Nature Precedings : doi:10.1038/npre.2007.11.1 : Posted 15 Jan 2007

Consortium for Functional Glycomics
Participating Investigator Meeting
Universal City, CA
November 19, 2006

Biology of glycan binding proteins: Insights from glycan microarrays

(CFG: Another 5 years!)

CFG PI 2006

Consortium for Functional Glycomics

Goal:

Define paradigms by which protein-carbohydrate interactions mediate cell communication

http://www.functionalglycomics.org

CFG PI 2006

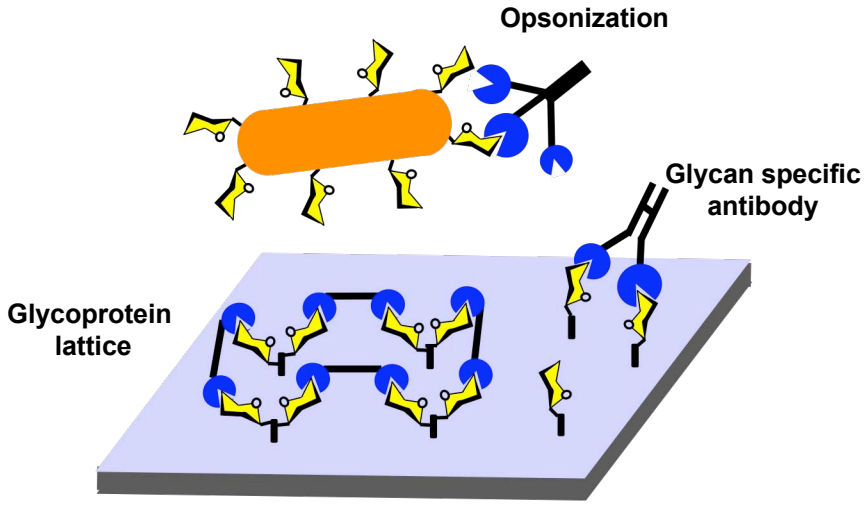
Nature Precedings : doi:10.1038/npre.2007.11.1 : Posted 15 Jan 2007

The next 5 years

- Funding of $41.8 million by NIGMS.
- Priority is to achieve the overarching goal to unfold the biology of glycan binding proteins, 'define the paradigms' using resources created in first 5 years.
- Enhance utility and availability of existing resources and databases
- Evergreen the unique resources and databases to insure availability to the community at the end of the 10 year project.

CFG PI 2006

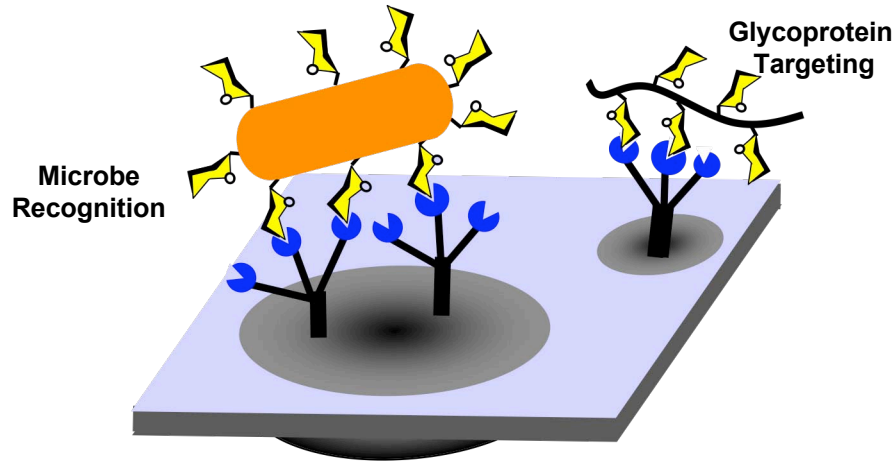
Soluble GBPs binding cell surface and pathogen glycans



CFG PI 2006

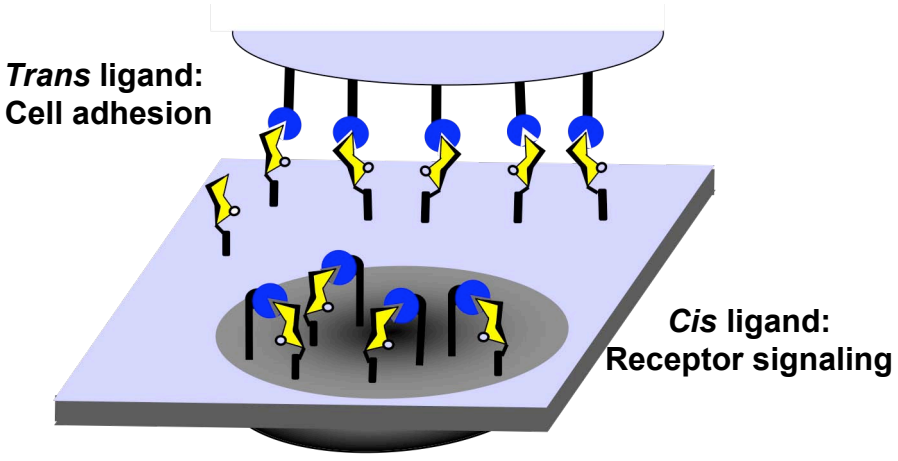
Nature Precedings : doi:10.1038/npre.2007.11.1 : Posted 15 Jan 2007

