Fibroblast growth factors (FGFs) are proteins responsible for transmitting various information between the cells of higher organisms, crucial both during embryonic development and in adult life. They provide signals, through four specific receptors (seven isoforms) on the cell surface (FGFRs), that trigger diverse responses, such as cell differentiation, division and migration, activation of metabolic pathways and tissue regeneration. Experimental studies confirm more than 60 FGF:FGFR interactions, making FGF/FGFR one of the most complex cell communication systems. Unfortunately, different aberrations in this system can lead to various diseases, including skeletal disorders and cancer. Current approaches based on low-molecular-weight drugs targeting FGF signaling are not specific, as such compounds mostly inhibit all variants of FGFR. This complicates our understanding of FGFR function and hinders progress in treating diseases caused by abnormal FGF signaling.

In this project, we will develop short DNA oligonucleotides, aptamers, that selectively interact with FGF receptors. We intend to generate both highly specific and potent inhibitors and activators of all individual FGFR variants. The effects of aptamers on complex processes regulated by FGF proteins will be analyzed using model cell lines and organ explants. We intend to demonstrate unprecedented control over the activity of individual components of the FGF/FGFR system, far beyond current methods. The results of the project should provide the basis for future aptamer applications, including anticancer and regenerative therapies.