The main aim of this project is to design and develop a library of peptide-based inhibitors against matrix metalloproteinases (MMPs) as a potential strategy to inhibit cancer metastasis.

Cancer is a group of over 200 diseases that occur when changes in normal cells within the body lead to uncontrolled, abnormal growth that forms a lump called a tumor. It is the world's second-leading cause of death, accounting for 9.6 million deaths in 2020. The situation is alarming, as about one in every four people is at risk of developing cancer in their lifetime. Traditional cancer treatments face a significant challenge in effectively delivering medicines directly to cancer cells while minimizing harm to healthy cells. Consequently, **there is an urgent need for new approaches to cancer treatment that can precisely target cancer cells, work more effectively, and have fewer side effects.**

In tumors, cancer cells can either stay in one tissue or spread to other parts of the body, which is called metastasis. This is the most dangerous step, accounting for approximately 90% of cancer-related illnesses and deaths. Understanding the mechanisms by which tumor cells acquire diversity and spread to other body tissues is crucial for developing new potential anti-tumor treatments. Despite significant progress in this area, there is still much more to uncover and explore. One crucial factor in cancer progression is the activity of enzymes called matrix metalloproteinases (MMPs). **These zinc-dependent enzymes play an important role in changing the environment surrounding tumors and helping them grow and spread.** Proper zinc coordination is essential for the proteolytic function of matrix metalloproteinases (MMPs). Therefore, targeting the zinc ion and/or the catalytic site of MMPs represents a promising strategy for inhibiting these enzymes and preventing tumor progression. **One of the aims of this project is to advance the understanding of matrix metalloproteinases' (MMPs') coordination chemistry and their interactions with zinc ions.**

To inhibit tumor progression, researchers have developed **MMP inhibitors (MMPIs).** These inhibitors consist of a zinc-binding group, enabling them to interact with and suppress the enzyme. However, small organic molecules used as MMPIs have drawbacks such as rapid excretion, low specificity, and poor water solubility. To overcome these challenges, **peptides have gained interest as potential cancer therapeutics**. Peptides have demonstrated superior efficacy, target specificity, and lower toxicity in humans compared to small molecules. Consequently, the next step of this project involves **investigating the structure and thermodynamic parameters of peptide-based inhibitors and their interactions with zinc ions and MMP's domain**. We will try to combine the advantages of the bioinorganic chemistry approach, potentiometry, ITC, solution NMR techniques, and other spectroscopic methods to fully understand and describe the structural and physicochemical properties of peptide-based inhibitors and their complexes at the molecular level. This approach will help us select the best candidates for effective interaction with the catalytic site of MMPs based on their physicochemical and thermodynamic properties.

We expect that the results obtained in the project will make a large contribution to the general knowledge of the coordination chemistry of matrix metalloproteinases associated with tumor metastasis and provide the basis for potential therapeutic options for cancer treatment. This step will bring us closer to a potential biomedical application of human-safe peptide-based inhibitors.