

**NCI - BSA Meeting
Alliance of Glycobiologists
June 29th., 2010**



Glycomics Resources Funded by NIH

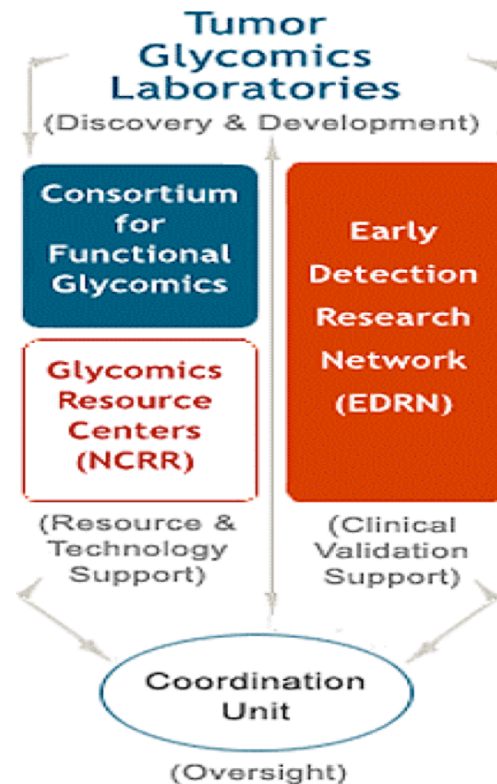
James C. Paulson

Departments of Chemical Physiology and Molecular Biology
The Scripps Research Institute, La Jolla, CA

Resources Available to the Alliance



STRUCTURE of the **ALLIANCE** of **GLYCOBIOLOGISTS** For Detection of Cancer and Cancer Risk



Glycomics Resources Funded by NIH



- **NCI**: Alliance of Glycobiologists (\$15 MM/5 years)
- **NIGMS**: Consortium for functional glycomics (\$75 MM 10 years; 2002-2011).
- **NCRR**:
 - Integrated Technology Resource for Biomedical Glycomics (Univ Georgia: CCRC)
 - Research Resource for Integrated Glycomics (CCRC,)
 - National Center for Glycomics and Glycoproteomics (Univ. Indiana)
 - Resource for Mass Spectrometry in Biology and Medicine (Boston Univ.)
- **NHLBI**: Programs of Excellence in Glycoscience (\$84 MM; 2011-2018).



Integrated Technology Resource for Biomedical Glycomics, Complex Carbohydrate Research Center, University of Georgia

Focus: develop technologies to analyze the changes in cell surface glycan expression and the regulation of these glycan changes during stem cell differentiation; exploit these changes to identify cell-specific markers.

Resource P.I., Michael Pierce

Core 1: Embryonic Stem Cell Platform: **Steve Dalton**

Core 2: Glycoproteomics: **Ron Orlando, Lance Wells, Mike Tiemeyer, Mike Pierce**
Glycosphingolipidomics: **Mike Tiemeyer**

Core 3: Glycotranscriptome Analysis by Kinetic RT-PCR: **Kelley Moremen**

Core 4: Bioinformatics of Glycan Expression: **Will York**

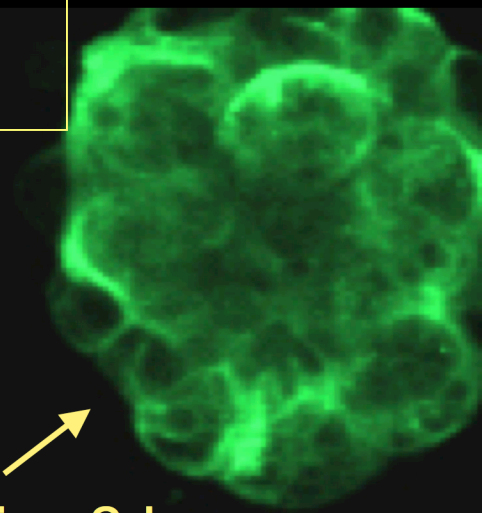
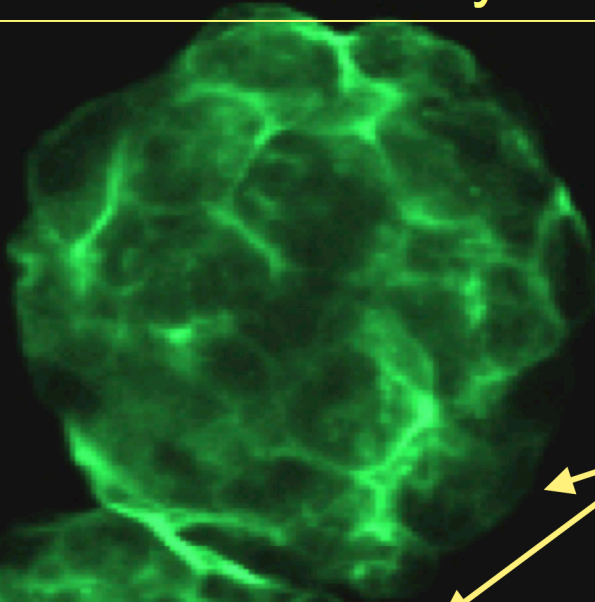
Service and Training: Parastoo Azadi; N- and O-linked analysis of glycoprotein glycans and identification of glycoproteins expressing particular glycans; glycosphingolipid analysis; bioinformatics databases via website

