Nuclear receptors group is a family of transcription factors responsible for the response of the cell to external and internal chemical signals, such as hormones, vitamins, and xenobiotics. Nuclear receptors allow the cells to adapt to changing conditions, for this reason, they play an important role in many biological processes, including development, reproduction, and metabolism. The **RORC** receptors we are interested in, occur in the body in two variants varying in length, called isoforms. **The broadly expressed, longer isoform of RORγ controls the metabolism of lipids and glucose**, and is involved in cyclic changes associated with the circadian cycle in the cell. **The shorter isoform, RORγT, is crucial for the development of Th17 helper lymphocytes**. The role of these cells in the body is complex and ambiguous. They **take part in pathogenic autoimmune processes** (in which the organism's immune system attacks its cells), **as well as are responsible for protection against extracellular bacteria and parasites**. Moreover, **they can be used to fight cancers because they can directly destroy cancer cells**. This property has been used in adoptive cellular immunotherapy, which consists of taking Th17 lymphocytes from the cancer microenvironment, multiplying them in laboratory conditions (as well as improving their anti-cancer properties) and administering them back into the patient's bloodstream.

We found that **AT7519**, a compound inhibiting the activity of cell cycle controling proteins (cyclin-dependent kinases), **is capable of interacting with RORγ/RORγT receptors**. We would like to investigate whether the biological effects we observe are the result of direct binding of AT7519 to the receptors that lead to changes in their activity, or are the result of modulation of other signal proteins in the cell, altering the expression of each of the isoforms. **What is extremely interesting is that it seems that this compound has opposite, isoform-dependent effects - it inhibits RORγ and induces RORγT. So far, a similar case is not known in the scientific literature!**

To find answers to our questions, we will conduct research using three cellular models. The HepG2 line of human hepatocytes expresses exclusively the RORγ isoform, while two types of lymphocytes (Jurkat T-cell lymphoma and Th17) express only the RORγT version. We will investigate the effect of AT7519 on the binding of RORγ/RORγT to the regulatory sites of their target genes, and changes in the signal transduction pathways induced by this inhibitor. Importantly, we will also examine how AT7519 affects the differentiation and persistence of Th17 cells.

Our results may contribute to a better understanding of the biology of RORγ/RORγT receptors and the mechanisms of their tissue-specific expression or function. If **AT7519 activates Th17 cells through interaction with RORγT, it may be used in immunological cell therapy to enhance the anti-cancer properties of Th17 cells**. The compound can be used during in vitro cell proliferation to quickly and efficiently increase their number and to improve their phenotype. **Discovery and characterization of the previously unknown properties of AT7519 may bring new benefits in therapy harnessing the body's natural immune responses to combat cancer**. Importantly, **due to the contribution of the RORγ isoform to the development of some types of cancer such as hepatocellular carcinoma or melanoma, the use of AT7519 as a potential inhibitor of this isoform may also be an interesting therapeutic option in the treatment of cancer diseases**.