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A systems model of phosphorylation for inflammatory signaling events

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Abstract

© 2014 Sadreev et al. Phosphorylation is a fundamental biochemical reaction that modulates protein activity in cells. While a single phosphorylation event is relatively easy to understand, multisite phosphorylation requires systems approaches for deeper elucidation of the underlying molecular mechanisms. In this paper we develop a mechanistic model for single- and multisite phosphorylation. The proposed model is compared with previously reported studies. We compare the predictions of our model with experiments published in the literature in the context of inflammatory signaling events in order to provide a mechanistic description of the multisite phosphorylation-mediated regulation of Signal Transducer and Activator of Transcription 3 (STAT3) and Interferon Regulatory Factor 5 (IRF-5) proteins. The presented model makes crucial predictions for transcription factor phosphorylation events in the immune system. The model proposes potential mechanisms for T cell phenotype switching and production of cytokines. This study also provides a generic framework for the better understanding of a large number of multisite phosphorylation-regulated biochemical circuits.

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