NCRR

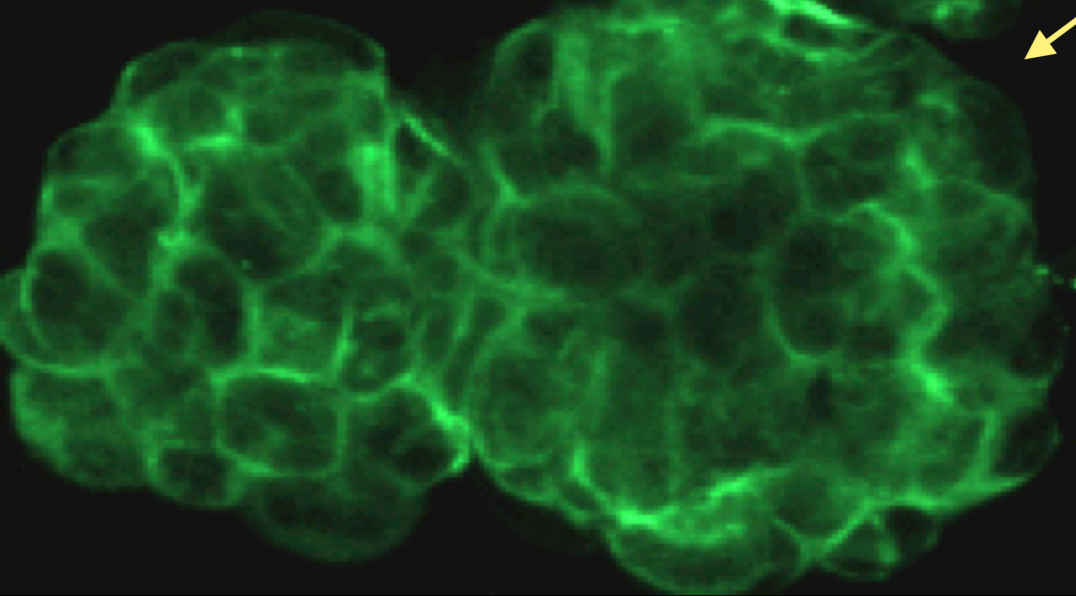
Biomedical
Glycomics

Poly-Sialic Acid is a marker for differentiated embryonic stem cells

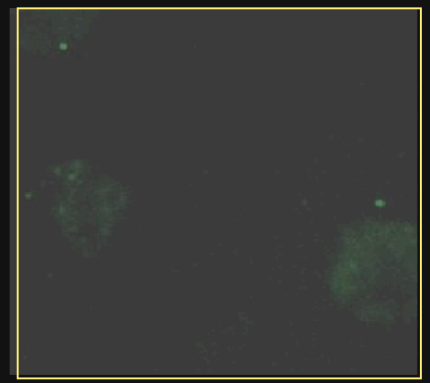
Anti-polysialic acid
antibody staining found
ONLY on embryoid bodies;
also found in some cancer
cells, including melanoma,
SCLC.

