First Data is Posted on the Consortium Website

An important milestone has been met by the Consortium – its first data sets are available for viewing on the website. In the interim period before the Consortium databases are fully functional this data is being posted in flat files. These files represent the broad spectrum of data that the Consortium is poised to produce – much of which is novel – and provide a preview of the types of information that will become increasingly available from the Consortium. The data pages can be accessed through the Core Status page at http://web.mit.edu/glycomics/consortium/organization/sciCores/coreCtoH.shtml. The following results can currently be viewed:

- From the Analytical Glycotechnology Core (C): Nine N- and O-linked glycan spectral profiles from the kidney, spleen, and thymus of FucT-IV and FucT-VII knockout mice
- From the Gene Microarray Core (E): Microarray data for nine tissues from a wild type mouse tissue survey
- From the Mouse Phenotype Core (G): Phenotype analysis results for Galectin3 (Lgals3) and Core 2 β(1,6)N-acetylglucosaminyltransferase-I (Gcnt1) knockout mice
- From the Protein-Carbohydrate Interaction Core (H): Galectin3 glycan array data

The Core Status page can be accessed from the “What’s New” button on the home page and will be updated as additional data becomes available.

Consortium-generated data will soon be entered into, and accessed directly from, relational databases currently under construction by the Information and Bioinformatics Core (B) under the leadership of Dr. Ganesh Venkataraman and Dr. Rahul Raman at the Massachusetts Institute of Technology. This group has the challenging task of developing the Consortium website with its accompanying powerful relational Central and specialized databases, necessary interfaces, presentation layers and search engines. This software infrastructure is a vital part of accelerating the progress of the Consortium. Much has been accomplished; extensive interactions with Core Directors have defined the data field requirements and helped establish data entry mechanisms, and data from several Cores has started being entered into the databases.
Molecule Pages Chosen As a Portal to Consortium Databases

The powerful relational Central Database will be used for acquiring, storing, analyzing, and disseminating data, tools, resources, and all program information related to the Consortium. The Consortium databases will store information on three main objects - glycan-binding proteins (the GBP database), glycosyltransferases (the GT database), and carbohydrate structures (the Carb database), and the relationships between them. The primary purpose of the GBP database is to provide Consortium members and the general scientific community with a web-based information resource for selected GBPs. The MIT scientists have selected the molecule page format as a mechanism for accessing the GBP database and interfacing it with the Central Database and the other specialized databases. The initial design of the GBP molecule page has been completed; finalization of the data fields and formats and of the mechanisms for data collection and entry is in progress. The intent of the molecule pages is to provide a format for allowing visitors easy access to a vast array of information and to allow customization of searches by following appropriate links. The visitor will be able to tailor her search to include as much specific detail as she desires, including experimental results and raw data files generated by the Consortium.

A sample molecule page for human Galectin3... can be accessed on the Consortium website where a wealth of public and Consortium-generated information is readily available.

The MIT scientists have selected the molecule page format as a mechanism for accessing the glycan-binding protein database. A sample molecule page for human Galectin3 contributed by Dr. Fu-Tong Liu and Dr. Dan Hsu can be accessed on the Consortium website at http://web.mit.edu/glycomics/molecul epages/cbp/galectins/gal3_human/, where a wealth of Galectin3-related public and Consortium-generated information is readily available.

The molecule page contains seven broad fields - General, Resources, Reference, Genome, Proteome, Glycome, and Biology - organized in a folder tab format with a horizontal navigation banner displayed at the top. Upon clicking a tab, specific information from each area is retrieved from the database and displayed. The displayed content can be text, graphic, or hyperlinks to other databases (such as PubMed or Swiss-Prot) or to Consortium results or raw data pages. A key word search capability with a search engine similar to that of Google will be incorporated, and an advanced search option will enable users to perform more specific queries. The molecule pages will be similar to those developed by the Alliance for Cellular Signaling, with differences in specific fields and formats.
The Consortium needs the help of experts to populate the molecule pages... and anticipates that they will represent an extraordinarily valuable resource in the field of glycobiology.

