

Tetracycline-regulated expression of a T cell epitope in dendritic cells *in vivo*

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In order to study the regulation of T cell responses by peptide/MHC complexes *in vivo*, we established a new mouse line that expresses an I-E^k-restricted T cell epitope derived from moth cytochrome c (MCC) under the dictates of the invariant chain transcriptional control sequences. Its expression can be regulated by feeding the animals with tetracycline or doxycycline in the food or drinking water. We show that: 1) In the absence of doxycycline, the reporter transgene was not expressed: AND transgenic thymocytes, specific for I-E^k/MCC, developed normally. However, AND thymocytes were deleted rapidly when the animals were fed with doxycycline. 2) For reasons unknown, MCC expression in the spleen was predominantly found in CD11c⁺ dendritic cells. Detection of the MCC epitope in the periphery by CFSE-labelled transferred T cells was strictly dependent on doxycycline. 3) The MCC peptide appeared quickly (within ca. 12 hours) and disappeared slowly (5-10 days) after doxycycline feeding and removal. Intriguingly, we did not find any signs of autoimmunity when the MCC transgene was switched on in adult AND transgenic animals, although the AND T cells had an activated phenotype. We are currently investigating how tolerance to this neo-self peptide is established and how it can be broken by costimulatory signals.

*equal contribution