Agent-based modelling demonstrates the impact of localised tumour cell proliferation and death on macrophage infiltration

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Growing tumours are infiltrated by a variety of immune cells, including macrophages, a type of immune cell which can adopt a range of pro- or anti-tumour phenotypes depending on microenvironmental cues. The spatial distribution of macrophages within a tumour varies from patient to patient and between different tumour types, and is related to patient outcome. There is considerable interest in understanding the mechanisms regulating the spatial localisation of macrophages within solid tumours and in exploiting tumour associated macrophages to deliver treatment to cancer cells [1, 4].

As a first step to understanding patterns of macrophage localisation within solid tumours, we consider the roles played by tumour cell proliferation and death in driving cell movement from proliferative tumour regions to hypoxic regions. This movement, induced by oxygen gradients within a tumour, must be taken into consideration when characterising patterns of macrophage infiltration. To understand the impact that this background movement has on macrophage infiltration, we first consider the infiltration of inert polystyrene microbeads into a tumour spheroid using data from [2]. We use the CHASTE modelling framework [3] to develop an agent-based model of microbead infiltration into a spheroid, and show how varying the rates of tumour cell proliferation and death influences the patterns of bead infiltration into the tumours.

We then extend our model to include macrophages and CSF-1, a macrophage chemoattractant produced by hypoxic tumour cells. By comparing the infiltration patterns of the macrophages in this model with those of the microbeads, we identify components of macrophage infiltration due to active (chemotactic) movement and passive components associated with tumour cell proliferation and death. Identifying which variations in macrophage distribution are due to active or passive processes may help determine which patients are most likely to respond to treatment with CSF-1 inhibitors [4].

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