"Modulation of Immune Response to Cancer via Nanotherapy: An Integrated Experimental/Mathematical Modeling Perspective"

Virtual Seminar
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Abstract

Tumor associated macrophages (TAMs) have been shown to both aid and hinder tumor growth, with patient outcomes, potentially hinging on the proportion of M1, pro-inflammatory/growth-inhibiting, to M2, growth-supporting, phenotypes. Strategies to stimulate tumor regression by promoting polarization to M1 are a novel approach that harnesses the immune system to enhance therapeutic outcomes, including chemotherapy. It was recently discovered that nanotherapy with mesoporous particles loaded with albumin-bound paclitaxel (MSV-nab-PTX) promotes macrophage polarization towards M1 in breast cancer liver metastases (BCLM). However, it remains unclear to what extent tumor regression can be maximized based on modulation of the macrophage phenotype, especially for poorly perfused tumors such as BCLM. To investigate in a controlled *in vitro* setting, 3D co-culture experiments mimicking the BCLM hypovascularized environment with various ratios of polarized macrophages were performed in collaboration with the Houston Methodist Research Institute. A mathematical modeling framework was applied to evaluate nanoparticle-mediated chemotherapy in conjunction with TAM polarization. The results show that the response is not linearly dependent on the M1:M2 ratio. To study this phenomenon, the response was simulated via the model for a variety of M1:M2 ratios, with results indicating that polarization to an all-M1 population may be less effective than a combination of both M1 and M2. Experimental observations with a CRISPR system that permanently modulates macrophage polarization confirm this model-driven hypothesis. Altogether, these studies indicate that response to nanoparticle-mediated chemotherapy targeting poorly perfused tumors may benefit from a fine-tuned M1:M2 ratio that maintains both phenotypes in the tumor microenvironment during treatment.

Bio

Dr. Frieboes pursues an improved understanding of cancer progression and response to treatment by applying principles from engineering and the physical sciences. His expertise is focused on an integrated application of mathematical modeling, computational simulation, and experimental biology techniques. This work is part of the burgeoning field of "Physical Oncology," in which cancer is studied not only from a biological standpoint, but also as a physical system using mathematics and physics. The aim of this research is to predict tumor behavior across spatio-temporal scales spanning from the omic to the organ, with the ultimate goal to personalize the treatment of individual patients. Dr. Frieboes received his Ph.D. degree in Bioemedical Engineering from the University of California, Irvine, and conducted post-doctoral training in collaboration with the University of Texas, Houston before joining the Bioengineering Department at the University of Louisville in 2010.

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