Chapter 18

Assessment of Anti-Angiogenic Drug in Cancer Therapy

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ABSTRACT

It has been documented in the literature that a solid tumor survives by the generation of micro-vessels around it. This phenomenon is known as angiogenesis. Angiogenesis is governed by two factors, namely Tumor Angiogenic Factor (TAF) secreted by the tumor cells and tissue Fibronectin (FNT) concentration in the extra-cellular space. These two factors help in mobilization of endothelial cells from nearby blood vessels. At the initial phase of angiogenesis, neighboring blood vessels affect in formation of capillary sprouts. In this work, to the authors develop a clinically relevant analytical model that could act as an effective tracing system of tumor growth. The author has performed a quantitative assessment of tumor angiogenesis. This analytical method is a correlation between tumor system and vasculature system through an analytical assessment at peripheral blood circulatory of tumor milieu.

INTRODUCTION

Creation of micro-vessel around solid tumor is known as angiogenesis. This phenomenon also happens in different hematological disorders (Risau, 1997). As an effect, malignant tumor survives by making a rapid growth. A tumor typically cannot grow in its diameter; while in response to hypoxia (shortage of oxygen and nutrients) tumor turns onto an angiogenic switch and begin to express vascular endothelial growth factor (VEGF). VEGF promotes the process of new blood vessel formation in the direction of tumor growth. Binding of VEGF to the endothelial cells uphold the migration and increase in count of the endothelial cells. Thus the growth and proliferation of blood vessels are propped up.

TAF and FNT the other two influencing factors of angiogenesis help in mobilization of endothelial cells from nearby blood vessels. This TAF emerges from the surrounding tissue and spread into the endothelial cells of blood vessels (Folkman & Klagsbrun, 1987). Endothelial cells also respond to the direction of increased TAF gradient and helps in formation of sprout. These sprouts gradually divide and migrate towards the tumor
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(Ausprank & Folkman, 1977). At the initial phase of angiogenesis, capillary sprouts are formed from the blood vessels of close proximity.

In an average it takes 15 days to establish the connection between tumor and parent vessel. This vascular connection subsequently supplies all nutrients required for tumor growth (Ausprank & Folkman, 1977). Same therapeutic efficacies have also been analyzed with the data of different chemotherapeutic treatments during this angiogenic phase. There it has been perceived that the dosage of chemotherapy effectively gives a stable outcome for small animals but in case of human being the effect grossly varies from patient to patient. Mainly it has been studied that the major drug components bypass the effective portion of tumor mass which leads to this undesirable behavior (Jain, 1987). This unstable behavior creates the demand for more analytical model based study of micro-vascular system.

Presently several cellular automation and hybrid continuum based analytical approaches have been taken (Cristini, Li, Jhon, Lowengrub, Steven, & Wise, 2009). These are targeted to tumor mass equation, momentum equation and constitutive relations. However, parametric evaluation of several factors like carcinogenic event, fluid viscosity at the tumor micro space, tumor mass and momentum is not clinically very feasible for an individual patient. This demands a simple but clinically applicable model for tracking the tumor system dynamics.

Here we make an attempt to develop an analytical model for the correlation between a distance point and an equivalent model. In doing so, we have considered a particular junction point is linearly linked with a distant vein. By calculating TAF concentration at that micro-vascular cell and several locations within the vein, we can track the tumor growth. This will be a very prominent invasive technique from different distance locations. This model gives an effective understanding of tracking tumor growth dynamics, which is clinically relevant. Also the model can establish a correlation with tumor vasculature system at the tumor milieu and it can perform a quantitative assessment of tumor growth.

SYSTEM ANALYSIS

Previously all modeling techniques were mainly targeted to endothelial cells, its effect on blood vessels, angiogenesis and apoptosis of tumor cells (Mukherjee, Majumder, & Iqbal, 2006). This approach was diversified from these areas to extracellular molecular effects for the process of angiogenesis (McDougall, Anderson, & Chaplain, 2006). A detailed overview of analytical study has been found in reference (Mantzaris, Webb, & Othmer, 2004). In recent time another mathematical model has been developed, which uses nonlinear equation of solid tumor growth using a mixture model (Cristini, Li, Jhon, Lowengrub, Steven, & Wise, 2009). This is based on cellular automation modelling, hybrid continuum – discrete models and agent based models, these approaches are particularly useful for studying carcinogenesis, natural selection, genetic instability, interactions of individual cells with each other and the micro-environment. A detailed overview of analytical study has been found in some references (Kansal, Torquato, Harsh, Chiocca, & Deisboeck, 2000; Dormann & Deutsch, 2002; Turner & Sherratt, 2002; Alarcon, Byrne, & Maini, 2003; Bartha & Rieger, 2006; Lee & Rieger, 2006). These references deal with the increase of computational cost of thermodynamically consistent mixture model for a vascular solid tumor growth which takes into account the effects of cell-to-cell adhesion, taxis inducing chemical and molecular species. All these models are concentrated on the modelling and remodeling of vascular network, different probabilistic equation of vessels diameter, shear
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