

Watching Class II MHC molecules move

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Antigen presentation requires the coordination of assembly, intracellular trafficking and display of MHC molecules. Class II MHC products sample endocytic compartments and there acquire peptides to be presented to CD4 T cells. The details of these pathways have been worked out mostly in established cell lines. With the growing awareness that professional antigen presenting cells, such as dendritic cells, are essential for the initiation of an immune response, the emphasis has shifted to the analysis of primary cells in culture, with all of the limitations inherent in the use of these biologicals. A further complication arises from the dynamic interactions that take place at the interface of the antigen presenting cell and the T cell. These interactions are spatially confined, and concern at best a fraction of total number of relevant molecules on both antigen presenting cell and T cell, thus limiting the usefulness of an exclusively biochemical approach to their study. Direct imaging has cast a new light on such interactions, as testified by the broad acceptance of the concept of an immunological synapse. Most of the detailed imaging experiments reported concern surface molecules on the T cell, while relatively little work has been done on the antigen presenting cell. I shall describe experiments that make use of a mouse in which all of its class II MHC molecules are tagged with GFP and expressed under the control of endogenous regulatory elements, as achieved by a knock-in approach. Dendritic cells obtained from such animals are used to image the events that occur upon contact of an antigen-loaded dendritic cell with an antigen specific T cell. The results show a remarkable level of specialization on the part of the antigen presenting cell in the handling of Class II MHC molecules to achieve full T cell activation.

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T-cell engagement of dendritic cells rapidly rearranges MHC class II transport.
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