

Vorschlag für ein Promotionsprojekt im Rahmen des VorSPrUNG-Programms

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Project Title: „Evaluation of trogocytotic transfer effects of anti-CD20 and anti-CD19 antibodies in multiple sclerosis therapy“

Multiple sclerosis (MS) is one of the most common immune-mediated neurological diseases of the central nervous system (CNS). Both peripheral and central pathomechanisms require targeted and effective therapy to prevent disease activity and progression. One highly successful treatment option are B cell-depleting anti-CD20 monoclonal antibodies (mabs) such as rituximab, ocrelizumab, or ofatumumab. However, also anti-CD19 B cell-depleting mabs such as inebilizumab are approved in CNS inflammation.

Trogocytosis is the intercellular transfer of membrane and membrane-associated proteins between cells. It could be shown that this phenomenon occurs in mab immunotherapy, in which cells that express Fcγ-receptors remove and internalize e.g. CD20 and bound mabs from malignant B cells. This process is also referred to as Shaving.

The aim of this project is to evaluate if various therapeutic mabs can shave their specified antigen, and also surrounding membrane-associated antigens, from the target cell. Thinking further, we also plan to analyze if the shaved antigens are transferred to the membrane of the shaving cell. This transfer could have far-ranging implications for mab therapies.

Experiments will be performed by stimulating whole blood or isolated neutrophils and peripheral blood mononuclear cells (PBMCs) with various mabs and afterwards analyzing them via flow cytometry. The isolation and flow cytometric staining of neutrophils and PBMCs are established. A special focus will be set on B cell lineage marker transfer.

This doctoral project aims to gain a profound understanding of the Fcγ-receptor trogocytotic transfer, occurring due to therapeutic mabs used in chronic CNS inflammation, and the far-ranging implications for all mab therapies.