

Publication**Contribution of IL-12R mediated feedback loop to Th1 cell differentiation****JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)****ID** 961801**Author(s)** Becskei, Attila; Grusby, Michael J.**Author(s) at UniBasel** [Becskei, Attila](#) ;**Year** 2007**Title** Contribution of IL-12R mediated feedback loop to Th1 cell differentiation**Journal** FEBS Letters**Volume** 581**Number** 27**Pages / Article-Number** 5199-206**Mesh terms** Animals; Cell Differentiation, immunology; Feedback; In Vitro Techniques; Interferon-gamma, biosynthesis; Interleukin-12, pharmacology; Interleukins, pharmacology; Mice; Mice, Knockout; RNA, Messenger, metabolism; Receptors, Interferon, metabolism; Receptors, Interleukin-12, metabolism; STAT1 Transcription Factor, metabolism; STAT4 Transcription Factor, metabolism; Th1 Cells, metabolism

T helper 1 (Th1) cell fate is induced by overlapping signaling pathways, whose kinetic principles and regulatory motifs are largely unknown. We identified a simple positive feedback loop in the STAT4 signaling pathway, whereby activation by IL-12 leads to the increased expression in IL-12 receptor. A computational analysis shows that this feedback loop synergizes with the one mediated by the IFN-gamma secreted by differentiating cells, when the induction of Th1 cell fate is weak. Positive feedback loops are often utilized to enhance phenotypic differentiation. This effect was confirmed by experiments showing that stochastic fluctuations in the expression of IL-12 receptor gene were amplified, leading to two discrete levels of expression in a cell population.

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