Engineering T cell immunity by TCR gene transfer

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STELLINGEN

behorende bij het proefschrift

ENGINEERING T CELL IMMUNITY BY TCR GENE TRANSFER

1. While both the targeting of CTLA-4 by Ipilimumab and the infusion of *ex vivo* expanded tumor-infiltrating lymphocytes have remarkable clinical effects in melanoma, their mode of action is largely unknown.
2. Unlike other T cell based immunotherapies, TCR gene transfer allows engineering T cell responses by targeted manipulation of T cell properties (*This thesis*).
3. The preclinical and clinical experience with engineered T cells suggests that no "windows of opportunity" exist with regards to expression of target antigens in vital tissues, and that the selection of safe target antigens will remain an open challenge (*This thesis*).
4. The modification of TCR affinity *in vitro* by affinity maturation is a safety concern if such TCRs are used for TCR gene transfer.
5. This thesis and work by others has helped to prevent toxicity, due to the formation of mixed-TCR dimers in TCR modified T cells, in clinical trials (*van Loenen MM et al. Proc Natl Acad Sci U S A. 107(24):10972-7 (2010) and this thesis).*
6. The tumoricidal TCR repertoire of tumor-infiltrating lymphocytes may be further harnessed by "autologous TCR gene transfer", a highly personalized treatment in which tumor-reactive TCRs are identified on a patient-specific basis and used for TCR gene transfer (*This thesis*).
7. The current regulations for the GMP-production of cell products do more harm than good for cancer patients by delaying entry of novel therapies into the clinic.
8. T cell receptors would deserve more interest from venture capital due to their potency for the treatment of cancer and other disease.
9. The current development of cancer therapies will only be beneficial for specific patient groups in high-income countries, while in low-income countries people primarily die from infectious disease.
10. "A man always needs to be busy with his thoughts if anything is to be accomplished." (*Antoni van Leeuwenhoek, 1632–1723*)