TP20: The role of TRIM proteins in colonization of the bone and bone microenvironment modulation of metastatic prostate cancer

Scientific staff

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Project description

This project investigates the role of family of tripartite motif containing proteins (TRIMs) for metastatic spread of prostate cancer (PCa) to the bone, the most common metastatic site of PCa. Besides well characterized genetic alterations affecting oncogenes and tumor suppressor genes, aberrant activity of regulatory elements for gene transcription and post-translational protein modification substantially contributes to the metastatic potential of PCa cells. TRIM proteins are essential regulators of protein degradation and are crucially involved in cellular processes driving metastasis. In our preliminary work, we found TRIM24 overexpression as frequent event in PCa bone metastases. In the literature, TRIM8, TRIM11, TRIM47 and TRIM68 have been described to be overexpressed in PCa or to influence mechanisms driving metastasis. **Based on these data, our overall hypothesis is that specific TRIM proteins have a crucial role in invasiveness and metastatic bone niche formation of PCa.** To test our hypothesis, we will characterize the expression and genetic status of TRIMs in a large cohort of PCa bone metastases. Subsequent in-vitro experiments using bone metastatic PCa cells will be conducted to investigate whether cellular features which are required for crucial steps during metastasis are influenced by specific TRIMs. In addition, 2D co-cultivation experiments will be applied to investigate whether TRIMs influence the communication between bone metastatic PCa cells and cells forming the bone microenvironment.
Results of this project will contribute to a better understanding of molecular processes promoting PCa metastasis to the bone. Due to the incurable nature of metastatic PCa to date, **targeting specific molecules like specific TRIM proteins might be a therapeutic option for patients suffering from metastatic PCa.**

Expertise

As pathologists, we have access to large tissue cohorts including prostate and breast cancer. Especially for prostate cancer, we have several independent cohorts including primary tumors and metastases from >1000 patients with well-characterized clinico-pathological data. For our own studies as well as in collaboration with other departments of the µBone consortium, we have expertise in pathology, morphology and tissue-based assays including immunohistochemistry, immunofluorescence, fluorescence-in-situ hybridization as well as different sequencing methods. Our infrastructure allows comprehensive in-vitro studies with several PCa cell lines.

Project-related publications

Offermann A, Vlasic I, Syring I, Vogel W, Ruiz C, Zellweger T, Rentsch CA, Hagedorn S, Behrends J, Nowak M, Merseburger A, Bubendorf L, Kirfel J, Duensing S, Shaikhibrahim Z, Perner S. MED15 overexpression in prostate cancer arises during androgen deprivation

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Queisser A, Hagedorn S, Wang H, Schaefer T, Konantz M, Alavi S, Deng M, Vogel W, von Mässenhausen A, Kristiansen G, Duensing S, Kirfel J, Lengerke C, Perner S. Ecotropic viral integration site 1, a novel oncogene in prostate cancer. Oncogene. 2016 Sep 12. doi: 10.1038/onc.2016.325.

Shaikhibrahim Z, Offermann A, Braun M, Menon R, Syring I, Nowak M, Halbach R, Vogel W, Ruiz C, Zellweger T, Rentsch C, Svensson M, Andren O, Bubendorf L, Biskup S, Duensing S, Kirfel J, Perner S. MED12 overexpression is a frequent event in castration-resistant prostate cancer. Endocr Relat Cancer. 2014 Aug;21(4):663-75

Shaikhibrahim Z, Menon R, Braun M, Offermann A, Queisser A, Boehm D, Vogel W, Rüenauver K, Ruiz C, Zellweger T, Svensson M, Andren O, Kristiansen G, Wernert N, Bubendorf L, Kirfel J, Biskup S, Perner S. MED15, encoding a subunit of the mediator complex, is overexpressed at high frequency in castration-resistant prostate cancer. Int J Cancer. 2014 Jul 1;135(1):19-26.

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Further information:

https://www.uksh.de/pathologie-luebeck/Research/PernerLab.html