Tita-Nwa, Dinga Nkom Freddy
Dr. sc. Hum.

Retargeting of cytokine induced killer cells against B-cell neoplasms using bispecific antibodies for adoptive immunotherapy

Geboren am 11.12.1973 in Bali-Nyonga, Cameroon
Master of Sciences in Biotechnology am 08.06.2002 an der Fachhochschule Mannheim.

Promotionsfach: Innere Medizin
Doktorvater: Prof. Dr. med. Anthony D. Ho

Bispecific antibodies (bsAb) can be used to crosslink cytotoxic effector cells with malignant targets and may thereby improve adoptive immunotherapy. In this study, the development and in vitro testing of a new quadroma-derived bsAb, HD37xT5.16 and of recombinant CD19xCD5 flexibodies is reported. These molecules recognize the CD19 antigen, expressed on B-cell lymphomas and the CD5 antigen expressed on effector T-cells. The recombinant flexibodies have four binding arms, two directed to each antigen, whereas the quadroma-derived bsAb has two binding arms, one for each antigen. The cytolytic efficiency of these antibodies was similar to that observed with a CD3 binding bsAb. Apart from cytolysis, apoptosis induction, cytokine production and proliferation of CIK cells targeted with newly established bsAbs was investigated. It was demonstrated that the CD5 binding BsAbs do not induce proliferation of T-cells and induce less of activation induced cell death than their CD3 binding counterparts. Anti-CD5 containing bsAbs may be used in combination with adoptive transfer of ex vivo activated T-cells in the setting of allogeneic stem cell transplantation since they will not activate and may be less capable of inducing graft versus host disease. The preclinical studies described here support the experimental use of bsAb HD37xT5.16 for treatment of minimal residual disease after allogeneic stem cell transplantation and may represent a promising strategy for immunotherapy of B-cell Neoplasm.