Accelerating Translation of Glycoscience: Integration and Accessibility

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Council of Councils

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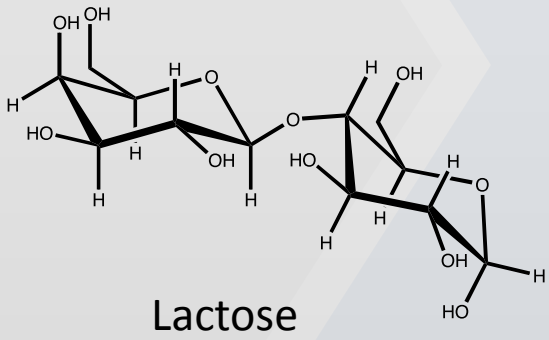
National Institutes of Health
Office of Strategic Coordination - The Common Fund

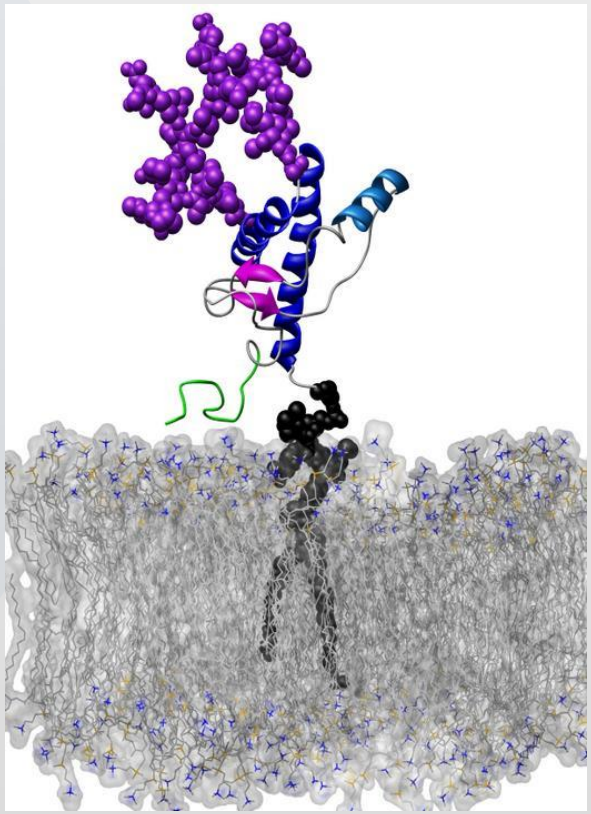
The Glycoscience Traffic Jam

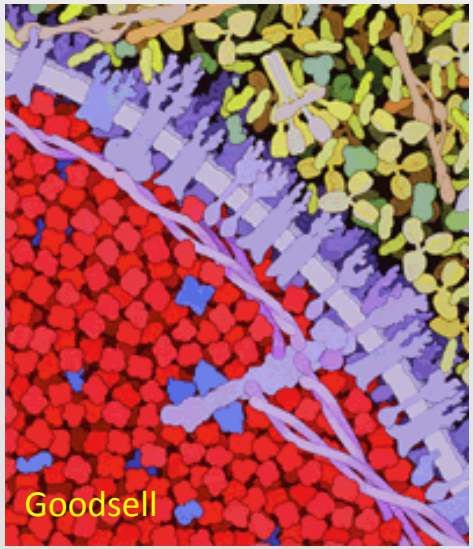
What are glycans?

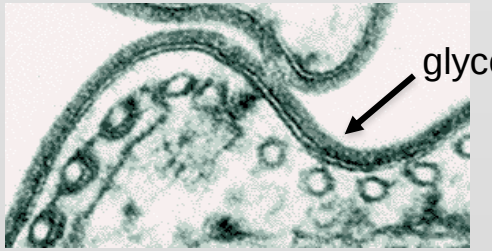
- **Glycans are complex chains of carbohydrates – also called oligosaccharides – that act in many biological pathways and diseases.**



