Summary

Post-transcriptional covalent modifications of RNA molecules are responsible for the control of gene expression, affecting the initiation and rate of translation, as well as miRNA binding, RNA stability, and RNA degradation. Understanding the molecular mechanisms underlying this process is currently the subject of many scientific studies. One of the aspects related to epitranscriptomics is to understand control mechanisms, molecular targets of RNA methylating enzymes, as well as their physiological effects. The characteristic of the proteins responsible for the modification of the epitranscriptome is particularly interesting in relation to processes such as cellular senescence or mechanisms related to the progression and development of drug resistance in cancer cells. The obtained results may be useful, e.g. in a) search of a new therapeutic strategies limiting the negative effects of chemo- and radiotherapy, b) searching for new therapeutic targets for the removal of cancer cells, including those resistant to conventional chemotherapeutics, c) identification of genes and pathways responsible, e.g. for tumor progression or drug resistance.

On the basis of current knowledge, including research conducted by the team from the University of Rzeszow, the m^5C RNA methyltransferase TRDMT1 seems to be interesting from the point of view of designing new therapeutic strategies in the future. TRDMT1 has an important role not only in the process of the response to cellular stress or embryogenesis, but also in cellular senescence, including the control of the lifespan of the organism. Interestingly, so far there have been no comprehensive data on the function of TRDMT1 during the senescence of cancer cells. There was also no information on the impact of the lack of a functional *TRDMT1* gene on genetic changes in cancer cells during the progression and senescence induced by chemotherapy.

Therefore, an attempt was made to determine the role of TRDMT1 during long-term *in vitro* culture of HeLa cervical cancer cells, MDA-MB-231 breast cancer cells, U-2 OS osteosarcoma cells, U-251 MG glioblastoma cells, as well as in chemotherapeutic-induced senescence. In particular, this thesis assessed the importance of the lack of a functional *TRDMT1* gene in relation to processes such as cell proliferation, cell death, DNA damage, DNA damage response pathway activity, control of telomere length, autophagy, oxidative stress and ability to form secondary chromosomal changes. During the implementation of the doctoral thesis, the use of DNA/RNA methyltransferase inhibitors on cells lacking the TRDMT1 protein was also evaluated.

Based on the obtained results, it was shown that the lack of TRDMT1 protein leads to changes in telomere lengths during subsequent passages of cancer cells, and also promotes secondary chromosomal changes. It was also observed that the TRDMT1 protein is able to interact with the telomerase of the tested cancer cells during doxorubicin-induced stress. Additionally, the level of TERRA telomerase RNA repeats was shown to be altered in cancer cells lacking a functional *TRDMT1* gene. It has also been proven that the lack of a functional *TRDMT1* gene modulates the process of accelerated cellular senescence through changes in the activity of pathways related to e.g. apoptosis, response to oxidative stress, RNA-dependent DNA repair, autophagy and secretion of pro-inflammatory factors. In addition, it was shown that the lack of TRDMT1 protein in cells with induced senescence modulates the level of NSUN enzymes responsible for post-transcriptional modifications of RNA. Thus, the obtained results indicate that the lack of a functional *TRDMT1* gene may promote intercellular variability within a subpopulation of cancer cells, as well as modulate the sensitivity of cancer cells to the chemotherapeutic agents. The presented results will provide a better understanding of the complex intracellular molecular mechanisms responsible for the plasticity of genomes and the variability of human cancer cells.