Characterizing Protein Interactions Employing a Genome-Wide siRNA Cellular Phenotyping Screen.

Suratanee A, Schaefer MH, Betts MJ, Soons Z, Mannsperger H, Harder N, Oswald M, Gipp M, Ramminger E, Marcus G, Männer R, Rohr K, Wanker E, Russell RB, Andrade-Navarro MA, Eils R, König R (2014) Characterizing Protein Interactions Employing a Genome-Wide siRNA Cellular Phenotyping Screen. *PLOS Comput Biol* 10(9), e1003814.

Abstract

Characterizing the activating and inhibiting effect of protein-protein interactions (PPI) is fundamental to gain insight into the complex signaling system of a human cell. A plethora of methods has been suggested to infer PPI from data on a large scale, but none of them is able to characterize the effect of this interaction. Here, we present a novel computational development that employs mitotic phenotypes of a genome-wide RNAi knockdown screen and enables identifying the activating and inhibiting effects of PPIs. Exemplarily, we applied our technique to a knockdown screen of HeLa cells cultivated at standard conditions. Using a machine learning approach, we obtained high accuracy (82% AUC of the receiver operating characteristics) by cross-validation using 6,870 known activating and inhibiting PPIs as gold standard. We predicted de novo unknown activating and inhibiting effects for 1,954 PPIs in HeLa cells covering the ten major signaling pathways of the Kyoto Encyclopedia of Genes and Genomes, and made these predictions publicly available in a database. We finally demonstrate that the predicted effects can

be used to cluster knockdown genes of similar biological processes in coherent subgroups. The characterization of the activating or inhibiting effect of individual PPIs opens up new perspectives for the interpretation of large datasets of PPIs and thus considerably increases the value of PPIs as an integrated resource for studying the detailed function of signaling pathways of the cellular system of interest.

Beteiligte Forschungseinheiten

Netzwerkmodellierung

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