ABSTRACT FOR GENERAL PUBLIC

The behavior of the cell is largely dictated by receptor proteins, which reside on cell surface and transmit signals from the extracellular space to the cell interior. The signaling of fibroblast growth factor receptors (FGFRs) regulates cell metabolism, motility, differentiation and proliferation. FGFRs are critical for human body development and proper functioning and alterations in FGFRs result in development of severe metabolic diseases and cancer. Due to their importance FGFRs are regulated at distinct levels. We have recently demonstrated the novel mode of FGFRs regulation. Extracellular galectin-1 and -3, sugar binding proteins, interact with sugar chains attached to FGFRs, adjusting signals transmission by these receptors. Human galectin family comprises of twelve proteins, and the contribution of most of galectins to the regulation of FGFRs is unknown. Importantly, galectins are also implicated in human diseases, including cancer.

We hypothesize that FGFR signaling is subjected to complex regulation by the extracellular galectin network, where galectins may directly activate FGFRs or adjust its function or cellular transport. The ultimate goal of the project is to uncover the role of all galectin family members in the regulation of FGFRs trafficking and activity. We will determine which galectins interact with FGFRs and characterize in detail identified complexes. We will elucidate how galectins affect the interaction of FGFRs with other cellular proteins. Furthermore, presented studies will determine the role of galectins in the regulation of FGFR-mediated signaling and cellular transport. Last but not least, we will uncover how galectin-FGFRs cross-communication determines fate of the cells.

The expected results generated during the project implementation will be of high novelty and significance for the field. Decoding how these pivotal cellular proteins co-operate in the determination of the cell fate is of fundamental importance for cell and cancer biology. Furthermore, the results obtained in the frame of this project may facilitate the design of novel therapeutic strategies against cancers with aberrant galectins and FGF/FGFR signaling and give directions to the new targets and approaches in metabolic diseases, including diabetes.