

# Signaling molecule identified as essential for maintaining a balanced immune response

July 26 2011

---

(Medical Xpress) -- St. Jude Children's Research Hospital investigators have identified a signaling molecule that functions like a factory supervisor to ensure that the right mix of specialized T cells is available to fight infections and guard against autoimmune disease.

The research also showed the molecule, phosphatase MKP-1, is an important regulator of immune balance. Working in laboratory cell lines and mice with specially engineered immune systems, scientists demonstrated that MKP-1 serves as a bridge between the innate immune response that is the body's first line of defense against infection and the more specialized adaptive immune response that follows. The results are published in the July 22 print edition of the scientific journal *Immunity*.

The results raise hopes that the MKP-1 pathway will lead to new tools for shaping the immune response, said Hongbo Chi, Ph.D., assistant member of the St. Jude Department of Immunology and the study's senior author. The co-first authors are Gonghua Huang, Ph.D., and Yanyan Wang, Ph.D., both postdoctoral fellows in Chi's laboratory.

The findings provide new details about how dendritic [cells](#) regulate the fate of naïve or undifferentiated T cells. Dendritic cells are the sentinels of the innate immune response, patrolling the body and ready to respond at the first sign of infection.

Investigators were surprised that a single molecule regulated production of three out of the four major subsets of T cells, which each play

different roles. MKP-1 is a negative regulator of the enzyme p38, which is part of the MAP kinase family of enzymes that control pathways involved in cell proliferation, differentiation and death.

Chi and his colleagues demonstrated that MKP-1 works in dendritic cells by altering production of protein messengers known as cytokines. Those cytokines determine which subset of specialized T cells the undifferentiated T cells are fated to become. In this study, scientists showed that MKP1 controls production of the cytokines that yield T helper 1 (Th1), T helper 17 (Th17) and regulatory T (Treg) cells. Th1 cells combat intracellular bacterial and viral infections. Th17 cells fight extracellular bacterial infections and fungi. Treg cells help with immune suppression, protecting against autoimmune diseases.

The study showed that suppression of p38 by MKP-1 promotes production of interleukin 12 (IL-12), which leads to an increase in Th1 cells. Rising IL-12 coincides with a drop in interleukin 6 (IL-6) and a corresponding dip in production of Th17. MKP-1 also inhibited the generation of Treg cells by down-regulating production of a third cytokine, TGF-beta.

Knocking out MKP-1 in mice disrupted production of IL-12 and IL-6 in dendritic cells as well as the anti-bacterial and anti-fungal [immune response](#), researchers reported. MKP-1 deficiency also promoted T-cell driven inflammation in a mouse model of colitis, an inflammatory disease.

“MKP-1 is the first signaling molecule found in dendritic cells to program differentiation of these diverse T- cell subsets,” Chi said.

Previous work by other scientists focused on T cell differentiation in response to stimulation by cytokines. “This research fills a gap in our understanding of dendritic cell-mediated control of T-cell lineage

choices,” Chi said. “T cells do not recognize pathogens directly, but dendritic cells do. T cells need dendritic cells to tell them what to do. In this study, we show that MKP-1 signaling in dendritic cells bridges the innate and adaptive immune responses by regulating cytokine production.”

Other authors are Lewis Shi and Thirumala-Devi Kanneganti, both of St. Jude.

**More information:** [DOI: 10.1016/j.immuni.2011.05.014](https://doi.org/10.1016/j.immuni.2011.05.014)

Provided by St. Jude Children's Research Hospital

Citation: Signaling molecule identified as essential for maintaining a balanced immune response (2011, July 26) retrieved 27 April 2024 from <https://medicalxpress.com/news/2011-07-molecule-essential-immune-response.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--