

Regulation of the antigen specific CD8 T cell response after vaccination with viral vectors

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Cancer is a life-threatening disease that is a major health problem in the western world, while many viral infections are a problem in both western world and third world countries. Vaccines may be able to effectively induce immune responses against both types of disease and are therefore important for the health of the world population. Prevention of viral infections by vaccination has been employed for many years, but the vaccines are not yet perfect, and optimization is necessary to improve protection against a number of viruses.

Treatment of cancer by vaccination is not a new idea, but we are still far from having a vaccine that effectively inhibits the growth of transformed cells.

The CD8⁺ T cell is the most important cell type involved in elimination of altered cells such as virus-infected cells and cancer. It is therefore of great importance to gain insight into the regulation of this cell type, in order to improve the current vaccine design, and thereby improve the immune response against a growing tumour or a chronic viral infection.

At present time, our laboratory has successfully prolonged the life of tumour-bearing animals by vaccination with an adenovirus vector encoding an exogenous tumour associated antigen. However, the immune response wanes over time, and eventually the tumour starts growing out again. The purpose of the current project is to identify some of the factors that limit the size and duration of a vaccine induced CD8⁺ T cell response, and in addition to investigate whether this response can be optimized through repeated immunizations.

These problems will be examined using an optimized adenoviral vaccine system with a vector encoding the glycoprotein of LCMV tethered to the invariant chain. The vaccine vector will be manipulated to identify parameters influencing the magnitude and quality of the antigen specific CD8⁺ T cell response.

Preliminary results have shown that animals that have encountered the adenoviral vector before, have a substantially diminished antigen specific CD8⁺ T cell response after the second encounter with the vector. These results suggest that pre-immunity has an effect on immunization with adenoviral vectors in the system used here.

The vaccine will also be used to vaccinate animals carrying a tumour expressing the dominant MHC class I presented epitope of the glycoprotein of LCMV (GP33) to evaluate tumour control by the antigen specific CD8⁺ T cell response induced by the vaccine.

Hopefully, identification of the parameters that influence the vaccine induced CD8⁺ T cell response will help us develop an optimized vaccine that can be used in the treatment of cancer.