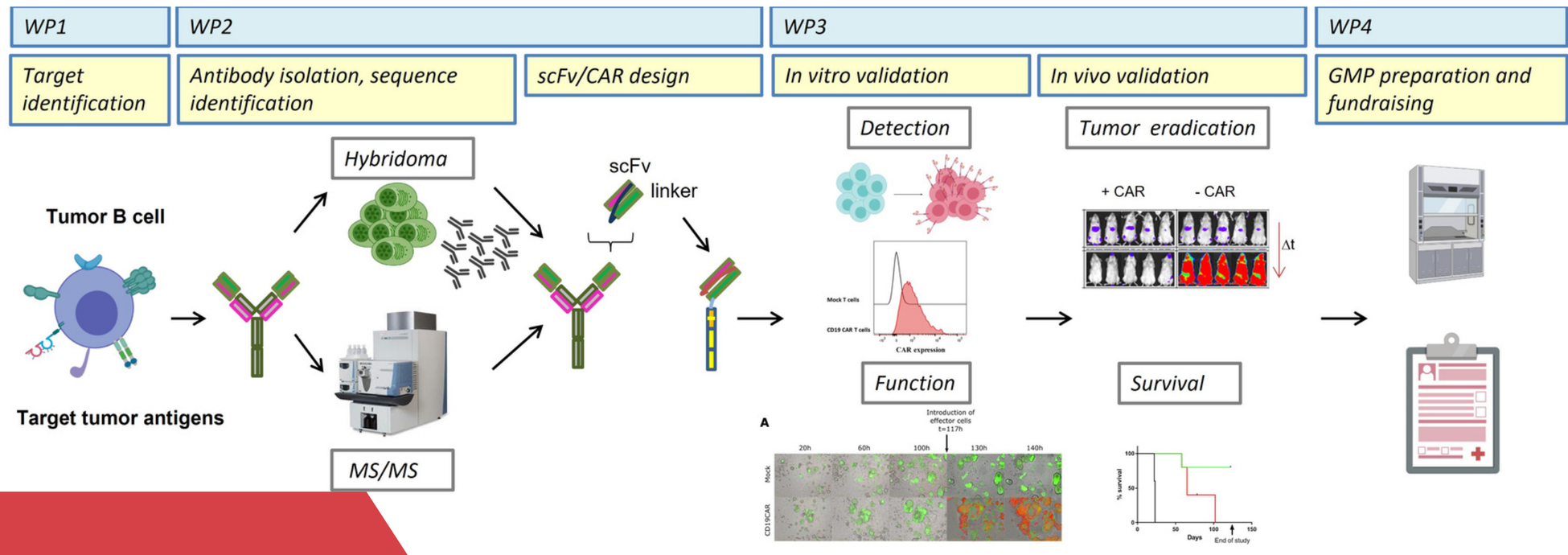

Development of alternative CAR constructs targeted against refractory B-cell malignancies

Principal Investigator: Magdalena Winiarska
Project Promoter: Medical University of Warsaw, Poland
Project Partners: Oslo University Hospital Norway, Pure Biologics S.A. Poland

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Immunotherapy employing CAR (chimeric antigen receptor)-modified T cells has become a breakthrough treatment for patients with B cell-derived malignancies who relapse after two or more lines of therapy. CAR T cells are able to specifically recognize selected antigens and directly eliminate cancer cells expressing them. So far, four CAR T cell products, all targeting CD19 molecule, have been approved for the treatment of Diffused Large B-Cell Lymphoma (DLBCL) and/or B-cell precursor acute lymphoblastic leukemia (BCP-ALL). Unfortunately, despite the significant success of the therapy, there are still patients who relapse following this treatment. The mechanism of tumor escape is frequently associated with CD19 antigen loss. Therefore, there is a need to explore alternative antigens as molecular targets for CAR T cell immunotherapies of B cell malignancies. Especially it is crucial to take into consideration possible changes in surface protein expression emerging on cancer cells throughout the course of the treatment. In our project, we employed a combined bioinformatics-transcriptomic-proteomic approach to define and validate surfaceome of relapsed/refractory BCP-ALL and lymphoma patients in order to select optimal new targets for CAR T cell immunotherapy. Chosen antigens were used for designing a panel of CAR candidates, which, after optimization of their affinity, will be validated in pre-clinical settings and prepared in GMP grade for the first-in-man study. The final product of this project will be one or more alternative CARs to be used in the treatment of patients with B cell malignancies refractory to all treatment options or patients who relapse after previous therapies.

ALTER CAR project aims to bring alternative solutions to patients with hematological malignancies who have relapsed/refractory disease. Solutions of personalized medicine developed within the project have the potential to increase the life expectancy and life quality of people affected by cancer.