

## **The role of CD4 T cells during vaccine induced immune responses against cancer**

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The importance of conventional CD4<sup>+</sup> T cells in orchestrating a CD8<sup>+</sup> T cell mediated immune response against cancer is widely accepted as they provide help by production of cytokines and by offering extra co-stimulation to keep the CD8<sup>+</sup> T cells alive and active. Regulatory CD4<sup>+</sup> T cells, on the other hand, are known to suppress CD8<sup>+</sup> T cell mediated responses.

To examine the role of CD4<sup>+</sup> T cells during control of B16 melanoma growth after therapeutic vaccination with a “strong” adenoviral vaccine encoding a tumor associated antigen (TAA) linked to the MHC class II associated invariant chain (Ii), which has previously shown to increase a CD8 T cell mediated anti-tumor response remarkably, or a “weak” adenoviral vaccine encoding the TAA alone, we used MHC class I deficient mice or anti-CD4 mAb treated mice.

The MHC class II deficient mice receiving the strong vaccine controlled their tumors as efficiently as the wild type counterparts, in contrast to MHC class II deficient mice receiving the weak vaccine in which the tumor control was significantly decreased compared with wild type mice. This indicates a redundant role of CD4<sup>+</sup> T cells after vaccination with a strong vaccine, whereas the efficiency of a weak vaccine depends on MHC class II restricted CD4<sup>+</sup> T cells.

The anti-CD4 mAb treated mice showed a different picture as the tumor control of mice receiving the strong vaccine was slightly increased, whereas tumor control in the mice receiving the weak vaccine was significantly increased compared with the untreated mice. This improvement might be due to blockage of some kind of regulatory CD4<sup>+</sup> T cells, which are still present in the MHC class II deficient mice.

The results question the need for CD4<sup>+</sup> T cell help during a CD8<sup>+</sup> T cell mediated anti-tumor response induced by a strong vaccine. In contrast, an anti-tumor response induced by a weak vaccine seems to depend on conventional CD4<sup>+</sup> T cells as long as regulatory CD4<sup>+</sup> T cells are also present, as blockage of all (conventional and regulatory) CD4<sup>+</sup> T cells improves the weak vaccine induced response to virtually obtain the quality of the strong vaccine induced response.