TP12: Wnt5a signaling in the bone microenvironment in prostate cancer

Scientific staff

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Project description

This project assesses the role of Wnt5a in bone metastases due to prostate cancer. Prostate cancer is one of the most common malignancies in older men and has a high propensity for to form bone metastasis, predominantly osteosclerotic lesions. The bone microenvironment and especially osteoblasts produce large amounts of Wnt5a, which may direct tumor cell homing into the bone microenvironment and/or foster tumor-bone interactions. Still it remains unclear, which cells in the bone microenvironment operate in Wnt5a signaling in bone metastases, and how targeted deletion of Wnt5a in mice affects the colonization and interactions of prostate cancer cells within the bone. **The central hypothesis is that non-tumor-derived Wnt5a from osteoblastic lineage cells controls critical aspects of prostate cancer cells in their interaction with the bone microenvironment.** To test this hypothesis, we will characterize bone-cancer interactions secondary to prostate cancer in syngeneic mouse models, analyze the role of involved exosomes, and investigate the impact of tumor-adjacent stroma. A clinician-scientist in the field of Tumor Orthopedics will collect and analyze human specimen of bone metastases obtained through established protocols.

The results of this project will yield **novel mechanistic insights into the role of Wnt5a and associated pathways in prostate cancer interactions with the bone microenvironment and the contribution of tumor vs. non-tumor tissues.** This may result in a refined and perhaps revised view of Wnt signaling in bone metastases and could provide a molecular basis for therapeutic intervention.

Expertise

We have established animal models with subcutaneous, intravenous, intratibial, and intracardiac injections of different tumor cell lines. In cooperation with the OncoRay, we expanded our imaging know-how, representing a platform to monitor tumor formation and tumor growth over time within the bone microenvironment. Our infrastructure includes a state-of-the-art facility for comprehensive characterization of bone phenotypes in mice and men. A unique achievement from a long-standing collaboration with the Department of Urology has been the generation of a primary prostate cancer tissue microarray, consisting of a cohort of 400 men, who underwent radical prostatectomy between 1996 and 2005 with a full clinical and laboratory data set, including the presence of skeletal metastasis.

Project-related publications

Rachner TD, Coleman R, Hadji P, Hofbauer LC. Bone health during endocrine therapy for cancer. Lancet Diabetes & Endocrinology. 2018;6:901-10.

Thiele S, Zimmer A, Göbel A, Rachner TD, Rother S, Fuessel S, Froehner M, Wirth MP, Muders MH, Baretton GB, Jakob F, Rauner M, Hofbauer LC. Role of WNT5A receptors FZD5 and RYK in prostate cancer cells. Oncotarget. 2018;9:27293-304.

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Baschant U, Rauner M, Balaian E, Weidner H, Roetto A, Platzbecker U, Hofbauer LC. Wnt5a is a key target for the pro-osteogenic effects of iron chelation on osteoblast progenitors. Haematologica 2016;101:1499-507.

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Hofbauer LC, Rachner TD, Coleman RE, Jakob F. Endocrine aspects of bone metastases. Lancet Diabetes & Endocrinology 2014;2:500-12.

Further information:
https://www.bone-lab.de