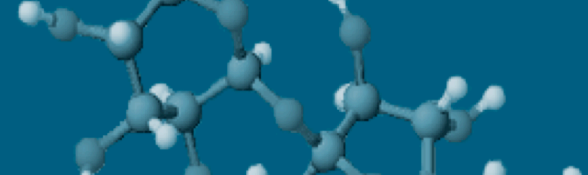


Embryoid Bodies 2d



Embryonic Stem Cells





Consortium for Functional Glycomics

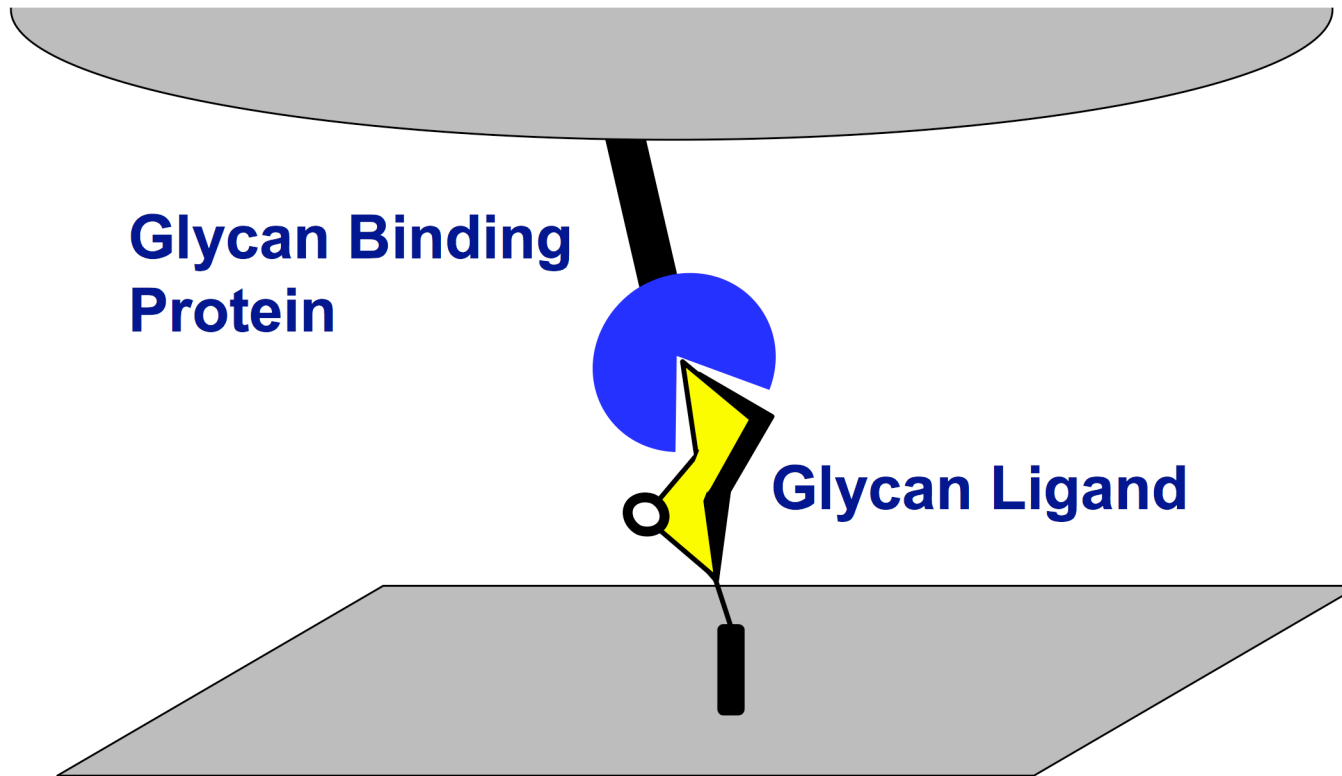
Goal:

Define paradigms by which glycan-binding proteins mediate cell communication

<http://www.functionalglycomics.org>

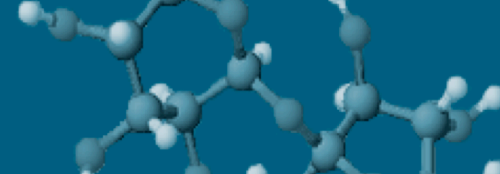


National Institute of
General Medical
Sciences

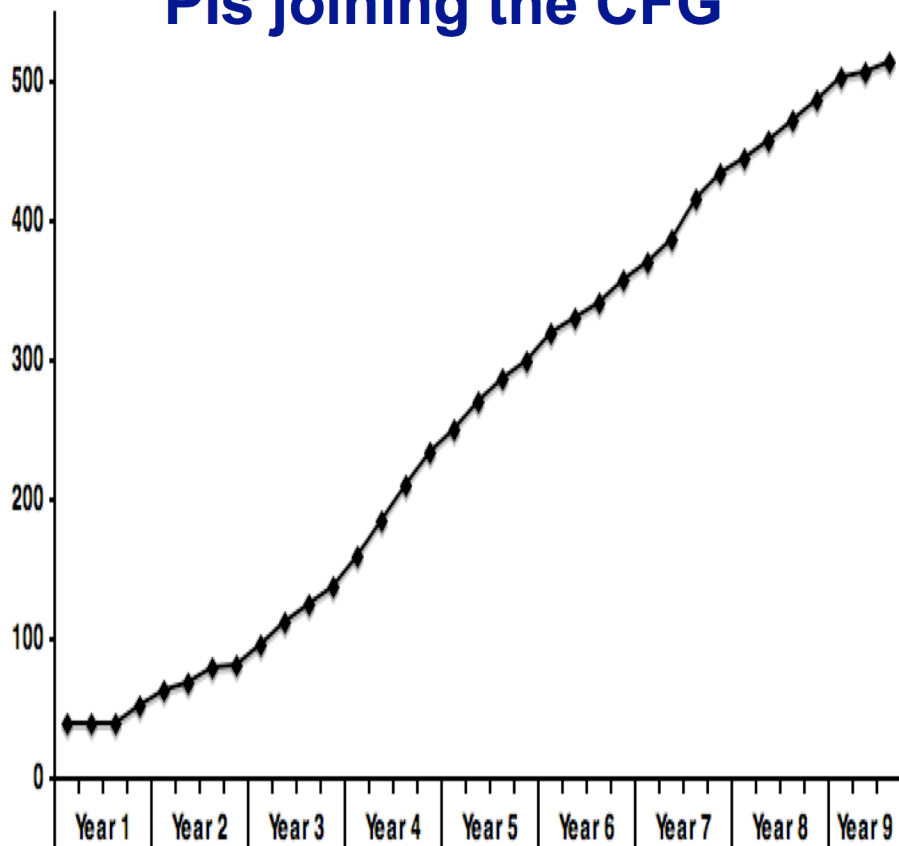


**Glycan Binding
Protein**

Glycan Ligand

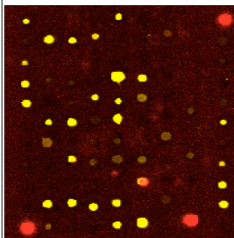


Steady increase in PIs joining the CFG



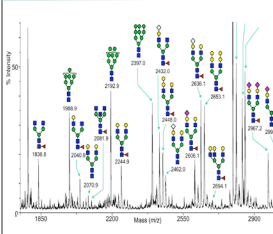
1. **Microorganism recognition of host glycans : Gillian Air**
2. **Immune recognition of glycans : Yvette van Kooyk**
3. **Glycans in immune cell communication : Paul Crocker**
4. **Glycans in development and physiology : John Hanover**
5. **Glycans in cancer biology : J. Taylor-Papadimitriou / Joy Burchell**
6. **Glycans in protein conformation and function : Jim Prestegard**
7. **Analytical glycomics : Mike Tiemeyer**
8. **Chemical synthesis and glycan microarrays : M.G. Finn**
9. **3-D Structural glycobiology : Rob Woods**
10. **Bioinformatics : Will York**

Glycan array and screening



Determine the specificity of your glycan-binding protein on a microarray with ~511 glycoprotein and glycolipid glycans

Glycan Analysis



Profile and characterize the *N*- and *O*-linked glycans from your tissues and cell lines

Mouse knockout strains



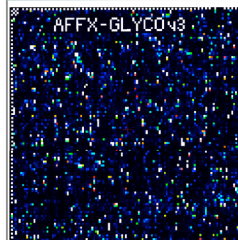
Novel knockout mouse strains with genes ablated for glycan-binding proteins

Carbohydrate compounds



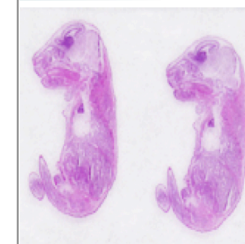
Over 230 carbohydrate compounds available with azido or biotin functional groups

Glyco-gene microarray



Analyze your mRNA on a custom gene microarray including 2,000 human and mouse glyco genes

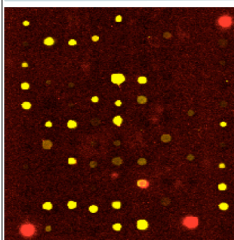
Mouse Phenotype Analysis



Phenotype characterization of mice in the public domain with deleted glycan-binding protein genes

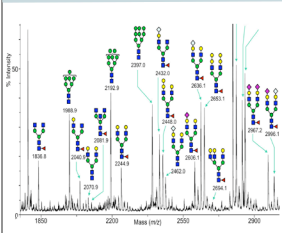
<http://www.functionalglycomics.org>

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Glycan Analysis



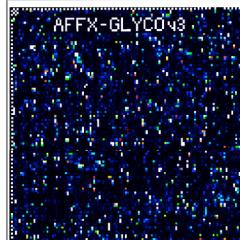
Profile and characterize the N- and O-linked glycans from your tissues and cell lines

Carbohydrate compounds



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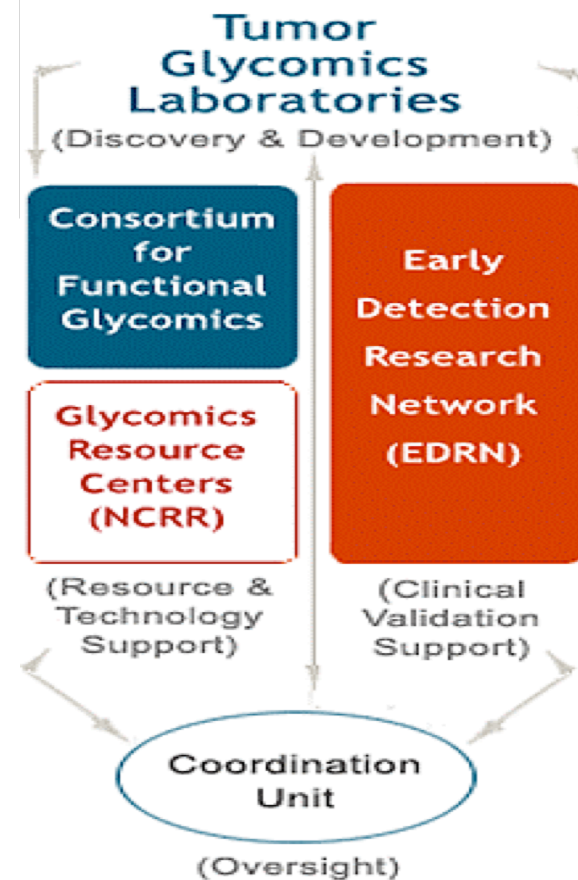
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Analyze your mRNA on a custom gene microarray including 2,000 human and mouse glyco genes

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For Detection of Cancer and Cancer Risk



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Strategy for production of glycan library



