The PM Map – A *P*roteomic and *M*etabolomic Data Visualization Network

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Αβστραχτ

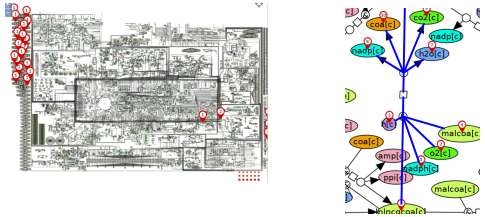
Metabolic pathways are developing as accurate markers of biological processes like the onset of disease. A current challenge in understanding these processes has been to find the exact mutations or protein changes that lead to up or downregulation of metabolic pathways[2]. The goal of this project was thus to develop a "Proteomic-Metabolomic" or "PM" Map, which visualizes both human metabolic reactions and proteins used in them. This tool was developed using data from ReconMap3, a currently available metabolism network from the Recon database. Parsing methods using Python programming were used to retrieve all of ReconMap's listed metabolites and Recon's gene products, and they were loaded onto Cytoscape, a network designing software. Finally, data on metabolite and protein abundance collected from proliferating and quiescent cells were displayed on the map to compare their activated metabolic pathways. Overall, the PM Map provides a promising method to understand changes in protein and metabolic activity in biological processes and diseases like cancer.

Ιντροδυχτιον

Mutation → **Functionality loss in protein/ enzyme** → **Abnormal activation/ deactivation of metabolic reaction(s)**

- Ex: Isodoro et. al developed an index that helps compare protein expression in normal vs cancerous tissues. They were able to correlate changes in glycolysis regulation to differentially expressed glycolytic proteins between the two tissue types.[1]
- Recon3D database was developed to link metabolic pathways with the genes and protein involved in them.
- ReconMap3 was also developed to help visualize these reactions, but does not visualize protein data.

ReconMap3 With Example of a Selected Pathway



Οβφεχτιωεσ

Motivation: How can we easily visualize activated/deactivated metabolic pathway(s) and mutations at the same time in a diseased or healthy tissue?

Goal of project: Expand ReconMap:

1. Reproduce ReconMap's reactions on Cytoscape software but filtering redundant metabolites
2. Adding proteins from Recon to PM Map as new nodes

Μετηοδσ

From XML Files to Visual Network

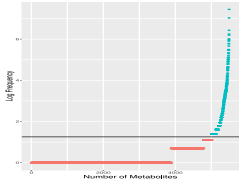
<species metaid = "s927 id = "s927 name = 34hpp[c]

ReconMap XML File → **XML File Parsing Using Python**

Name	ID	Species ID
34hpp[c]	sa1620	s927

Metabolite Name Added to a Node Table

Node Table → **Remove repetitive metabolites**



Frequency Plot of Repetitive Metabolites (In Blue)

Retrieve Corresponding Reaction IDs From XML file

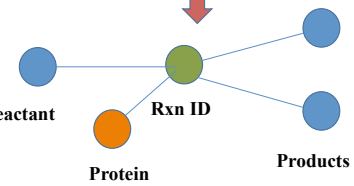
<reaction metaid = "r_HMR_6770" id = "r_HMR_6770"

ReconMap XML File → **Produce Edge Table with Metabolites and Reaction IDs**

Source Node	Target Node
s927	R_HMR_6770

Edge Table With Metabolite and Matching Reaction ID

Edge Table → **Load Tables Onto Cytoscape Software, Add Proteins From Recon XML File**



PM Map Format

Ρεσυλτσ

Application of PM Map to Experimental Data

- Study: Coloff, et. al – "Differential Glutamate Metabolism in Proliferating and Quiescent Mammary Epithelial Cells" [3]

Goal: Determine Metabolic Differences Between Proliferating and Quiescent Cells

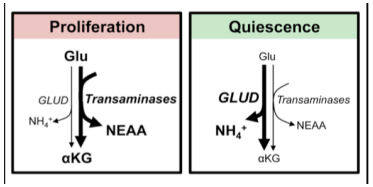
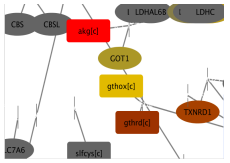


Diagram from study showing mechanism for proliferating cells deriving amino acids (NEAAs) used in growth[3]

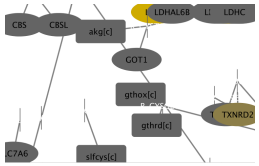
Methods:

- Researchers developed 3D culture of maturing mammary epithelial cells
- Collected protein and metabolite samples as they transitioned from proliferation (day 5) to quiescence (day 15)

PM Map After Loading Sample and Abundance Data



Day 5 (Proliferation)



Day 10 (Quiescence)

Potential Role of PM Map

- Blocking a transaminase in cancer cells can serve as form of therapy
- However, knowledge of overall metabolic pathways needed first because of potential flux of other pathways that support tumor growth
- PM map can serve as a way to visualize entire pathways surrounding the detected metabolites/proteins
- May help researchers find more effective protein targets for cancer therapy

Ρεφερενχεσ

1. Brunk, Elizabeth, et al. "Recon3D enables a three-dimensional view of gene variation in human metabolism." *Nature biotechnology* 36.3 (2018): 272.
2. Isidoro, Antonio, et al. "Breast carcinomas fulfill the Warburg hypothesis and provide metabolic markers of cancer prognosis." *Carcinogenesis* 26.12 (2005): 2095-2104.
3. Coloff, Jonathan L., et al. "Differential glutamate metabolism in proliferating and quiescent mammary epithelial cells." *Cell metabolism* 23.5 (2016): 867-880.
4. Sompairac, Nicolas, et al. "Metabolic and signalling network maps integration: application to cross-talk studies and omics data analysis in cancer." *BMC bioinformatics* 20.4 (2019): 140.

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