Introduction
Pathway and network analysis is used to understand genomics data from transcriptomics, proteomics and metabolomics experiments. It uses prior knowledge of biological relationships and can evaluate related effects that strengthen each other. Genetic variants analysis (such as SNPs, indels..) would also benefit from this approach because of the evaluation of related variations in different genes, and integration of variant data with other omics results. Currently, genetic variations cannot easily be combined in pathway representations. It is also not clear how to better visualize and interpret variation data once we connected it to pathway content programmatically.

In this project we take up the challenge to integrate genetic information in the open source pathway analysis program PathVisio (pathvisio.org).

Design and analysis ideas
We connected variants with related genes, using bioinformatic mapping approaches (see bridgedb.org). With this we can visualize variants on a pathway. We now aim for meaningful presentations showing some design studies:

- Variants information for selected genes is shown in a separate panel (see right side in the figure).
- Genetic variations with statistical values from large genetic datasets (e.g. GWAS) can be highlighted for the annotated variants (colors in the panel and clickable values).
- Specific information about variants like HapMap environment or function predictions can be shown as popups (popup) or via linkouts to genome browsers.

We will also map variants and genes for statistical approaches using larger sets of biological pathways (e.g. from WikiPathways), to find those where many variants occur in specific phenotypes. This is comparable to the over representation and gene set enrichment analyses. Finally, we will investigate the use of existing advanced tools (like sift and polyphen) to integrate predictions of biological functional changes.

The figure shows a first implementations for SNPs representation (from GWAS data) in a pathway, using PathVisio.

Pathways as a bridge to networks
Pathway and network biology can be easily combined: our tools convert one into the other and we can use the same mappings between database identifies in both. Variations are evaluated in pathways as networks, increasing network extensions (e.g. with miRNA or drugs) and topology studies. This will combine network connectivity, betweenness and shortest path analysis with the occurrence of deleterious variants in disease phenotypes.