Abstract

Fibroblasts are the principal cellular component of the connective tissue. They are a heterogeneous group of cells which contribute to the structure of connective tissue and wound healing by their ability to produce extracellular matrix (ECM). Fibroblasts and cells derived from them are involved in many pathological processes such as formation of malignant tumors and fibrosis. Tumor progression which finally leads to metastasis is a serious biomedical problem. There is a growing body of the recent evidence showing an important role of the tumor stroma and its interaction with cancer cells in cancer progression.

Tumor stroma comprises mainly of myofibroblasts and their products, namely ECM, soluble factors, and enzymes. Myofibroblasts contribute more or less to all steps of cancer progression. Furthermore myofibroblasts play a key role in fibrosis, another serious human disease which is not efficiently treatable and which is associated with cancer progression. These facts made us to search for molecular means capable of eliminating the myofibroblastic phenotype. We succeeded to entirely dedifferentiate primary myofibroblasts by concomitant inhibition of TGFβ signaling and perturbation of MAPK signaling in a chick model that we have introduced.

Malignant fibroblasts form sarcomas. ECM is the first barrier interfering with the migration of primary tumor cells and sarcoma metastasis. We have identified an expression profile and its regulator EGR1 which are necessary for fibrosarcoma cells migration and metastasis. Furthermore, we have shown that the amoeboid mode of invasion and the Rho/ROCK/MLC signaling play a crucial role in metastasis of both experimental chicken and rat sarcoma cells. The evolutionary conservation of these molecular mechanisms in birds and mammals suggests their general importance for invasiveness of sarcoma cells.