Regulatory Interaction plugin: a PathVisio plugin to visualize microRNA-target interactions

Stefan van Helden, Martina Kutmon, Lars M. Eijssen, Susan L. Coort, Chris T. Evelo
Bioinformatics-BiGCaT, Maastricht University, the Netherlands.

Since the discovery of microRNAs (miRNAs), which are post-transcriptional regulators, many studies are performed to investigate their role in physiological and disease processes. Microarray technology makes it possible to measure miRNA expression on a large scale. The pathway visualization tool PathVisio (www.pathvisio.org) can provide valuable assistance to gain insight in which biological processes miRNAs play a role. In PathVisio pathways are schematic representations of the interactions between biological entities such as genes and proteins. These biological entities are annotated with identifiers and accession numbers from online databases with additional information about the selected item.

To include miRNAs in the pathway analysis, PathVisio should be able to visualize them. WikiPathways is an open, public platform dedicated to the curation of biological pathways by and for the scientific community. At the moment, most of the 1674 available pathways do not contain information about miRNAs. By expanding PathVisio’s functionality with the Regulatory Interaction plugin, it is possible to automatically visualize the regulatory interaction partners of a selected pathway element in a side panel, as well as show the expression levels of these biological entities by loading a data set containing regulator and target expression data, e.g. miRNA and mRNA expression data.

To do this, we use a simple text file format containing two columns, regulator and target identifiers, in our case-study these are the interactions between miRNAs and genes. It is possible to load multiple interaction files simultaneously, e.g. MicroCosm Targets, miRTarBase and miRecords. If the user selects an element in a pathway, the plugin displays the interaction partners in a side panel. By loading an expression data set, this will also show the expression levels of the biological entities involved in the regulatory interaction.

The regulatory interaction plugin enables the integration of miRNA regulation in pathway analysis. In the near future, we will add the functionality to perform pathway statistics based on a set of miRNAs. The target genes of those miRNAs will be used to perform a gene set enrichment analysis. This could give some indication if a pathway is regulated by a set of miRNAs or not.