Chemical synthesis

Enzymatic synthesis



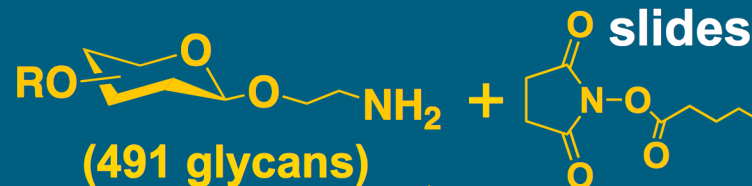
Reducing end Derivatization



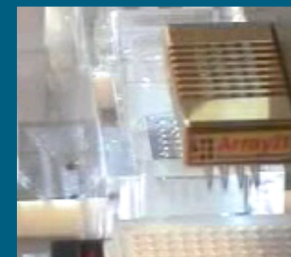
Glycoprotein and Glycolipid Glycans

Glycan Library

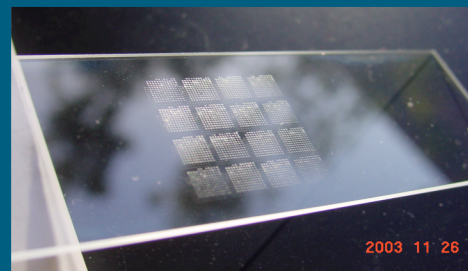
NHS Activated slides



Standard Microarray robotics



Stable Amide Bond

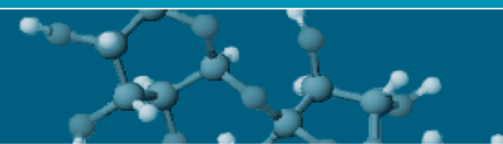


Blixt et al (2004)
PNAS

Glycan microarrays used in alliance tumor glycomics laboratories



- **Ajit Varki** :Detection of anti-Neu5Gc antibodies and urinary Neu5Gc levels for the early diagnosis of cancer.
- **Margaret Huflejt**: Detection of anti-glycan antibody-based signatures of non-small cell lung cancer (NSCLC), mesothelioma, melanoma, and ovarian and breast cancers
- **Denang Wang** : Identification of anti-glycan autoantibody signatures as markers of prostate cancers.
- **Michael Hollingsworth** : Detection of auto-antibodies to glycopeptide epitopes as biomarkers for early detection of pancreatic cancer and adenocarcinomas



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Search by keyword to find CFG data and resources:
(Examples: SNA; galectin-1; influenza; galb1-4GlcNAc)

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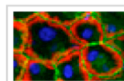
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Last updated: 10 June 2010

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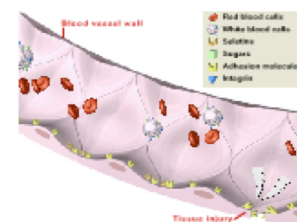


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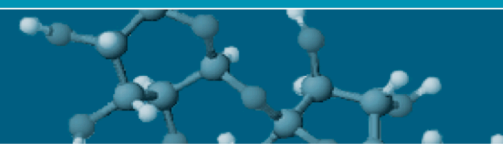
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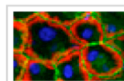
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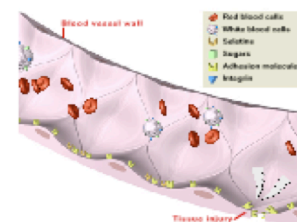
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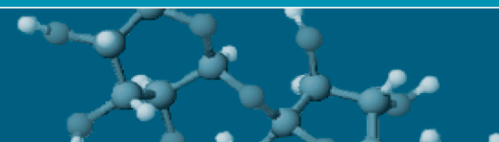
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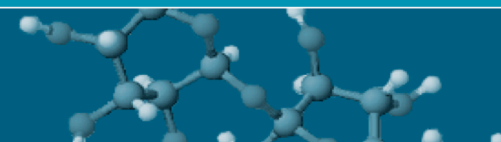
Glycan Profiling: Glycan profiling experiments performed by the Analytical Glycotechnology Core (C) identify the presence of various N- and O-linked glycans in human and mouse tissues. For each species, the data is organized by tissue type.

Gene Microarray: A microarray chip with an up-to-date glycogene list has been produced by the Gene Microarray Core (E) and is being used to screen RNA samples for investigators. The gene list has been highly annotated by Participating Investigators.

Mouse Phenotyping: Results from the Mouse Phenotype Core (G) are presented here. Information on experiments, their summaries and raw downloadable data, are provided.

Glycan Array: Results from high-throughput screening for identifying lectin-ligand interactions performed by the Protein-Carbohydrate Interaction Core (H) are summarized here.

If you are a participating investigator and want to submit a resource request, please click "[here](#)" .

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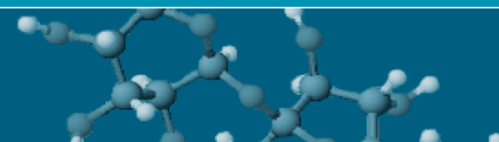
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species
















participating investigator

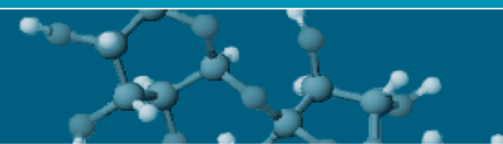
glycan type analyzed

cell type

Here is a listing of all the investigator samples. Each sample entry follows an outline (template) recommended and decided by the core directors. An investigator sample may be added by using the "Add New Sample" link and by choosing the appropriate template determined mutually by the investigator and the core director. Once a sample is added, it is saved in the system, and is available for modification (Edit) or removal (Delete) until the Finalize option is chosen in the operations menu.