Cell surface GBPs binding pathogen and glycoprotein glycans



CFG PI 2006

Cell surface GBPs binding cell surface glycans



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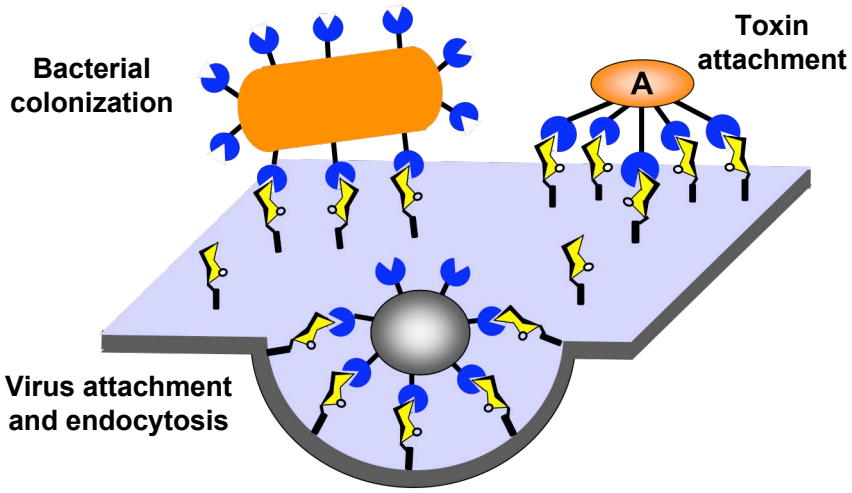
Attachment of microbial pathogens to host cell glycans



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Information needed to elucidate GBP function

- Specificity of GBP for its glycan ligands
- Cell type expression of GBPs and its ligands
- Glycan structures expressed on cell types/glycoproteins recognized by GBP
- Glycosyltransferases responsible for synthesis and regulated expression of GBP ligands
- Structures of GBPs

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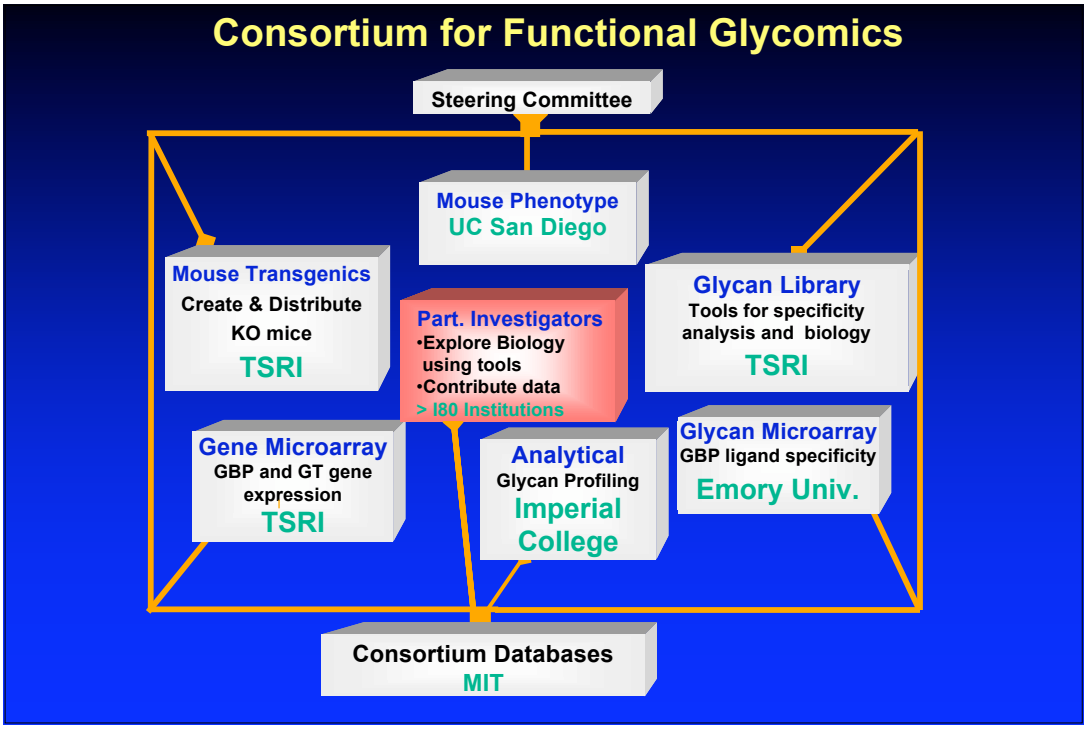
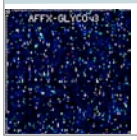


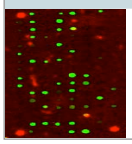
Consortium for Functional Glycomics : Glycobiology resources offered

Glyco-gene microarray



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

Glycan array screening

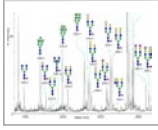


Determine the specificity of your glycan-binding protein on a microarray with ~300 glycoprotein and glycolipid glycans

Carbohydrate compounds

Over 230 carbohydrate compounds available with azido or biotin functional groups

Glycan Analysis

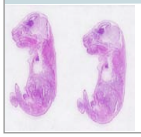


Profile and characterize the *N*- and *O*-linked glycans from your tissues and cell lines

Mouse knockout strains

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

Mouse Phenotype Analysis



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

www.functionalglycomics.org

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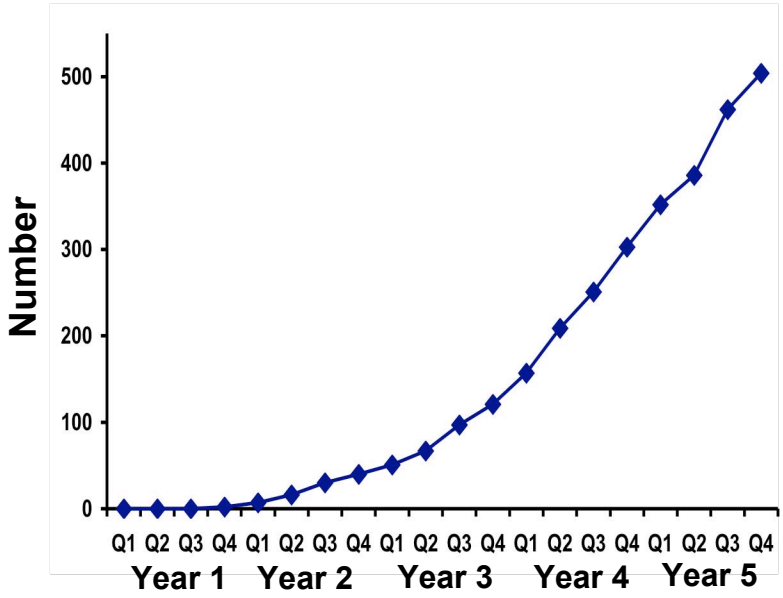
Accelerating rate of resource requests

