

Inferring Novel Functional Links between Different Metabolic Pathways from Genomic Associations - (session: Comparative Genomics and Molecular Evolution)

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The way the metabolic pathways are represented is usually based on information derived from biochemical and physiological studies, which mainly focus on the direct interactions between metabolites but tend to miss the wide-ranging connections. New and intriguing associations between apparently unrelated proteins are now inferable from comparative analyses of localization and distribution of the corresponding genes in different genomes. Inferring functional associations between proteins is based on the evidence that, during evolution, genes functionally associated are subjected to a similar selection pressure. As a result of this pressure, they tend to have the same species distribution (same phylogenetic profile), to be located in close proximity within the genome, particularly in prokaryotes (gene neighborhood) or to be fused together (gene fusion). STRING is an integrated database, which collects all the genomic evidences for functional links between proteins. Additionally, it offers a benchmarked scoring scheme to integrate the different association evidences and gives a confidence value for each prediction. Using the STRING collection as the starting database of gene associations, we analyzed all the predicted links between two Clusters of Orthologous Groups (COGs) associated to two unrelated metabolic pathways as mapped in the KEGG database and with a confidence value threshold of 0.700. The thus defined dataset comprises 132 associations, 54 of whose are already known in literature but not reported in the KEGG database, 40 can be attributed to a lack of resolution in the orthology detection, and 38 are novel and previously undescribed associations. Interestingly, the 38 binary associations can be organized in 8 main groups, each linking two pathways. From the analysis of these 8 novel connections, new and interesting hypotheses on metabolic pathways interactions and evolution can be derived.