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Mathematical modelling of cancer cell morphological and phenotypic plasticity in response to the extracellular matrix

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The occurrence of distant metastases greatly reduces or even removes the possibilities of curative treatment for cancer patients. The development of tools for predicting and diagnosing the onset of secondary tumours has long been a significant subject of cancer research effort. Moreover, it is widely known that while in some tissues cancer cells exhibit higher proliferation, in others they are more invasive so the best treatment strategy should be chosen accordingly.

A novel tissue engineering approach was created in our group in order to gain insight into the processes of cell growth, motility and invasion. Organ-specific scaffolds were seeded with highly invasive triple negative breast cancer cells. These tissue engineering constructs (TECs) were then cultured in vitro for 4 weeks and the resulting patterns of cell colonisation of extracellular matrix (ECM) were analysed.

One of the most noteworthy results of this experiment is the emergence of two alternative strategies of matrix colonisation depending on the origin and structure of the underlying ECM. In particular, we observed significant differences in cellular attachment efficiency, morphology, density and invasion of the breast cancer cells.

To gain a better understanding of cellular behaviours and validate the hypothesis that colonisation pattern strongly depends on the properties of ECM, we developed a corresponding mathematical model of tumour growth in TECs. For these purposes, we used a lattice-based stochastic approach based on the energy formalism, where the concept of cell adhesion is considered the key mechanism of cell-cell and cell-ECM interactions. Our model reproduces the early stage of the experiment (the stage characterised by rapid colonisation of surface and subsurface matrix layers) showing a clear distinction in cell morphology and spatial distribution when varying the density of adhesion molecules expressed on the matrix.

Further, to expand the computational model and attribute the role of the underlying ECM to cell invasion and clustering inside the tissue, we ran a set of single-factor experiments, each designed to reveal the effect of a specific physical property of the matrix. Statistical analysis of the experimental data provides estimations of model parameters and complements the picture of cell-matrix interactions.

We believe that this data-driven approach will allow predicting phenotypical and morphological changes of cancer cells and the subsequent preferred mode of tissue colonisation, which is essential for the choice of appropriate treatment.

Primary author: Ms ROZOVA, Vlada (Macquarie University)

Co-authors: Dr GULLER, Anna (Macquarie University); Prof. ZVYAGIN, Andrei (Macquarie University)

Presenter: Ms ROZOVA, Vlada (Macquarie University)

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