Cells participating in such processes as embryogenesis, wound healing and tissue regeneration have to be guided specifically to the site of action in order to perform their functions. For example, cell migration through an increasing gradient of soluble chemoattractant created in the healing tissue is a common way of cell recruitment to the wound site. However, cells may also respond to other factors such as adhesion site gradient, matrix topography or matrix stiffness by directed migration. Moreover, one of the first directional cues that appear in the skin immediately after wounding is a direct current electric field. The presence of endogenous electric fields (EFs) within extracellular spaces has been known for more than 150 years; however the significance of the EFs for numerous physiological processes has only recently been confirmed by several modern techniques. It was documented in a number of reports that the EFs are present in all developing and regenerating animal tissues and play a key role in major biological processes such as embryogenesis, wound healing and tissue regeneration. Most organs and embryos surrounded by a layer of epithelial cells produce potential difference or transepithelial potentials of few millivolts to tens of millivolts. A major cellular effect of the EF is electrotaxis, that is a directional movement towards the cathode or anode. It should be noted that the active migratory response is completely different from the movement of a non-live charged particle due to a pure physical force, because cells respond to the EF by active directional migration!

In vitro application of the EF of strengths comparable with those detected in vivo produces electrotaxis in a variety of cultured cells. Although several mechanisms and signalling pathways were suggested to be involved in the electrotactic movement, still very little is known regarding the general mechanisms used by cells to detect such small EFs and to respond to them by directed translocation. In particular, no single sensor of the EF employed in electrotaxis has been identified. One possible reason is that such single sensor does not exist and the electrotactic reaction has a bi- or multimodal character. Two main hypotheses on the mechanism of electrotaxis are based either on activation of specific ion channels or on redistribution of cell membrane receptors responsible for sensing of directional signals from chemokines/growth factors on the cell surface. Since both mentioned above mechanisms are in fact not mutually exclusive, we suggest here the biphasic mechanism of electrotaxis and a complementary role of ion channels and chemoattractant receptors in this process. Our hypothesis assumes that the activity of ion channels is necessary for the first very fast cell reaction but after a sufficiently long time (a time scale of the order of dozen minutes) redistribution of receptors on the cell membrane may be sufficiently clear to be responsible for directing cell migration in the electric field.

To verify this hypothesis, we are going: (1) to characterize the dynamics of electrotactic reaction of mouse 3T3 fibroblasts, (2) to identify ion channel genes that are crucial in the electrotaxis of 3T3 cells by a screening strategy for the electrotaxis phenotype, (3) to identify genes of chemoattractants/growth factors receptors that are necessary for efficient electrotaxis of 3T3 cells (4) to prove that identified ion channels are necessary only for the first, very fast, reaction of cells for the EF and chemoattractant receptors redistribution for the second part of reaction observed after a prolonged time.

We think that our model may allow explanation of some valid questions concerning the mechanism of electrotaxis. Moreover, the results will be beneficial also for regenerative medicine, as endogenous dcEFs and electrotaxis play a significant role in wound healing and tissue regeneration. Since, the detailed understanding of signaling pathways regulating electrotaxis is crucial for establishing an efficient treatment in several disorders, the results of our project will be of high importance not only for science, but also for the entire society.