Sample Search Results

| Species | Comments | Cell Type | Glycan type Analyzed | Participating Investigator | Data | Resource Request |
|---------|-------------------|-------------|----------------------|----------------------------|--|-------------------|
| Human | Human Neutrophils | Neutrophils | N-Linked | Cummings,Richard D. | View     | cfg_rRequest_1685 |
| Human | Human Monocytes | Monocytes | N-Linked | Crocker,Paul | View     | cfg_rRequest_1686 |
| Human | Human B-Cells | B-Cells | N-Linked | Crocker,Paul | View     | cfg_rRequest_1686 |
| Human | Human T-Cells | T-Cells | N-Linked | Crocker,Paul | View    | cfg_rRequest_1686 |



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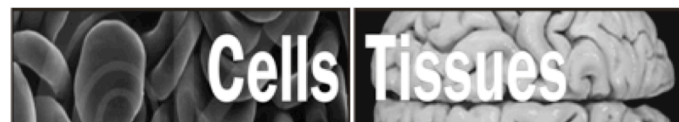
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










participating investigator

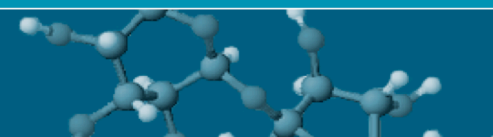
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| Human | Human T-Cells | T-Cells | N-Linked | Crocker,Paul | View    | cfg_rRequest_1686 |



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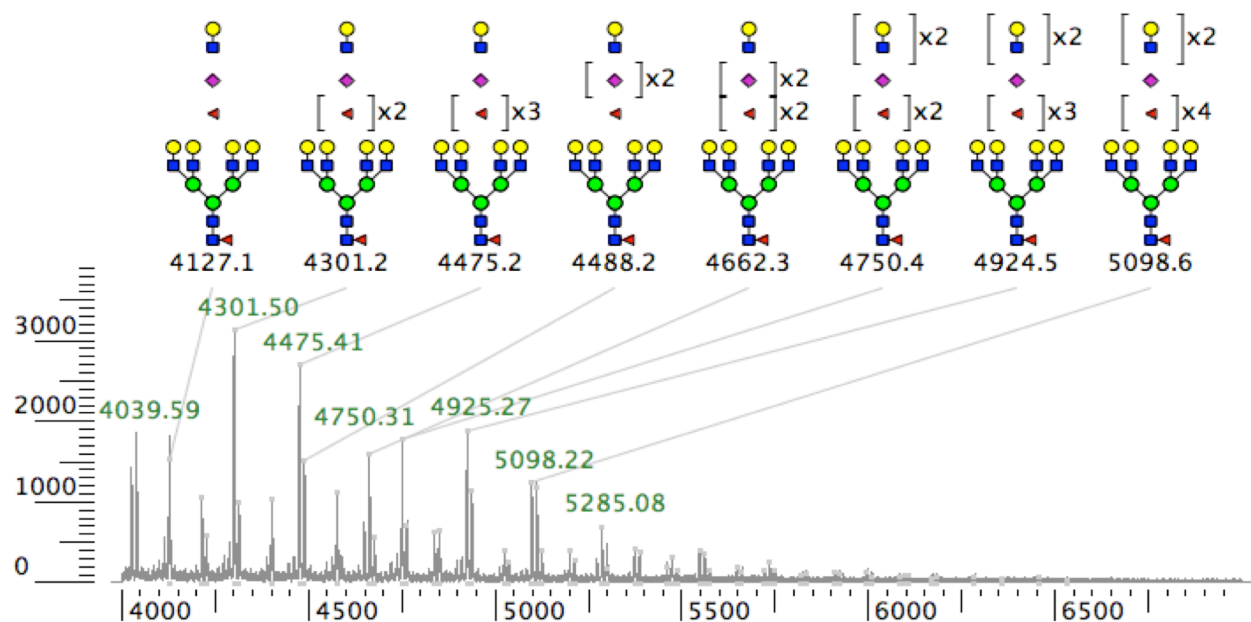
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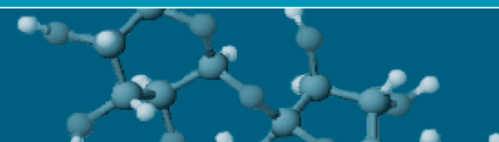
File View Tools Help

Loaded /coreCStatic/allmsdfiles/205_2.msd and /coreCStatic/allmsdfiles/205_2.msa
 mass: 3969.98 ... 7030.02, intensity: 0.0 ... 3125.7



Click-drag to zoom in on a region. ESC to undo a zoom.

Control-click a cartoon to see CFG glycan database entries (Command-click on a Mac). Click on an entry to expand or contract it.



