Mechanistic models of cancer-immune cycle and immunotherapies

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Abstract

Immo-ono-cology is at the forefront of drug development. New therapies are being developed to target the cancer-immune cycle, a dynamic system of non-linear interactions between the cellular and molecular players of the immune system and tumour. The design of an effective cancer immunotherapy is complicated by various factors, including a potentially immunosuppressive tumour microenvironment, immune-modulating effects of conventional treatments and therapy-related toxicities. Quantitative and mechanistic understanding of this system is crucial to unravel these complexities, which can only be achieved by the use of mathematical models. Mathematical models are increasingly being used to support diverse clinical decisions in drug discovery and development.

Here, we systematically surveyed 136 published mechanistic models describing various components of Cancer-Immune System dynamics, and Immunotherapies. We distill and discuss several example models that have grown in complexity by incorporating the advances in cancer-immune biology. In addition, we have developed a unified biological process map by integrating the processes described in these models. This comprehensive analysis of literature models on the cancer-immune cycle can potentially benefit modelling efforts in pharmaceutical industry.

Landscape of Cancer-Immune System Models

- An overview of the literature-based models of cancer-immune system dynamics that is reviewed in this study
- The models continuously evolve (e.g. see blue shaded region), grow in size (see node size) and complexities with the inclusion of new experimental/clinical findings in cancer-immune biology

Cell-cell communication mediated by molecular players

Cytokines, chemokines, growth factors, cell-surface receptors and other molecular players (middle panel) that mediate cell-cell communication as described in the above models

Unified biological process map

The processes and the immunotherapies incorporated in 136 models are represented here as a unified biological process map. This map reflects the extent of cancer-immune system dynamics and therapies that have been addressed by the published models in order to elucidate mechanistic insights.

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