A comprehensive program for the creation and phenotyping of novel mouse knockout strains... is expected to produce valuable information on the biological functions of many genes of interest.

The Mouse Transgenics Core is now a fully functional facility creating new, as well as breeding existing, genetically modified mouse strains. This Core provides mice to the Mouse Phenotype Core for phenotype analysis. Eleven genes selected by the Steering Committee to be of high priority interest to the Consortium are currently being targeted...
for the creation of knockout mice: Langerin, DcSign (CD209a), SignR1 (CD209b), Mincle (Clec9f9), Galectin9 (Lgals9), Dectin2 (Clec9f10), SiglecH, Dcir (Clec9f6), SignR3 (CD209d), Mcl (Clec9f8), and Dcar. Targeting vectors for many of these genes have been constructed and embryonic stem cell clones bearing an ablated gene have been obtained for a number of them. Conditional gene modification using Cre/loxP technology is being used for all of the targeted genes except Langerin and DcSign. One of the targets, Galectin9, was identified from a commercial source and acquired by the Mouse Transgenics Core.

In addition to providing mice to the Mouse Phenotype Core, the Mouse Transgenics Core also provides breeding pairs of mice to investigators for use in experiments designed to address scientific issues of interest to the Consortium. Galectin9, a novel knockout mouse, is now available to investigators. Galectin9 is a developmentally-regulated pro-apoptotic lectin that has been implicated in the chemotraction and activation of eosinophils in tissues during inflammation. The list of 24 mouse lines now available can be viewed on the Consortium webpage [http://web.mit.edu/glycomics/consortium/resources/resourcecoref.shtml](http://web.mit.edu/glycomics/consortium/resources/resourcecoref.shtml).

Breeding pairs of mice have been provided to investigators for studies of the role of Galectin3 in breast cancer, the roles of Galectin1 and Galectin3 in adaptive immunity, and B cell homing to bone marrow in ST6Gal-1 knockout mice.

Mice that are transferred to the Mouse Phenotype Core from the Mouse Transgenics Core, as well as certain existing mouse strains contributed by Participating Investigators and selected by the Steering Committee for their relevance to the Consortium, undergo extensive phenotypic analyses under the auspices of four Sub-Cores of the Mouse Phenotype Core. The facility measures more than 100 physiological parameters and responses among genetically altered mice and compares its findings to those identically obtained from sibling control genotypes.

Galectin9, a novel knockout mouse, is now available to investigators.

The Mouse Phenotype Core measures more than 100 physiological parameters and responses among genetically altered mice and compares its findings to those identically obtained from sibling control genotypes.

- The Hematology, Chemistry and Coagulation Sub-Core identifies abnormalities in blood cell homeostasis and morphology, as well as abnormalities in plasma and serum lipids, proteins, coagulation factors, and basic chemistry.
- The Immunology Sub-Core identifies abnormalities in immune cell development and function by employing a variety of assays - both analytical and involving immunologic challenge to the innate and acquired immune systems.
- The Histology Sub-Core examines the morphologic variation in mutant mice by initial autopsy and histological examination of multiple tissues, organs, and cell types.
• The **Behavior and Metabolism Sub-Core** investigates the presence of phenotypic abnormalities in basic metabolism, such as pulmonary function, cardiac output, and caloric homeostasis. Other basic and behavioral tests include assays of hearing, fear, nociception, learning, memory, and locomotor skills.

An intriguing finding that has emerged is that **Galectin3 knockout mice appear to be more socially dominant than their wild type littermates**.

Results for Galectin3 (Lgals) and Core 2 β(1,6)N-acetylgalactosaminyltransferase-I (Gcnt1) knockout mice are accessible from the Consortium web page [http://web.mit.edu/glycomics/consortium/organization/sciCores/coreg1.shtml](http://web.mit.edu/glycomics/consortium/organization/sciCores/coreg1.shtml). An intriguing finding that has emerged is that Galectin3 knockout mice appear to be more socially dominant than their wild type littermates. In a “tube test”, where a mouse of each genotype is introduced into one end of a tube and their respective behaviors observed, the wild type littermate mice backed out more often than would be expected by chance. The results of this and two other behavioral tests suggest that the Galectin3 mutant mice exhibit increased aggressive behavior.

