

Non-Confidential Disclosure

 Immune Disease Institute	Office of Technology Development 800 Huntington Avenue Boston, Massachusetts 02115 www.idi.harvard.edu
IDI 98-001	SELECTIVE INHIBITION OF CALCINEURIN- NFAT SIGNALING

Application: Organ transplantation, allergy, inflammatory and autoimmune diseases

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Invention Summary:

This invention relates to the NFAT-family proteins, which are transcription factors that play a key role in the inducible expression of cytokine genes during the activation of T-cells and other immune system cells. The activation of NFAT in cells requires its dephosphorylation by the protein phosphatase calcineurin. There are currently immunosuppressant drugs that inhibit dephosphorylation of calcineurin but they display considerable toxicity and are known to inhibit dephosphorylation of calcineurin substrates other than NFAT. The division of signaling pathways downstream of calcineurin, into a branch that depends on NFAT and branches that do not, lead the inventor to devise more selective ways of blocking calcineurin-NFAT signaling. The present invention is an optimized peptide ligand that inhibits NFAT recognition and dephosphorylation by calcineurin. Studies have shown that this peptide inhibits calcineurin-NFAT transcriptional signaling in T cells and is more selective and less toxic than cyclosporin A.

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