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Current Research

Our research objective is to decipher molecular mechanisms that regulate dynamic interactions in intracellular signaling networks and thereby control cellular decisions. When these control mechanisms fail cancer and other diseases arise. Signal transduction in intracellular networks comprises the transmission of information from cell surface receptors to the nucleus where the activity of genes is regulated. To elucidate key regulatory mechanisms it is not sufficient to identify the network components but rather essential to understand the dynamic behavior. In close collaboration with modeling partners we are following a systems biology approach and combine quantitative data with mathematical models to investigate alterations in signaling networks that promote the onset of cancer. As an example we are studying cellular decisions in hematopoietic and hepatocellular cells. The data-based mathematical models enable rapid testing of hypotheses, the targeted design of experiments and the prediction of steps most suitable for intervention. Thereby our approach can contribute to a more rapid development of effective anti-cancer therapies.

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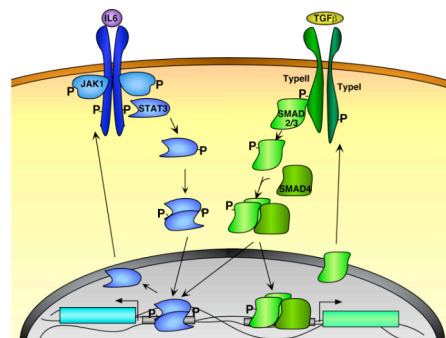


Future Projects and Goals

The aim of the group is to understand molecular mechanisms determining cellular decisions, cell-context specific effects and predict targets for efficient intervention to correct alterations promoting tumor formation. Future projects are to generate time-resolved and spatially-resolved quantitative data for multiple signaling pathways to extend our data-based mathematical models with the aim to capture cross-talk of signaling pathways and to identify general building principles.

Selected Publications

- I. Swameye, T. G. Müller, J. Timmer, O. Sandra, and U. Klingmüller. Identification of nucleocytoplasmic cycling as a remote sensor in cellular signaling by data-based dynamic modeling. PNAS (2003) 100:1028-33.
- A. C. Heinrich, R. Pelanda, and U. Klingmüller. A mouse model for visualization and targeted mutations in the erythroid lineage. Blood. (2004) 104(3):659-66.
- M. Schilling, T. Maiwald, S. Bohl, M. Kollmann, C. Kreutz, J. Timmer, and U. Klingmüller. Computational processing and error reduction strategies for standardized quantitative data in biological networks. FEBS Journal (2005), 272:6400-6411.



Cross-talk of signaling through the interleukin (IL)-6 receptor and the transforming growth factor (TGF) beta receptors is schematically depicted.