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An Integrated Systems Approach to Deconstructing Glycosylation

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AN INTEGRATED SYSTEMS APPROACH TO DECONSTRUCTING GLYCOSYLATION

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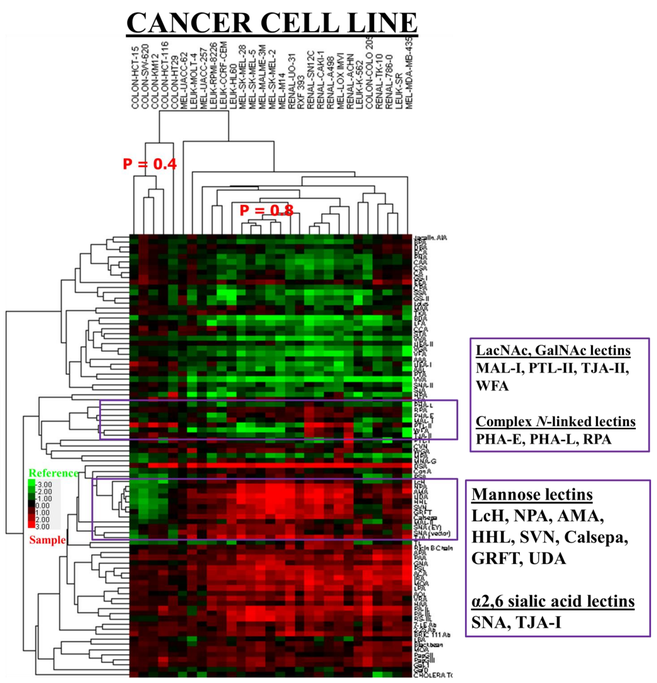
Lectin Microarray Results



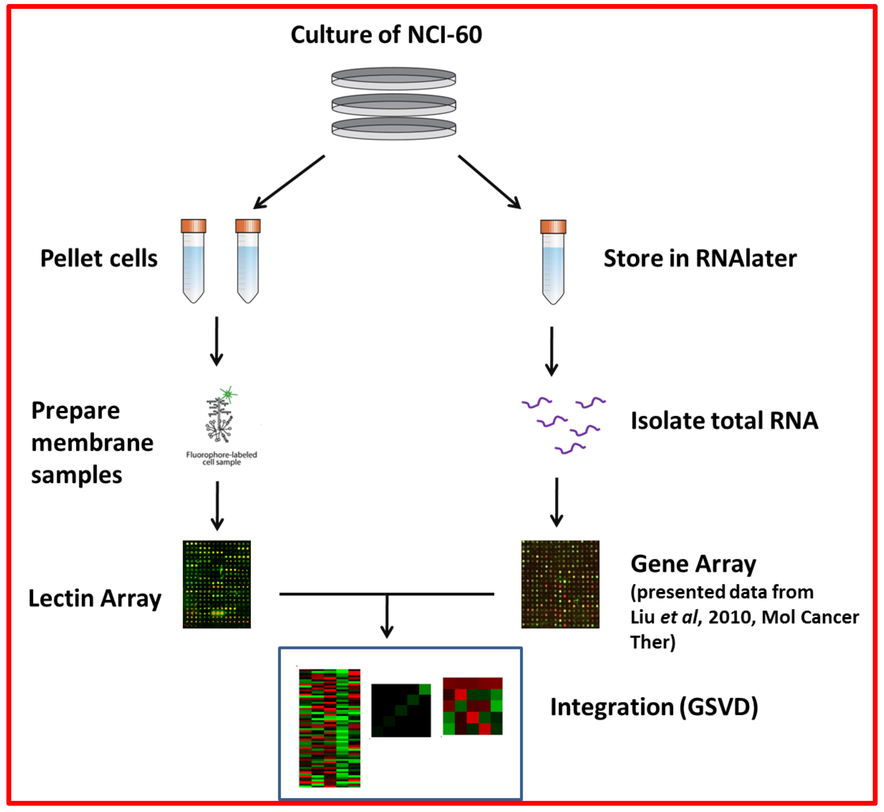
CANCER TYPE	GLYCAN SIGNATURE	EXAMPLE STRUCTURES
Colon	Decreased in high mannose and α2,6 sialic acid Increased LacNAc, complex *N*-linked	
Melanoma	Increased in high mannose and α2,6 sialic acid Decreased LacNAc, complex *N*-linked	
Renal	Increased in high mannose and α2,6-sialic acid Increased LacNAc, complex *N*-linked	
Leukemia	No distinct signature based on these data	

CONCLUSION: The lectin microarray platform is suitable to identify distinct, carbohydrate-based cell surface features which differentiate certain cancer tissue types.

GOAL: To deconstruct the regulation of the complex, non-template driven synthesis of carbohydrates using high-throughput microarray methods

STRATEGY: Isolate matched glycomic and transcriptomic samples from the NCI-60 panel, or metabolically perturbed cell lines and subject to a "systems biology" approach of lectin and genomic microarray followed by the decomposition and integration of the data sets

Experimental Workflow



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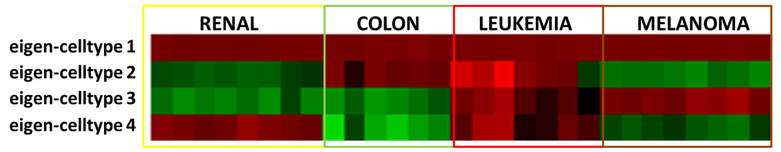
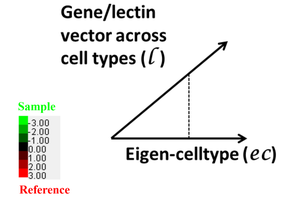
Decomposition Analysis

GSVD Matrix

$$M = U\,\Sigma\,V^{T}$$

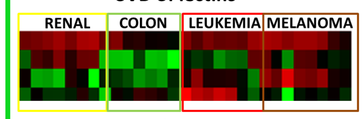


Projection correlation = $\mathcal{C}\,||\,ec$

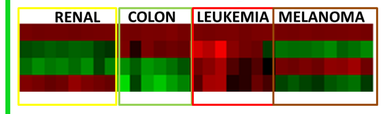


eigen-celltype 2	APA, Con A, DSA , GNA, LcH, LPA, NPA, PAA ,SNA (vector), UDA, HHL, MAL-II, CVN, SVN, GRFT, ACA, PSL, TJA-I, AMA, Calsepa, IRA, RS-IIL	High mannose, α2,6 sialic acid (*N*-linked)
eigen-celltype 3	VRA, PTL-II, HAA	Terminal GalNAc (*O*-linked)
eigen-celltype 4	TKA, PapGII	Glycolipid

SVD of lectins



GSVD of lectins-genes



CONCLUSION: Decomposing the lectin and gene expression data reveals 3 unique glycosylation patterns. *N*-linked expression is inversely correlated, *O*-linked positively. Each eigen-celltype has process specific gene/glycosylation patterns (not shown).

Future Directions

-We have used a "systems" approach to identify regulatory effects on the glycome

-We are now expanding our analysis to include glycomic analysis of the entire NCI-60 panel and genomic analysis with our custom designed arrays

-We are perturbing the metabolic state of select cell lines in order to determine the effect on glycome expression