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Anna Konstorum* (konstorum@uchc.edu), **Anthony T. Vella**, **Adam J. Adler** and **Reinhard C. Laubenbacher**. *An intracellular model of synergistic CD8 T cell costimulation by 4-1BB (CD134) and OX40 (CD137)*.

Combined agonist stimulation of the CD8 T cell costimulatory receptors OX40 (CD137) and 4-1BB (CD134) has been shown to generate supereffector T cells that survive longer and produce a greater quantity of cytokines that mediate tumor cell killing in vivo compared to T cells stimulated with an agonist of either costimulatory receptor individually. In order to understand the mechanisms for this synergy, we have created a multistate discrete logic-based mathematical model for the activation of the CD8 T cell intracellular signaling network by mono- or dual-costimulation (DCo). We show that synergy occurs from downstream interacting pathways that are activated upon activation of both receptors, and in silico simulation of the model supports published experimental results. We propose that the model can be used to identify critical molecular targets of synergy in the context of cancer immunotherapy. (Received September 24, 2018)