Functional gap junctions accumulate at the immunological synapse and contribute to T cell activation

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Gap junction (GJ) mediates intercellular communication through linked hemichannels from each of two adjacent cells. Using human and mouse models, we show that connexin 43 (Cx43), the main GJ protein in the immune system, was recruited to the immunological synapse during T cell priming as both GJs and stand-alone hemichannels. Cx43 accumulation at the synapse was Ag specific and time dependent, and required an intact actin cytoskeleton. Fluorescence recovery after photobleaching and Cx43- specific inhibitors were used to prove that intercellular communication between T cells and dendritic cells is bidirectional and specifically mediated by Cx43. Moreover, this intercellular cross talk contributed to T cell activation as silencing of Cx43 with an antisense or inhibition of GJ docking impaired intracellular Ca2+ responses and cytokine release by T cells. These findings identify Cx43 as an important functional component of the immunological synapse and reveal a crucial role for GJs and hem