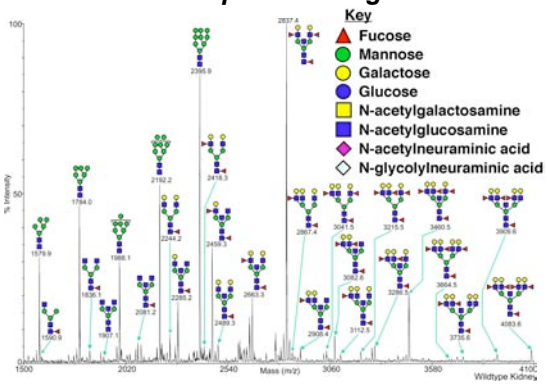


CFG PI 2006

Analytical Glycomics Core

- Focused glycan MS profiling of purified human and murine cell populations and glycoprotein ligands of GBPs.
- Coordinate glycan profiling and GT gene expression datasets with Gene Microarray Core (E).
- ✳ Goal to increase throughput with automated annotation and improved micro-sample handling.
- ✳ Goal to integrate data with other database and informatics features.

Analytical Core
Stuart Haslam, Simon North, Anne Dell
Imperial College



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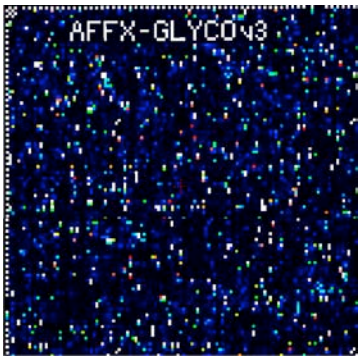
Glyco-gene Microarray Core

- GLYCO-gene chip v3 with human and murine GBP and GT families represented (>200 GT genes).
- Highly annotated by experts in each gene family .
- 'Popular' resource by investigators
- Strategic goal to match gene expression of human and murine cell populations with glycan profiling by Core C.
- Data accessible with data mining tools posted on the CFG website.
- ✳ Regularly update technology and chip design
- ✳ Interogate data from database interfaces.

Glyco-gene Microarray Core
Steven Head
Tim Gilmartin
The Scripps Research Institute



CFG PI 2006

Mouse Transgenics / Phenotyping

- Major success in germline transmission from C57Bl/6 ES cells.
- Six novel KO strains available and 18 additional in development.
- Additional ~50 'published' KO strains available from Jackson Laboratories, MMRC and Participating investigators.
- Phenotype data deposited into the CFG database.
- ✳ Develop mentor program for generation and phenotyping of KO mice.

Mouse Transgenics Core
Bo Ma
James Paulson
TSRI
Mouse Phenotyping Core
Sally Orr
Jamey Marth
UCSD

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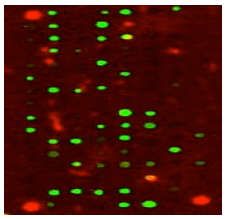
Glycan micro-array for GBP specificity

- Glycan library with ~230 synthetic glycans and glycan derivatives available on request.
- Printed glycan array with ~300 synthetic glycans represented.
- ✳ Expand Reagent Library to include glycan specific antibodies and glycosyltransferases.
- ✳ Expand uses of existing glycan microarray
- ✳ Develop a pathogen glycan microarray.

Glycan Microarray Synthesis Core
Ola Blixt,
James Paulson /
Chi-Huey Wong
TSRI



Glycan-Protein Interaction Core
David Smith
Richard Cummings
Emory University

CFG PI 2006

Initiatives emerging from glycan array

- **Centers for Disease Control** agreement with CFG to make custom glycan microarray for evaluation of its utility for screening specificity of influenza virus field isolates
- **National Cancer Institute** Early Diagnosis Research Network (RFA) for glycomics biomarkers with CFG as partner, targeting ~$3 million per year in grants.

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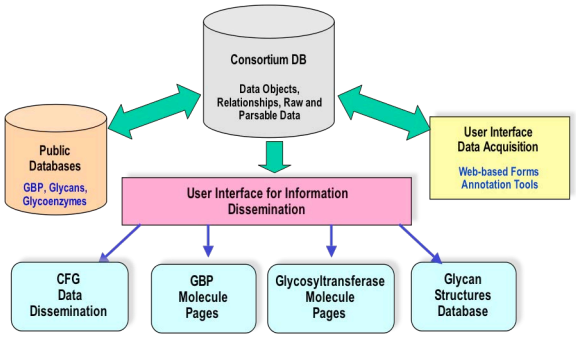
Bioinformatics

Bioinformatics

Rahul Raman
Ram Sasisekharan
MIT

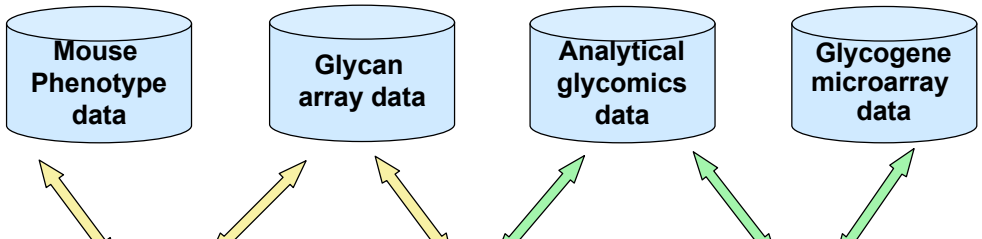


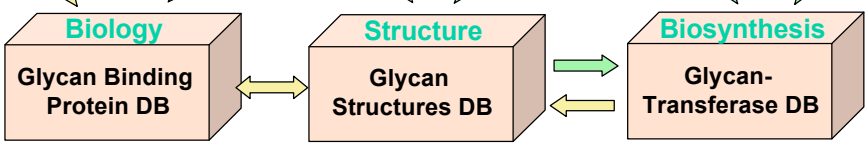
- Implement vision for CFG databases developed with the SC, Scientific Cores and Participating Investigators.
- Develop interfaces for acquisition and dissemination of Consortium data.
- Develop specialty databases integrated with CFG data as resources for PIs and the scientific community.

