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Résumé

CD8+ T cells are important for immune responses against viruses and bacteria, as well as for tumor surveillance. When the CD8+ T cell recognizes its antigen (i.e. it enters in contact with an antigen presenting cell), it gets activated, it then differentiates into an effector, and kills infected or malignant cells bearing the antigen. Meanwhile, part of activated CD8+ T cells differentiate into memory cells. CD8+ T cell activation, differentiation, proliferation and death are controlled by intracellular signaling based on cell interactions with their microenvironment and gene regulation (1), (2). Here we present a multiscale model for CD8+ T cell immune response.

The model is implemented in the modelling platform Simuscale developed at Inria. Simuscale provides an efficient numerical framework for integrating and simulating different physical and temporal scales involved in the CD8 T cell immune response. First, a gene regulatory network (GRN), described by a Piecewise-deterministic Markov process (PDMP), is integrated and simulated in each individual T cell. Second, the internal GRN dynamics affects cellular fate: it changes cell activation status and triggers either proliferation, apoptosis, or differentiation. Third, interactions between cells modify the GRN dynamics via cell signaling, generating feedback regulation of CD8 T cell dynamics.

Through simulations, we explore conditions (for example threshold values of the protein concentration of a given gene, or the volume of a cell) that can lead to decisions about division, death, and differentiation states of a cell. We introduce a GRN consisting of 8 different genes. Simulations of this complex, multiscale model show that the model is able to reproduce key features of the CD8 T cell response (3).

References

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