Prenylation is a covalent post-translational modification that tightly controls the signaling activity of many cellular proteins. Rab geranylgeranyl transferase (RGGT) is an enzyme responsible for the prenylation of Rab proteins, which are key factors involved in the regulation of intracellular vesicular transport. Fully functional Rab proteins must undergo single or double geranylgeranylation. Thanks to this post-translational modification, they can be anchored to the appropriate membrane, where they can fulfill their role. It was found that defects in the prenylation process may lead to the development of many diseases, e.g., cancer or neurological diseases. One way to reduce the adverse effects of Rab proteins is to inhibit the enzymatic activity of RGGT. The main goal of this project is to develop an innovative strategy of targeting RGGT to degradation using low-molecular chemical compounds, the so-called PROTAC (PROteolysis TArgeting Chimera) based on RGGT inhibitors developed in our group. PROTAC molecules will be investigated as a research tool to determine the mechanisms by which RGGT influences the prenylation of various Rab GTPases. In the future, PROTAC preparations targeting RGGT could be used as potential therapeutic agents for the treatment of prenylation related diseases.

The second goal of this project is to verify the hypothesis that PROTAC molecules targeting RGGT can degrade not only the target protein but also proteins (e.g., Rab).