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# HLA-DR-specific γδ T-cell receptor to treat proliferative disorders of HLA-DR$^+$ cells

Keywords: Immunotherapy, Cell therapy, Cancer, Chimeric antigen receptor, T-cell receptor

## INVENTION NOVELTY

αβ T-cell receptor (TCRs) based immunotherapeutic approaches require prior knowledge of the HLA-haplotype in addition to the presented tumor-specific peptide fragment of a patient. In contrast to αβ TCRs, most identified γδ TCRs bind target molecules independent of MHC mediated peptide presentation in a way similar to antibodies. The novel receptor molecules represent promising candidates for the development of cell and immunotherapeutic treatments for the whole class of HLA-DR$^+$ malignancies.

## VALUE PROPOSITION

The MHC restriction limits the applicability of αβ TCRs to a certain subset of the population, a major disadvantage not inherent to γδ TCRs. The proprietary technology of Hannover Medical School (MHH) enables the development of an immunotherapy specifically targeting HLA-DR$^+$ cells for a broad range of malignancies of hematopoietic and lymphoid tissues with a naturally occurring receptor molecule. This enables the development of T-cell based immunotherapeutics characterized by properties closely resembling the physiologic immune response.

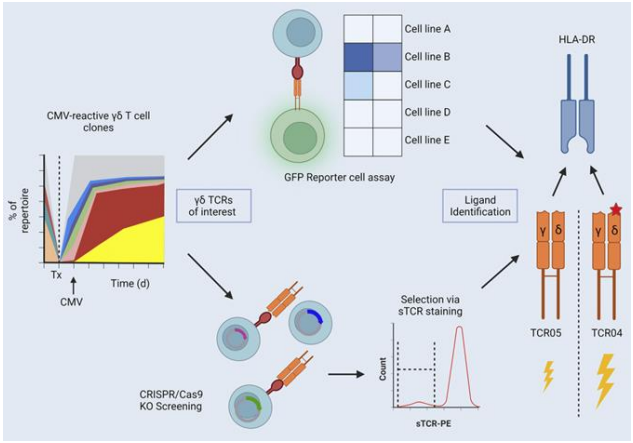


*Figure 1: Isolation and identification of HLA-DR specific γδ TCRs in response to CMV reactivation (Deseke2022).*

## TECHNOLOGY DESCRIPTION

HLA-DR is an MHC class II cell surface receptor presenting peptide fragments to immune cells. The technology covers two Vγ3Vδ1+ TCRs that recognize HLA-DR with a nanomolar and micromolar affinity in the liganded and unliganded form, respectively (TCR04: KD = 32 nM, TCR05: KD = 2.7 µM). One specific receptor (TCR05) likely binds exclusively to loaded HLA-DR complexes but irrespective of peptide presentation. The receptor with supraphysiologic high affinity (TCR04) represents a further promising candidate in the context of immunotherapeutic approaches involving γδ T-cells and their TCRs. The TCR specificity is predominantly mediated by the δ-chain of the γδ TCR constructs with an inferior role of the γ-chain. The receptors were isolated in a screen identifying γδ TCRs in response to CMV reactivation.

## COMMERCIAL OPPORTUNITY

In-licensing or collaboration for further development is possible.

## DEVELOPMENT STATUS

*In vitro* studies have been performed at Hannover Medical School.

## PATENT SITUATION

International patent application PCT/EP2022/057144 with priority of March 2021 is pending.

## FURTHER READING

1) **Deseke et al., 2022.** A CMV-induced adaptive human Vδ1+ γδ T cell clone recognizes HLA-DR. *J. Exp. Med.* DOI: 10.1084/jem.20212525

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