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Modulation of T Cell Signaling Via SLAT Association with IP3R1

Researchers at the La Jolla Institute for Immunology have discovered the interaction of two proteins, SWAP-70-like adaptor of T cells (SLAT) and inositol 1,4,5-trisphosphate receptor type 1 (IP3R1). This interaction was found to regulate Ca^{2+} signaling in T cells and represents a specific drug target for treating immune disease.

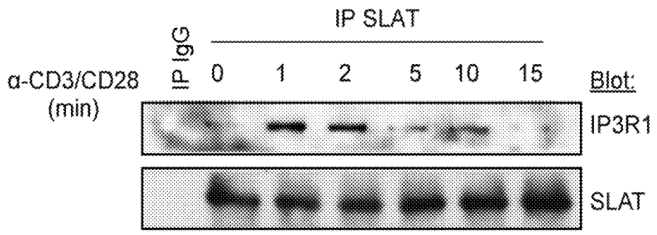
SAWP-70-like adaptor of T cells (SLAT) is a guanine nucleotide exchange factor that regulates T cell activation and differentiation by enabling Ca^{2+} release from intracellular stores in response to T cell receptor stimulation. However, the underlying mechanism and its relevance in T cell activation were previously unknown.

As such, researchers at LJI have discovered a TCR-induced direct association between SLAT and the inositol 1,4,5-trisphosphate receptor type 1 (IP3R1), mediated by an N-terminal putative EF hand domain and the pleckstrin homology domain of SLAT which independently bind a distinct motif within the IP3R1 ligand-binding domain. Disruption of the SLT-IP3R1 interaction inhibited TCR-induced Ca^{2+}-NFAT signaling and cytokine production. Thus, SLAT is a novel IP3R1-interacting regulator of T cell activation, implicating this interaction as a potentially selective immunosuppression drug target.

ADVANTAGES:

- Describes previously unknown interaction between two proteins
- Gives specific drug target for treating immune disease
- Useful for any immune disease caused by aberrant T cell activation

Modulation of SLAT interaction with IP3R1 regulates T cell activation



SLAT interacts with IP3R1 in stimulated CD4+ T cells

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