Mechanistic models of cancer-immune cycle and immunotherapies

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Viji Chelliah[1], Georgia Lazarou[2], Andrzej Kierzek[2], Piet van der Graaf[1]

[1] Certara UK Limited, Unit 43, Canterbury Innovation Centre, University Road, Canterbury, CB2 7FG, United Kingdom

[2] Certara UK Limited, Level 2-Acero, 1 Concourse Way, Sheffield, S1 2BJ, United Kingdom

Abstract

Immuno-oncology is at the forefront of drug development. New therapies are being developed to target the cancer-immunity 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.
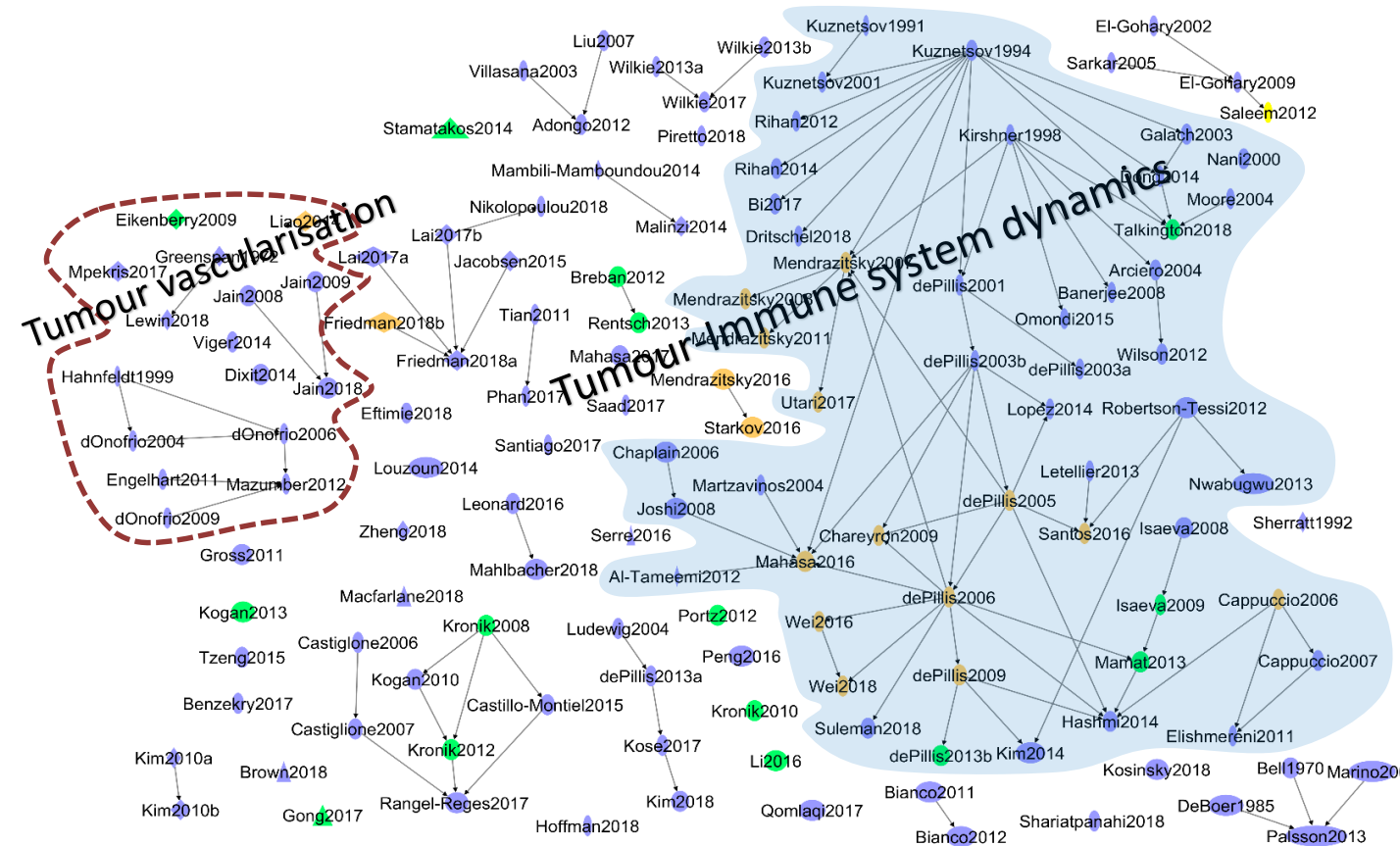
Here, we systematically surveyed 136 published mechanistic models describing various components of Cancer-Immune System dynamics, and Immunotherapies. We distill and discuss several example models that have grown in complexity by incorporating the advances in cancer-immune biology. In addition, we have 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.

