Multi-omics reaction pattern recognition reveals signatures of mitochondrial dysfunction

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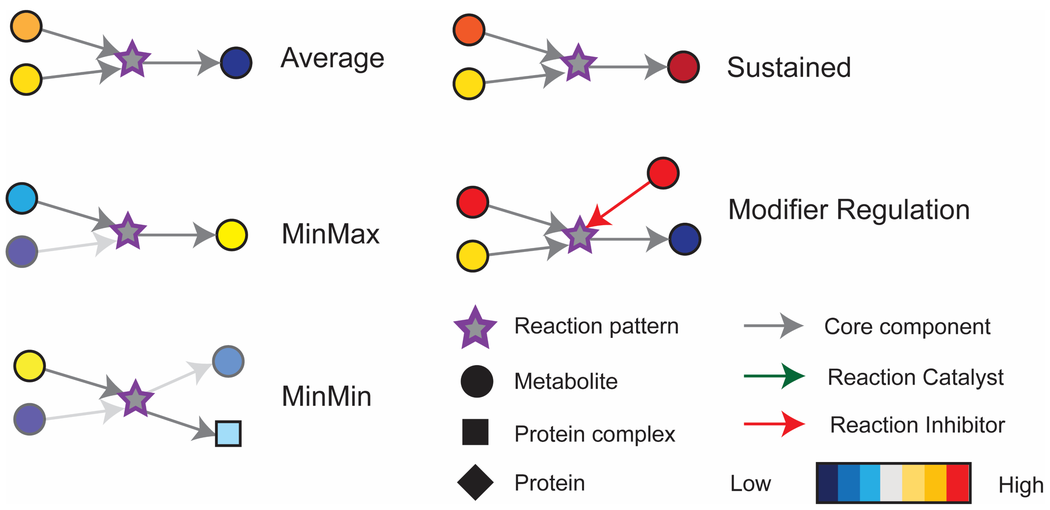
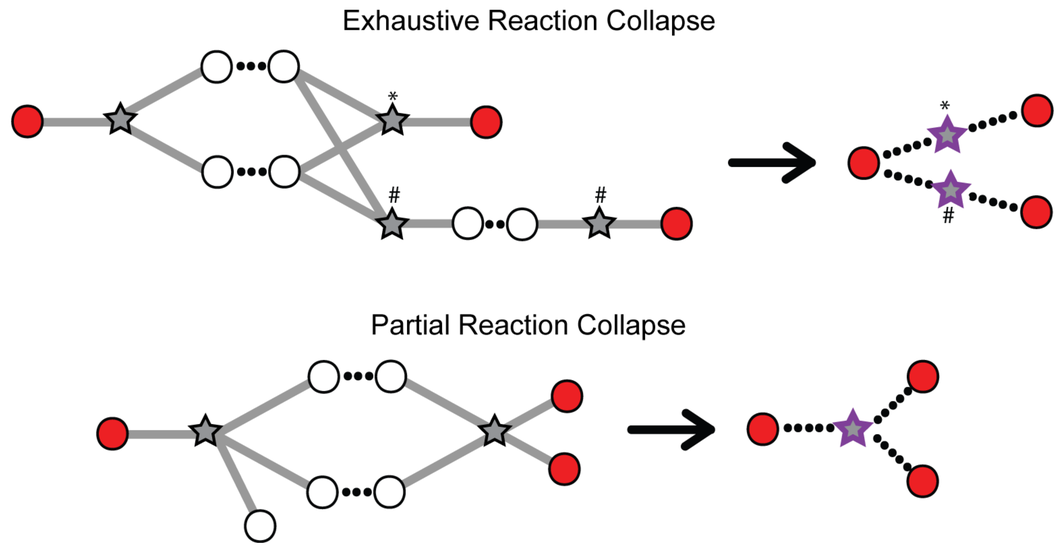
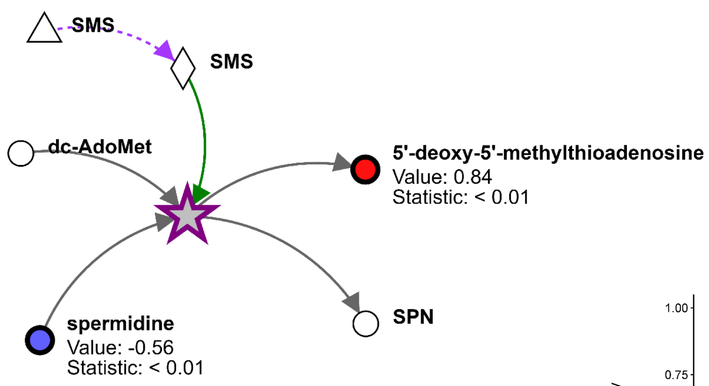
Metaboverse offers the ability to perform comprehensive reaction pattern searching across the biological network.

