VAMP7 controls T cell activation by regulating the recruitment and phosphorylation of vesicular Lat at TCR-activation sites

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Abstract

The mechanisms by which Lat (a key adaptor in the T cell antigen receptor (TCR) signaling pathway) and the TCR come together after TCR triggering are not well understood. We investigate here the role of SNARE proteins, which are part of protein complexes involved in the docking, priming and fusion of vesicles with opposing membranes, in this process. Here we found, by silencing approaches and genetically modified mice, that the vesicular SNARE VAMP7 was required for the recruitment of Lat-containing vesicles to TCR-activation sites. Our results indicated that this did not involve fusion of Lat-containing vesicles with the plasma membrane. VAMP7, which localized together with Lat on the subsynaptic vesicles, controlled the phosphorylation of Lat, formation of the TCR-Lat-signaling complex and, ultimately, activation of T cells. Our findings suggest that the transport and docking of Lat-containing vesicles with target membranes containing TCRs regulates TCR-induced signaling.

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