In silico generation of tumor invasion patterns

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Background There is much bibliography about mathematical models of tumor growth based on reaction-diffusion equations that describe during the time the proliferation and invasion of tumor cells into peripheric host tissue. In a previous work we have developed a model of this kind that describe a glioma growth inside the human brain [1]. Here we present a derived of this model applied to the growth and invasion of multicellular spheroids of the LM3 cell line immersed in a collagen I matrix, an in vitro model of a microtumor in avascular stage (preangiogenic). It is known that invasion patterns in this model depend on the cell line used as well as on the physical characteristics and chemical components of the surrounding matrix.

Mathematical model The mathematical model initiates from a unique tumor cell that proliferates (monoclonal tumor origin) and then considers two stages: an initial benign stage with only proliferation and a later malign stage where invasion starts. The reaction term of the equation considers a logistic cell proliferation and the diffusion term, based on the Fick's law, simulates the volumetric growth of the spheroid as well as the invasion of tumor cells in host tissue. There is also a third term of radial invasion derived from a source of cells located in the spheroid surface. The model may be described as: being Ci the concentration of tumor cells in the node i, P the net cell proliferation rate, Cmax the carrying capacity of the system, D the diffusion coefficient, S the cell source, δ the Dirac delta function, r the radial distance to the spheroid center, R the spheroid radius and Vi the radial velocity of cellular invasion in the node i.

$$\frac{\partial Ci}{\partial t} = P\,Ci\left(1 - \frac{Ci}{Cmax}\right) + D\,\nabla^2 Ci + S\,\delta\,(r\text{-}R(t)) - Vi\,\nabla r\,Ci$$

Results Parameter ranges related to invasion patterns and morphology were obtained from the analysis of experimental images of spheroid invasion. When the model were breed with these ranges, it was able of generate aleatory invasion patterns similar to the experimentally observed.

Conclusion This kind of experimental-numerical interaction has a wide application potential at the moment of predicting the clinical behaviour of a tumor in a patient-specific way in base on biopsy tissue obtained from a given patient.

References

1. Suárez C, Maglietti F, Colonna M, Breitburd K, Marshall G: Mathematical modeling of human glioma growth based on brain topological structures: study of two clinical cases. PlosOne 2012, 7(6): e39616.