**First Published Use of Consortium Gene Microarray**

With the publication earlier this year of a paper by Participating Investigator **Dr. Jeffrey Esko** and colleagues, the application of microarray data from the Gene Microarray Core (E) to a wide variety of problems of interest to the Consortium is officially underway. The paper, entitled “Expression Patterns of α2,3-Sialyltransferases and α1,3-Fucosyltransferases Determine the Mode of Sialyl Lewis X Inhibition by Disaccharide Decoys”, appeared in the June 27 issue of the *Journal of Biological Chemistry*. (The paper is available on the Consortium website at [http://glycomics.scripps.edu/Brown2003.pdf](http://glycomics.scripps.edu/Brown2003.pdf).)

The paper reports the use of two disaccharide glycosides (peracetylated forms of Galβ1,4GlcNAcβ-O-naphthalenemethanol and GlcNAcβ1,3Galβ-O-naphthalenemethanol) to divert the cellular glycosylation machinery in LS180 human colon carcinoma cells and U937 human lymphoma cells from the synthesis of cellular glycoproteins to the assembly of free oligosaccharides including sialylated, sulfated, and fucosylated products. In LS180 cells, expression of α2,3-sialylated oligosaccharides on the cell surface, as assayed by altered binding of lectins and carbohydrate-specific antibodies, was diminished by the presence of the glycosides, whereas α2,6-sialylation and fucosylation were not. In U937 cells, the glycosides decreased fucosylation without affecting sialylation.
Gene microarray analysis added insight by providing evidence for the selective effects on subsets of enzymes expressed in each cell type. The microarray data revealed that ST3Gal-IV is the only sialyltransferase expressed in LS180 cells, whereas U937 cells express ST3Gal-IV, ST3Gal-V, and ST3Gal-VI. LS180 cells express fucosyltransferases FucT-III and FucT-VI, while U937 cells express FucT-IV and FucT-VII.

The findings from this paper suggest that, taken together, priming data, lectin binding data, enzyme assays and microarray data provide a way to evaluate the potential efficacy of primer-based decoys and possibly other inhibitors of glycosylation.

Under the direction of Steve Head, the Gene Microarray Core’s GLYCOv1 GeneChip has been used for the evaluation of gene expression in more than a dozen models of protein-carbohydrate interactions using RNA samples provided by investigators within and outside of the Consortium. These projects range from the response of T cells to viral infection, glycosyltransferase and GBP expression during mouse B and T cell development, gene expression in cystic fibrosis airway epithelial cells and gene expression in Galectin3 and Mgat3 knockout mice, among others. The Consortium looks forward to the knowledge that these microarray experiments will yield and the contribution that these collaborations will make to the field of glycobiology.

**Second Annual Participating Investigators’ Meeting To Be Held on December 7th**

The Consortium is looking forward to the second annual meeting of its Participating Investigators at the Catamaran Resort Hotel in San Diego on December 7th. The full-day meeting will be held following the conclusion of the 2003 Annual Conference of the Society for Glycobiology. Core Directors will present the last year’s results and progress from their Cores. The afternoon session will consist of selected presentations by Participating Investigators, and subgroup break-out sessions chaired by the Subgroup leaders to solicit community feedback and recommendations will follow.
Crystal Structure Determination of Murine Glycan-Binding Proteins

Dr. Ian Wilson, a Consortium Participating Investigator and Principal Investigator of the Joint Center for Structural Genomics (JCSG), noted that both Consortia have an overlapping goal of determining the structures of murine proteins, specifically glycan-binding proteins (GBPs) in our case. He has offered to set up crystallization arrays of high purity GBPs, which will become candidates for crystallization by the JCSG. If you are interested please contact Dr. James Paulson or your Subgroup leader. (Visit http://web.mit.edu/glycomics/consortium/organization/people/peoplesubgroup.shtml for contact information.)

