

## Targeting breast cancer stem cells

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Heterogeneity is a common feature of all tumours, which has been tried to be explained by two models: the clonal evolution theory and the cancer stem cell (CSC) hypothesis. However, both experimental and clinical data suggest that both theories are not mutually exclusive and can complement each other. According to the cancer stem cell hypothesis, once CSC are eliminated the rest of the tumour degenerates and die. Breast cancer stem cells (BCSCs) are a small drug-resistant population within breast tumours responsible for metastatic disease. Given that metastasis accounts for more than 90% of cancer-related deaths, therapeutic strategies aiming at targeting CSC are currently being explored. The aim of this study is to generate tools to test whether depleting CSC is sufficient to prevent metastasis and/or eradicate a given primary tumour. To achieve this objective, I have designed a CSC reporter based on intrinsic features of this subpopulation of cells, namely the higher activity of the Hippo pathway. My results indicate that enforcing the constitutive expression of YAP in cancer cells increases the frequency of CSC, as seen by the mammosphere assay. These results prompt us to design constructs containing a CSC reporter driving expression of the Herpes Virus thymidine kinase gene to selectively kill BCSC. Overall, these data suggest that the proposed experimental strategy may prove suitable to provide a proof-of-concept for the CSC hypothesis.

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