Integration of interfaces for CFG data and specialty databases

Implemented
Planned

Consortium Data





Specialty Databases

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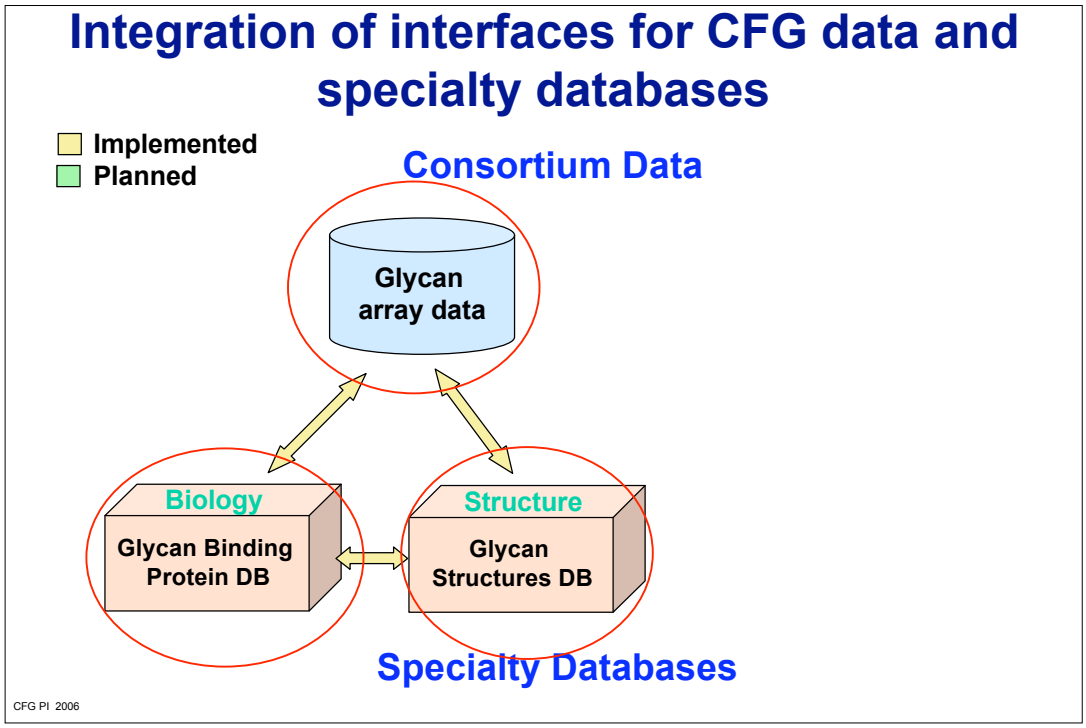

