Identification of cancer signaling pathways from published gene expession signatures using PubLiME

ID - 97

Muller Heiko[1,2], Mancuso Francesco Mattia[1,2], Cittaro Davide[1], Finocchiaro Giacomo[1,2]
[1]FIRC Institute of Molecular Oncology Foundation (IFOM), Via Adamello 16, 20139 Milan, Italy
[2]European Institute of Oncology (IEO), Via Ripamonti 435, 20141 Milan, Italy

Motivation

Gene expression technology has become a routine application in many laboratories and has provided large amounts of gene expression signatures that have been identified in a variety of cancer types. Interpretation of gene expression signatures would profit from the availability of a procedure capable of assigning differentially regulated genes or entire gene signatures to defined cancer signaling pathways. Here we describe a graph based approach that identifies cancer signaling pathways from published gene expression signatures.

Methods

Published gene expression signatures are collected in a database (PubLiME: Published Lists of Microarray Experiments) enabled for cross-platform gene annotation.

Significant co-occurrence modules composed of up to ten genes in different gene expression signatures are identified. Significantly co-occurring genes are linked by an edge in an undirected graph. Edge betweenness and k-clique clustering combined with graph modularity as a quality measure are used to identify communities in the resulting graph.

Results

The identified communities consist of cell cycle, apoptosis, phosphorylation cascade, extra cellular matrix, interferon and immune response regulators as well as communities of unknown function. The genes constituting different communities are characterized by common genomic features and strongly enriched cis-regulatory modules in their upstream regulatory regions that are consistent with pathway assignment of those genes.

Email: heiko.muller@ifom-ieo-campus.it