

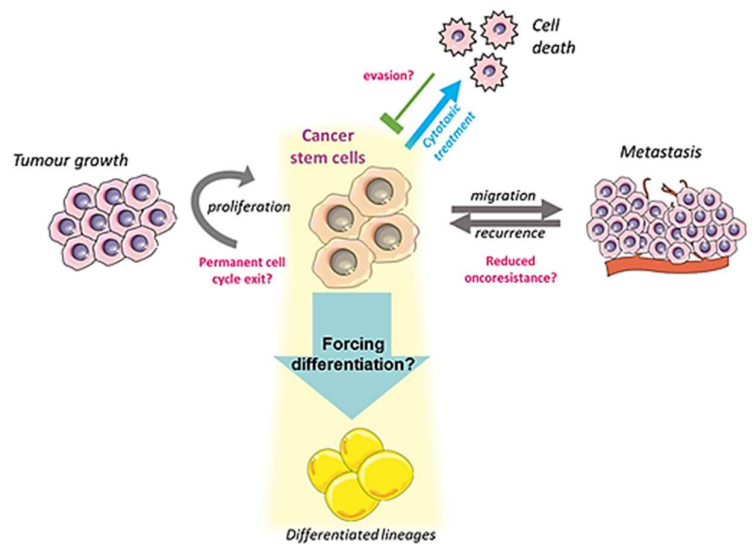
3D spheroid cancer models to develop treatments targeting tumour stem cell and potentiate oncotherapies.

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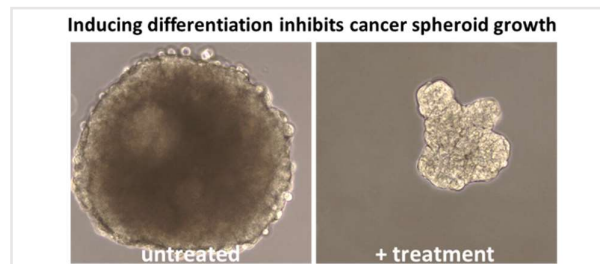
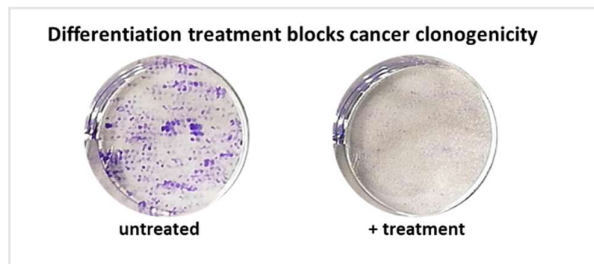
Research Theme: Cellular and molecular regulation of stem cells & cancer

Project rationale:

Cancer growth and recurrence is linked to the ability of a small population of stem cells within the tumour able to evade oncotherapies and regrow new tumours after the end of chemotherapy. These cancer stem cells (CSCs) represent a key target to reduce cancer recurrence and improve the efficacy of existing therapies. Since undifferentiated cancer stem cells are notoriously resistant to standard antiproliferative and cytotoxic chemotherapy drugs, inducing their differentiation towards more differentiated cell types, which are typically less pathogenic, offers a new alternative approach against cancer recurrence.



Aim of the project: to develop treatments targeted against cancer stem cells, using a 3D tumour spheroid model to recapitulate the process of tumorigenesis in vitro. We are designing new treatments to force the differentiation of CSCs in order to reduce their proliferative and migratory capacity. By using a 3D tumour model rather than monolayer cultures to develop new treatments, the results produced will be more physiologically relevant to the in vivo situation, where CSCs within the tumour are shielded by surrounding cells.



Experimental plan in 4 steps:

- 1) 3D tumour models of 2 prominent cancer models (lung and breast cancer) will be treated with a set of molecules inducing differentiation pathways to identify the most effective treatment for differentiation.
- 2) The differentiated cell types within the tumour models will be monitored both by direct imaging (using confocal/light sheet microscopy) and validated by marker expression analysis at the protein (immunodetection) and transcript level (RT-qPCR) to confirm their phenotypic switch.
- 3) The frequency of CSCs within treated tumour samples will be measured by flow cytometry, and their stem cell characteristics will be analysed using established stemness and cancer assays (eg proliferation, clonogenicity, EMT, migration).
- 4) The effect of the differentiation treatment will be validated in an ex vivo model of tumour propagation looking at changes in chemoresistance to standard chemotherapy drugs, to measure the treatment's capacity to block cancer recurrence, regrowth and invasiveness after chemotherapy.

Techniques involved: Human cancer cell cultures, 3D spheroid culture, disease modelling, stem cell marker detection, confocal/light-sheet imaging & 3D reconstruction, clonogenic & migration assays, protein expression & transcriptome analyses, flow cytometry & cell sorting, cryosectioning and immuno-histological analyses.

Outcome of the project: Design and ex vivo validation of a new treatment inducing cancer stem cell differentiation as an anti-cancer strategy for prominent types of solid cancers.