warrior and thwart the pathogens from invading our body. One of the most important classes of effector cells that protect against bacterial invasion are the Th17 cells, whose differentiation is opposed by Vitamin A present abundantly in the gut. Interestingly both iTreg and Th17 cellular differentiations require a common

signalling pathway that intrinsically links their developmental axis. The talk will briefly focus on the roles of differentiation of these 2 types of T helper subsets on protection against an enteropathogenic bacteria *Citrobacter rodentium*, a murine gut bacteria that closely mimics enterohemorrhagic *Escherichia coli* infection of humans and serves as a useful model for studying intestinal immune response; and briefly discuss the mechanism of their orchestration to confer protective immunity to the enteropathogenic bacteria. This talk will also highlight the emerging role of intestinal immune system in human health and focuses on dynamics of intestinal immune system capable of thwarting the microbial onslaught from trillions of microbes.

Speaker Biography

Rajatava Basu received his Doctoral training from India and Germany and is working at Indian Institute of Chemical Biology, India and Charité Medical School, Humboldt University, Germany where he characterized immuno-dominant epitopes by proteomic analysis to develop an effective DNA vaccination strategy against infectious diseases. After completing a stint at Charité – Universitätsmedizin in Berlin as a Visiting Scientist, he visited USA and joined the laboratory of Prof. Casey Weaver at UAB for pursuing his Post-doctoral training on the area of cellular and molecular mechanisms controlling T cell-mediated immune regulation during autoimmune inflammation. Currently, he is an Assistant Professor of Pathology at UAB School of Medicine and a Crohn's and Colitis Foundation (CCFA, USA) fellow. He has published in leading journals like *Nature Immunology*, *Immunity* and *Immunological Reviews*. He has received prestigious international scholarships and has been awarded Alexander von Humboldt fellowship and Volkswagen Stiftung fellowship.

e: rajatavbasu@uabmc.edu

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