Case study: viral activation of immune cells

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Predicting Network Activity from High Throughput Metabolomics

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Abstract

The functional interpretation of high throughput metabolomics by mass spectrometry is hindered by the identification of metabolites, a tedious and challenging task. We present a set of computational algorithms which, by leveraging the collective power of metabolic pathways and networks, predict functional activity directly from spectral feature tables without a priori identification of metabolites. The algorithms were experimentally validated on the activation of innate immune cells.

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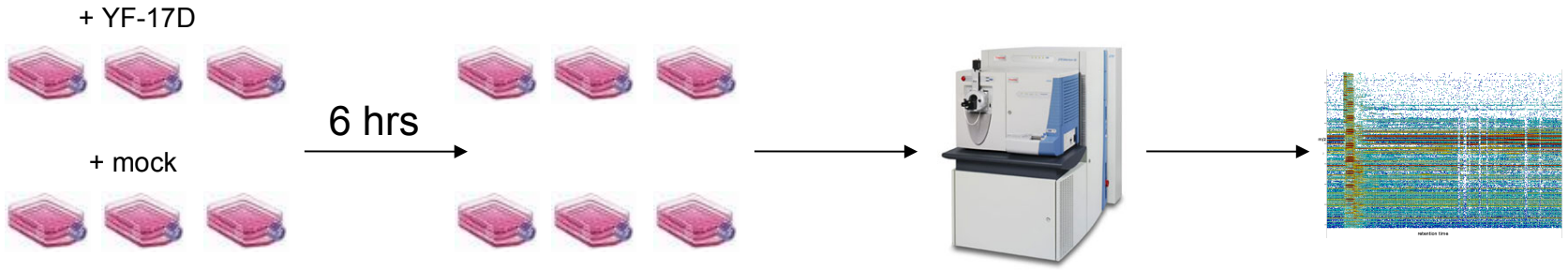
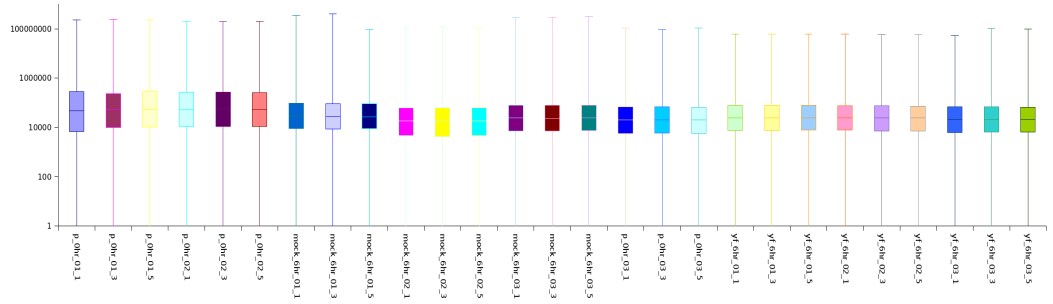
Experiment

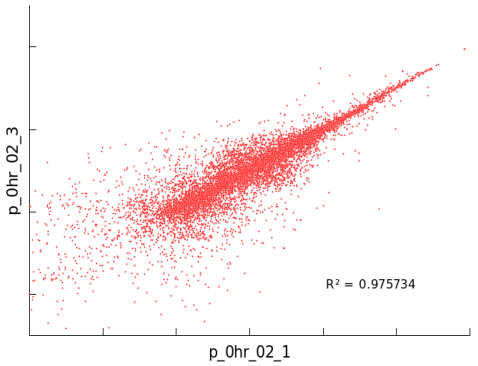
Monocyte derived dendritic cells (moDC)



