Department of Biological Sciences

VISITOR'S TALK

Speaker: Dr. Akansha Chaturvedi, PhD

Date/Time: Friday, 23rd February, 2018 at 10:30 am
Venue: AB3-401

Spatial regulation of the B cell receptor and Toll-like receptor signaling in B Cells

Antibody responses are initiated by B cells that recognize and respond to foreign antigens through clonally expressed antigen-specific B cell receptors (BCRs). Antigen binding to the BCR triggers both BCR signaling and internalization. However, how internalization regulates signaling was not known for the BCR and multiple other immune receptors. In a novel study, we demonstrated that the BCR signaling is compartmentalized. We showed that the BCR signaling is a dynamic process, which begins at the cell surface with the transient recruitment and phosphorylation of the early proximal signaling kinases and continues as the BCR traffics into the cell with the sequential recruitment and phosphorylation of downstream kinases. Moreover, BCR localization and trafficking are essential for optimal signaling. Interestingly, blocking endocytosis of the BCRs completely perturbs the spatiotemporal regulation of major signaling pathways leading to the dysregulation of gene transcription controlled by these pathways. This intracellular location of BCR not only serves to regulate the BCR signaling but also provides a platform where internalized BCR interacts with the intracellular Toll-like receptor (TLRs), in particular, TLR9. We showed that in resting B cells, TLR9 is localized in early endosomal compartments and signals from these compartments. BCR crosslinking results in the relocalization of TLR9 to the autophagosome-like compartments into which the BCR is internalized and where synergistic signaling between BCR and TLR9 occurs. Besides regulating BCR and TLR9 responses, intracellular location is also important in governing responses to different TLR9 ligands.