Adoptive immunotherapy is a promising therapeutic approach for the treatment of chronic infections and cancer. T cells within a certain range of high avidity for their cognate ligand are believed to be most effective. T cell receptor (TCR) transfer experiments indicate that a major part of avidity is hardwired within the structure of the TCR. Unfortunately, rapid measurement of structural avidity of TCRs is difficult on living T cells. We developed a technology where dissociation (koff rate) of truly monomeric peptide-major histocompatibility complex (pMHC) molecules bound to surface-expressed TCRs can be monitored by real-time microscopy in a highly reliable manner. A first evaluation of this method on distinct human cytomegalovirus (CMV)-specific T cell populations revealed unexpected differences in the koff rates. CMV-specific T cells are currently being evaluated in clinical trials for efficacy in adoptive immunotherapy; therefore, determination of koff rates could guide selection of the most effective donor cells. Indeed, in two different murine infection models, we demonstrate that...
T cell populations with lower koff rates confer significantly better protection than populations with fast koff rates. These data indicate that koff rate measurements can improve the predictability of adoptive immunotherapy and provide diagnostic information on the in vivo quality of T cells.