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Huia-Chia Chuang

National Health Research Institutes, Taiwan

The phosphatase JKAP/DUSP22 attenuates T-cell receptor signaling and autoimmunity

NK pathway-associated phosphatase (JKAP, also named DUSP22) was originally identified as a JNK activator. Recently, JKAP has been shown to play a critical role in immune regulation. In T-cell receptor (TCR) signaling, JKAP directly inactivates Lck by dephosphorylating tyrosine-394 residue. JKAP-knockout T cells display enhanced cell proliferation and cytokine production. Moreover, JKAP-knockout mice display enhanced serum levels of pro-inflammatory cytokines (TNFa, IFNy, IL-6, IL-17A) and autoantibodies (ANA, anti-dsDNA). JKAP-knockout mice also show enhanced T-cell-mediated immune responses and are more susceptible to experimental autoimmune encephalomyelitis (EAE). Adoptive transfer experiments further show that the recipient mice with JKAP-knockout T cells display exacerbated EAE symptoms. In addition, aged JKAPknockout mice spontaneously develop systemic inflammation and autoimmune diseases, including nephritis. Furthermore, T-cell-specific JKAP mutant transgenic mice show induction of autoantibodies (ANA, anti-dsDNA) and display a lupus nephritis-like phenotype. To study the clinical relevance of JKAP downregulation in T cells, peripheral blood T cells from systemic lupus erythematosus (SLE) patients were isolated and subjected to immunoblotting. The data showed that JKAP protein levels in the peripheral blood T cells of SLE patients were significantly decreased compared to those in healthy controls. Remarkably, JKAP downregulation in SLE T cells were correlated with proteinuria and poor renal outcome. In summary, JKAP is an important phosphatase that inactivates Lck in the turn-off stage of TCR signaling, leading to suppression of T-cellmediated autoimmunity. Furthermore, JKAP downregulation in T cells is a diagnostic and prognostic biomarker for SLE nephritis.

Biography

Huia-Chia Chuang received her PhD degree in Basic Medical Sciences in 2008 and conducted Postdoctoral studies at National Health Research Institutes (NHRI). She is currently an Assistant Investigator of Immunology Research Center, NHRI. She has published 20 papers in reputed journals such as *Nature Immunology, Nature Communications, Arthritis & Rheumatism,* and *Blood.*

cinth@nhri.org.tw

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