Cancer Immunity (16 May 2007) Vol. 7 Suppl.1, p. 14

CANCER
IMMUNITY
Meeting Abstract

Cross-priming and cancer vaccines

Danila Valmori

Columbia University, College of Physicians & Surgeons, New York, NY, USA

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

1. Heath WR, Belz GT, Behrens GM, Smith CM, Forehan SP, Parish IA, Davey GM, Wilson NS, Carbone FR, Villadangos JA. Cross-presentation, dendritic cell subsets, and the generation of immunity to cellular antigens. *Immunol Rev* 2004; **199:** 9-26. (PMID: 15233723)

2. Groothuis TA, Neefjes J. The many roads to cross-presentation. *J Exp Med* 2005; **202:** 1313-1318. (PMID: 16287713)

3. Ochsenbein AF, Sierro S, Odermatt B, Pericin M, Karrer U, Hermans J, Hemmi S, Hengartner H, Zinkernagel RM. Roles of tumor localization, second signals and cross priming in cytotoxic T-cell induction. *Nature* 2001; **411:** 1058-1064. (PMID: 11429607)

4. Chen W, Masterman KA, Basta S, Haeryfar SM, Dimopoulos N, Knowles B, Bennink JR, Yewdell JW. Cross-priming of CD8+ T cells by viral and tumor antigens is a robust phenomenon. *Eur J Immunol* 2004; **34:** 194-199. (PMID: 14971045)

5. Melief CJ. Regulation of cytotoxic T lymphocyte responses by dendritic cells: peaceful coexistence of cross-priming and direct priming? *Eur J Immunol* 2003; **33:** 2645-2654. (PMID: 14515248)