

## Antigen encoded by vaccine vectors derived from human adenovirus serotype 5 is preferentially presented to CD8+ T lymphocytes by the CD8alpha+ dendritic cell subset

Muhammad Suleman, Sandra Galea, Francoise Gavard, Bernard Klonjkowski, Eric Tartour, Jennifer Richardson

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Suleman M, Galea S, Gavard F, Klonjkowski B, Tartour E, Richardson J

Different subsets of dendritic cells (DC) elicit qualitatively different immune responses. In mice, two lymphoid tissue-resident subsets, CD8alpha⁺ and CD8alpha⁻, have been implicated in the induction of T helper 1 (Th1) or Th2 responses, respectively. Moreover, CD8alpha<sup>+</sup> DC play a major role in priming CD8<sup>+</sup> T lymphocyte responses to viral antigens during viral infections. These considerations have been less extensively explored for vaccine vectors derived from viruses. Despite inefficient ex vivo transduction of DC, vectored vaccines derived from human adenoviruses of serotype 5 (Ad5) elicit robust immune responses, predominantly of the Th1 orientation, in humans and mice. At present it is unknown whether Ad5 interacts with DC subsets in a differential manner, thereby influencing the quality of the elicited IR. To address this issue, successive steps (attachment, transgene expression, MHC class I antigen presentation and activation of antigen-specific T lymphocytes) involved in induction of immune responses by Ad5-based vectors were examined in CD8alpha<sup>+</sup> or CD8alpha<sup>-</sup> murine DC subsets. Although in both *ex vivo* and *in vivo* experiments  $CD8\alpha^+$  and  $CD8\alpha^-$  DC subsets captured an Ad5-based vector to a similar extent, transgene expression and subsequent MHC class I display of a transgeneencoded antigen were more efficient in CD8alpha<sup>+</sup> DC. Moreover, following *in vivo* and *ex vivo* transduction with an Ad5-based vaccine, antigen-specific CD8<sup>+</sup> T lymphocytes were more efficiently activated by CD8alpha<sup>+</sup> DC than by CD8alpha DC. Thus, superior antigen expression and MHC class I display in CD8alpha<sup>+</sup> DC may contribute to preferred priming of antigen-specific CD8+ lymphocytes by Ad5-transduced CD8alpha+ DC.