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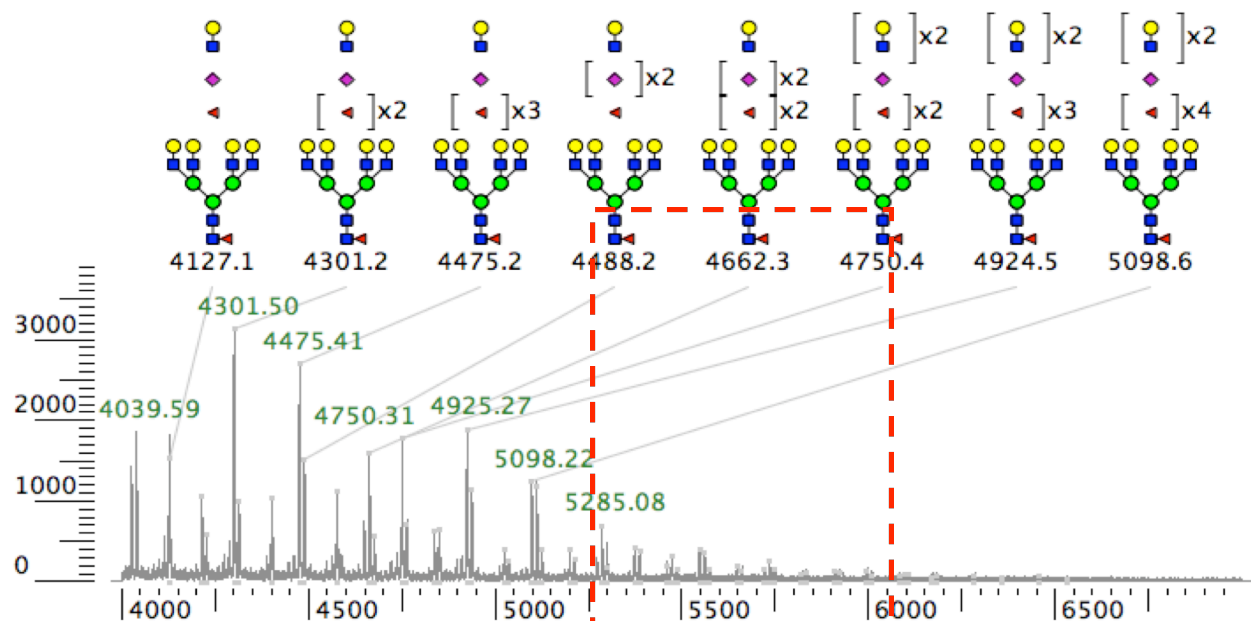
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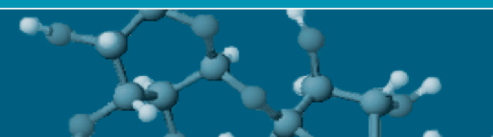
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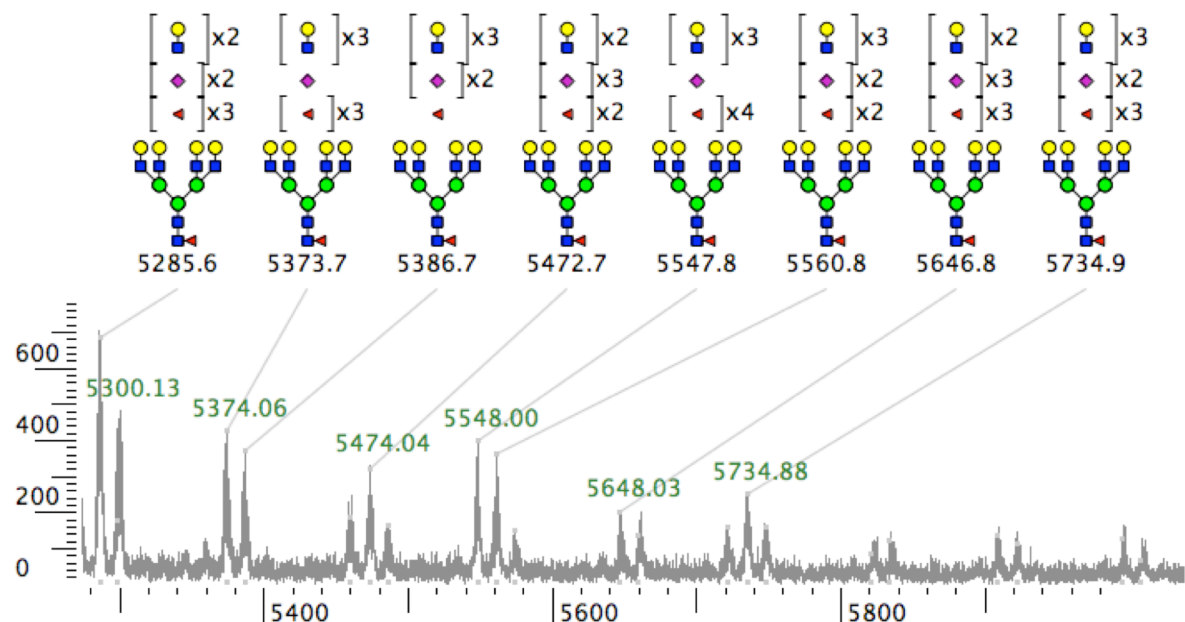
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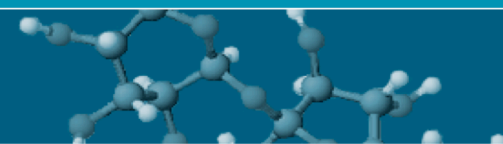
FAQs

