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Heterogeneity in Tumour Necrosis Factor induced Pro- and Anti-Apoptotic Signalling from a Systems Biology Perspective

By Monica Schliemann

Shaker Verlag Mrz 2013, 2013. Buch. Book Condition: Neu. Neuware - Many immune hormones are pleiotropic, i.e. they can induce a broad, even contradictory pattern of cellular responses. This also holds true for the cytokine tumour necrosis factor (TNF), which is able to trigger apoptosis, but can also stimulate cellular growth. The final fate of a given cell after TNF stimulation is highly dependent on the balance between the implicated pathways in combination with the cellular context. This study analyses the complex interplay of the crosstalk of TNF receptor type 1 (TNF-R1) induced pro- and anti-apoptotic signalling pathways. Both signalling pathways are regulated via feedback loops. For example, the mutual activation of caspases includes a positive feedback loop, while I κ B α and NF- κ B form a negative feedback loop. A well defined model of TNF-induced apoptosis is the human cell line KYM-1, on which experimental kinetic data (life cell imaging, western blotting, cytotoxicity and caspase activity assays as well as microinjections) were obtained at various concentrations of TNF. A useful tool integrating quantitative, dynamical data with the corresponding hypotheses is mathematical modelling, which formalises the biological knowledge and allows for generating model-based predictions. Based on this thesis' experimental findings, in particular that...



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