An emerging and promising target for anticancer drugs are telomeres – DNA-protein complexes that protect the ends of chromosomes from damage. They consist of repetitive TTAGGG DNA sequences and proteins known as shelterins. In typical somatic cells, telomeres shorten during cell divisions, leading to their dysfunction. This phenomenon, known as the 3' end replication problem, results in chromosomal instability, contributing to genome reorganization and potentially leading to cancer development.

In most cancers, the activation of telomerase – an enzyme responsible for elongating telomeres – is essential for tumor cell survival. Telomerase is active in approximately 85% of cancer cells, while its expression remains low in normal cells. Furthermore, cancer cells usually possess short telomeres, creating an opportunity for selective targeting of these structures without harmful effects on healthy cells. Inhibition of telomerase in cancer cells leads to further telomere shortening, triggering cellular senescence and apoptosis.

One of the key molecular targets for telomerase inhibitors is the catalytic subunit hTERT, responsible for the enzymatic activity of telomerase. Despite extensive research on hTERT as a potential therapeutic target, no compounds have yet been approved as anticancer drugs. Therefore, the exploration of novel compounds acting as telomerase inhibitors, particularly those targeting hTERT, remains an urgent need.

Our project builds on prior research in which we successfully identified two promising small-molecule compounds from the anthraquinone class that directly inhibit telomerase activity, leading to telomere damage. The project aims to expand these findings through comprehensive biological evaluations in cellular and *in vivo* models. These studies seek to confirm the efficacy and elucidate the mechanism of action of these compounds as potential anticancer agents.

Additionally, the project will assess the impact of these compounds on cancer stem cells (CSCs), which are responsible for cancer relapse and therapy resistance. Special focus will be placed on the role of the hTERT subunit in regulating CSC functions and the potential effects of inhibitors on their survival and self-renewal capabilities.

The realization of this project will provide new, original data on the biological activity of telomerase inhibitors and their influence on key molecular processes in cancer cells. The results have the potential to be published in prestigious scientific journals, significantly contributing to advancements in the development of novel therapeutic strategies in oncology.