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SAP/SH2D1A Knockout Mouse: A Model for X-Linked Lymphoproliferative Disease

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Key Words

SLAM-associated protein, SAP, X-linked lymphoproliferative disease, XLP, asthma, hypersensitivity, Th2 cells

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Summary

SAP (SLAM-associated protein, also known as SH2D1A and DSHP) is a small lymphocyte-specific signaling molecule that is critical in normal immune function, especially in the regulation of T cell responses, such as cytokine roles (e.g., T helper type 2 cytokines) and effects on antibody production by B cells. SAP is also defective or absent in patients with X-linked lymphoproliferative disease (XLP), a genetic disorder characterized by immune dysregulation and lymphoproliferation upon exposure to Epstein-Barr virus. NHGRI investigators generated a mouse deficient in SAP, which upon challenge with infectious agents, recapitulates features of XLP. SAP-deficient mice have normal lymphocyte development and life expectancy under wild type conditions. Upon infection, however, SAP mutant mice show evidence of T cell hyperactivation, decreased B cell function, and, in a model of chronic infection, increased morbidity and mortality.

Potential Commercial Applications

This knockout mouse can be used to study and design therapeutics or gene therapy for XLP. It can also help in investigating other T cell-mediated diseases, such as asthma and hypersensitivity. This model is also useful for researchers interested in T- cell signaling and cytokine production by T-helper cells

Related Articles

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