THE ROLE OF ANGIOGENESIS IN MATHEMATICAL MODELING OF TRIPLE-NEGATIVE BREAST CANCER

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In this study, a mathematical model of triple-negative breast cancer (TNBC) is proposed. The mathematical model includes interactions between tumor cells, innate and adaptive immune cells, and the angiogenic factor. Without the angiogenic factor, the mathematical model exhibits three coexisting stable equilibria, representing the tumor-free equilibrium (immune surveillance), the microscopic tumor equilibrium (equilibrium phase), and the large-tumor equilibrium (immune escape). However, the microscopic tumor equilibrium can break down when the angiogenic factor is included. The tumor may start to grow larger depending on how rapidly the angiogenic factor increases, which indicates how quickly new blood vessels are recruited to nourish the tumor. The microscopic tumor equilibrium can last for months, years, or even a lifetime. Experimental data in three independent studies are used to estimate the parameter values. The parameter values are consistent across all three studies. Further estimation of parameter distributions using the MCMC method is performed to study individual variation. Mathematical analysis, such as the nonnegativity and boundedness of solutions as well as stability analysis of the equilibria, is conducted. In addition, global sensitivity analysis and bifurcation analysis are investigated. The results of the numerical simulations are compared with the observed medical phenomena. The model can serve as a foundation for further investigation of angiogenesis-related treatments and other therapeutic approaches, including immunotherapy and chemotherapy.

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