Modeling the kinetics of T helper cell fate establishment

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Résumé

Naive T helper cells integrate a large range of signals into the fate decision of becoming Th1, Th2, Th17 or iTreg, expressing distinct sets of transcription factors and cytokines. Improper differentiation in vivo leads to asthma, tumor tolerance or autoimmunity, and recent therapies consist in engineering or differentiating T helper cells from patients in order to optimize the immune response. However, therapies are challenged by the poor stability and persistence of these cells in vivo. Assessment of the kinetics of expression of helper-specific transcription factors and cytokines during in vitro differentiation allowed us to develop a mathematical model to extract the strength of interactions between these molecules and further predict differentiation in pathological conditions. The challenges faced during the development of the model, including identification of parameters, choice of the variables to simulate, correlation between mRNA and protein expression over time, as well as the to-and-fro between wet experiments and modelling will be discussed. The model will be able to predict the robustness of differentiation as well as conditions where improper differentiation or plasticity occurs, leading to targeted experiments.

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