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The inhibition of PxIxIT motif-containing Calcineurin substrates induces the expansion of murine Cancer Stem Cells

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Abstract:

Introduction: Calcineurin is a calcium-dependent serine/threonine phosphatase reported as involved in many different tumorigenic processes such as tumor cell survival, proliferation, migration and metastatization. More recently, calcineurin has also been characterized as a protein involved in the stemness of cancer stem cells (CSCs), as it regulates transcription factors and other proteins involved in the differentiation processes, but also in pathways that concern the metabolism and the autophagic mechanisms, all of which are important aspects of stem cells.

Aim: Our principal goal is the phenotypical and functional characterization of genetically engineered tumor cell lines in which the interaction between calcineurin and the PxIxIT motif-bearing substrates has been constitutively inhibited (cells called Calcineurin Impaired or CN^{IMP}. Controls that do not have this kind of inhibition are called Mock). From preliminary studies, this kind of inhibition allows for the expansion of Cancer Stem Cells (CSCs), which are to be subsequently selected and further characterized.

Conclusion: Our model has allowed us to isolate the CSC population from the murine melanoma line B16. The characterization of this population has confirmed that these cells do indeed possess many stem cell-characteristic properties, such as slow proliferation, alterations in the cell cycle and expression of transcription factors characteristic of the epithelial-to-mesenchymal transition.

Future developments: We aim to further explore whether our model also works in different tumor cell lines, with particular focus on human cell lines, and also characterize their stem cell populations.