Cancer-Immune System and Immunotherapies
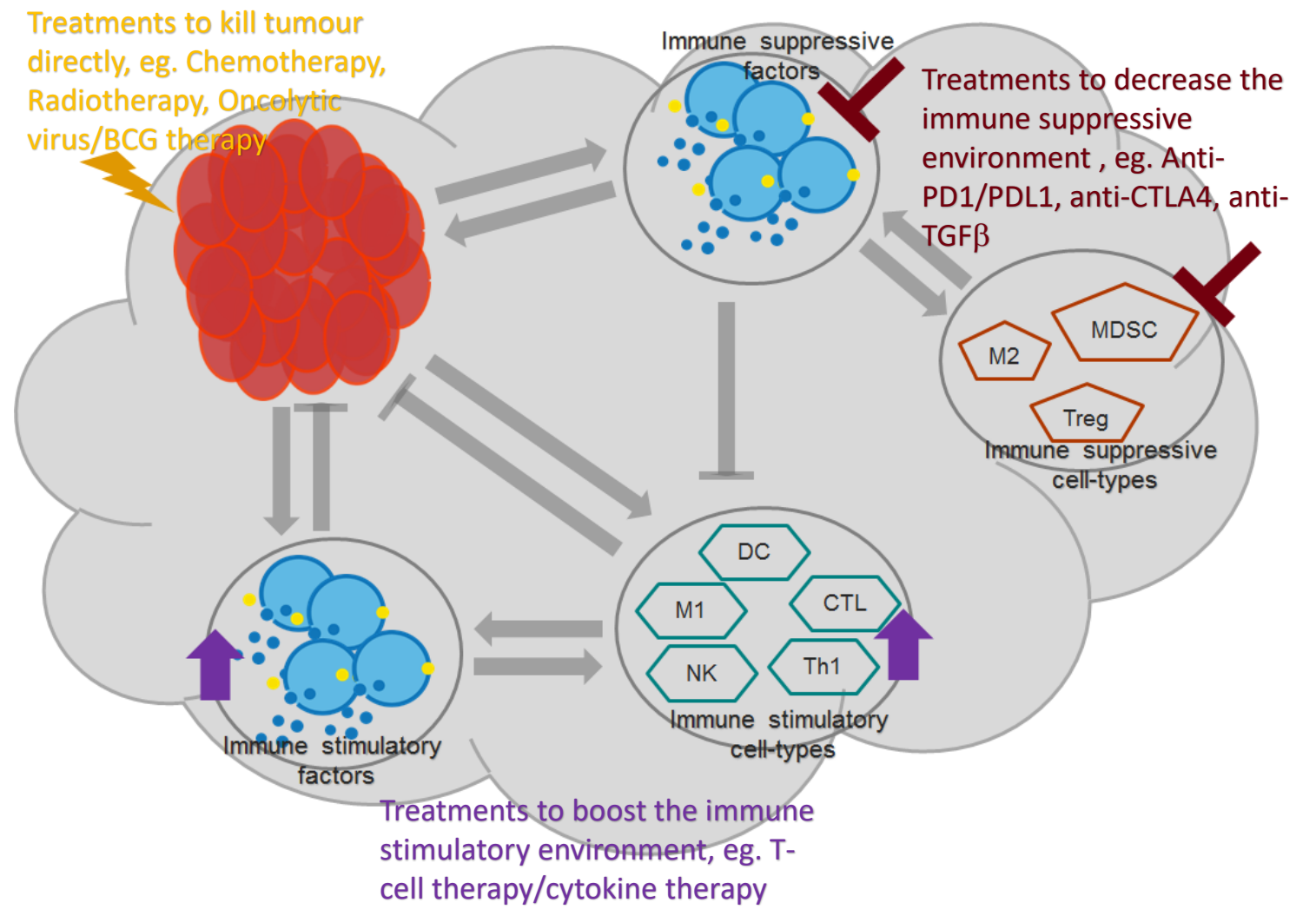
Landscape of Cancer-Immune System Models

- An overview of the literature-based models of cancer-immune system dynamics that is reviewed in this study

- The models continuously evolve (eg. see blue shaded region), grow in size (see node size) and complexities with the inclusion of new experimental/clinical findings in cancer-immune biology

| Modelling approaches/ Study Type	ODE/DDE - 115 models	PDE - 16 models	Spatial/ABM,DTE - 5 models
Clinical	●	◆	▲
Preclinical	●	◆	▲
Both	●	◆	▲

- Good consensus of biological processes are captured by these models with reasonable agreement with preclinical and clinical data.