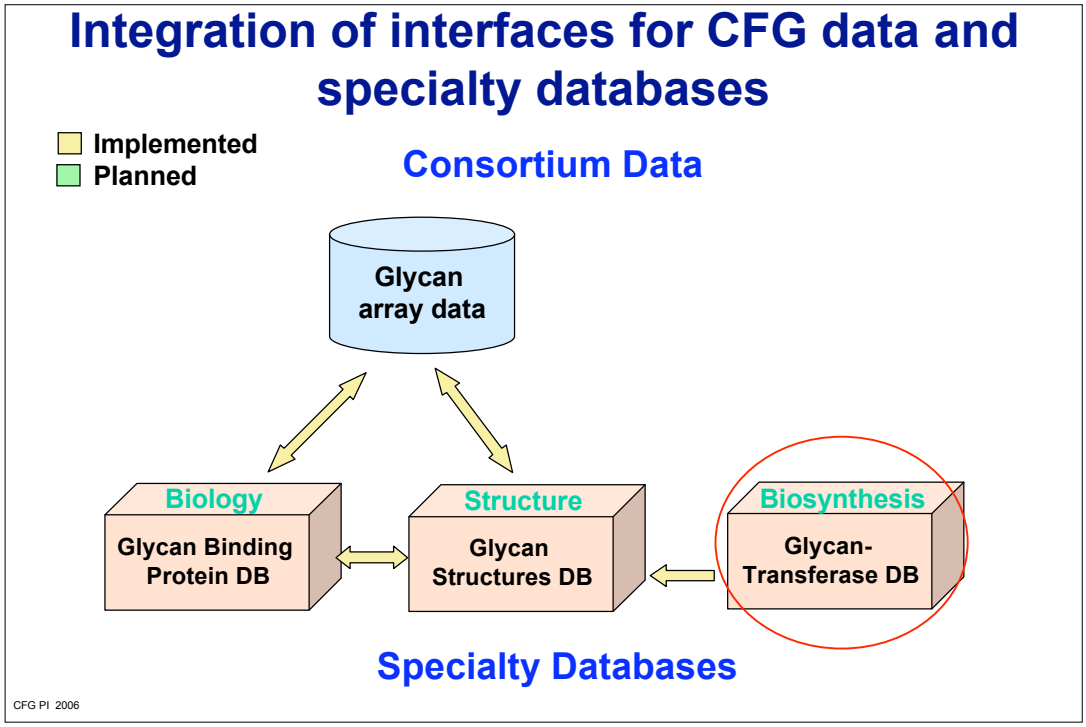

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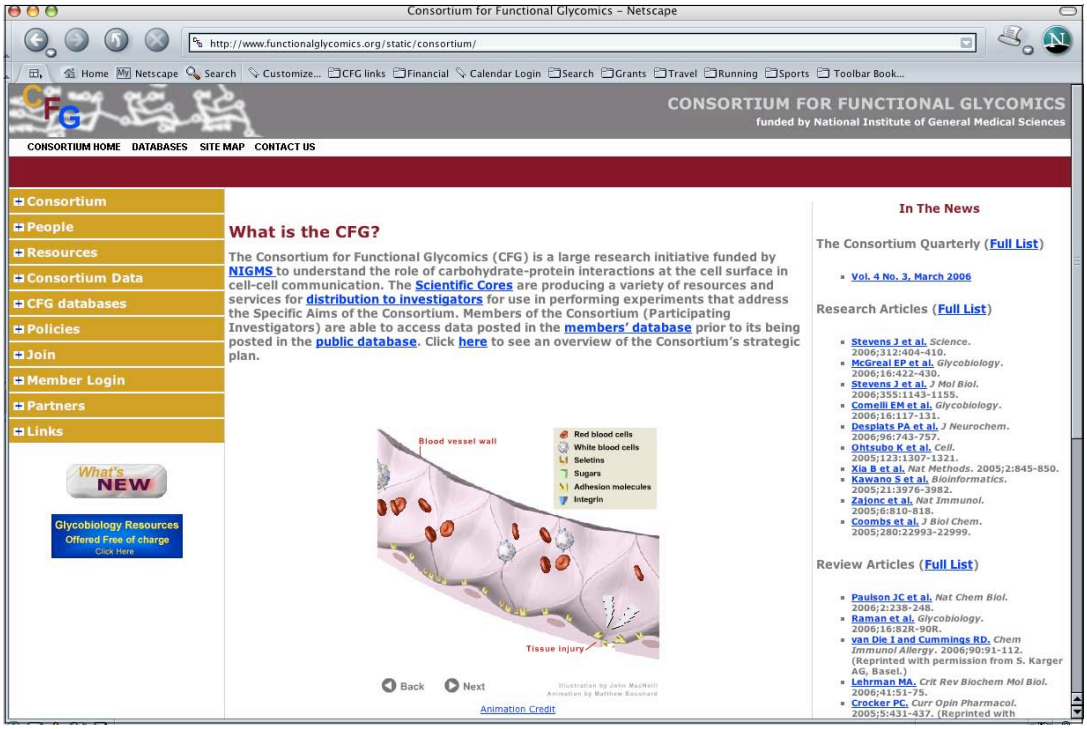

