海外特別講演

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Personal Statement

The PI is a physician-scientist who has directed a NIH-funded laboratory since 1989. As an investigator, he directs four R01-funded research programs, one of which has achieved M.E.R.I.T. status, that are focused on mucosal immunology with a particular emphasis on the immunologic functions of the intestinal epithelium; a field that his laboratory has pioneered through the study of nonclassical MHC class I molecules (e.g. CD1 and FcRn) and more recently the unfolded protein response and Paneth cell function (XBP1). In addition, the PI is a leading authority on carcinoembryonic antigen cell adhesion molecule 1 (CEACAM1) function in T cells. His fundamental research has significant applications to inflammation and inflammatory bowel disease in particular; an area for which the PI is considered to be an international expert. The PI is also an accomplished academic leader at Brigham and Women's Hospital and Harvard Medical School where he is a Division Chief and Program Director of an Institutional Training Grant for training physician-scientists in digestive disease-related research and co-Director of the Harvard Digestive Diseases Center which is funded by a P30 award.

Positions and Honors

1979–1982	Medical Intern, Resident and Chief Resident, The New York Hospital/Cornell Medical Center, New York, NY
1982–1986	Clinical and Research Fellow in Medicine (Infectious Diseases), Massachusetts General Hospital, Harvard Medical School, Boston, MA
1986–1990	Clinical and Research Fellow in Medicine, Brigham and Women's Hospital and Laboratory of Molecular Immunology, Dana Farber Cancer Institute, Harvard Medical School
1989–1991	Instructor in Medicine, Harvard Medical School; Associate Physician, Brigham and Women's Hospital
1991–1996	Assistant Professor in Medicine, Harvard Medical School
1996–2005	Associate Professor of Medicine, Harvard Medical School; Physician, Brigham and Women's Hospital
1998–	Chief, Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital
2005–	Professor of Medicine, Harvard Medical School

Other Experience and Professional Memberships

1986	Diplomate, American Board of Internal Medicine/Infectious Diseases
1989	Diplomate, American Board of Internal Medicine/Gastroenterology
1996–2001	Associate Editor, Gastroenterology
1996–2000	Member, Immunology Sciences Study Section, National Institutes of Health (NIH)
1998–2004	Chair, Microbiology, Immunology and Inflammatory Bowel Disease Section, American Gastroenterological Association; Gastroenterology Research Group Steering

Honors

1978 Alpha Omega Alpha, 1979 M.D. cum laude, 1995 American Society of Clinical Investigation
1996 American Digestive Health Foundation/AGA Basic Research Award, 2001 Association of American Physicians, 2002 CCFA Humanitarian Man of the Year, 2005 NIH Method to Extend Research in Time (M.E.R.I.T) Award, 2012 AGA William Beaumont Prize in Gastroenterology

CD1-NKT Interactions in Mucosal Immunity

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CD1 consists of two groups of molecules that are conserved across species: type 1 CD1 (CD1a-c) and type 2 CD1 (CD1d). These molecules are MHC class I-like in their structure but traffic broadly throughout the secretory and endolysosmal systems wherein their function is in the presentation of cell associated (endogenous) and microbial (exogenous) lipids to T cells which are specific for these lipids in the context of CD1 on an antigen presenting cell. In the case of T cells that are specific for CD1d-restricted lipids, they are considered to be natural killer T (NKT) cells which express either a canonical (invariant) or noncanonical (noninvariant) T cell receptor-α chain. CD1d is expressed by both parenchymal cells (e.g. intestinal epithelial cells) and hematopoietic cells (macrophages, dendritic cells and B cells) in the intestines and regulate iNKT cells. CD1d-restricted pathways regulate the composition of commensal microbiota in the intestines and protect the mucosal surfaces such as in the lung from pathogens. In addition, CD1d-restricted pathways have been shown to regulate and promote colitis as modeled in the oxazalone-induced colitis model which is prevented by CD1d- and Jα18-deficiency, which in the latter case deletes iNKT cells. Moreover, iNKT cells are regulated by the microbiota such that in their absence, as in germ-free mice, or their reduction, as in antibiotic-treated mice, iNKT cells increase in number within the colon. As a consequence, GF mice are highly susceptible to oxazolone-induced colitis in a pathway that is CD1d- and CXCL16-dependent. The regulation of this pathway is age-dependent and requires microbial exposure during the neonatal, but not adult, period of life; a finding which has provided support to the validity of the hygiene hypothesis. This lecture will focus on recent insights into the biology CD1 and NKT cells in mucosal immune responses during inflammation and in response to the commensal microbiota and the manner and consequences of perturbations as a consequence of normal microbial colonization.