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Impact of HCMV on HLA-I and Consequences on Gamma Delta T cell and Alpha Beta T cell Activation

Layal Massara
University of Bordeaux, College of Health Sciences, France

Cytomegalovirus (CMV), a Beta Herpes virus, is considered as a paradigm for viral evasion. It is an important opportunistic pathogen in immunocompromised patients and a major cause of congenital birth defects when acquired in utero. CMV encodes molecules to prevent antigen presentation to αβ T cells through inhibition of MHC Class I expression and to suppress NK cell functions by mimicking or down-regulating ligands of NK receptors (NKR). These evasion mechanisms are not expected to affect γδ T cells and, as a matter of fact, their response to CMV has been widely reported in many different physio-pathological contexts as well as in CMV-seropositive healthy donors (*Dechanet et al, 1999)(Scheper, 2013).*

Our aim was to understand how CMV induces γδ T cell response. We used recombinant adenovir uses expressing each of the four US genes, and a mutant HCMV deleted for these 4 genes (CMV-DUS). We observed an induction of HLA-I expression by the control adenovirus, and an inhibition by US2, US3 and US11. When using CMV-DUS, infected cells expressed much more native HLA-I than CMV-WT infected cells. Interestingly and in sharp contrast to αβ Tcells, γδ T cell were activated to produce IFNg when cultured with fibroblasts infected with CMV-WT, but not when fibroblasts were infected with CMV-DUS. These results indicate that HLA-I molecules regulate γδ T cells through mechanisms that are under investigation in our team. The immune escape processes developed by CMV could thus promote γδ over αβ T cell response and explain the important response of γδ T cells to the virus in immune suppressed individuals.