Pathway and Gene Selection with Guided Regularized Random Forests

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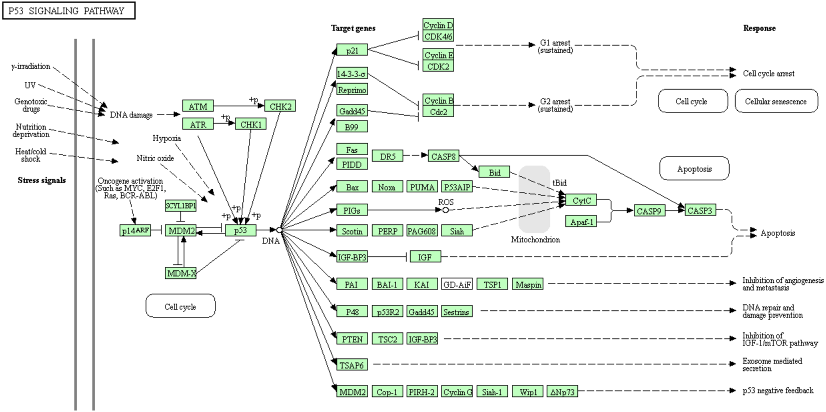
- The earliest methodological approaches focused on analyzing such data at the level of individual genes. For biological outcomes that depend on single mutations (e.g., cystic fibrosis) this is an effective approach.
- For diseases and disorders that are the result of complex interactions between many genes, such as cancer, this approach is less effective.
- Current cancer research improves upon the previous methodology by incorporating **genetic pathway** information into the analysis.

So, What Are Gene Pathways?



Source: KEGG Database

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- Rank pathways according to their out-of-bag (OOB) error rate.
- Within each pathway, rank the individual genes by comparing variable importance scores.

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- In a Random Forest, splitting variables are determined by maximal information gain.
- GRRF uses a regularized information gain that penalizes variables that are not already in the feature set.
- The regularization parameter $\gamma \in [0, 1]$ is calculated from the variable importance scores of a preliminary Random Forest.

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- GRRF models were constructed for each pathway, and pathways were then ranked according to OOB error rate.

Breast Cancer Results

Pathway	Length	Gamma	Error
Glycolysis-Gluconeogenesis	68	0.10	0.022
BC Downregulated of MTA-3 in ER-negative Breast Tumors	19	0.15	0.029
BC GATA3 Participate in Activating the Th2 Cytokine Genes Expression	21	0.05	0.031
Pentose Phosphate	22	0.05	0.051
Fructose and Mannose Metabolism	39	0.05	0.055