An Interactive Digital Pathway Map: A Resource for Interpreting Metabolomic Data

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Introduction

Interpretation of mass spectrometry-based metabolomic data in the context of biochemistry requires a high level of familiarity with metabolic pathways. Metabolomic investigators need to know specific details about the particular pathway of interest and understand how it is integrated within the bigger picture of comprehensive metabolism. Our objective is to provide an all-in-one resource for biochemical interpretation of metabolomic data. Contrary to physical pathway maps, we have created a digital version of comprehensive metabolism that can be viewed at any level. Metabolism can be viewed at the aerial perspective or, with multiple mouse clicks, at the "zoomed-in" molecular level of specific metabolic reactions. This resource can also be used effectively for teaching metabolism in the classroom.

Methods

We developed our metabolic map by reviewing and compiling information from metabolic pathway maps and databases, including METLIN and KEGG. We organized metabolic reactions on a systems-level by identifying those taking place in somatic cells, renal cells, myocytes, adipocytes, enterocytes, hepatocytes, and neurons. The reactions were digitally reconstructed in their specified organ cells and subcellular locations. We created a systems-level map using the reconstructions and the Google Maps API. Metabolites were grouped by their chemical properties and reactions by their pathways and cycles. We used this information to construct layers of complexity, allowing users to explore the depth of metabolism without being overwhelmed (see figure below). Additionally, users can view pathways at the systems level by theme (e.g., oxidative pathways, single-carbon pathways, etc.).

Preliminary data

Our interactive digital platform called Connex, currently in the beta development stage, is being used by our laboratory as a research tool in addition to students of Dr. Gary Patti's General

Biochemistry II course at Washington University in St. Louis. We will highlight the efficacy of our digital platform for interpreting metabolomic data in the context of biochemistry by using a dataset acquired from cancer cells. These data include both conventional LC/MS-based metabolomic data revealing pool sizes in addition to LC/MS-based metabolomic data from samples that have been enriched with various stable isotopes to learn about alterations in pathway dynamics. Together, these results suggest various points of dysregulation in basic metabolism. We will visualize these specific alterations within our digital map at a detailed level, showing chemical structures, free energies, and background information about the reactions compiled from multiple resources. We will also show how these results can then be simultaneously visualized at the systems level with just a few mouse clicks.

Novel aspect

To our knowledge, this is the only digital, systems-level metabolic map that arranges pathways by levels of complexity and detail.