Repopulation of the antigen-specific memory $CD8^+$ T cell pool following re-exposure to antigen

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Upon antigenic stimulation, naïve $CD8^+$ T cells become activated effector cells. This population of effector cells later decreases in size and remains as a small pool of resting memory cells, capable of a rapid response on re-exposure to the same antigen. However, new naïve cells undergo an effector response during re-exposure, resulting in new memory cells. The number of circulating memory $CD8^+$ T cells remains constant; therefore, a mechanism for homeostatic control of antigen-specific memory cells must exist. To investigate regulation of memory cells, we utilized two genetically marked strains of mice, both with a transgenic TCR that recognises the peptide 257-264 of the OVA protein in association with MHC Class I. Naïve transgenic $CD8^+$ T cells from the first donor were transferred with peptide–loaded bone marrow-derived dendritic cells (bmDCs) into syngeneic mice. These T cells expanded, acquired an effector phenotype, then became quiescent memory cells. The same mice then received a transfer of peptide-loaded bmDCs and naïve transgenic $CD8^+$ T cells from the second donor. These cells also become effector, and then memory, cells. The composition of the memory pool in these mice was analysed following a third challenge with antigen. The recall memory population was composed almost entirely of memory cells generated from the second response, whereas memory cells generated from the first response had been eliminated. We propose that memory cells generated in a subsequent exposure to the same antigen delete existing antigen-specific memory cells, at least under the conditions of these experiments. This may be a mechanism for homeostatic control of memory cell populations.