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Identification of CD4+ T cell epitopes specific for the breast cancer associated antigen NY-BR-1

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Adoptive transfer of autologous tumor antigen-specific T cells provides an innovative strategy for cancer immunotherapy. The differentiation antigen NY-BR-1 is over-expressed in approx. 60% of all invasive mammary carcinomas, thus representing a potential target for T cell based immunotherapy. As efficient immune attack of tumors depends on the activity of tumor antigen-specific CD4+ effector T cells, NY-BR-1 was screened for the presence of HLA-restricted CD4+ T cell epitopes that could be included in immunological treatment approaches. Splenocytes from HLA-transgenic (HLAtg) mice immunized with recombinant adenovirus (Ad.NY-BR-1) were screened ex vivo for specific activity against a NY-BR-1-derived peptide library. In silico predicted candidate epitopes present among recognized library peptides were used to establish murine CD4+ T cell lines whose HLA-restriction was determined in vitro on peptide loaded T2/DR3 and T2/DR4 target cells. Natural processing of these epitopes by human cells was proven upon specific recognition of human dendritic cells loaded with cell lysates from Ad5. NY-BR-1 infected melanoma cells through the established murine HLA-restricted CD4+ T cell lines. Importantly, reactive CD4+ T cells specific for the identified NY-BR-1-derived epitopes were detected among PBMC of HLA-matched breast cancer patients after long term in vitrorestimulation with synthetic 15mers by intracellular cytokine staining. Moreover, deep sequencing performed on the murine HLA-restricted CD4+ T cell lines established with the new epitopes identified two NY-BR-1-specific TCRs that could potentially serve tools for the generation of autologous TCR-transduced T cells lines for future NY-BR-1-specific adoptive immunotherapy approaches against breast cancer.

Biography

Stefan B Eichmüller gained his PhD at the Free University of Berlin, where he continued his work as a Postdoc in the Dermatology Section of the Virchow Hospital Berlin. In 1997, he moved to the German Cancer Research Institute in Heidelberg, Germany, where he has been heading his own research group focusing on tumor-specific T cell immunology. Furthermore, he set up a GMP facility for the establishment of autologous immune cells as therapeutics, where he currently holds the positions as QP and head of QC. He has published more than 70 papers and is Editorial Board Member of several journals.

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