RNA molecules regulate all vital cellular processes. On the other hand, RNA drives the development of incurable neurodegenerative diseases and serves as the genetic material of many dangerous viruses. RNA molecules are also important research objects. They have been applied in biotechnology as tools for regulation of gene expression, biosensors or nano-materials. In medicine, they are used as drugs, carriers of low-molecular compounds and recently as an active component of vaccines used to fight the COVID-19 pandemic. The activity of RNA molecules can be regulated by small molecules (ligands) inducing specific biological or therapeutic effect. Therefore, in recent years, scientists have focused on the search for small molecules interacting specifically with nucleic acids. Unfortunately, structural studies of RNA-ligand complexes are still uncommon, which makes it difficult to rationally design synthetic RNA-interacting compounds.

The aim of this project is to analyze the atomic structures of complexes of various ligands with RNA molecules important in the physiology and pathogenesis of human diseases. We will use crystallography, which is based on X-ray diffraction on crystals. This powerful technique yields real, spatial models of biomolecules determining the ligand binding sites and describing details of their interaction. The obtained crystallographic models will allow to observe which ligand elements are responsible for the selectivity and affinity for target RNA molecules. Our research will expand the knowledge regarding structure and function of nucleic acids as well as small RNA binders. It will also contribute to the understanding of the role of RNA in the pathomechanism of neurodegenerative diseases and viral infections. We will formulate fundamental principles facilitating design of low-molecular compounds that can be used to develop new molecular tools and, in the future, effective therapies against as yet incurable disorders.