

Licensing Opportunity



Acceleration of the development of new vaccines peptide-MHC exchange technology to identify T-cell epitopes

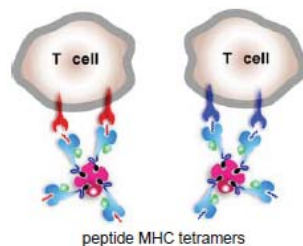
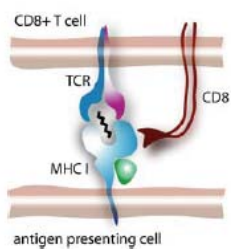
- This technology will reduce the time and costs of vaccine discovery, preclinical and clinical studies.
- This technology offers a superior antigen discovery platform enabling design of novel and more effective vaccines.
- This technology can be used for high-throughput antigen specific screening of killer T cells, allowing for the monitoring of vaccine efficacy at the level of killer T cells.

Biological Therapeutics | Monoclonal Antibodies

2011

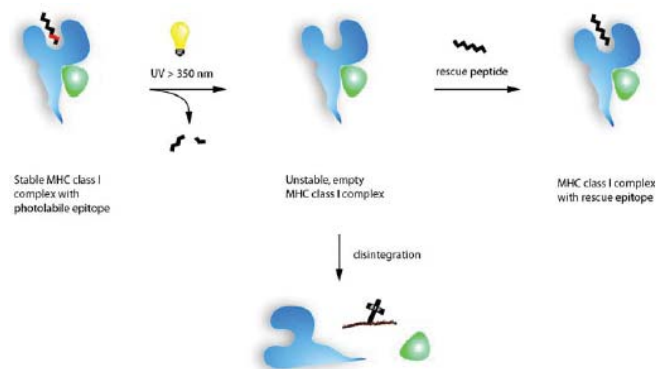
Background

Major histocompatibility complex (MHC) class I molecules present peptides on the cell surface for recognition by appropriate cytotoxic T-cells. MHC-bound peptides are critical for the stability of the MHC complex, and standard strategies for the production of recombinant MHC complexes are based on in vitro refolding reactions with specific peptides. This strategy is not amenable to high-throughput production of vast collections of MHC molecules.



The Technology

Sanquin and The Netherlands Cancer Institute have developed conditional MHC ligands that form stable complexes with MHC complexes but can be cleaved upon UV irradiation. The resulting empty, peptide-receptive MHC molecules can be charged with epitopes of choice under native conditions. This allows for the high-throughput production of peptide-MHC (pMHC) complexes.

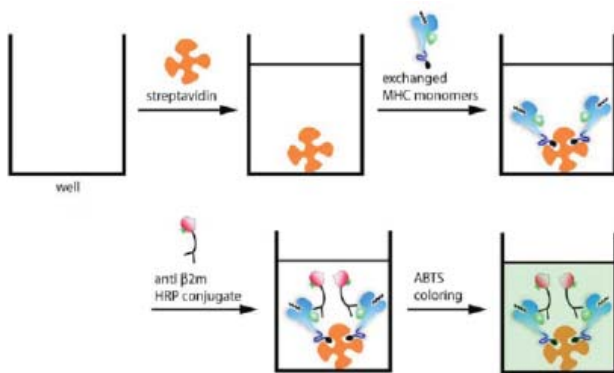


Applications of the pMHC exchange technology & status:

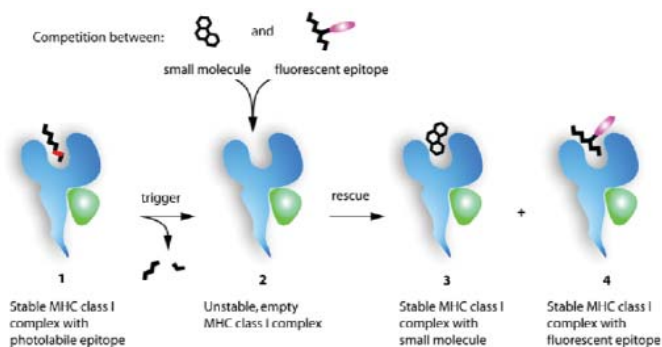
1. Platform for rapid and high-throughput identification of MHC ligands within pathogen genomes and disease associated genes (ELISA and FP-based assay operational; MHC micro-array under development, also for functional study of cytotoxic T cells).
2. Production platform for generation of MHC multimers for (high-throughput) detection of T-cells (operational; increasing number of UV-sensitive ligands for different HLA-alleles to widen applicability)
3. Production platform for clinical grade MHC reagents for T-cell purification (under development). Areas of potential clinical use of MHC multimers: cancer, viral infectious diseases, transplantation, autoimmune diseases.