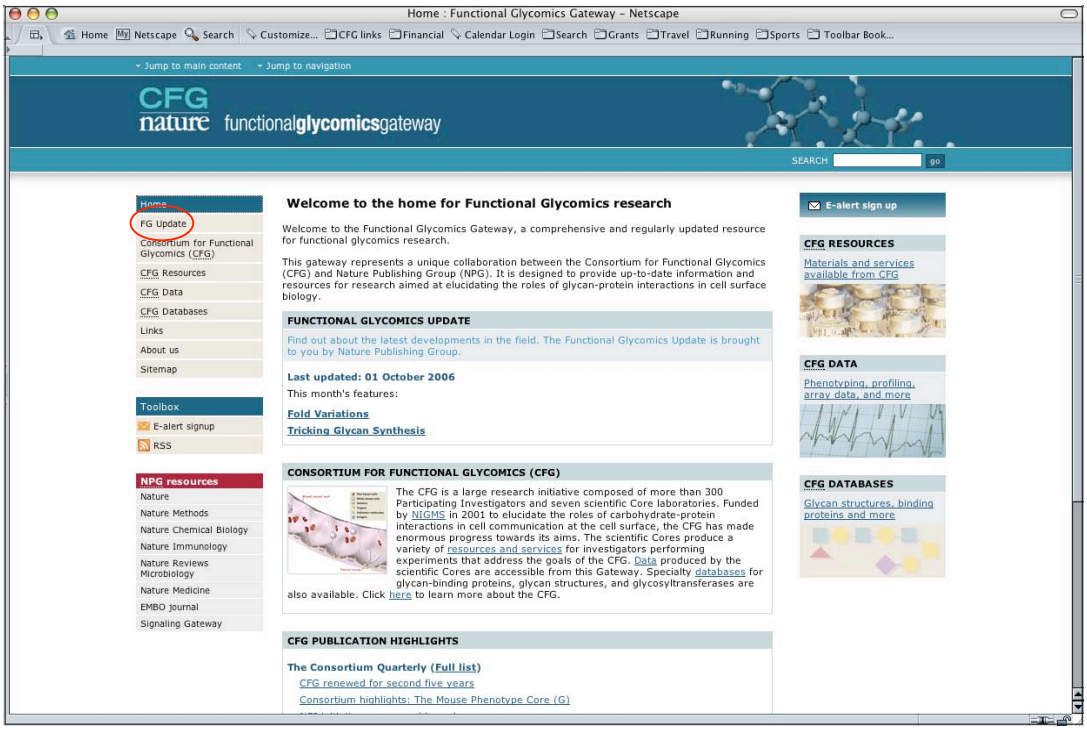

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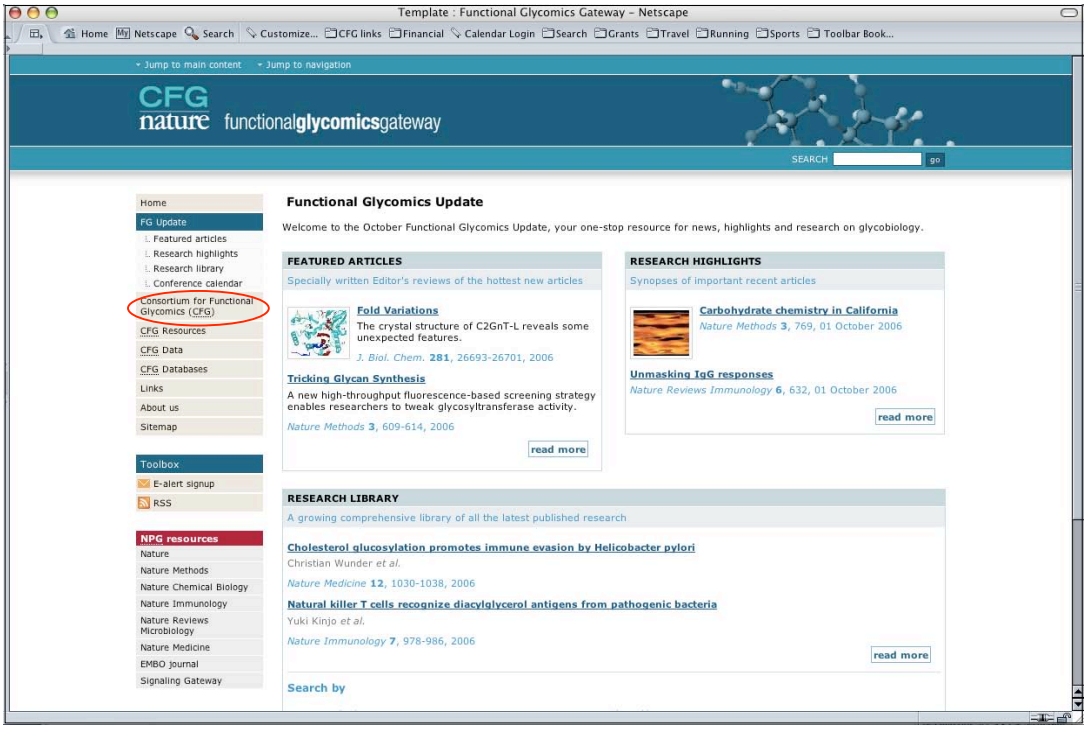

