

The mechanisms of invasivity and regulation of transcription of cancer cells

Cancer originates in cells that overcome the control mechanisms of the organism. Cancer cells can be eventually released from the site of origin and spread through tissues. Cancer cells can acquire certain mechanisms that enable them to more effectively invade surrounding tissue or layers of other cells. The research on the migration of cancer cells is important for the understanding of the origin and spreading of metastases and consequently for anticancer therapy. In my Ph.D. work, I participated in the research of the properties of invasive metastatic cells. We compared non-invasive rat sarcoma cell line with a highly metastatic cell line derived from it. We showed that cells of the invasive cell line use amoeboid mode of migration, have upregulated Rho/ROCK signaling, and have accumulated actin and myosin at the leading edge. It is at the leading edge where the cells generate their traction forces. Cells of non-invasive cell line use mesenchymal mode of migration and generate forces mainly at their retracting end. We also compared two breast cancer cell lines derived from a single carcinoma. We showed that the more invasive cell line, derived from its parental line by neoplastic transformation, displayed elevated cytoskeletal dynamics. Moreover, we showed the presence of invadopodia at the sites of extracellular matrix degradation. We introduced the usage of acellular dermis for the study of invasive structures of cancer cells and described the morphology of these structures in complex three dimensional environment.

In our laboratory, the research of the mechanisms of cellular regulations involved in cancer biology concerns also the study of SNW proteins that act in regulation of transcription and splicing. We showed that stress induced accumulation of p53 is resistant to SNW1 downregulation by siRNA. We also showed that p53 response genes are induced independently of SNW1 depletion. Our results indicate that SNW1 is dispensable for the transcription and splicing of certain stress induced genes.