Cell Biology – Molecular Cell Dynamics Laboratory
together with the
Microscopical Imaging Centre and the Preclinical Animal Imaging Centre

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The laboratory has year-long open internship positions for Bachelors and Masters students (duration 3 to 9 months), integrated in ongoing research projects.

The lab is dedicated to the cellular, molecular and physical mechanisms governing different types of normal and cancer cell invasion into 3D tissues. We further study applied aspects of cytotoxic T cell mediated killing of tumor cells and microenvironmental control of cancer therapy response to radiation, immuno- and chemotherapy. Previous work of the lab contributed to establish a classification on different types of cell migration, their main molecular adhesion and protease pathways, and types and mechanisms of plasticity of migration, with relevance to cancer invasion and metastasis as well as immune cell migration. Current themes address how and when migrating cells switch the mechanisms of migration (plasticity), and integrate guidance from the tissue and neighboring cells, , using chemical versus physical information from the environment.

Ongoing projects focus on: cell migration, cell-matrix adhesion/interactions, protease function and signaling in cell migration; immune effector function in tumors; and how imaging can be applied to detect and surgically remove tumors better.

M**ethods** in the lab include: 2D and 3D tissue culture of cells, generation of tumor-like spheroids, time-lapse microscopy of cell migration, confocal microscoy of 2D and 3D cultures, cell transfection, protein biochemistry (e.g. Western blot, immunoprecipitation), molecular biology techniques (RNA interference, quantitative PCR), flow cytometry, automated high-content microscopy, image segmentation and quantification, live-cell imaging in mice and zebrafish embryos.

The techniques used in a particular project may vary, dependent on the topic and major question.

Selection of cancer topics:
Cancer invasion and metastasis
To enhance understanding in cancer invasion and metastasis, we address the rate-limiting steps of cancer metastasis, including local invasion, intravasation and distant seeding in the secondary organ, as well as the consequences of invasion and metastatic colonization including invasive growth and cancer resistance. Specifically, we aim to interfere with adhesion and signaling pathways controlling cell-cell and cell-matrix interactions, and detect the effects on cancer cell invasion, survival and proliferation, and apoptosis rates in the primary lesion as well as metastatic sites. We further study the role of proteases in cancer invasion and resistance, and the mechanisms of collective invasion in 3D tissues, particularly the cell-cell interaction mechanisms (cadherins, connexins). Main tumor types are: melanoma, breast cancer, sarcoma, glioma, head and neck tumors.

Cancer immunology and immunotherapy
We study how cytotoxic T lymphocytes move to the tumor, engage with target cells, induce cytotoxic killing, and resolve the interaction for consecutive killing events (serial killing). We particularly study how T cells kill tumor cells in 3D tissue culture models and in vivo, and how this important process is disturbed by factors of the microenvironment (hypoxia, cytokines, lack of nutrients). Main models are melanoma and sarcoma.

Cell-cell communication during morphogenesis
The cell-cell communication and signaling pathways required for epithelial cell migration (normal and cancer cells) are studied in 3D invasion models. Main models are Madin-Darby kidney cells and polarity signaling pathways.