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Uncovering the relations between signaling, gene expression and phenotype in the EGFR network

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Ligand binding to cell surface receptors initiates a cascade of signaling events regulated by dynamic phosphorylation on a multitude of pathway proteins. Quantitative features, including intensity, timing, and duration of phosphorylation of particular residues play a role in determining cellular response. We have designed a mass spectrometry technique allowing site-specific quantification of dynamic phosphorylation in the cell and we have applied it to study signaling events triggered by the activation of the epidermal growth factor receptor (EGFR). To further understand cellular regulatory processes and their relationship to cellular phenotype we have used RNAseq to measure dynamics changes in gene expression as a consequence of EGFR activation and real time reverse contrast microscopy to quantify cellular proliferation and migration rates. Hierarchical clustering and Self organizing maps (SOMs) analysis of our data has highlighted potential biological functions for phosphorylation sites previously unrelated to EGFR signaling and identified network modules regulated by different combinations of phosphorylation sites and gene expression events. Partial least square regression (PLSR) analysis of our data identified combination of signals strongly correlating with cellular proliferation and migration. Overall, our approach reveals the interdependencies between cellular signaling and gene regulatory networks as well as their role in combined role in the regulation of basic cellular phenotype.

Biography

Alejandro Wolf-Yadlin got his PhD from MIT Bioengineering Department 5 years ago. He worked for Doug Lauffenburger and Forest White developing and applying proteomics tools to study cell biology. He did his postdoc in Gavin MacBeath's Lab at Harvard University where he developed high throughput protein arrays. Currently he is a Professor in the Department of Genome Sciences at the University of Washington.

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