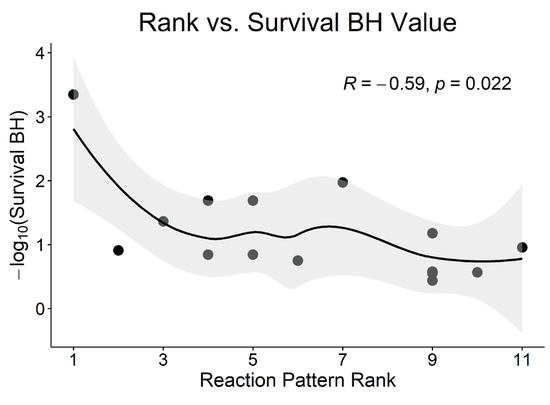


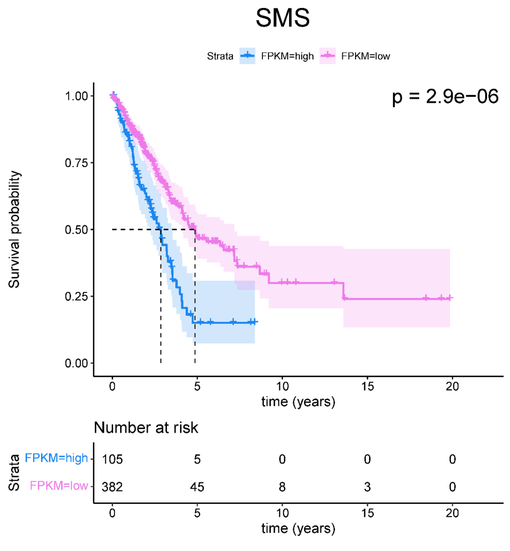
Metaboverse enables the identification of such patterns across multiple reactions where data are missing in intermediate reaction steps.



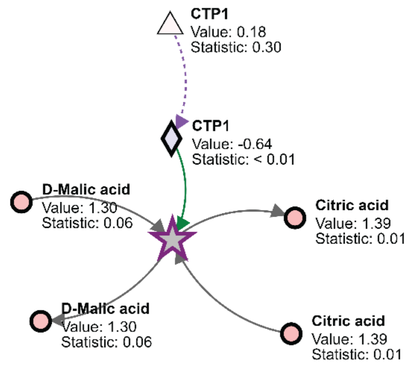
The top reaction pattern result from Metaboverse in a paired patient tumor/non-tumor lung adenocarcinoma steady-state metabolomics datasets reveals regulatory action catalyzed by spermine synthase (SMS). In the TCGA LUAD RNA-seq dataset, higher expression of SMS also corresponded with poorer patient survival. We noticed that these correlations held with the other top-ranking reaction patterns' enzyme rank and patient survival.



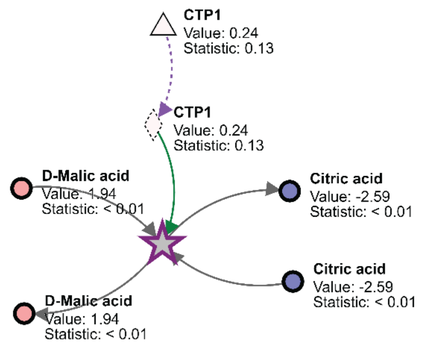




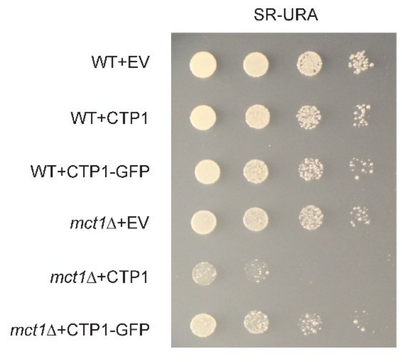
In an RNA-seq, proteomics, steady-state metabolomics experiment in a model of mitochondrial dysfunction, where we knock out the mitochondrial fatty acid synthesis (mtFAS) pathway by knocking out *MCT1*, we noticed a top-ranking reaction pattern revolving around citrate export (via Ctp1). Overexpression of *CTP1* in the *mct1*Δ background showed a specific phenotype, suggesting that *CTP1* downregulation was an adaptation to mitochondrial dysfunction. *CTP1* expression correlated with biosynthetic pathways across >6000 S. cerevisiae RNA-seq datasets.

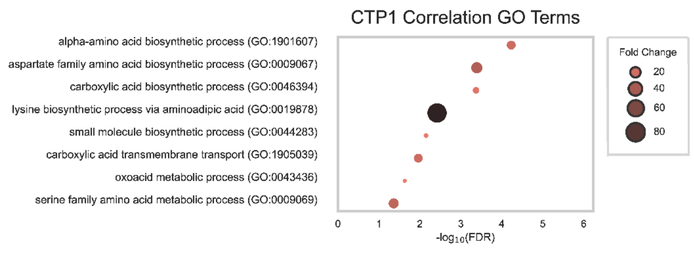


log₂(*mct1*Δ / WT) (12 hr)



log₂(*mct1*Δ / WT) (3 hr)





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References:
Wikoff, 2015, *Cancer Prev Res*; Berg, 2020, *bioRxiv*; Uhlén, 2015, *Science; Van Vranken, 2018, Mol. Cell*

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