Genome-scale reconstruction of the human astrocyte metabolic network

Martín-Jiménez C.A.

Salazar-Barreto D.

Barreto G.E.

González J.

Astrocytes are the most abundant cells of the central nervous system; they have a predominant role in maintaining brain metabolism. In this sense, abnormal metabolic states have been found in different neuropathological diseases. Determination of metabolic states of astrocytes is difficult to model using current experimental approaches given the high number of reactions and metabolites present. Thus, genome-scale metabolic networks derived from transcriptomic data can be used as a framework to elucidate how astrocytes modulate human brain metabolic states during normal conditions and in neurodegenerative diseases. We performed a Genome-Scale Reconstruction of the Human Astrocyte Metabolic Network with the purpose of elucidating a significant portion of the metabolic map of the astrocyte. This is the first global high-quality, manually curated metabolic reconstruction network of a human astrocyte. It includes 5,007 metabolites and 5,659 reactions distributed among 8 cell compartments, (extracellular, cytoplasm, mitochondria, endoplasmic reticle, Golgi apparatus, lysosome, peroxisome and nucleus). Using the reconstructed network, the metabolic capabilities of human astrocytes were calculated and compared both in normal and ischemic conditions. We identified reactions activated in these two states, which can be useful for understanding the astrocytic pathways that are affected during brain disease. Additionally, we also showed that the obtained flux distributions in the model, are in accordance with literature-based findings. Up to date, this is the most complete representation of the human astrocyte in terms of inclusion of genes, proteins, reactions and metabolic pathways, being a useful guide for in-silico analysis of several metabolic behaviors of the astrocyte during normal and pathologic states. © 2017 Martín-Jiménez, Salazar-Barreto, Barreto and González.

Astrocyte

Genomic-scale metabolic network

Ischemia

Model

Systems biology

acetoacetic acid

adenosine triphosphate

arginine

asparagine

carbon dioxide

cystine

glucose

glutamic acid

glutamine

glycine

histidine

isoleucine

leucine

linoleic acid

linolenic acid

lysine

methionine

ornithine

oxygen

proline

pyruvic acid

serine

threonine

tyrosine

valine

Article

astrocyte

brain ischemia

brain metabolism

brain mitochondrion

cell nucleus

cytoplasm

endoplasmic reticulum

energy metabolism

extracellular space

genomics

Golgi complex

human

lysosome

mathematical model

metabolic rate

metabolite

peroxisome