Lactose







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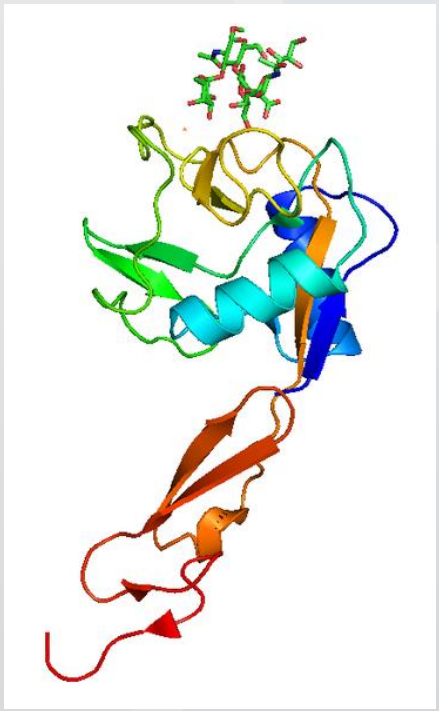
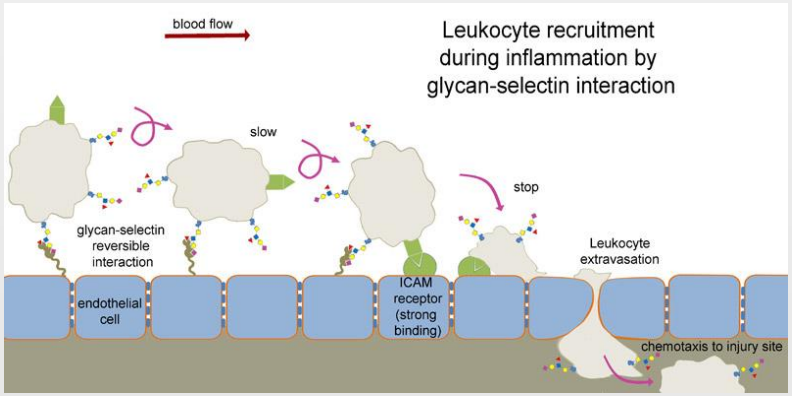
Why is glycoscience important for medicine?

Glycans and the proteins that bind them play key roles in many diseases



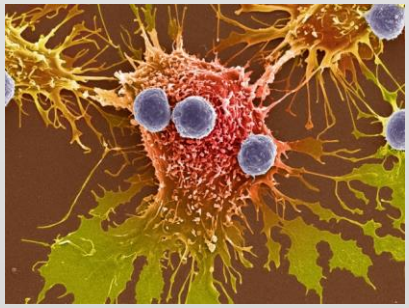
Selectin

Immune Response



Sickle Cell Disease

Cancer



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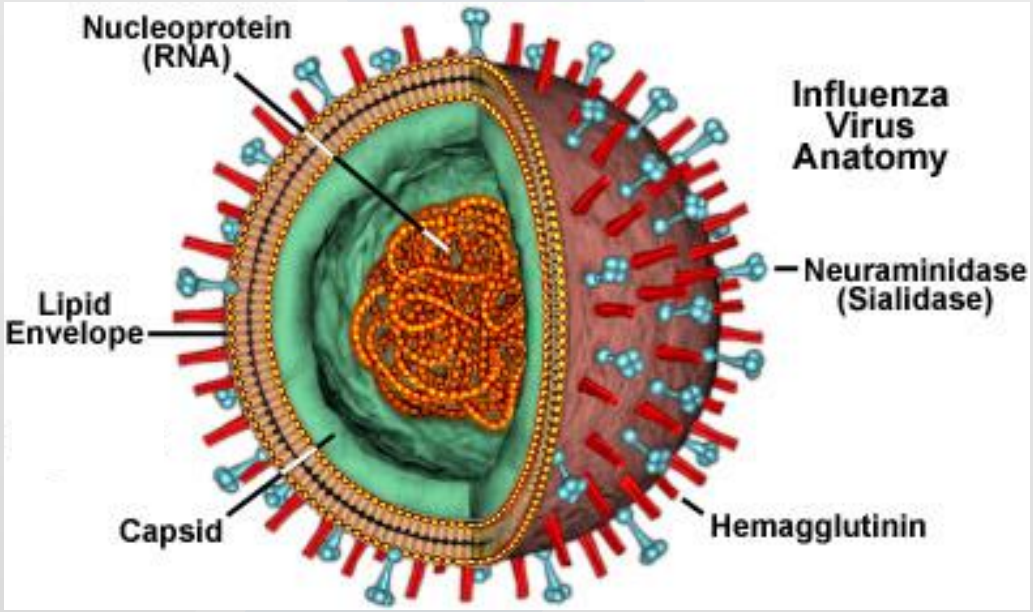
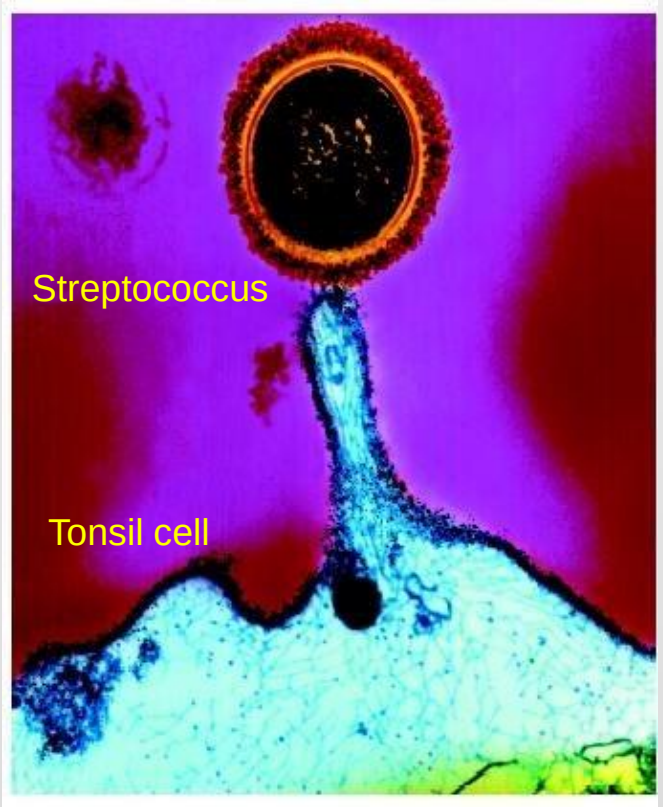


