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Host Defense & Pathophysiology

The calcineurin - NFAT axis contributes to host defense during *Pseudomonas aeruginosa* lung infection

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Abstract

Infection with the opportunistic pathogen *Pseudomonas aeruginosa* is effectively controlled through tightly coordinated inflammation in healthy individuals. Dysregulated inflammation in cystic fibrosis greatly increases susceptibility to *P. aeruginosa* and lung damage. Recently, we identified regulator of calcineurin - 1, a small, conserved protein that suppresses the NFAT pathway by inhibition of calcineurin and functions as a central negative regulator of multiple inflammatory transcription factors after *P. aeruginosa* lung infection, implying a role for the canonical NFAT pathway in *P. aeruginosa* infection. Calcineurin is a calcium - calmodulin–responsive phosphatase that dephosphorylates NFAT and promotes NFAT nuclear translocation and transcriptional activity. The contribution of the NFAT pathway to host defense against *P. aeruginosa* remains poorly characterized. In this study, we found that NFAT was rapidly and transiently activated after *P. aeruginosa* infection both in vitro and in vivo. Deficiency of calcineurin A β caused impaired activation of NFAT and decreased inflammatory cytokine production in vivo. Finally, we demonstrated that the cross - talk between the NFAT and NF κ B pathways coordinately transactivate host response genes during *P. aeruginosa* infection. Together, these results demonstrate for the first time that NFAT is activated through calcineurin and interacts with NF κ B after *P. aeruginosa* lung infection, and contributes to the host inflammatory response.

Supporting Information