Abstract

In solid tumors, there can be various types of non-cancerous cells, including immune cells, fibroblasts, endothelial cells, etc. These different types of cells form the so-called tumor microenvironment (TM) that strongly affects the growth and survival of cancer cells, and hence are very important for successful treatment, including the immune checkpoint blockade (ICB) therapy that won Nobel Prize in 2018. Even though the ICB therapy can cure about 20% of patients with melanoma (one type of skin cancer) and non-small-cell lung cancer (NSCLC), most patients either do not respond to the therapy or develop resistance later on. Furthermore, the therapy does not work so well in many other types of cancer. It has been suggested that the interactions between cancer cells and other cells can be one of reasons for the failure of immune surveillance and ICB therapy. In our work, through studying the population dynamics of immune cells (ODE-based models) in the TM, we demonstrated the immune system can reach a steady state in which immune-suppressing populations dominate and the activity of cancer-killing immune cells (e.g., CD8+ T cells) is thus suppressed. Furthermore, by characterizing the spatial infiltration patterns of CD8+ T cells in patient samples and developing mathematical (PDE-based) models to recapitulate the patterns, we concluded that cancer cells or other cells inside cancer-cell islands can secrete certain repellents which prevent the infiltration of CD8+ T cells1. In the end, I will show our agent-based simulation studies on the mechanism underlying the long-range circumferential alignment of fibroblasts and collagen fibers around cancer-cell islands2. The pattern of collagen fibers has been suggested to be responsible for limiting the infiltration of CD8+ T cells into cancer-cell islands. In summary, our studies provide mechanistic understandings regarding the immune-suppressing TM, which could help the development of new therapeutic options.

1. Li, X., Gruosso, T., et al., “Infiltration of CD8+ T cells into tumor- cell clusters in Triple Negative Breast Cancer.” Proc Natl Acad Sci U S A, 116(9): 3678–3687, 2019.

2. Li, X., Balagam, R., et al., “On the mechanism of long-range orientational order of fibroblasts.” Proc Natl Acad Sci U S A, 114(34): 8974–8979, 2017.