TP7: Dissecting the role/s of breast cancer cell membrane protrusions in invasion, colonization and transformation of the bone marrow microenvironment: From cell biology to clinical applications

Scientific staff

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Project description

This project assesses the role of plasma membrane protrusions emerging from breast cancer (BC) cells in the invasion and transformation of bone marrow hematopoietic stem and progenitor cell niche. The bone metastasizing capacity of breast cancer is subtype dependent. Moreover, only little is known about the biology and molecular principles of BC metastasis and it remains elusive, how breast cancer cells modify and exploit the hematopoietic niche in the bone. **Since the underlying functional mechanisms of this phenomenon are largely unknown, we plan to dissect the implication of plasma membrane protrusions emerging from BC cells in migration, adhesion and invasion of bone marrow microenvironment.** The morphological impact of factors and/or signaling pathways that modulate the metastatic capacity of cancer cells will be evaluated. As cellular representatives of bone marrow niches, mesenchymal stromal cells (and osteoblasts derived therefrom) will be used. **Mechanisms of intercellular communication between BC cells and bone-derived cells will be investigated as well and a particular attention will be devoted to thin membrane processes that could act as tunneling nanotubes.** For clinical translation, we will study the role of those plasma membrane protrusions and communication pathways with regard to drug response, metastatic potential and the intrinsic molecular subtypes of BC.

The results of this project will shed light on the cellular and molecular mechanisms underlying the **invasion**, **colonization** and **intercellular communication** of the bone marrow niche under metastatic environment conditioned by breast cancer cells.

Expertise

[We have all techniques, biological tools and know-how to study the molecular and cellular biology of breast cancers particularly the mechanisms of invasion and transformation of the hematopoietic stem cell niches. We have also a long-standing experience of exosomes and other extracellular membrane vesicles, which could benefit for several other groups particularly whom will search for new biomarkers. We will also provide primary breast cancer cells based on collaboration, methods for the detection of disseminated tumor cells (DTCs) and drug-screening assay.]

Project-related publications

Fonseca A-V, Freund D, Bornhäuser M and Corbeil D. Polarization and migration of hematopoietic stem and progenitor cells rely on the RhoA/ROCK I pathway and an active reorganization of the microtubule network. J Biol Chem. 2010;285:31661-71.

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Link T, Kuithan F, Ehninger A, Kuhlmann JD, Kramer M, Werner A, Gatzweiler A, Richter B, Ehninger G, Baretton G, Bachmann M, Wimberger P, Friedrich K. Exploratory investigation of PSCA-protein expression in primary breast cancer patients reveals a link to HER2/neu overexpression. Oncotarget.2017;8:54592-54603.

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Rappa G, Green TM, Karbanová J, Corbeil D, Lorico A. Tetraspanin CD9 determines invasiveness and tumorigenicity of human breast cancer cells. Oncotarget. 2015;6:7970-91.

Reichert D, Friedrichs J, Ritter S, Käubler T, Werner C, Bornhäuser M and Corbeil D. Phenotypic, morphological and adhesive differences of human hematopoietic progenitor cells cultured on murine versus human mesenchymal stromal cells. Sci Rep. 2015;5: 15680.]

Further information:

https://www.uniklinikum-dresden.de/de/das-klinikum/kliniken-polikliniken-institute/gyn
http://www.biotec.tu-dresden.de/research/corbeil.html