Mathematical model of senescence-mediated modulation of tumor growth and invasion

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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 [1]. We have developed an agent-based model of solid tumour growth [2] whose input population composition is based on the cancer stem-cell hypothesis [3]. It is 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 show that intratumoural competition between the two cell types may arise to modulate tumour progression and ultimately cancer presentation risk. Model simulations reveal 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 long-term through increasing constraints on stem-cell compartment kinetics. Reactivation of replicative senescence can prolong CC competition with cancer stem cells, thereby ultimately inhibiting malignant progression regardless of tumour size.

References

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