

Cross-priming and cancer vaccines

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Abstract

Whereas virtually any antigen expressing MHC class I+ cell can present tumor antigens to CD8+ T cells, only professional antigen-presenting cells (APC) have the capacity to prime tumor antigen specific naïve CD8+ T cells *in vivo*. Professional APC can acquire exogenous tumor antigens and present them via their own MHC class I molecules to CD8+ T cells in a process known as antigen cross-presentation (1). The precise molecular pathways leading to cross-priming, however, remain controversial (2), and even the relevance of tumor antigen cross-presentation for the induction of anti-tumor responses has been questioned (3-5). In this presentation, I will review the proposed molecular basis for cross-presentation, the APC subsets which are known to be involved in this phenomenon and the *in vivo* conditions which may result in cross-priming of tumor antigen specific CD8+ T cells versus cross-tolerance. I will then show recent evidence that vaccination of cancer patients with NY-ESO-1 recombinant protein, Montanide® ISA-51 and the TLR9 ligand CpG 7909, can result in the *in vivo* cross-priming of NY-ESO-1 specific CD8+ T cells able to recognize endogenously expressed NY-ESO-1 antigen, indicating that cross-presentation of tumor antigens is highly relevant for tumor immunotherapy and can occur, following activation of professional APC, in the presence of appropriate levels of integrated humoral and CD4+ T-cell responses. The presented data provide direct evidence of *in vivo* cross-priming of specific CD8+ T cells by a recombinant full-length tumor antigen vaccine in cancer patients and support the use of this type of formulation for the further development of efficient cancer vaccines.

References

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