

Carvalho A, De Luca A, Bozza S, Cunha C, D'Angelo C, Moretti S, Perruccio K, Iannitti RG, Fallarino F, Pierini A, Latgé JP, Velardi A, Aversa F and Romani L. (2011). TLR3 essentially promotes protective class I-restricted memory CD8⁺ T-cell responses to *Aspergillus fumigatus* in hematopoietic transplanted patients. *Blood*, 119:967-77

Aspergillus fumigatus is a model fungal pathogen and a common cause of severe infections and diseases. CD8⁺ T cells are present in the human and murine T cell repertoire to the fungus. However, CD8⁺ T cell function in infection as well as the molecular mechanisms that control their priming and differentiation into effector and memory cells in vivo remains elusive. In this study, we report that both CD4⁺ and CD8⁺ T cells mediate protective memory responses to the fungus contingent upon the nature of the fungal vaccine. Mechanistically, class I MHC-restricted, CD8⁺ memory T cells were activated through TLR3 sensing of fungal RNA by cross-presenting dendritic cells. Genetic deficiency of TLR3 was associated with susceptibility to aspergillosis and concomitant failure to activate memory protective CD8⁺ T cells both in mice and in stem cell-transplanted patients. Thus, TLR3 essentially promotes antifungal memory CD8⁺ T cell responses and its deficiency is a novel susceptibility factor for aspergillosis in high-risk patients.