QA: total ion counts are similar among samples

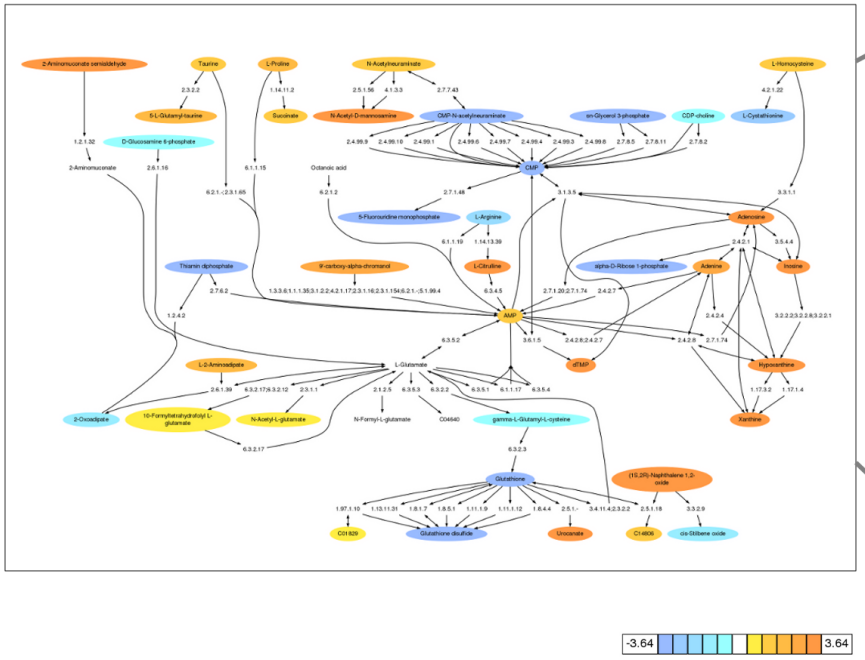


technical replicates, 10,000 features

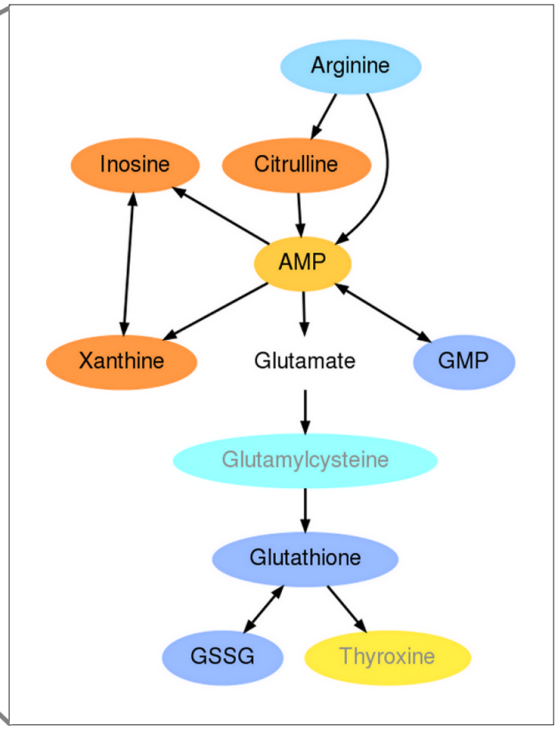


Mummichog: viral activation of immune cells

A

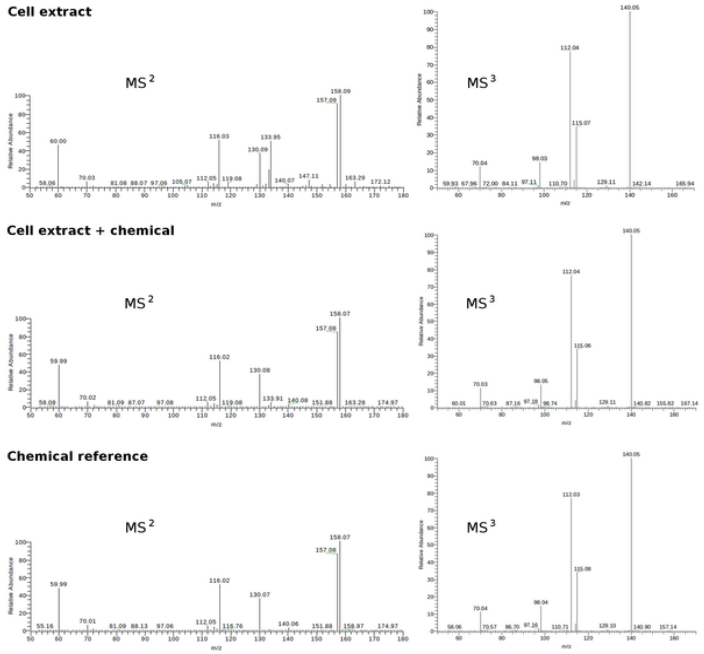


B

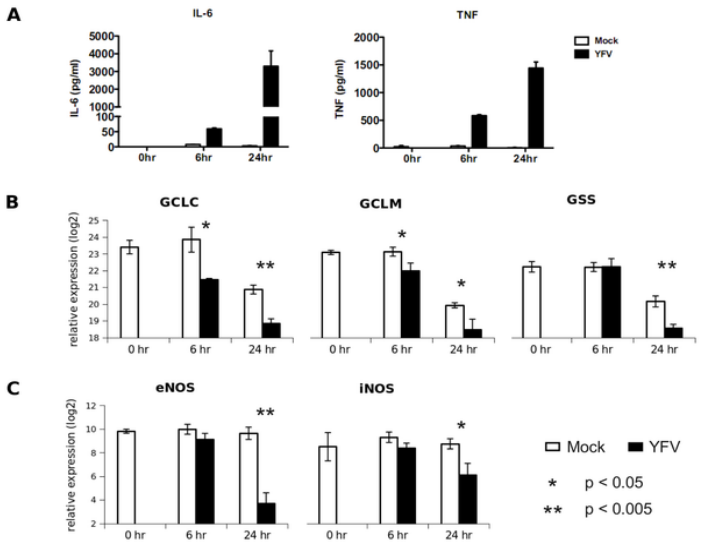


Li et al. 2013. PLoS Computational Biology. 9:e10031323

Experimental validation of *mummichog* prediction



Tandem mass spectrometry confirmed 9/11 metabolites



