Zebrafish xenograft model: Identification of novel mechanisms driving prostate cancer metastasis

Chen, L.

Stellingen behorend bij het proefschrift getiteld

Zebrafish xenograft model: identification of novel mechanisms driving prostate cancer metastasis

1. Human prostate cancer cells display a comparable response to the microenvironment in both zebrafish and mice xenografts that lead to experimental metastasis (Chapter 3 and 5).

2. The zebrafish microenvironment induces epithelial-mesenchymal transition of xenografted prostate cancer cells partially through elevation of Cripto expression (Chapter 3).

3. Mechanosensing and mechanotransduction driven by the integrin-CDC42-N-Wasp axis governs stem-like phenotypes of prostate cancer cells inducing initiation of metastatic growth (Chapter 4).

4. The microenvironment-dependent NF-κB-activin A axis promotes metastasis of prostate cancer cells through co-activation of the SMAD2/3-SMAD4 and ERK1/2 signaling pathways (Chapter 5).

5. AMPK-autophagy signaling activated by metabolic stress promotes cancer cell survival and invasion and can be considered as a putative target to combat advanced prostate cancer (Chapter 6).

6. Disseminated non-stem cancer cells induce metastases after dedifferentiation into cancer stem cells at the pre-metastatic site. This dedifferentiation is regulated by both cell autonomous and microenvironment factors (Adapted from Arianna Fumagalli et al, *Cell Stem Cell*, 2020).

7. A metabolic switch is indispensable for disseminated cancer cells to survive oxidative stress in blood flow (Adapted from Elena Piskounova et al, *Nature*, 2015).

8. AMPK signaling protects cancer stem cells in acute myeloid leukemia from metabolic and oxidative stresses in the bone marrow (Adapted from Yusuke Saito et al, *Cell Stem Cell* 2015).

9. Mechanosignaling reprograms metabolic features of cancer stem cells through activation of the AMPK-autophagy axis controlling metastatic progression (Adapted from Antonio Totaro et al, *Proceedings of the National Academy of Sciences*, 2019).

10. All models have their own special values. A combination of multiple model systems provides multidimensional answers towards scientific questions.

Lanpeng Chen, Leiden, 17 September 2020