DOI 10.18699/SbPCD-2018-17

Towards understanding of apoptosis regulation using computational biology

I.N. Lavrik
Department of Translational Inflammation Research, Institute of Experimental Internal Medicine, Otto von Guericke University, Magdeburg, Germany
Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia
e-mail: inna.lavrik@med.ovgu.de

Key words: apoptosis, system biology, CD95, death receptor

Apoptosis is a programme of cell death, which is essential to all multicellular organisms. There are two signaling pathways of apoptosis: intrinsic that is mediated by mitochondria and extrinsic, that is mediated by a family of death receptors. CD95 (APO-1/Fas) is a member of the death receptor family. The CD95 death-inducing signaling complex (DISC), comprising CD95, FADD, procaspase-8, procaspase-10, and c-FLIP; serves as a key platform for initiator procaspase-8 activation leading to induction of apoptotic and non-apoptotic pathways. The enormous advantage for studies of the death receptor networks is provided by the state of the art computational technologies, in particular by systems biology. Systems biology is an emerging field of science that combines mathematical modeling with quantitative experimental methods, providing a quantitative assessment of the signaling pathways. Despite the fact that death receptor-mediated signaling has been studied to a high level of detail, its quantitative regulation until recently has been poorly understood. This situation has dramatically changed in the last years. Creation of mathematical models of death receptor signaling, in particular in immune cells, led to an enormous progress in the quantitative understanding of the network regulation and provided fascinating insights into the mechanisms of death receptor control. It will be discussed how our systems biology studies provide new understanding of the death receptor signaling in cancer cells and create a platform for the drug development in the context of diseases associated to defects in death receptor signaling pathways.