

The Edinburgh human metabolic network reconstruction

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Extended abstract

Many Human diseases are caused by or resulted in an abnormal metabolic state. Detecting the unusual level of certain specific metabolites in a patient's blood or urine has long been established as an effective method to identify biomarkers for diagnosing particular diseases. Recent rapid developments of advanced metabolomics technology is opening up new horizons as thousands of metabolites can be measured simultaneously, providing a much more comprehensive assessment of a patient's health status. To better understand the huge amount of metabolomics data, a high quality human metabolic network which links the change of metabolite concentration with the corresponding enzymes and genes is necessary.

In this poster, we presented a high quality human metabolic network reconstructed by integrating genome annotation information from different databases and metabolic reaction information from literature. The main processes for the reconstruction of the human network are shown in Figure 1. A preliminary network was first reconstructed by integrating genome annotation information from different databases such as Entrez gene, KEGG, HGNC and Uniprot. Then the genome based network was merged with the literature based network from EMP by matching compounds in the two networks. The integrated network was further consolidated and complemented with information obtained directly from literature. The final network contains more than 2000 metabolic genes and nearly 3000 reactions.

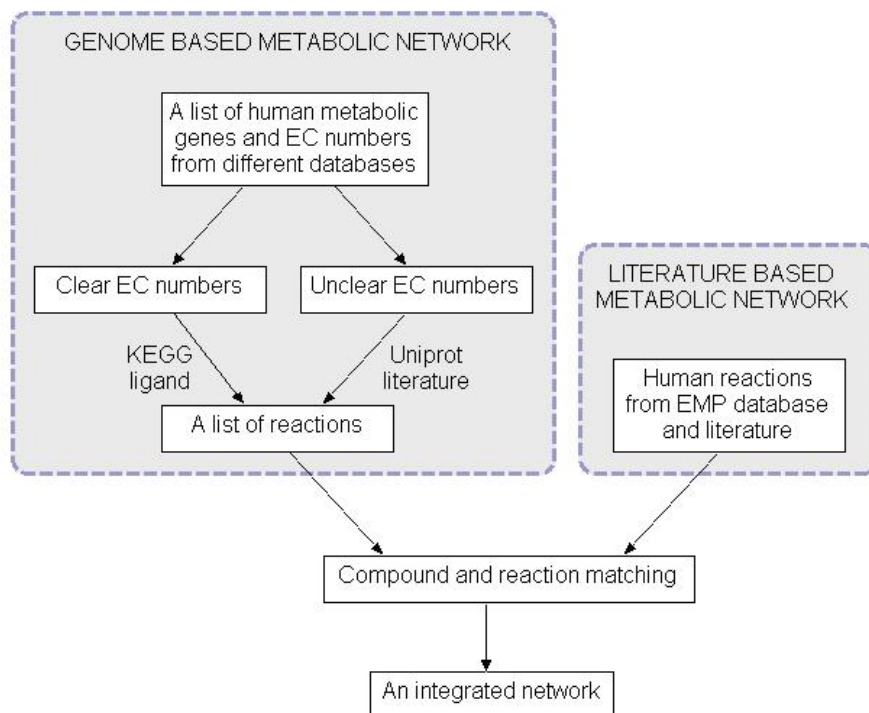


Figure 1: Processes for the reconstruction of the high quality human metabolic network.

To better understand the organization of the human metabolic network, we reorganized the reactions into about 70 human specific metabolic pathways according to their functional relationships and manually drew all the pathways in Edinburgh Pathway Editor (EPE) for visualization. The tyrosine derived monoamines metabolism pathway is shown in Figure 2 as an example. Based on the connection with the central metabolites (in glycolysis, Pentose phosphate pathway and TCA cycle pathway), we classified the metabolites as exchangeable, degradable, and based on pathway analysis. This classification leads to the confirmation of the bow-tie connectivity structure from a functional rather than structural point of view.

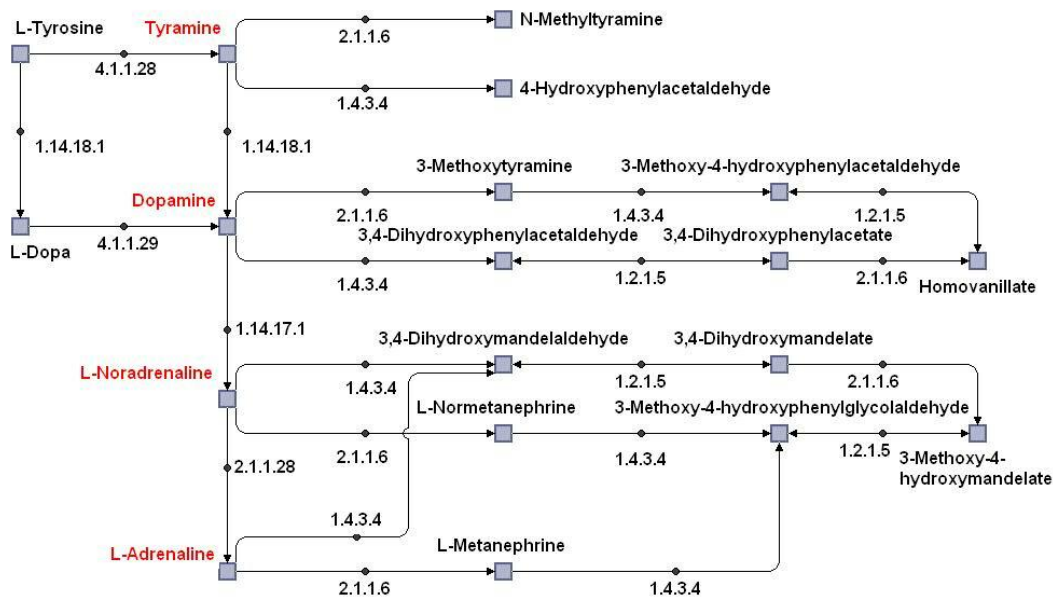


Figure 2: Metabolic pathways for the tyrosine derived monoamine neurotransmitters.

A main objective of human metabolic network analysis is to see how it is related with human disease. To examine this, we obtained diseases and drugs information from OMIM and DrugBank. More than half of the genes in the network are related with one or more human diseases in the OMIM database. More than 300 of them have been selected as drug targets according to the information in DrugBank. By checking with literature, we found that many metabolites are signal metabolites which can bind to certain protein receptors and through signal transduction pathways affecting the expression of many genes (for example, the four metabolites in red colour in Figure 2). The dysfunction of the enzymes in the synthesis and degradation pathways of these metabolites often leads to disease because of the resulting abnormal concentration of these metabolites. Consequently, these enzymes are often selected as drug targets. In Figure 2, enzymes 1.4.3.4, 4.1.1.28 and 2.1.1.6 are all drug targets.