TP19: RAI2 as novel suppressor of cancer cell homing & survival in the bone marrow

Scientific staff

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Project description

Our research is based on the aim to detect and characterize disseminated tumor cells (DTCs) in bone marrow (BM) and circulating tumor cells (CTCs) in blood, in order to understand and characterize the mechanisms that enable early tumor cell dissemination, and to identify genes and pathways important for site specific metastasis in epithelial tumors. Our initial study identified RAI2 to be down-regulated among DTC-positive breast cancer patients and to be an independent prognostic factor (Werner et al 2015). RAI2 can furthermore regulate AKT activity. AKT has been shown to be an important mediator of cancer cell dormancy and regulator of the proliferation and survival of DTCs. Therefore RAI2 might also be involved in the dormancy control and of overt bone metastasis formation. The aim of this project is to better understand this rather poorly characterized but clinical highly interesting protein in the context of bone metastasis. Here we want to investigate whether **RAI2 is directly involved in the formation of bone metastasis through its interactions with the local bone environment.** To test this hypothesis, we will use both in vitro models but also generated different xenograft and transgenic mouse models. The obtained data will finally be validated in patient-derived material. Should the proposed project demonstrate that RAI2 plays a critical role in the communication between bone and tumor cells, our results would have important implications for novel therapeutic strategies.

Expertise

We have established various high sensitive assays for CTC and DTC detection and characterization suitable for both patient-derived samples and mouse models. Our infrastructure includes a state-of-the-art facility for liquid biopsy research including a large biobank of patient-derived material.

Project-related publications

Bidard, F.C.; Michiels, S.; Riethdorf, S.; Mueller, V.; Esserman, L.J.; Lucci, A.; Naume, B.; Horiguchi, J.; Gisbert-Criado, R.; Sleijfer, S., et al. Circulating Tumor Cells in Breast Cancer Patients Treated by Neoadjuvant Chemotherapy: A Meta-analysis. JNCI 2018, 110, 560-567, doi:10.1093/jnci/djy018.

Mohme, M.; Riethdorf, S.; Dreimann, M.; Werner, S.; Maire, C.L.; Joosse, S.A.; Bludau, F.; Mueller, V.; Neves, R.P.L.; Stoecklein, N.H., et al. Circulating Tumour Cell Release after Cement Augmentation of Vertebral Metastases. Sci Rep 2017, 7, 7196, doi:10.1038/s41598-017-07649-z.

Bardelli, A.; Pantel, K. Liquid Biopsies, What We Do Not Know (Yet). Cancer Cell 2017, 31, 172-179, doi:10.1016/j.ccell.2017.01.002.

Riethdorf, S.; Muller, V.; Loibl, S.; Nekljudova, V.; Weber, K.; Huober, J.; Fehm, T.; Schrader, I.; Hilfrich, J.; Holms, F., et al. Prognostic Impact of Circulating Tumor Cells for Breast Cancer

Patients Treated in the Neoadjuvant "Geparquattro" Trial. Clin Cancer Res 2017, 23, 5384-5393, doi:10.1158/1078-0432.CCR-17-0255.

Bartkowiak, K.; Kwiatkowski, M.; Buck, F.; Gorges, T.M.; Nilse, L.; Assmann, V.; Andreas, A.; Muller, V.; Wikman, H.; Riethdorf, S., et al. Disseminated Tumor Cells Persist in the Bone Marrow of Breast Cancer Patients through Sustained Activation of the Unfolded Protein Response. Cancer Res 2015, 75, 5367-5377, doi:10.1158/0008-5472.CAN-14-3728.

Werner, S.; Brors, B.; Eick, J.; Marques, E.; Pogenberg, V.; Parret, A.; Kemming, D.; Wood, A.W.; Edgren, H.; Neubauer, H., et al. Suppression of early hematogenous dissemination of human breast cancer cells to bone marrow by retinoic Acid-induced 2. Cancer Discov 2015, 5, 506-519, doi:10.1158/2159-8290.CD-14-1042.

Further information:
www.uke.de/tumorbiologie