Identification of MHC ligands

High throughput analysis of peptide exchange efficiency is performed by ELISA and Fluorescence Anisotropy-based Assay.

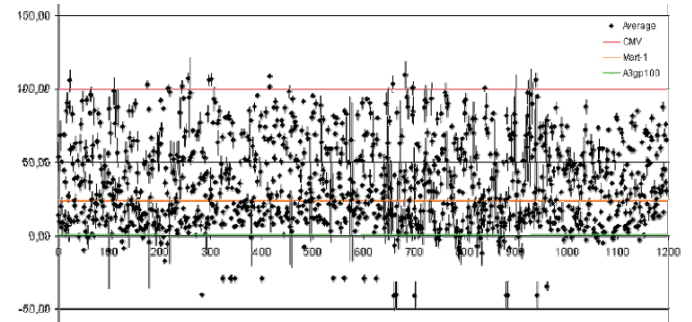


Fluorescence polarisation assay



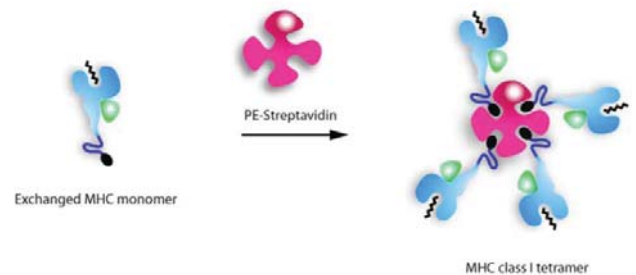
High-throughput epitope screening of HLA-A*201

Absorption normalised to CMV peptide = 100%; peptides with score above 60%: 262 out of 1197

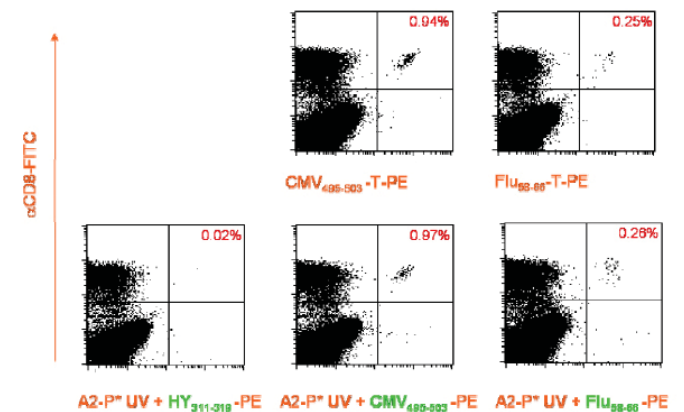


Generation of MHC tetramers for T-cell detection

Standard MHC exchange reactions are performed in multiwell plates. The biotin-tagged pMHC molecules are used for multimerization, using a fluorochrome (PE-Streptavidin). The pMHC multimer has an increased affinity for binding to the T cell receptor (TCR).



Analysis of T-responses using MHC exchange tetramers



Intellectual Property

Patent application: PCT WO 2006/080837

[Direct link.](#)

Inventors

- Schumacher, prof.dr. T.N.M.

Key publications

1. Schumacher, T.N. et al. Direct binding of peptide to empty MHC class I molecules on intact cells and in vitro. *Cell* 1990; 62: 563-7.
2. Schumacher, T.N. et al. Peptide selection by MHC class I molecules. *Nature* 1991; 350:703-6.
3. Bakker, A.H & Schumacher, T.N. MHC multimer technology: current status and future prospects. *Curr Opin Immunol* 2005; 17:428-33.
4. Toebes, M. et al. Design and use of conditional MHC class I ligands. *Nature Medicine* 2006; 12 (2):246-51.
5. Rodenko B. et al. Generation of peptide-MHC class I complexes through UV-mediated ligand exchange. *Nature Protocols* 2006; 1(3):1120-32.
6. Bakker AH, et al. Conditional MHC class I ligands and peptide exchange technology for the human MHC gene products HLA-A1, -A3, -A11, and -B7. *Proc Natl Acad Sci U S A.* 2008; 105(10):3825-30.
7. Gijsbert M. Grotenbreg, et. al. Discovery of CD8_ T cell epitopes in *Chlamydia trachomatis* infection through use of caged class I MHC tetramers. *Proc Natl Acad Sci U S A.* 2008; 105(10):3831-36.