File View Tools Help


 Loaded /coreCStatic/allmsdfiles/205_2.msd and /coreCStatic/allmsdfiles/205_2.msa
 mass: 5273.33 ... 6038.34, intensity: 0.0 ... 702.4


Click-drag to zoom in on a region. ESC to undo a zoom.

Control-click a cartoon to see CFG glycan database entries (Command-click on a Mac). Click on an entry to expand or contract it.



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Functional Glycomics Update

Consortium for Functional Glycomics (CFG)

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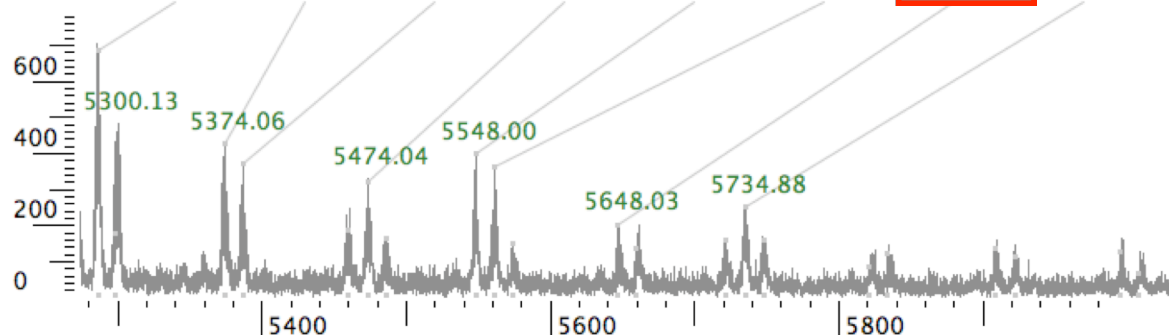
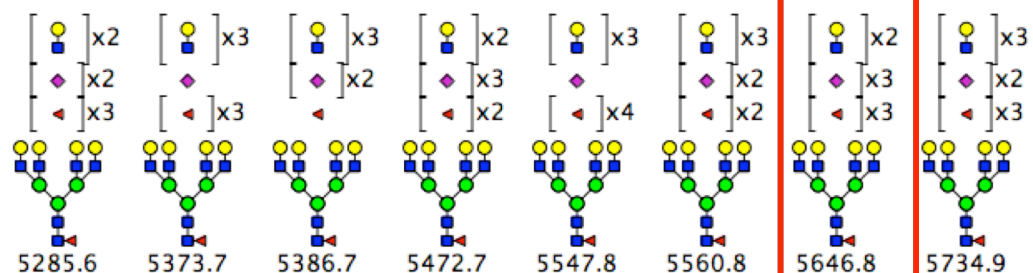
Suggestion

Sitemap

FAQs

File View Tools Help

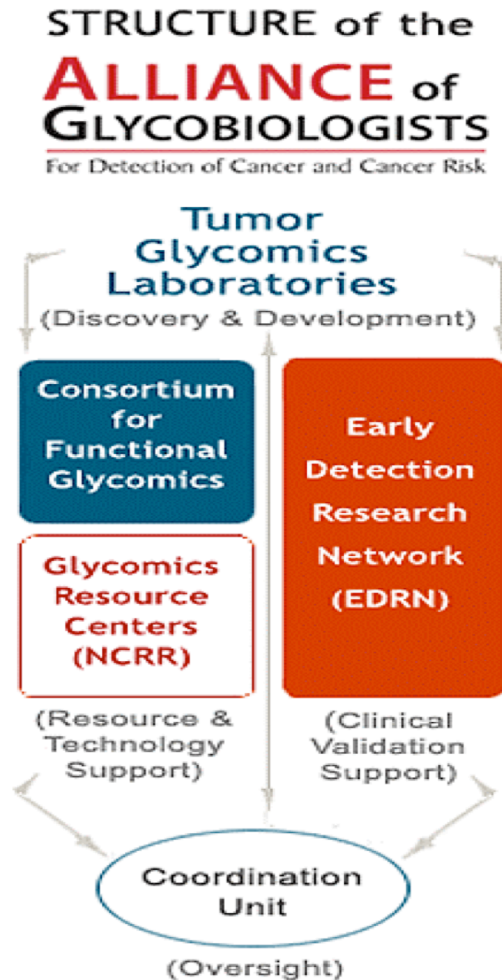
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Benefits from other NIH Glycomics Efforts



- Infrastructure that offers specialized resources
- Growing and highly collaborative community with interests in cancer
- Integrated databases and bioinformatics efforts that provide access to glycomics data to 'non-experts'