Available Resources and Services

The Consortium is producing novel resources and services for Participating Investigators and interested scientists. These reagents and tools are detailed on the Consortium website, where visitors can also find instructions for completing and submitting resource requests online. Request forms received online are forwarded to the Director and Coordinator of the appropriate Core for evaluation. If needed, the Director will request additional information from the applicant. All requests are given the same consideration regardless of Consortium member status; non-members proposing experiments within the scope of the Consortium agree to submit their data to the Consortium database prior to publication. Most requests, along with the Director’s recommendation, are reviewed at the following Steering Committee meeting. The website is updated with new offerings as additional resources become available.

Carbohydrate compounds (available at http://web.mit.edu/glycomics/consortium/resources/resourcecored.shtml)
- 40 saccharides, from monosaccharides up to decasaccharides, in 1 and 5 mg quantities
- 39 biotinylated structures in 250 µg quantities
- 4 polyacrylamide derivatives in 250 µg quantities

- Human Siglec-2 and human Siglec-10 in 100 µg vials
- Mouse Siglec-4, 50 µg in 10 ml, as a non-purified protein in media
- Mouse CD1d in 500 µg vials
Mouse knockout strains (available at http://web.mit.edu/glycomics/consortium/resources/resourcecoref.shtml)
  o 24 glycosyltransferase and GBP knockout strains, including several double knockout strains

Glycan array screening (available at http://web.mit.edu/glycomics/consortium/resources/resourcecoreh.shtml)
  o Glycan array version 2.2, a 384-well plate using a streptavidin/biotin format, with 170 unique glycans plus controls
  o Instructions for human and murine lectin preparation

Gene microarray screening (available at http://web.mit.edu/glycomics/consortium/resources/resourcecoree.shtml)
  o A custom-designed glyco-gene chip array (GLYCOv1) contains probe sets for 1,814 human and mouse transcripts relevant to the Consortium (developed using Affimetrax technology)
    ▪ Gene list and probe set annotation
    ▪ Instructions for RNA sample purification and shipping
  o Glyco-gene chips for analysis in your own DNA microarray facility

People and News

New Relationships:
  ➞ A collaboration with The Palo Alto Research Center (USA) has been established for the development of an algorithm which will greatly assist in the annotation of MALDI glycan mass spectral data. This work has been funded by a supplement from the NCRR.
  ➞ The Protein-Carbohydrate Interaction Core has received a supplemental equipment grant from the NIGMS for a plate robot and a radiometric flow detector.

Acknowledgements:
  ➞ The Consortium thanks Dr. Fu-Tong Liu and Dr. Dan Hsu for contributing the Galectin3 molecule page.
  ➞ The Consortium gratefully acknowledges contributions of enzymes, glycan-binding proteins and mouse lines from a number of investigators. Their names are on the website acknowledgement page at http://web.mit.edu/glycomics/consortium/acknowledgement.shtml.
New members:

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<tr>
<th>Investigator</th>
<th>Institution</th>
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<tr>
<td>Pablo Argueso, PhD</td>
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<td>Thomas Edgington, MD</td>
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<td>Yong-Jian Geng, MD, PhD</td>
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<td>Jill Gready, PhD</td>
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Calendar of Upcoming Events:

⇒ The Annual Conference of The Society for Glycobiology
   San Diego, CA
   December 3-6, 2003
   [http://www.glycobiology.org/conference/default.asp](http://www.glycobiology.org/conference/default.asp)

⇒ Annual Meeting for Participating Investigators of the Consortium for Functional Glycomics
   San Diego, CA
   December 7, 2003

⇒ The 7th Annual San Diego Glycobiology Symposium
   San Diego, CA
   February 20-21, 2004
   [http://grtc.ucsd.edu/sdgs.html](http://grtc.ucsd.edu/sdgs.html)