According to the World Health Organization (WHO), in 2018 cancer was the second leading cause of death, causing over 9.6 million deaths worldwide. The continuous increase in multidrug resistance of tumors, as well as dynamically changing epigenetic factors, create the need to search for new, more selective anticancer compounds. Advances in molecular biology and the human genome project have contributed to remarkable advances in the identification of new molecular targets and thus the development of new therapeutic targets against cancer. A promising target for drugs used in cancer therapy are telomeres, DNA-protein complexes composed of repeating tandem TTAGGG DNA sequences at the ends of chromosomes and proteins called shelterins. In normal somatic cells, dysfunctional telomeres arise because of their critical shortening during successive cell divisions (3 'end replication problem). Loss of telomeres induces chromosomal instability and contributes significantly to genome rearrangement, which can lead to tumor formation. In the vast majority of tumors, telomerase activation is required to maintenance telomeres length. Telomerase is activated in approximately 85% of tumor cells while exhibiting low expression in normal cells. In addition, cancer cells, unlike normal cells, are characterized by short telomeres. This creates the possibility of blocking, the process of carcinogenesis by inhibiting the activity of telomerase without side effects for normal cells. Inhibition of the enzyme in cancer cells can lead to a decrease in telomere length and, consequently, to cell ageing and apoptosis. One of the methods of telomerase inhibition is the use of small-molecule chemical compounds targeting the hTERT telomerase catalytic subunit, responsible for enzymatic activity. Although this subunit has been exhaustively researched as a molecular target, so far none of the promising molecules has been registered as a drug. Therefore, there is still a need for new compounds that are inhibitors of telomerase, and in particular of this subunit.

The aim of the proposed research is to evaluate the cellular response to the new 9,10-anthraquinone derivatives in order to determine the molecular mechanism of action of these compounds. Preliminary studies have shown that these compounds exhibit high cytotoxic activity against non-small cell lung cancer A-549 and that they inhibit telomerase activity *in vitro*. Numerous reports indicate anthraquinone derivatives as telomerase inhibitors, but our preliminary results show that the new anthraquinone derivatives exhibit a completely different telomerase inhibition mechanism than other known compounds of this chemical class. This finding suggests that the compounds may have low toxicity to normal cells.

The first step of the research will be determining the cytotoxic activity of 9 compounds on a panel of lung cancer cells (A-549, H226, H460) and determining the effect of these compounds on the proliferation of normal cells (NHBE 2954). Selected, most active compounds will be thoroughly tested to prove the activity of the compounds against telomerase *in vivo* (cellular lines). Since the goal of the test compounds is to induce tumor cell death, the signaling pathways responsible for inducing cell death will be investigated, including the determination of the exact molecular mechanism. The final test will be to check whether the compounds shorten the telomere length, which should lead to inhibition of the proliferation of cancer cells.

The results of this project will confirm the anti-tumor activity of the new 9,10-anthraquinone derivatives as telomerase inhibitors on a broad panel of lung cancer cell lines, by investigating their mechanism of action. The study will bring fully original and novel results important for extending our knowledge on the new small-molecules telomerase inhibitors from the anthraquinone class, which could be a good starting point for further development of new anticancer agents targeting telomere.