

Parallel detection of tumor-specific T-cell responses by multidimensional encoding of peptide-Major Histocompatibility Complexes

Sine Reker Hadrup^{#,*,^}, Arnold H. Bakker^{#,*}, Chengyi J. Shu[#], Rikke S. Andersen[¶], Jerre van Veluw[#], Pleun Hombrink⁺, Emilie Castermans[#] Per thor Straten[¶], Christian Blank[#], John B. Haanen[#], Mirjam H. Heemskerk⁺ and Ton N. Schumacher^{#, @}

* These authors contributed equally, # Division of Immunology, The Netherlands Cancer Institute, Amsterdam, The Netherlands, ¶ Centre for Cancer Immune Therapy (CCIT), Department of Hematology, Herlev University Hospital, Herlev, Denmark. + Department of Hematology, Leiden University Medical Center, The Netherlands, ^ Present address: Centre for Cancer Immune Therapy (CCIT), Department of Hematology, Herlev University Hospital, Herlev, Denmark.

The use of fluorescently labeled MHC multimers has become an essential technique for the analysis of disease- and therapy-induced T cell immunity. While classical MHC multimer analyses are well-suited for the detection of immune responses against a few epitopes, limitations on patient sample size preclude a comprehensive analysis of T cell immunity.

To address this issue, we have developed a combinatorial encoding strategy that allows the parallel detection of a multitude of different T cell populations within a single sample. Detection of antigen-specific T cells from peripheral blood by combinatorial encoding is as efficient as detection with conventional PE labeled multimers, but results in a significantly increased sensitivity, and most importantly, allows comprehensive screens to be performed on patient material. Proof of principle for the feasibility of large-scale screening of patient material was obtained by analysis of HLA-A3 restricted T cell responses against known and potential melanoma-associated antigens in peripheral blood from melanoma patients. Melanoma specific T cell reactivity was detected much more frequent than previously described.

This method will form an ideal platform for CD8 T cell epitope discovery and monitoring of therapy-induced T cell responses following vaccination.