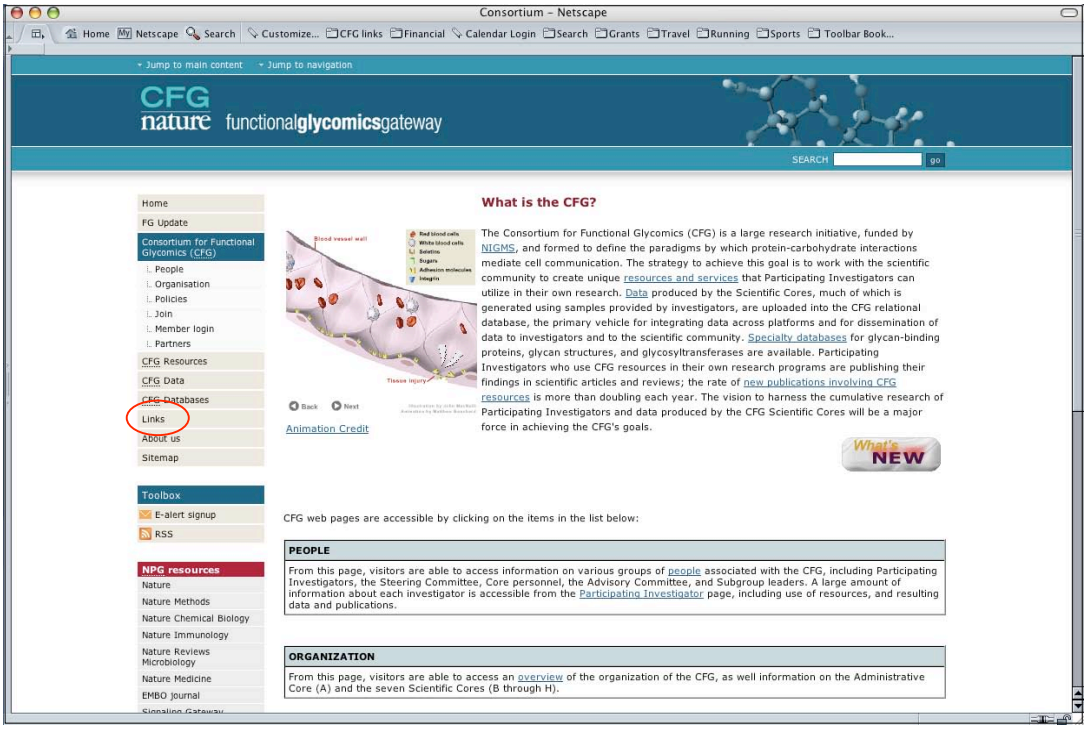

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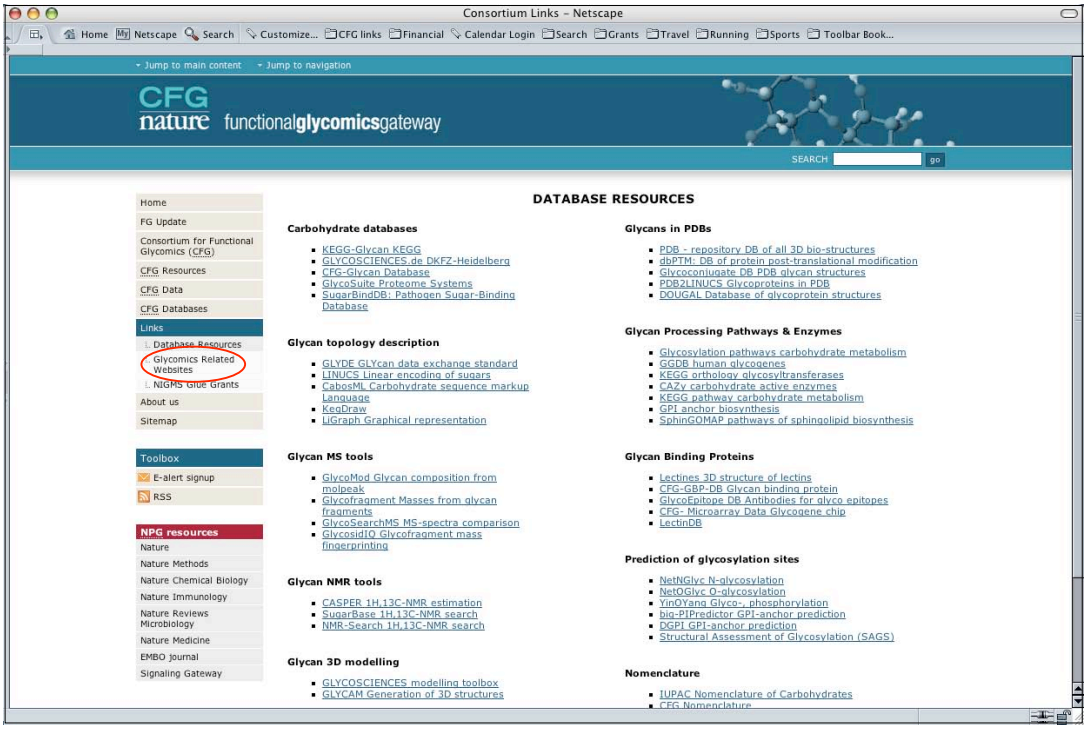
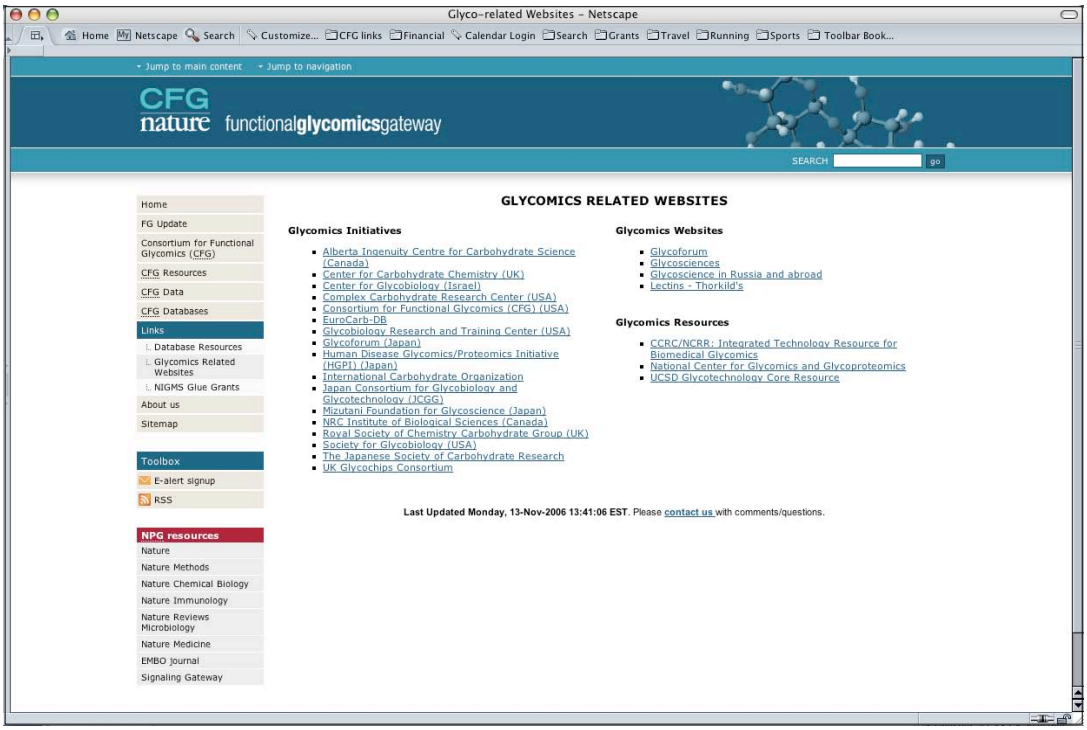
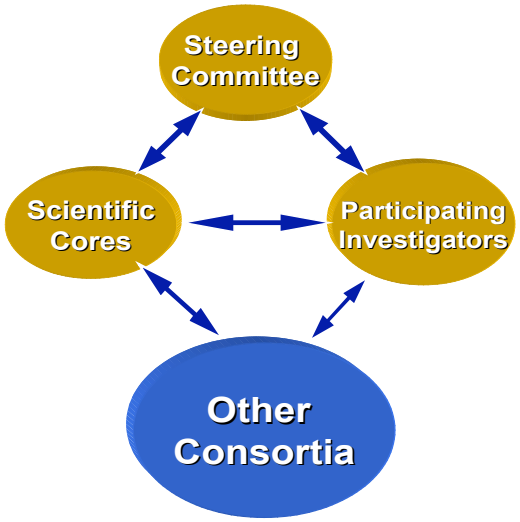




Nature Precedings : doi:10.1038/npre.2007.11.1 : Posted 15 Jan 2007

Forge Alliances with Other Consortia and Database Organizations



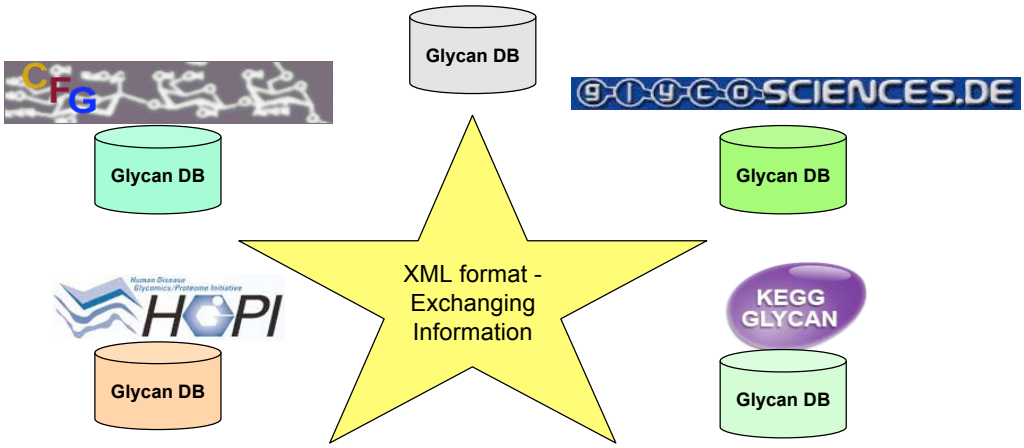
- Identify synergies with existing consortia and databases.
- Leverage resources to mutual benefit.
- Develop uniform standards for depositing and sharing data
- Facilitate ever-greening resources and databases

