Multiscale Modeling of the Competing Roles of the Immune System in EMT-Mediated Cancer

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During tumorigenesis and throughout the lifetime of a tumor, the immune system is constantly engaged in complex interactions in and around the tumor. These interactions are influenced by the tumor microenvironment (TME) and in particular by the cellular process of epithelial-to-mesenchymal transition (EMT) in an as-yet unexplained manner. In turn, both the tumor and the immune system exert substantial influence over the TME in competition to influence the fate of the host. Determining the critical factors and mechanisms involved remains a crucial task for cancer immunotherapy. Here, we seek to understand how interplay between the tumor, the immune system, and EMT can determine the outcome of cancer. We developed a multiscale agent-based model that describes tumor-immune interactions and how EMT modulates these. Exploration of the model revealed that increasing the growth arrest of mesenchymal cells in some circumstances results in a more tumor-friendly environment and sometimes less. In contrast, enhancing the immune evasiveness of mesenchymal cells always leads to a more tumor-friendly microenvironment. Moreover, encouraging the TME towards a pro-EMT state also benefits the tumor. Together, these results indicate that the joint regulation of the TME by the immune system and the tumor itself provides possible targets for future cancer therapies, in particular cancers such as pancreatic cancer in which EMT is speculated to play a role.

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