Clonal expansion of cytotoxic T cells: The role of the immunoproteasome in infection

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We show how the proteasome, a protease ubiquitously present inside every cell of all organisms, may affect the dynamics of cytotoxic T cell clo! nes during an immune response. It is well documented how T cell clones interact with antigen presenting cells via MHC class I/peptide complexes in order to get signals regulating their survival, differentiation and death. The peptides mounted on the MHC complexes are mainly generated by the proteasome. During an immune response, some proteasomes are replaced by immunoproteasomes, which are believed to process antigenic peptides more efficiently. In the present model, we investigate the homeostasis and the clonal expansion of cytotoxic T cell clones taking into account peptide processing and the effect of changes in the cellular proteasome composition. The model is based on a classical theoretical description of T cells competing for resources. It shows that the shaping of different peptide distributions by the proteasome can strongly influence the dynamics of the T cell repertoire. We found that the immunoproteasome may represent a major contribution to ! the selection of the appropriate T cell distribution during an immune response, enhancing possibly its effectivity by several orders of magnitude. We show that, without immunoproteasome upregulation, infections tend become chronic, and compare our findings to data of LCMV infected mice.