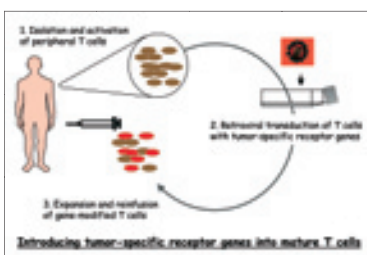


Experimental immunogene therapy of cancers: gene-modified T lymphocytes to provide tumour-specific immunity



CLINICAL and tumour immunology research at the Erasmus MC in Rotterdam focuses on immunogene therapy of cancer in general, and the therapeutic use of T lymphocytes genetically endowed with a cancer-specificity in particular. Our research has led to successful generation of tumour-specific T lymphocytes following genetic introduction of genes encoding receptors such as antibodies or T cell receptors (TCR), and we have initiated a phase I study to treat metastatic renal cancer with gene-modified T lymphocytes, the first clinical study of its nature in Europe (www.erasmusmc.nl/interne_oncologie).

Current research efforts are an integral part of the ATTACK project (www.attack-cancer.org) and directed towards improvement of efficacy and safety of T cell therapy. To this end, genetic T cell engineering is further optimized,



and molecular strategies are designed to enhance the immune control of tumors. Targeting technologies;

T cell selection and expansion methods; and the persistence, anti-tumor activities, as well as the safety of adoptively transferred T lymphocytes are assessed in various mouse tumor models.

Core elements of the Erasmus MC research include:

- Target antigens of choice, such as MAGE antigens, show an expression that is as much as possible restricted to malignant tissue and are therefore considered safe.
- Design of alternative receptors that are less prone to result in possibly dangerous T cell reactivities when compared to 'natural' TCR.
- Genetic strategies to help T lymphocytes to counteract the immunosuppressive milieu of tumours.
- Real-time in vivo monitoring of gene-modified T lymphocytes via advanced intravital fluorescence microscopy (Laboratory of Experimental and Surgical Oncology, Erasmus MC).

The generation of tumour-specific T lymphocytes that are able to confer specific immune responses in vivo with no or limited side-effects is considered an important step to successfully translate genetic T cell retargeting to the clinic.

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