An essential role for NOD2 in mitigation of experimental autoimmune uveitis

Holly L Rosenzweig
Oregon Health & Science University, USA

As a leading cause of blindness worldwide, there is a most pressing need to define mechanisms of uveitis (intraocular inflammation). Despite its prevalence, uveitis remains an enigmatic group of diseases that are often inadequately treated. An emerging hypothesis proposes that uveitis arises from complex interplay between adaptive, T cell responses and innate immune activation. Innate receptors such as Toll-like receptors (TLRs) and NOD-like receptors (NLRs) have evolved to respond to microbial structures and activate innate immune signaling responses. The recently identified NLR, NOD2, is the genetic cause of the inflammatory disease Blau syndrome, a granulomatous uveitis that is accompanied by arthritis and dermatitis. Despite the unequivocal connection between NOD2 and uveitis in humans, we know very little of its biological functions within the eye. In our endeavor to understand how NOD2 may shape adaptive, T cell-dependent ocular inflammation we explored its contribution in murine experimental autoimmune uveitis (EAU). EAU ensues in response to immunization with the retinal antigen, interphotoreceptor retinoid-binding protein (IRBP). Topical endoscopic fundus imaging (TEFI) revealed severe papillary inflammation, extensive retinal vascular cuffing, and florid retinitis associated with NOD2-deficiency. Histopathology supported the susceptibility of NOD2-deficient mice, and granuloma formation was a defining immunopathological feature. To determine the cellular compartment associated with uveitis susceptibility in NOD2-deficient animals, bone-marrow chimeras were subjected to EAU. These data support NOD2 expression in the hematopoietic compartment as the foremost contributor to uveitis susceptibility. These data reveal a critical role for NOD2 in dampening uveitogenic T cell responses of the eye.

Biography
Holly Rosenzweig completed her Ph.D. in Immunology at Oregon Health & Science University and subsequently pursued a fellowship in uveitis at Casey Eye Institute, Portland, OR. She is currently Assistant Professor at the VA Medical Center with a dual faculty appointment in Department of Ophthalmology at Oregon Health & Science University. Her research interests involve innate mechanisms of chronic inflammatory diseases such as uveitis and arthritis.

rosenzwh@ohsu.edu