T CELLS

Sharing through a synapse

A close look at the behaviour of activated T cells in lymph nodes reveals that they engage with each other in dynamic clusters to share interleukin-2 (IL-2).

To become activated, T cells engage with antigen-presenting cells (APCs), an interaction that is characterized by the formation of an immunological synapse. Once activated, T cells tend to have reduced motility and have been shown to associate in large clusters, but what might be the purpose of these T-cell clusters? To investigate this in detail, Krummel and colleagues used two-photon laser scanning microscopy to visualize the dynamics of activated T cells *in vivo*. Deep within the lymph nodes of mice that had received labelled antigen-specific T cells activated by subsequent immunization, the authors observed clusters of T cells. These clusters, which persisted for >30 minutes or were more transient, were highly dynamic, with T cells observed joining and leaving them. The clusters could form even if activation stimuli were not provided by APCs, which suggests that the capacity to self-aggregate is gained after T-cell activation but is not dependent on APCs.

Further *in vitro* analysis showed that the activation-induced T-cell clustering is mediated by the integrin LFA1 (lymphocyte function-associated antigen 1), as fewer clusters were found in LFA1-deficient mice, and LFA1-specific antibody disrupted aggregates of wild-type T cells *in vitro*. In addition, electron microscopy analysis revealed that, similar to APC–T-cell interactions, multifocal synapses formed between the activated T cells. These synapses were characterized by the polarization of the microtubule-organizing complex and IL-2-containing vesicles towards the point of contact.

This suggested that T-cell clustering might be of benefit to the T cells by facilitating the capture of IL-2 that is directionally secreted across the synapse. Indeed, synapse-engaged T cells were found to accumulate more IL-2 than those that were not engaged in synaptic contact and this resulted in substantially higher levels of phosphorylated STAT5 (signal transducer and activator of transcription 5), which is a transcription factor downstream of IL-2-receptor signalling.

So, this study shows that T-cell activation is facilitated by the formation of T-cell clusters that allow polarized secretion of cytokines across a synapse.

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