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Targeting ITK Signaling in T-cell Mediated Diseases: A Review

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Investigation of ITK signaling in disease pathogenesis and the potential efficacy of its inhibition in malignant, autoimmune, and other illnesses is an exciting area of both pre-clinical and clinical study. ITK is a Tec family kinase which are primarily expressed in cells of hematopoietic lineage. Following TCR ligation, ITK is recruited to the cell membrane where it interacts with Linker for activation of T cells (LAT) and SH2-domain-containing leukocyte protein of 76 kDa (SLP76). Proper positioning of ITK and Phospholipase C (PLC)γ-1 within the LAT-SLP76 complex leads to the phosphorylation and activation of PLCγ1. ITK signaling can lead to aberrant immune behavior and disease pathogenesis in various malignant and immunological disorders. These diseases include T-cell derived malignancies as well as immune-subversion mechanisms seen in other malignancies, allergic diseases such as asthma and atopic dermatitis, certain infectious diseases such as leishmaniasis, and several autoimmune disorders such as rheumatoid arthritis and psoriasis. ITK signaling also has implications in bone marrow and solid organs transplants. Here, we will review the clinically relevant material for each T-cell derived disease, examine the efficacy of ITK inhibition in disease models and clinical studies, postulate potential avenues for further research, and finally, discuss our new data observed following the attenuation of the SLP76:ITK interaction in a murine model of graft versus-host disease.