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Adenoviral vaccine alters the program of pathogen-specific protective CD8$^+$ T cells expanded after an infectious challenge by selectively blocking the apoptotic signalling receptor CD95 (Fas) expression.

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Introduction: Recombinant replication deficient adenoviruses (human and simian) are being used for the development of new vaccines against diseases caused by intra-cellular pathogens such HIV, TB, malaria, Leishmaniasis, Chagas´disease, Toxoplasmosis, etc. due to their capacity to elicit CD8$^+$ T-cell mediated protective immune responses. Although efficient in relevant experimental models, it is still obscure the reason(s) why these vectors are particularly potent. We hypothesized that their unusual potency may rely on their capacity to generate a distinct type of specific CD8$^+$ T cell when compared to the pathogen itself.

Methods: To gain further information on that subject, we compared the CD8-epitope specific immune response elicited by the human intracellular parasite *Trypanosoma cruzi* or a replication deficient human adenovirus type 5 expressing its immunodominant CD8 epitopes followed or not by a challenge with *T. cruzi*.

Results: We found that functional and phenotypic aspects of the specific CD8$^+$ T cells greatly overlap. In both cases, mice developed highly cytotoxic CD8$^+$ T cells expressing CD107a, IFN-gamma and/or TNF-alpha with a typical T effector surface phenotype. The only remarkable difference we observed was that the expression of the apoptotic signaling receptor CD95 (Fas) was significantly up-regulated only on the surface of T cells following pathogen infection. Specific CD8$^+$ T cells expanded following adenoviral vaccination were not only refractory to apoptosis *in vivo* induced by parasite infection, but they **selectively block** CD95 expression on protective CD8$^+$ T cells expanded after the challenge.

Conclusions: Our results suggest that, as expected for an efficient vaccine, immunization with a recombinant adenoviral vector generates effector immune cells prior to the pathogen encounter. In addition, unexpectedly, adenoviral vaccination selectively altered the program of pathogen-specific CD8$^+$ T cells expanded after an infectious challenge, a fact that may add another important aspect for the improved protective potential of these vectors.

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