

# VACCINES AND INNATE IMMUNITY: LESSONS FROM CYTOMEGALOVIRUS IMMUNOEVASION

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Cytomegalovirus (CMV) establishes life-long infection of its host, ensuring continuous supply of effector memory CD8<sup>+</sup> T cells. CMVs possess numerous immunoevasion genes able to modulate basically any part of immune response, including NK cell and CD8<sup>+</sup> T cell response. It is well established that deletion of these viral inhibitors leads to virus attenuation *in vivo*. These features make CMV a very attractive CD8<sup>+</sup> T cell vaccine-vector candidate. Control of CMV infection is in great part dependent on NKG2D, an activating receptor when expressed on NK cells and co-stimulatory one when expressed on CD8<sup>+</sup> T cells. We have constructed highly attenuated mouse CMV (MCMV) expressing NKG2D ligand RAE-1 $\gamma$  inserted in place of its viral inhibitor (Slavuljica et al, 2010) and foreign CD8<sup>+</sup> T cell epitope as well (Trsan et al, 2013). Such a recombinant vaccine-vector provided outstanding and long-lasting CD8<sup>+</sup> T cell-mediated protection against challenge infections. Moreover, RAE-1 $\gamma$ MCMV-vector circumvented MCMV interference of antigen presentation, improved antigen presentation to CD8<sup>+</sup> T cells and potentiated memory CD8<sup>+</sup> T cell response. Surprisingly, these immuno enhancing properties of RAE-1 $\gamma$  expressing MCMV vector were retained even in NKG2D deficient mice, pointing to additional NKG2D-independent immune function of RAE-1 $\gamma$ . In my talk, I will discuss the capacity of MCMV expressing RAE-1 $\gamma$  as a vaccine vector against other pathogens, as well as tumors.

SPEAKERS ABSTRACTS

Day 3

