Project goal:

Immunoglobulin E (IgE) plays a central role in acute allergic reactions and chronic inflammatory diseases. IgE is produced by activated B cells and plasmocytes. B cell differentiation into antibody-secreting cells requires interactions between B cells and T follicular helper cells (Tfh). Work over the past decade has highlighted the critical role of both, B and Tfh cells in the development of IgE-associated diseases. Nowadays these disorders are the most common inflammatory conditions, and their effective treatment is a significant challenge. Millions of people worldwide have asthma, allergies and other IgE-related inflammatory conditions, which is a huge medical, social and financial problem. Nowadays, the standard therapy of IgE-mediated chronic diseases (antihistamines, corticoids, and others) is often not effective, therefore, searching for new therapies must continue. A new hope is immunotherapy with monoclonal antibody-derivatives, including bispecific Abs (bsAbs) and chimeric antigen receptor (CAR) effector cells. Adoptive cell therapy (ACT) with CARs and bsAbs has been used efficiently in the treatment of various hematological malignancies. And is currently in the preliminary stages of clinical research in some inflammatory and autoimmune diseases.

Therefore, the development of a drug able to neutralize IgE and prevent its production represents a breakthrough in the treatment of inflammatory pathologies with a probable allergic basis.

Hereby, we hypothesize that development of an CAR effector cells targeting IgE-producing cells and inducibly secreting bsAbs targeting Tfh cells able to prevent IgE production, represents a breakthrough in the treatment of IgE-related disorders, including severe asthma, as well as IgE multiple myeloma (MM) and closely related with it amyloidosis.

Description of research:

To generate the proof of concept for the efficacy of the specific anti-IgE CAR-expressing cells, in the current project we will focus on few research goals. We will optimize the production of anti-IgE CAR-expressing immune cells able to inducibly produce bsAbs against Tfh and evaluate their killing efficacy against a special model cell line, as well as IgE-producing immune cells (B cells and plasmocytes) and Tfh from patients with severe asthma, IgE multiple myeloma and IgE amyloidosis (chronic disorders related to IgE) and healthy controls.

The reasons for attempting the research topic:

IgE-associated diseases belong to the most common inflammatory conditions, and their effective treatment is a significant challenge for physicians. Therefore, these problems prompt us to plan the research described in this project.

Targeting and eliminating only these cells which produce IgE with the specific CAR cells holds the promise of achieving long-term symptom relief or even a cure of IgE-related diseases with the single treatment.

Indeed, we expect the development of such a ‘living drug’ will represent a significant breakthrough in the treatment of numerous inflammatory pathologies.

Substantial results expected:

In the current project, we use modern CAR technology to provide evidence for the experimental effectiveness and safety of eliminating immune cells that produce IgE. In addition, the project will increase general knowledge about how the immune system works. In summary, the results of this project can have a direct impact on improving the effectiveness and safety of immunotherapeutic strategies used in modern therapy of autoimmune and inflammatory diseases.

The most important achievement of this project will be obtaining a validated product-candidate(s) for translational development of anti-IgE CAR-expressing cells inducibly producing bsAbs able to prevent IgE production.