- The analysis highlights the gaps in the knowledge incorporation in models where new interventions can be applied.

- Integration of well characterized processes defined in individual models will provide a comprehensive cancer-immune cycle model.

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
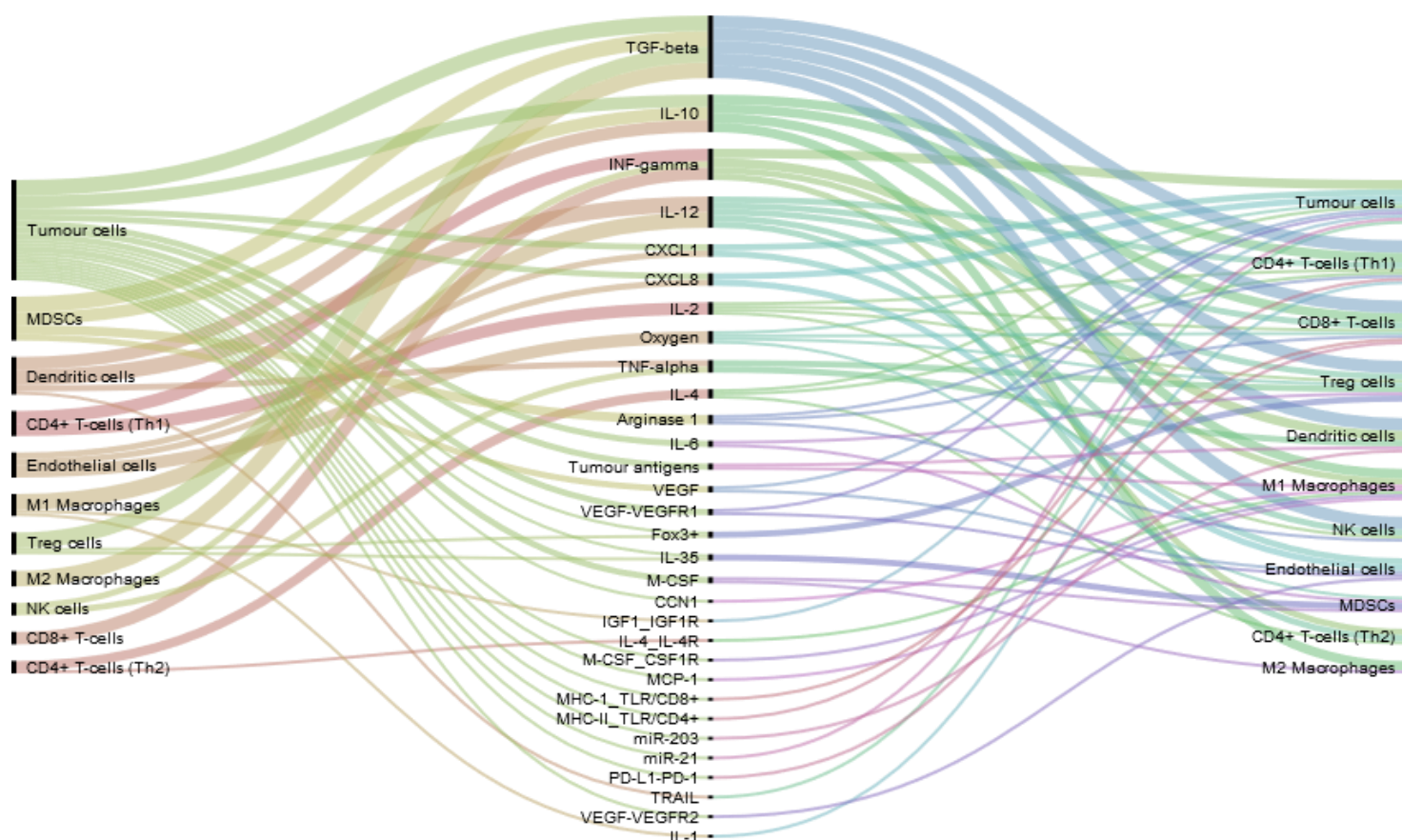
Unified biological process map

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.