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**Discrete dynamic modeling of T cell survival signaling networks**

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Biochemistry-based frameworks are often not applicable for the modeling of heterogeneous regulatory systems that are sparsely documented in terms of quantitative information. As an alternative, qualitative models assuming a small set of discrete states are gaining acceptance. This talk will present a discrete dynamic model of the signaling network responsible for the survival and long-term competence of cytotoxic T cells in the blood cancer T-LGL leukemia. We integrated the signaling pathways involved in normal T cell activation and the known deregulations of survival signaling in leukemic T-LGL, and formulated the regulation of each network element as a Boolean (logic) rule. Our model suggests that the persistence of two signals is sufficient to reproduce all known deregulations in leukemic T-LGL. It also indicates the nodes whose inactivity is necessary and sufficient for the reversal of the T-LGL state. We have experimentally validated several model predictions, including: (*i*) Inhibiting PDGF signaling induces apoptosis in leukemic T-LGL. (*ii*) Sphingosine kinase 1 and NF$\kappa$B are essential for the long-term survival of T cells in T-LGL leukemia. (*iii*) T box expressed in T cells (T-bet) is constitutively activated in the T-LGL state. The model has identified potential therapeutic targets for T-LGL leukemia and can be used for generating long-term competent CTL necessary for tumor and cancer vaccine development. The success of this model, and of other discrete dynamic models, suggests that the organization of signaling networks has an determining role in their dynamics. Reference: R. Zhang, M. V. Shah, J. Yang, S. B. Nyland, X. Liu, J. K. Yun, R. Albert, T. P. Loughran, Jr., Network Model of Survival Signaling in LGL Leukemia, PNAS 105, 16308-16313 (2008).