Have you ever wondered what makes it possible for your cells to move? The interior of the cell is filled with a bunch of fibres made of a protein called actin. These fibres form a structure generally called the actin cytoskeleton. The cytoskeleton gives shape to the cell, participates in intracellular transport and provides to the cells the ability to move. The actin cytoskeleton has great importance for the functioning of every cell, and it is not surprising that it also plays an important role in pathological conditions. For example, cancer cells use a cytoskeleton to move across surrounding tissues to form metastases.

The cytoskeleton itself would be useless if its formation and movements were not regulated by a number of proteins. These proteins have a different function in the actin cytoskeleton organization. A very important group is the family of so-called actin nucleators. These proteins allow the formation of actin nuclei and subsequent polymerization of actin into filaments. These proteins include, among others Spire protein and FMN2 formin. Interestingly, despite the fact that these proteins represent different families of actin nuclei, they have been shown to be able to interact directly with each other to form a Spire-FMN2 complex. The role of this complex, both for the actin polymerization process itself and the significance of Spire-FMN2 interaction for cells, however, is still unknown. The precise mechanism of the actin polymerization in the presence of the Spire-FMN2 complex also remains elusive. To answer these important questions, small-molecule compounds that are able to disrupt the interaction between Spire and FMN2 are needed. Such compounds often called as molecular probes can be used in biology to study the mechanism and the role of the Spire-FMN2 complex.

The present project aims the development of specific molecular probes, inhibiting the Spire-FMN2 interaction, which could contribute to the answer to the most fundamental questions regarding this interaction. To achieve this goal, we plan to use a combination of molecular biology techniques, organic chemistry, virtual screening, nuclear magnetic resonance spectroscopy and X-ray crystallography. As a result, we expect to receive high-quality chemical probes that can be used by a wide range of scientists working on unravelling the mechanisms associated with actin nucleation.