CFG PI 2006

Glycan structure database

Data exchange with other initiatives

Complex Carbohydrate Research Center
The University of Georgia



NIH Workshop on Glycomics Bioinformatics and Biomarkers in Disease September 11-13, 2006

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Leverage resources through alliances

- CAZy: Carbohydrate Active-EnZYmes (Bernard Henrissat)
- CCRC/NCRR : Integrated Technology Resource for Biomedical Glycomics (Michael Pierce)
  - Correlation of microarray/RT-PCR methods for GT expression
  - Link Glycan Database to 3D-Glycan Structure Resource (Rob Woods
  - Database XML standards (Will York)
- EuroCarbDB : - (Willi von der Lieth)
  - Coordination of carbohydrate databases and data exchange standards
- KEGG glycan project (Minoru Kanehisa)
  - Annotation of GT database; analysis of microarray data
- HGPI: HUPO glycomics disease initiative (Naoyuki Taniguchi)
- Japanese Consortium for Glycobiology and Glycotechnology (JCGG) (Yoshi Nagai / Hisashi Narimatsu)
- Joint Center for Structural Genomics (Ian Wilson)
  - Crystal Structures of Glycan Binding Proteins and GTs
- Lipid MAPS Consortium (Ed Dennis/Al Merrill)
  - Annotation of glycolipid biosynthetic pathways
- UK Glycochip Consortium (Sabine Flitch)
  - Coordinate efforts on design of glycan microarrays

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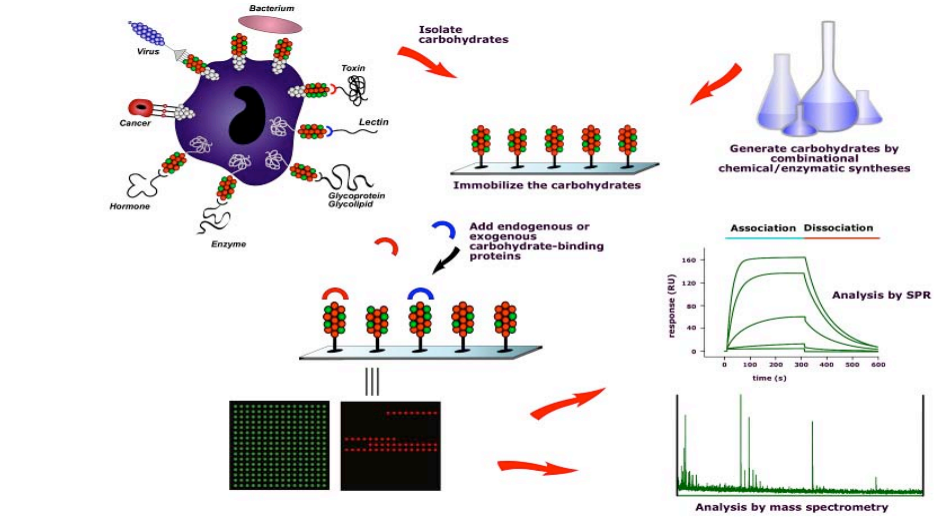
GLYCOARRAYS – STRATEGIES FOR HIGH THROUGHPUT ANALYSIS OF THE GLYCOME

http://www.glycochips.org.uk/

RESEARCH COUNCILS UK



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Nature Precedings : doi:10.1038/npre.2007.11.1 : Posted 15 Jan 2007

Biology of glycan binding proteins: Insights from glycan microarrays

8:55 – 9:20 **Dave Smith**
(Emory University)
CFG Glycan array analysis

9:20 – 9:45 **Kurt Drickamer**
(Imperial College of London)
Glycan array analysis of receptors that bind endogenous and pathogen glycans

9:45 – 10:10 **Mavis Agbandje-McKenna**
(University of Florida)
Glycan array and structural analyses of parvoviral-host cell receptor interactions

10:10 – 10:35 **Els van Damme**
(Ghent University)
Diverse specificities of plant lectins revealed on glycan microarrays

10:35 – 11:05 MORNING BREAK

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Biology of glycan binding proteins: Insights from glycan microarrays

11:05 – 11:30 **David Miller**
(University of Illinois at Urbana-Champaign)
Glycomic approach to identify oligosaccharides that bind sperm

11:30 – 11:55 **Ola Blixt**
(The Scripps Research Institute)
Developments in CFG glycan and pathogen polysaccharide arrays

11:55 – 1:00 LUNCH

1:00 – 1:30 **Rahul Raman**
(Massachusetts Institute of Technology)
Enhancements to CFG databases and interfaces

1:30 – 2:30 **Investigator Feedback on CFG Initiatives**
Co-Chairs: Rick Cummings & Steve Rosen

CFG PI 2006

Acknowledgments

Steering Committee

Paul Crocker
Richard Cummings
Anne Dell
Kurt Drickamer
Pamela Marino
Jamey Marth
James Paulson
Steve Rosen
Ram Sasisekharan
Ron Schnaar
Pamela Stanley

Scientific Cores

Ola Blixt
Steve Head
Stuart Haslam
Bo Ma
Sally Orr
Rahul Raman
David Smith

Participating Investigators

~300

Advisory Committee

Elizabeth Neufeld
Ellis Reinherz
Nathan Sharon

Sponsors:

NIGMS
Neose Technologies
Kyowa Hakko
Otsuka Phamaceuticals
NRC Ottawa

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