Gene expression supported GSH/GSSG depletion and Arg/Cit conversion

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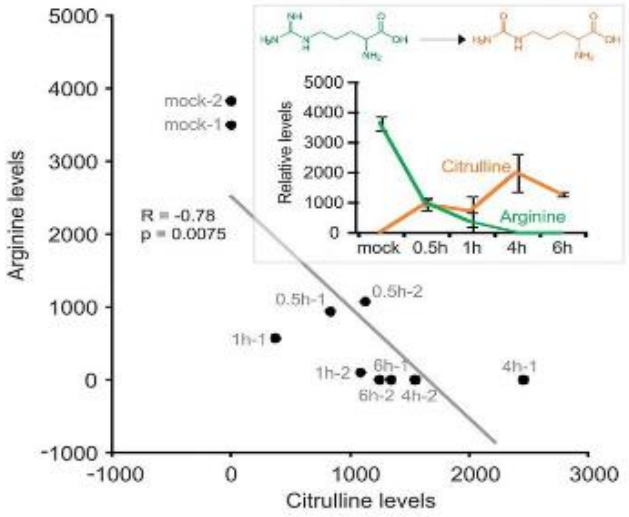
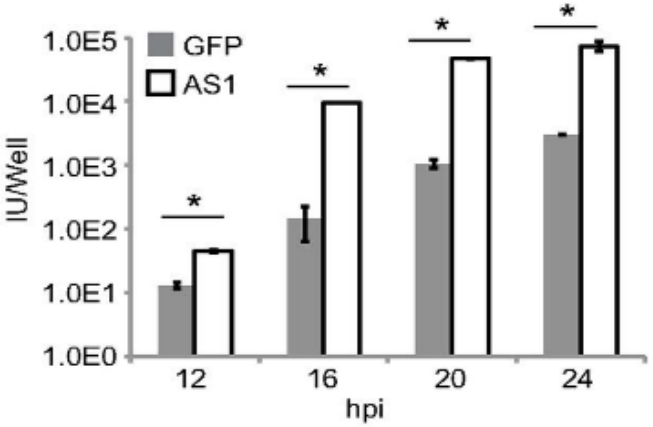
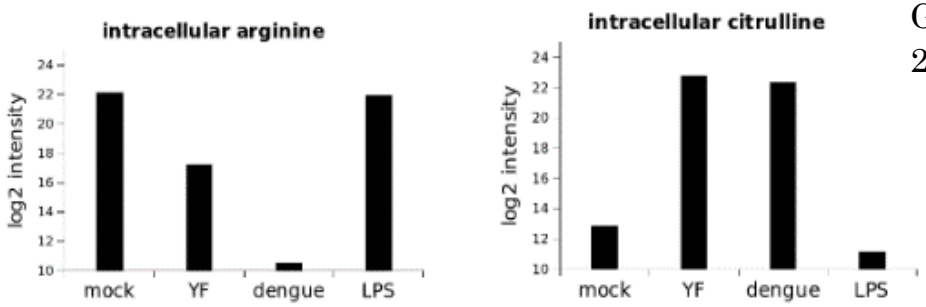
Arginine as master regulator of viral response



Ravindran et al. 2014. Science 343:313



Argininosuccinate synthetase 1 knockdown led to increased replication of HSV-1.
Grady, Purdy, Rabinowitz & Shenk. 2013. PNAS 110:E5006.



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