Seminar/Talk

Cytoskeletal regulation of B cell receptor (BCR) spatial organization and signalling

Bolger-Munro, Madison
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Host: Carl-Philipp Heisenberg

When B cells encounter antigens on the surface of an antigen-presenting cell (APC), B cell receptors (BCRs) are gathered into microclusters that recruit signalling enzymes. These microclusters then move centripetally and coalesce into the central supramolecular activation cluster of an immune synapse. The mechanisms controlling BCR organization during immune synapse formation, and how this impacts BCR signalling, are not fully understood. We show that this coalescence of BCR microclusters depends on the actin-related protein 2/3 (Arp2/3) complex, which nucleates branched actin networks. Moreover, in murine B cells, this dynamic spatial reorganization of BCR microclusters amplifies proximal BCR signalling reactions and enhances the ability of membrane-associated antigens to induce transcriptional responses and proliferation. Our finding that Arp2/3 complex activity is important for B cell responses to spatially restricted membrane-bound antigens, but not for soluble antigens, highlights a critical role for Arp2/3 complex-dependent actin remodeling in B cell responses to APC-bound antigens. These findings indicate that Arp2/3-dependent actin retrograde flow amplifies microcluster-based BCR signalling. However, the underlying mechanism is not known. Because the BCR is a mechanosenstive receptor, we are now testing the hypothesis that Arp2/3 activity generates force that is exerted on antigen-bound BCRs and that this increases BCR signalling output and promotes antigen internalization.

Wednesday, October 23, 2019 11:00am - 12:30pm

Meeting room 2nd floor / Bertalanffy Bldg. (I04.2OG - LAB)

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