

CPB 69700 RESEARCH SEMINAR

DEPARTMENT OF COMPARATIVE PATHOBIOLOGY

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VPTH 112
3:30 pm

“SHARPIN Regulates Inflammatory Response Via NF- κ B Signaling”

Abstract:

Improper regulation of inflammation contributes to the pathogenesis of many chronic diseases. Therefore, the identification and understanding of critical regulators of the inflammatory response may reveal potential therapeutic targets. The protein SHARPIN appears to play a role in the control of inflammation. Previous studies have shown that deletion mutations of the *Sharpin* gene result in multiorgan chronic inflammation in mutant mice. The aim of the present study was to determine the effect of SHARPIN-deficiency on the secretion of pro-inflammatory mediators and cell signaling. Dendritic cells were generated from the bone marrow of SHARPIN-deficient and wild-type mice and stimulated with ligands of Toll-like receptors. The SHARPIN-deficient dendritic cells had decreased production of the cytokines IL-1 β , IL-6, and IL-12, and the inflammatory mediator nitric oxide as compared with WT counterparts. This was associated with decreased signaling through the NF- κ B pathway, while MAPK signaling pathways appeared to be intact. Overexpression of SHARPIN in fibroblasts increased IL-6 production in a dose-dependent manner. These data suggest that SHARPIN is specifically involved in NF- κ B signaling activation and thus necessary for complete activation of inflammatory pathways. Therefore, SHARPIN may be a potential therapeutic target for chronic inflammatory diseases.