Effect of anti-CD147 drug on Tumor Angiogenesis using Nano-Based Drug Delivery – A Mathematical Model

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Abstract: Tumor angiogenesis is the development of new vasculature from existing vasculature. Most tumors rely on angiogenesis for their growth. There are many important factors that assist during the process of angiogenesis in a tumor like Tumor Angiogenesis Factors (TAFs), Matrix Metallo Proteinases (MMPs), fibronectin etc. These factors are responsible for the migration of Endothelial Cells (ECs) from the parent blood vessel to the tumor. Extracellular Matrix Metallo Proteinases Inducer / Cluster of Differentiation 147 (EMMPRIN / CD147), a transmembrane glycoprotein, advances the speed of tumor angiogenesis by increasing the TAF and MMP concentrations. An anti-CD147 drug which is encapsulated in a nanoparticle is applied to prevent or delay the completion of angiogenesis. The mathematical formulation consists of partial differential equations (PDEs), incorporating the concentration equations of ECs, TAFs, fibronectin, MMPs, CD147, anti-CD147 drug, tumor cells and nanoparticle. The encapsulation of the drug in the nanoparticle ensures that the drug is delivered to the site of interest. Further, release of the drug from the nanoparticle and its impact are modeled. The simulations are performed in COMSOL Multiphysics 5.4 software. The results show that having a high concentration of the drug in the delivery site, through a controlled release, is more effective than single administration of the drug.

Keywords: tumor angiogenesis; mathematical model; CD147; anti-CD147 drug; nanoparticle drug delivery.

Introduction

Tumor angiogenesis is one of the processes by which tumors grow. In the initial stages, a tumor solely depends on the nutrients from the neighboring blood vessels. After reaching 1 – 2 mm in diameter, the nutrients from the neighboring blood vessels alone are insufficient for the tumor to grow. In this juncture, the tumor secretes Tumor Angiogenesis Factors (TAFs) and Matrix Metallo Proteinases (MMPs) in the neighborhood. The TAFs set up a gradient that pulls the Endothelial Cells (ECs), which line the walls of the blood vessels, towards the tumor. This set-up leads to the lining of ECs to form new blood vessels. This process is called angiogenesis. This set-up is the vascular network, henceforth used by the tumor for its growth [1]. The MMPs are responsible for degrading the Extra Cellular Matrix (ECM) and creating a space for the new blood vessels [2, 3]. Cluster of Differentiation 147 (CD147) is a transmembrane glycoprotein that influences the rise of TAFs and MMPs accelerating the pace of angiogenesis. Thus, targeting CD147 molecule becomes essential to slow down tumor angiogenesis [4, 5]. This is achieved by the use of a

suitable anti-CD147 drug encapsulated in a nanoparticle. The drug encapsulation in a nanoparticle ensures that the drug is delivered to the desired site.

Related work

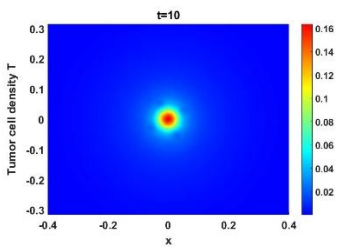
In 2025, Tsiros et al. [6], have developed a compartmental model to study the drug delivery through nanoparticle. Also, they have studied the physicochemical properties and their impact on the nanoparticle accumulation, localization and disposition. They concluded that the properties of nanoparticle are optimized leading to an improvement in drug delivery to the target site. In 2025, Koutsi et al. [7], have studied mechanotherapeutics and sonopermeation with the help of a mechanistic model. They have considered nano-immunotherapy in the treatment of cancer. They concluded that the model effectively describes the interactions between various molecules and the therapeutic modalities. Shabbir et al. [8] have studied the movement of nanoparticles in the vicinity of a tumor. They concluded that the enlargement in the vessel diameter enhanced the flow of nanoparticles.

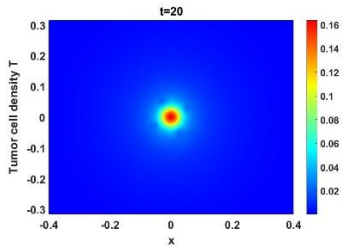
Key Contribution

In this study, the delivery of drug encapsulated in nanoparticles is discussed. Specifically, an anti-CD147 drug, which targets the CD147 molecules, is encapsulated in a nanoparticle and the delivery of the drug through nanoparticle to the desired site is studied. Further, the effect of the drug on tumor angiogenesis is explored.

Methods, Results and Discussion

A mathematical model is developed to study the effects of anti-CD147 drug encapsulated in a nanoparticle on tumor angiogenesis. The concentration of TAFs, MMPs, CD147, anti-CD147 drug, tumor cells and nanoparticles are modeled as partial differential equations (PDEs). The TAFs and MMPs aid in the angiogenesis process while CD147 rapidly advances angiogenesis. This results in the growth of the tumor. To combat the progress of angiogenesis, a drug that specifically targets CD147 molecule which in turn affects the TAFs and MMPs, is considered. This drug is further encapsulated in a nanoparticle to ensure the drug is delivered to the exact tumor site. The equation for free drug (the drug that is not encapsulated in the NP) and the equation for the NP-drug (the drug that is encapsulated in the NP) are considered. They are modeled as reaction-diffusion equations. The parameter values are borrowed from available literature. Sensitivity analysis is performed for certain parameters that are not available in literature. The simulations are executed in COMSOL Multiphysics software. The results show that there is a reduction in the occurrence of angiogenesis due to the effect of the drug. The drug encapsulated in the NP reduces the concentration of CD147. This results in reduction of TAFs and MMPs. As such, there is a decrease in the progression of angiogenesis.





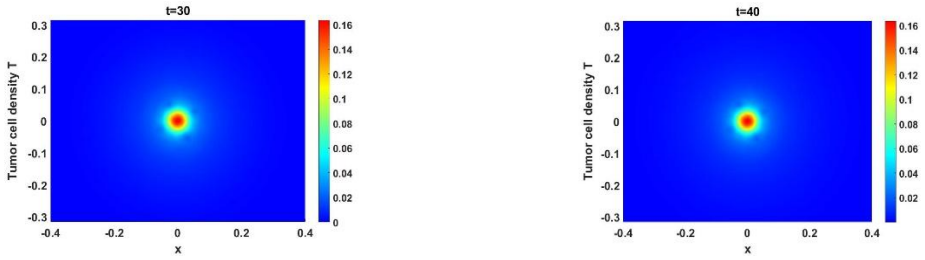


Fig.1: The density of tumor cells for different times.

Figure 1 depicts the density of tumor cells for various times. It is seen from the figure that there is no change in the tumor as time progresses. Typically, the tumor grows as time progresses. However, in this study, the effect of anti-CD147 drug, which is specifically encapsulated in a Nano Particle, has stopped the tumor growth. Even for time as high as t=40 (60 days), there is no growth of the tumor. This is in fact, a very promising strategy to stop the tumor angiogenesis.

Conclusions

1. The targeting of tumor angiogenesis is achieved. The focus was on the CD147 molecule and the ways to curb the effects of CD147 was studied.
2. The anti-CD147 drug encapsulated in a NP was observed to be effective in curbing the influence of CD147 on tumor angiogenesis.
3. The limitations of the present work are – the study does not consider combinatorial therapy. Also, there are various pathways involved in the angiogenesis process. Targeting such pathways along with targeting CD147 may provide better treatment strategies to combat tumor angiogenesis.

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