TP10: Molecular Characterization of Bone Metastasis Founder Cells in Prostate Cancer

Scientific staff

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Project description

Prostate cancer is relatively slow progressing cancer, ultimately being the cause of death of only a fraction of diagnosed patients. However, its unpredictable course makes it impossible to predict which patients will be affected. Major site of metastasis of prostate cancer is the bone. Disseminated cancer cells remaining in the body after surgical removal of primary tumor comprises the pool from which metastasis founder cells are recruited. The ultimate goal of this project is is to understand early steps of colonization of bone by prostate cancer metastasis founder cells. To this end, we have defined two major aims of this project: (1) molecular characterization of disseminated prostate cancer cells from M0-stage patients, and (2) modeling of interaction of early-stage disseminated prostate cancer cells with the bone marrow. We hypothesize that the molecular characterization of metastasis founder cells, and correlation of the molecular data with the outcome will enable us to: (i) establish new markers for detection of metastasis founder cells, (ii) understand the fate of early disseminated cancer cells, with emphasis on dormancy, (iii) enable development of novel models to study early steps of metastatic colonization, (iv) identify therapy targets on metastasis founder cells, and (v) improve drug screening approaches by targeting metastasis founder cells within the microenvironment of the bone.

Expertise

Our sample bank contains several hundred genomes and transcriptomes of disseminated single cancer cells isolated from the bone marrow of M0 and M1 patients with various bone-seeking and non-seeking tumors (e.g. prostate, breast, NSCLC). Our key expertise is molecular analysis of genome and transcriptome of single cells. To this end, we have established different methods – e.g. qPCR, SNV analysis, CNA analysis, RNA-seq, etc. This is further supported by a team of bioinformaticians from Fraunhofer ITEM-R.

Project-related publications

Werner-Klein M, Scheitler S, Hoffmann M, Hodak I, Dietz K, Lehnert P, Naimer V, Polzer B, Treitschke S, Werno C, Markiewicz A, Weidele K, Czyz Z, Hohenleutner U, Hafner C, Haferkamp S, Berneburg M, Rümmele P, Ulmer A, **Klein CA**. Genetic alterations driving metastatic colony formation are acquired outside of the primary tumour in melanoma. Nat Commun. 2018; 9(1):595.

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Gužvić M, **Klein CA**. Towards prevention of metastatic prostate cancer: recent molecular insights from the direct analysis of metastatic precursor cells. Translational Cancer Research 2016, 5(S2):S182-S186.

Gužvić M, Braun B, Ganzer R, Burger M, Nerlich M, Winkler S, Werner-Klein M, Czyż ZT, Polzer B, **Klein CA**. Combined genome and transcriptome analysis of single disseminated cancer cells from bone marrow of prostate cancer patients reveals unexpected transcriptomes. Cancer Res. 2014; 74(24):7383-94.

Klein CA. Selection and adaptation during metastatic cancer progression. Nature. 2013; 501(7467):365-72.

Weckermann D, Polzer B, Ragg T, Blana A, Schlimok G, Arnholdt H, Bertz S, Harzmann R, **Klein CA**. Perioperative activation of disseminated tumor cells in bone marrow of patients with prostate cancer. J Clin Oncol. 2009; 27(10):1549-56.

Further information:
http://www.experimentelle-medizin.de/