Developing A Multi Scale Cellular Automata Simulation Model Of A Vascularised Brain Tumour Environment To Predict Angiogenic Potential Of Brain Endothelial Cells.

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Project Background

Angiogenesis, the growth and formation of capillaries from pre-existing vessels, is involved in various disease pathologies including brain tumours which require new blood vessels for their growth and survival. Several aspects of angiogenesis have been investigated, based on which novel agents have been developed to counteract tumour-induced angiogenesis. Within this project, a tool is developed to predict angiogenic potential in brain endothelial cells in a vascular tumour environment, based on a simulation of cell-to-cell Delta-Notch signalling in response to VEGF leading to cell migration and hereby vascular development using CompuCell3D.

Methods

- Creating A Vascularised Tumour Environment In CompuCell3D: Converting experimental data into virtual data.
- Delta-Notch Patterning in Response To VEGF: Simulating development and migration.
- Tracking Tip Cell Formation, Sprouting And Migration: Developing a tool to simulate development and migration.

Results

- Simulating Tumour Angiogenesis: Creating a simulated vascularised brain tumour environment including VEGF secretion, Delta-Notch signalling in response to VEGF and angiogenic potential.
- Visualising Tip Cell Migration: Tracking tip cell formation and migration.

Conclusions

This study demonstrates the potential of combining experimental data with computational simulations to better understand angiogenesis and predict angiogenic potential. The model can be further extended to incorporate vessel networks and vessel structures, which is relevant for drug development and clinical trials.

Relevance

We enhance the accuracy of studying biological processes occurring in tumour angiogenesis by combining experimental data and computational modelling based on theory. This can be used in the investigation of treatment strategies and aid in drug efficiency and clinical trials.

Discussion

Limitations

1. Cellular automata modelling can't incorporate off-lattice biomechanics and interactions.
2. Models are restricted through limited dynamic range and number of cells.
3. Models cannot adapt to nitric and morph its macroscopic to survive as soon as new.
4. Evolutionary learning requires further advances in computational modelling, possibly through machine learning and AI.

Translational Potential

Application And Relevance In Cancer Research

Today, a cure for brain cancers e.g. Glioblastoma multiforme (GBM) is still extremely rare. GBM is often treated surgically, followed by radiotherapy and chemotherapy. The study of anti-angiogenic agents is key to developing treatment where new anti-angiogenic agents can be investigated through tissue specific simulation models and institutional and metamorphic factors.

Future Directions

1. Personalised Medicine: Patient cells can be linked to experimental data via cell lines, and used to simulate and predict likely anti-angiogenic treatment responses and outcomes.
2. Modelling Vessel Density: High microvascular density indicates metastatic risk and can facilitate cancer cell migration into blood circulation. Implementing vessel density as a parameter in this model will aid in studying tumour recurrence and cancer spread.
3. Retinal Vascular Disease: The quantification of angiogenesis in a tumour biopsy specimen can be used to predict metastasis and recurrence risks. Using biopsy data within our simulation model can be used to predict metastasis and recurrence, and gain a deeper understanding of underlying mechanisms.
4. Modelling With Biopsy Specimen: The simulation of angiogenesis in a tumour biopsy specimen can be used to predict metastasis and recurrence risks. Using biopsy data within our simulation model can be used to predict metastasis and recurrence, and gain a deeper understanding of underlying mechanisms.