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Genetic analysis of differentiation of T-helper lymphocytes

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ABSTRACT. In the human immune system, T-helper cells are able to differentiate into two lymphocyte subsets: Th1 and Th2. The intracellular signaling pathways of differentiation form a dynamic regulation network by secreting distinctive types of cytokines, while differentiation is regulated by two major gene loci: T-bet and GATA-3. We developed a system dynamics model to simulate the differentiation and re-differentiation process of T-helper cells, based on gene expression levels of T-bet and GATA-3 during differentiation of these cells. We arrived at three ultimate states of the model and came to the conclusion that cell differentiation potential exists as long as the system dynamics is at an unstable equilibrium point; the T-helper cells will no

longer have the potential of differentiation when the model reaches a stable equilibrium point. In addition, the time lag caused by expression of transcription factors can lead to oscillations in the secretion of cytokines during differentiation.

Key words: Genetic analysis; System dynamics model; Th1-Th2; Equilibrium point

