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BIPHASIC MODULATION OF CANCER STEM CELL-DRIVEN SOLID TUMOUR DYNAMICS IN RESPONSE TO REACTIVATED REPLICATIVE SENESCENCE

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ABSTRACT

Cell senescence is a physiological programme of irreversible mitotic arrest that is triggered after a variety of intracellular and extracellular events. Its purpose is to protect tissue integrity by disabling mitosis in stressed or damaged cells. The senescence program serves as a tumour suppressor, and cancer cells are believed to bypass senescence to advance to malignancy. Recent studies have shown that senescence can be reactivated in cancer cells through a number of external perturbations, including oncogene activation, tumour suppressor gene withdrawal and irradiation.

In [1] we have developed an agent-based model of solid tumour growth whose input population composition is based on the cancer stem-cell hypothesis. It was used to show how cancer stem cells can drive tumour progression, while non-stem cancer cells (CCs) interfere with this by impeding cancer stem-cell dynamics. We showed that intratumoural competition between the two cell types may arise to modulate tumour progression and ultimately cancer presentation risk. Model simulations revealed that reactivation of the replicative senescence programme in CCs initially increases total tumour burden, as attrition from cell death is partially averted, but evolves to provide tumour control in the longterm through increasing constraints on stem-cell compartment kinetics.

In [1] we conclude that reactivation of replicative senescence can prolong CC competition with cancer stem cells, thereby ultimately inhibiting malignant progression regardless of tumour size.

REFERENCES

[1] J. Poleszczuk, P. Hahnfeldt, and H. Enderling: *Biphasic modulation of cancer stem cell-driven solid tumour dynamics in response to reactivated replicative senescence*, Cell Proliferation **47** (2014), 267–276.