EDITORIAL

Scope of Mathematical Biology in Cancer Research

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INTRODUCTION

Mathematical biology involves the use of mathematical models derived from biological data to predict the course or outcome of a biological event. In oncology, mathematics plays a vital role in determining the tumor behavior and the optimal treatment strategy including the right combination of treatment modality to be used, and the timing and duration of the treatment. The major limiting factor in mathematical oncology is the inability to obtain accurate biological data to formulate appropriate mathematical models.[1] Development of molecular biology has enabled us to overcome these limitations. An example of such development is an accurate measurement of cell cycle phases,[2] based on which optimal schedule

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for chemo- or radiotherapy can be formulated.[1] Thus, the evolution of molecular techniques has aided in the formulation of accurate mathematical prediction models for diseases. Further, in diseases with several potentially successful treatment options, a mathematical model may aid in identifying the most optimal treatment strategy.

Mathematical oncology translates each of the components in cancer pathogenesis into a mathematical representation using which predictive models can be formulated to describe the complex interaction of these factors and their potential influence on the therapy design and prognosis. Mathematical oncology can be broadly divided into two categories, computational and physical oncology.[3] In computation oncology, computational resources including databases (proteomic, genomic data sets) will be analyzed using biostatistics to formulate mathematical models capable of predicting the tumor behavior.[3,4] Physical oncology is based on the presumption that carcinogenesis is a result of complex biophysical interactions. Thus, physical oncology predicts tumor behavior based on mechanistic models which in turn are derived from the analysis of biophysical laws of interactions.[3] Recent studies have led to the development of mathematical models capable of accurately determining several aspects of the tumor biology including invasion, metastasis, and treatment outcome. Gatenby and Gawlinksi[4] developed a glycolysis model for cancer which showed the role of anaerobic metabolism as a major determinant in the development of invasive behavior. Due to the nonuniform distribution of oxygen, the tumor developed heterogeneous environment causing loss of morphological stability leading to the invasive behavior. Byrne and Chaplain[5] model decoded the variations in the diffusion of nutrients based on the vasculature of a tumor. Understanding the tumor vasculature pattern provided an explanation for the heterogenicity in the tumor microenvironments which in turn could explain the variations in the tumor behavioral patterns. Formulation of a vascular model for cancer also aided in improving

the efficiency of drug delivery systems. Apart from the diffusion gradient based on the vasculature, it was shown that cell density also plays a major role in determining the efficiency of drug delivery.[3] Thus, formulating models capable of assessing the diffusion gradient, drug penetration, and potential drug modification could aid in predicting the outcome of treatment modalities.

Szeto et al[6] combined the pre-and postoperative images of cancer with experimental growth models, to accurately predict the survival pattern in glioblastoma. Gatenby and Gillies[7] provided a model to explain the mechanism of tumor growth and progression. The model predicted that phenotypic and genotypic heterogenicity of tumor cells aided in circumventing the constraints of the tumor microenvironment, thereby allowing unrestrained tumor growth. Brú et al[8] used *in vivo* and *in vitro* models to study the microstructures of the host–tumor interface, through which they mathematically characterized the tumor interface. An example of interface characterization was the identification of "fingering" morphology as a risk factor for invasion.[9] The "fingering" morphology was presumed to be the result of an overall mechanical instability induced by loss of cancer cell adhesion.

In addition to the development in mathematical biology, the past decade has seen significant stride being made to integrate artificial intelligence (AI) in medical sciences. Artificial intelligence has been successfully used to detect and grade a variety of diseases including cancer.[10] Thus, framing diagnostic and therapeutic mathematical models using AI could increase the overall prediction rate of these models. To conclude, formulating customized computational and physical models for specific cancer types using AI would aid us in accurately predicting the cancer behavioral patterns and in formulating the most optimal diagnostic and treatment strategies.

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