Fibroblast growth factors (FGF) are proteins responsible for the transfer of various information between the cells of higher organisms, crucial both during embryonic development and in adult life. They provide signals that trigger diverse responses, such as cell division, cell migration, activation of metabolic pathways, tissue regeneration, as well as protection against programmed cell death and ageing. This multitude of evoked reactions is of great therapeutic potential of FGF family proteins, however, poor understanding of the mechanisms differentiating specific cell response makes their clinical use significantly difficult. Some differences in sequences and structures of individual growth factors, their physicochemical properties, stability, as well as the manner and time of interaction with a particular type of receptor seem to be of key importance for cell behaviour.

We will conduct a detailed analysis of how changes in the stability of FGF proteins (i.e. their resistance to both thermal and proteolytic degradation) and in the strength of their binding to FGF receptors influence the effects observed in cells. We have selected four members of the FGF family: FGF8, FGF9, FGF10 and FGF18 with relatively low intrinsic stability, which have not been analyzed for modification of their activity so far. We will design, obtain and characterize in detail the mutants of these proteins with different properties to indicate the structural elements that determine the specific cellular response. The proposed research will increase the knowledge about the relationship between the structure and function of FGF proteins, enable to obtain variants with strictly defined activities and help to verify the features of growth factors determining cell fate. The results of the project should form the basis for future FGFs applications, including regenerative and anti-aging therapies.