TP18: The role of stromal cells in cancer cell homing and growth

Scientific staff

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Project description

The project focuses on evaluating the role of stromal cells on cancer cell homing to the bone marrow and on cancer growth in bone. Based on the gained knowledge, we will then explore possibilities for modifying mesenchymal cell numbers, their immune modulatory effects and their interactions with matrix molecules.
Breast and prostate cancer cells home to the bone marrow, where they presumably hijack the hematopoietic stem cell niche, and develop metastatic lesions. We aim to characterize the elusive premetastatic niche by examining the role of mesenchymal stromal cells (MSCs) in cancer cell homing and growth of bone metastases. Decreasing the number of MSCs pharmacologically enhanced cancer cell homing to the bone marrow in mice. Initial characterization confirmed a relationship with a mesenchymal subpopulation. We would like to characterize this subpopulation further. This will be followed by both genetic and pharmacologic manipulation in mice in order to increase the identified subpopulation and diminish cancer cell homing.

Preliminary work also suggests that this subpopulation suppresses cancer growth in an in vivo model of breast cancer metastasis in mice. We therefore aim to characterize how this subpopulation modulates the immune response towards cancer in vivo. In addition, we will also evaluate whether modifying matrix components and matrix receptors affects the immune cell response to cancer and/or growth. The goal is to take advantage of the lessons learned in this work to maximize the immune inhibitory effect on cancer.

Expertise

Various murine tumor models have been established to evaluate homing of cancer cells and cancer growth. The role of stromal cells originating from the bone marrow and the microenvironment as well as various immune cells are being characterized with and without modulation of the microenvironment.

Project-related publications

1. S. Rossnagl, H. Ghura, C. Groth, E. Altrock, F. Jakob, S. Schott, P. Wimberger, T. Link, J.-D. Kuhlmann, A. Stenzl, J. Hennenlotter, T. Todenhöfer, M. Rojewski, K. Bieback, **I.A. Nakchbandi**. “A Subpopulation of Stromal Cells Controls Cancer Cell Homing to The Bone Marrow”. **2018**; Cancer Research, 2018 Jan 1;78(1):129-142.
2. S. Rossnagl, E. Altrock, C. Sens, S. Kraft, K. Rau, M.D. Milsom, T. Giese, Y. Samstag, **I.A. Nakchbandi**. “EDA-Fibronectin Originating from Osteoblasts Inhibits the Immune Response against Cancer”. **2016**; PLoS Biol 14(9):e1002562.
3. S. Rossnagl, A. von Au, M. Vasel, M. G. Cecchini, **I. A. Nakchbandi**. “Blood Clot Formation Does Not Affect Metastasis Formation or Tumor Growth in a Murine Model of Breast Cancer”. **2014**; PLoSOne. 2014;9(4):e94922.
4. C. Sens, K. Huck, S. Pettera, S. Uebel, G. Wabnitz. M. Moser, **I.A. Nakchbandi**. “Fibronectins Containing Extradomain A or B Enhance Osteoblast Differentiation Via Distinct Integrins”. J Biol Chem. **2017** May 12;292(19):7745-7760.
5. C. Sens, E. Altrock, K. Rau, V. Klemis, S. Pettera, S. Uebel, M. Moser, **I.A. Nakchbandi**. “An O-Glycosylation of Fibronectin Mediates Hepatic Osteodystrophy Through $\alpha 4\beta 1$ Integrin”. J Bone Miner Res. **2017** Jan;32(1):70-81.
6. S. Kraft, V. Klemis, C. Sens, T. Lenhard, C. Jacobi, Y. Samstag, G. Wabnitz, M. Kirschfink, R. Wallich, G.M. Hänsch, **I.A. Nakchbandi**, “Identification and characterization of a unique role for EDB fibronectin in phagocytosis”. J Mol Med (Berl). **2016** May;94(5):567-81.

Further information: Website: http://www.biochem.mpg.de/en/rg/nakchbandi