TP15: The role of tumor-associated macrophages in bone metastasis formation in zebrafish

Scientific staff

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Project description

Besides metastases in the lung, liver and brain, bone metastases are common among patients with breast cancer. The bone microenvironment provides a fruitful soil for disseminated tumor cells, which represent cells that have separated from the primary tumor, spread via the circulation and reached distant sites such as bone where they then settled. Some of these cells are eventually responsible for metastasis in bone, but it is currently unclear how they successfully engraft at the appropriate sites. Recent evidence suggests that a subpopulation of macrophages (tumor associated macrophages) supports cancer metastasis. Here, by using a zebrafish xenotransplantation model combined with state of the art in vivo imaging and macrophage ablation, we investigate whether macrophages and tumor cells interact in niches of bone formation in zebrafish larvae and how this leads to bone metastasis. In addition, we alter macrophage-bone cell crosstalk by genetic and pharmacologic approaches in order to decrease the bone metastatic potential of breast cancer cells in vivo.

Expertise

We have established a zebrafish larval xenotransplantation model in which we use time lapse imaging to monitor macrophage interaction with osteoblasts and other cells of the bone niche. Other methods in the lab include RNA in situ hybridization, transcriptome analysis and qRT-PCR as well as immunohistochemistry. Zebrafish larvae will also be used in a chemical screening approach (Vast BioImager).

Project-related publications

1. Geurtzen K*, **Knopf F***, Wehner D, Huitema LF, Schulte-Merker S, Weidinger G. Mature osteoblasts dedifferentiate in response to traumatic bone injury in the zebrafish fin and skull. *Development* 2014;141:2225-34. (*equal contribution).
2. Geurtzen K, Vernet A, Freidin A, Rauner M, Hofbauer LC, Schneider JE, Brand M, **Knopf F**. Immune suppressive and bone inhibitory effects of prednisolone in growing and regenerating zebrafish tissues. *JBMR* 2017; 32:2476-2488.
3. **Knopf F**, Hammond C, Chekuru A, Kurth T, Hans S, Weber CW, Mahatma G, Fisher S, Brand M, Schulte-Merker S, Weidinger G. Bone regenerates via dedifferentiation of osteoblasts in the zebrafish fin. *Dev Cell* 2011;20:713-24.
4. **Knopf F.*,** Schnabel K*, Haase C, Pfeifer K, Anastassiadis K, Weidinger G. Dually inducible TetON systems for tissue-specific conditional gene expression in zebrafish. *PNAS* 2010;107(46)**:**19933-8. (*equal contribution).
5. Masselink W, Cole N, Berger S, Fenyes F, Sonntag C, Wood A, Nguyen PD, Cohen N, **Knopf F**, Weidinger G, Hall TE, Currie PD. A somitic contribution to the apical ectodermal ridge is essential for fin formation. *Nature* 2016; 535(7613): 542-546.

Further information:

https://www.crt-dresden.de/de/forschung/research-groups/core-groups/crtd-core-groups/knopf/