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Mathematical Modelling of Cancer Growth and Spread: The Role of Enzyme Degradation of Tissue

Metastatic spread of cancer is the main cause of death in patients suffering from the disease - cancer cells from a primary tumour break away from the central mass and are disseminated throughout the body where they re-grow to form secondary tumours or metastases. A crucial aspect of metastatic spread is the process of local invasion of the surrounding tissue. The cancer cells achieve this by the secretion of certain enzymes involved in proteolysis (tissue degradation), namely plasmin and matrix metalloproteinases (MMPs). These overly-expressed proteolytic enzymes then proceed to degrade the host tissue allowing the cancer cells to spread throughout the microenvironment by active migration and interaction with components of the extracellular matrix such as collagen.

Here, we present a mathematical model of cancer cell invasion of a host tissue at the macro-scale (cell population) level. The model considers cancer cells and a number of different matrix-degrading enzymes (MDEs) from the MMP family and their interaction with, and effect on, the extracellular matrix (ECM) using systems of reaction-diffusion-taxis partial differential equations in an attempt to capture the qualitative dynamics of the migratory response of the cancer cells, with a specific focus placed on the membrane-bound MMPs. We use mathematical analysis and computational simulations of the equations in both one- and two-space dimensions to predict the spatio-temporal evolution of the cancer cell density, the concentration levels of the various enzymes and the density of the extracellular matrix. The model exhibits either travelling-wave solutions of cancer cells, which can be used to determine the maximum speed of invasion into the tissue, or very dynamic and heterogeneous spatio-temporal solutions, which match experimentally and clinically observed results for aggressive invading carcinoma.