Matzavinos, Anastasios; **Chaplain, Mark A. J.**; **Kuznetsov, Vladimir A.**

Mathematical modelling of the spatio-temporal response of cytotoxic T-lymphocytes to a solid tumour. (English) Zbl 1061.92038

Math. Med. Biol. 21, No. 1, 1-34 (2004).

Summary: A mathematical model describing the growth of a solid tumour in the presence of an immune system response is presented. In particular, attention is focused upon the attack of tumour cells by so-called tumour-infiltrating cytotoxic lymphocytes (TICLs), in a small, multicellular tumour, without necrosis and at some stage prior to (tumour-induced) angiogenesis. At this stage the immune cells and the tumour cells are considered to be in a state of dynamic equilibrium – cancer dormancy – a phenomenon which has been observed in primary tumours, micrometastases and residual disease after ablation of the primary tumour. Nonetheless, the precise biochemical and cellular mechanisms by which TICLs control cancer dormancy are still poorly understood from a biological and immunological point of view. Therefore we focus on the analysis of the spatio-temporal dynamics of tumour cells, immune cells and chemokines in an immunogenic tumour.

The lymphocytes are assumed to migrate into the growing solid tumour and interact with the tumour cells in such a way that lymphocyte-tumour cell complexes are formed. These complexes result in either the death of the tumour cells (the normal situation) or the inactivation (sometimes even the death) of the lymphocytes. The migration of the TICLs is determined by a combination of random motility and chemotaxis in response to the presence of chemokines. The resulting system of four nonlinear partial differential equations (TICLs, tumour cells, complexes and chemokines) is analysed and numerical simulations are presented. We consider two different tumour geometries – multi-layered cell growth and multi-cellular spheroid growth. The numerical simulations demonstrate the existence of cell distributions that are quasi-stationary in time and heterogeneous in space.

A linear stability analysis of the underlying (spatially homogeneous) ordinary differential equation (ODE) kinetics coupled with a numerical investigation of the ODE system reveals the existence of a stable limit cycle. This is verified further when a subsequent bifurcation analysis is undertaken using a numerical continuation package. These results then explain the complex heterogeneous spatio-temporal dynamics observed in the partial differential equations (PDE) system. Our approach may lead to a deeper understanding of the phenomenon of cancer dormancy and may be helpful in the future development of more effective anti-cancer vaccines.

MSC:

92C50	Medical applications (general)
35Q80	Applications of PDE in areas other than physics (MSC2000)
34C60	Qualitative investigation and simulation of ordinary differential equation models
65C20	Probabilistic models, generic numerical methods in probability and statistics

Cited in **1** Review
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Keywords:

solid tumour growth; immune response; T-lymphocytes; chemokines; spatio-temporal heterogeneity; simulations

Software:

XPPAUT

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