Project description

The essence of the project entitled "*Biophysical mechanism of synergy of integrins and syndecans in adhesion of bladder cells to structural elements of the extracellular matrix*" was to elaborate the mechanism of mutual interaction between integrins and syndecans, two families of receptors present on the cell surface. The most important achievement of the project is the development of a biophysical model of the interaction between integrin and syndecan receptors binding to extracellular matrix proteins, based on theoretical models of thermally-driven unbind of individual complexes under the influence of external force (Figure 1).

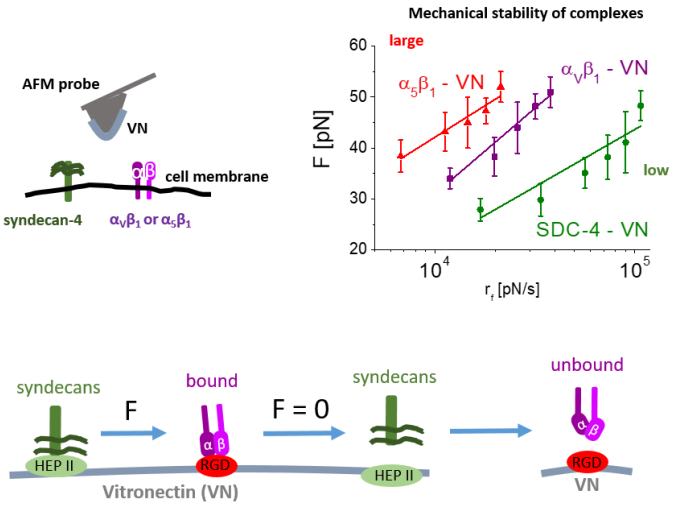

Figure 1. *Biophysical model of the interaction between integrin and syndecan receptors, developed on the basis of single-molecule unbinding measurements.*

The mechanical stability of individual complexes can be determined by measuring the unbinding force.

Mutual interactions among molecular complexes will affect the adhesive properties of cells in a given environment.

Obtained parameters describing the kinetic properties of the unbinding process of individual complexes will allow the development of the interaction models for specific molecular complexes. The model developed, within the frame of this project, shows that syndecans can control (turn on and off) the binding of integrins to extracellular matrix proteins through the transmission of small portions of forces. Thereby, such interaction will strongly influence the kinetics of changes in cells exposed to mechanical stimuli.

The interaction of cells with the surrounding environment begins at the nanoscale, i.e. at the level of interaction arising between a single molecule of the ECM matrix protein and the corresponding receptor located on the cell surface. Atomic force microscopy (AFM) allows us to study the properties of individual molecular complexes, which has been widely used in research on the adhesive properties of many types of complexes studied mainly in isolated systems without the participation of living cells. Despite the published studies on the integrin interactions, there are no data describing the properties of syndecans – ECM protein complexes as well as there is no data on mechanism of synergy between integrins and syndecans in tumor cells, for which the increased expression of some integrins and syndecans is observed. Understanding the biophysical basis of the interaction of ECM proteins with integrins and syndecans will shed light on a recognition of one molecule by another while knowledge about energy profiles allows us to reconstruction of interaction mechanisms of given receptor pairs. Prediction of pathways and affinity binding of a complex formed by two or more molecules with known structures may find applications in modern drug design understood as an alternative to macroscopic methods for determining affinity in complexes formed between receptor and ligand. This is particularly important for the identification of molecular markers associated with the response of normal and cancerous cells to an altered surrounding microenvironment. This will contribute to a better understanding of the molecular mechanisms of bladder cancer, and may improve the effectiveness of its treatment in the future.