Abstract for the general public

The proper functioning of our body at all stages of development depends largely on the precise interaction of cells. They communicate with each other through a wide range of signalling molecules, including growth factors, among them fibroblast growth factors (FGFs). To transmit information, FGFs bind to their specific receptors (FGFR) on the cell surface and, by activating them, initiate signalling cascades leading to a specific cellular response. This response can vary and includes: cell division, growth, migration, protection against apoptosis and regulation of metabolism. Signals generated by FGF/FGFR units are responsible for important vital processes, but without tight control they can lead to abnormal cellular functioning and the development of many disorders, including cancer. The molecular basis of these regulatory processes, which dictate the ultimate cellular outcome, has yet to be fully described.

The goal of our project is to identify and characterize the regulatory module in the FGF receptor 1 (FGFR1) responsible for determining cell fate upon growth factor stimulation. We postulate that the terminal fragment of FGFR functions inside the cell as an interaction hub for regulatory proteins, controlling which cellular response is triggered under certain conditions and preventing uncontrolled cell division leading to oncogenesis.

Within the project an extensive study of proteins that interact with the C-terminal part of FGFR1 will be performed. We expect to discover novel receptor- binding proteins and signalling routes that underlie variation in FGF/FGFR function. We will conduct research that will provide information on modification to the terminal fragment of the receptor, in particular the phosphorylation responsible for turning on and off protein activity. We will also investigate how the identified interactions with partner proteins, including kinases, affect endocytosis, cell division, cell motility, apoptotic response and glucose metabolism.

FGF/FGFR deregulation is frequently observed in diseases of civilization. Deciphering the mechanisms responsible for regulating signal transduction induced by FGF proteins is particularly important in FGF receptor-dependent cancers. The results obtained will also contribute to the expansion of basic knowledge of cell biology and the function of other types of receptors responsible for intercellular communication.