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Metabolic Network Analysis: Implication And Application

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Availability

Pathway Alignment Tool (PAT) executables are available upon request; Pathway Hunter Tool (PHT) is available on http://www.pht.uni-koeln.de

Local metabolic demand and supply regulate network components and control their activity globally. The use of metabolite structural information to calculate the shortest path generates valid biochemical connectivity [1]. We introduce a new concept of "load points" for identifying and empirically ranking the important points (metabolites/enzymes) in the network. The load point analysis provides a global insight into the metabolic network, which cannot be obtained from connectivity information or metabolic concentration data. We propose a new computational model based on extended graph theory to find "Choke point (CP)" and "Load point" enzymes (enzymes that uniquely consume or produce a certain metabolite in the network) [2]. Identifying such enzymes is the key to network-based potential drug targeting [3]. We obtained few potential drug targets based on the "choke point" analysis of the network in the malarial parasite *Plasmodium falciparum* and pathogenic bacterium *Helicobacter pylori*. A comparative study was performed between human network and pathogenic network. Each potential target is ranked by its load value and results were divided in sub-classes based on the homology. This was done in order to make our results biologically more meaningful. Since this method screens the entire pathogenic network, it is more valuable than other existing methods which report the potential target by looking at specific pathways or certain biological activity like reverse transcriptase in case of HIV. These modules are implemented in Pathway Hunter Tool (PHT) and available via web.

A new algorithm to perform metabolic pathway alignment (based on the shortest path) highlights the conserved (isoenzmes) and variable connectivity (alternate paths) in various genomes. Gibbs free energy (G°) [4][§], enzyme connectivity and enzyme occurrence matrix was used to rank the aligned pathways. Gaps (insertion and deletion) can be allowed during the alignment for obtaining more flexible results since most of the annotated networks have missing links. This method highlights the application and implication of metabolic networks [5,6] and it also suggests enzymes for "hole filling" in the metabolic network. This module is implemented in Pathway Alignment Tool (PAT).

[§]For bringing the molecules into the correct standard state at pH 7, see: ChemAxon Ltd., Máramaros köz 3/a, Budapest, 1037 Hungary.

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