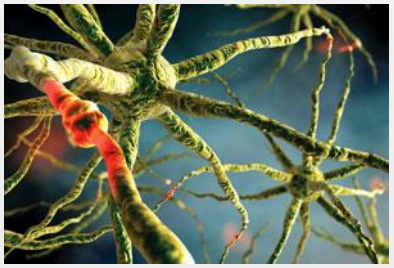


So What's the Problem?

- **Although great progress has been made in glycoscience over the past decade, studying glycans is still almost entirely the province of highly specialized experts.**

This presents a huge roadblock for studies supported by almost every Institute and Center

Case Study



Mueller TM, Haroutunian V, Meador-Woodruff JH.
(2013) *Neuropsychopharmacology*
N-Glycosylation of GABAA Receptor Subunits is Altered in Schizophrenia.

The authors' data indicate that there are changes in the glycans attached to key proteins on the surfaces of cells in the brains of people with schizophrenia.

Roadblock	Accessible Tool Needed
What are the glycans and how are they changed?	Easy ways to sequence glycans
What proteins do the glycans bind to?	Easy ways to identify binding partners
How could the researchers study the roles of the glycans and the effects of the changes?	Efficient synthesis of any glycan

Common Fund Glycoscience Working Group

Co-Chairs:

Jon Lorsch, Director, NIGMS
Martha Somerman, Director, NIDCR

Co-Coordinators:

Penny Wung Burgoon, NIDCR
Pamela Marino, NIGMS
Douglas Sheeley, NIGMS

Houman Araj, NEI
Gilman Grave, NICHD
Karl Krueger, NCI
Amanda Melillo, NIDCR
Thandi Onami, NIAID
Rao Rapaka, NIDA
Rita Sarkar, NHLBI
Salvatore Sechi, NIDDK
Craig Thomas, NCATS
Ravi Basavappa, OD

Advice from the Research Community

- **Experts Consulted:**
  - ❖ 2012 National Academy of Sciences consensus report: *Transforming Glycoscience: A Roadmap for the Future*
  - ❖ May 2013 Common Fund Glycoscience Workshop
  - ❖ May 2013 Council of Councils

- **Portfolio Analysis is currently underway:**
  - ❖Research investment appears to be wide-reaching but not deep. In 2013, less than 1% percent of the approximately 80,000 NIH awards had a relationship to glycoscience, but these awards were issued by 19 of the 23 ICs that issue grants and contracts

Goals & Deliverables

To develop accessible new tools and technologies that make glycoscience possible for any biomedical investigator.

- ***less complex***
- ***easily available and affordable***
- ***easy to understand and adapt to different systems***

Proposed Strategy

- **Initiative 1: Accessible tools for probing and analyzing carbohydrates and their interaction partners ($16M)**

  - Sequencing and binding partner identification

- **Initiative 2: Facile methods and technologies for synthesis of biomedically relevant glycans and their glycoconjugates ($27M)**

  - Ability to easily and cost-effectively make all microbial and mammalian glycans

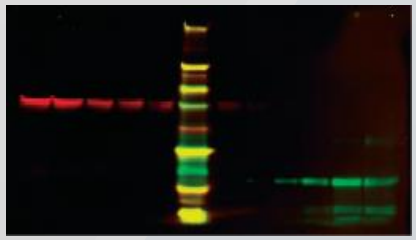
- **Initiative 3: Data Integration tools ($17M)**

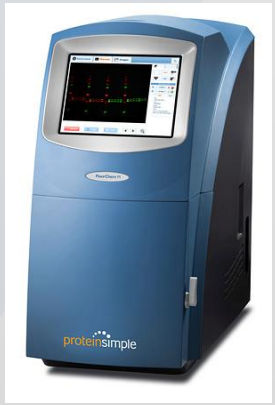
  - Connect genome and proteome to glycome

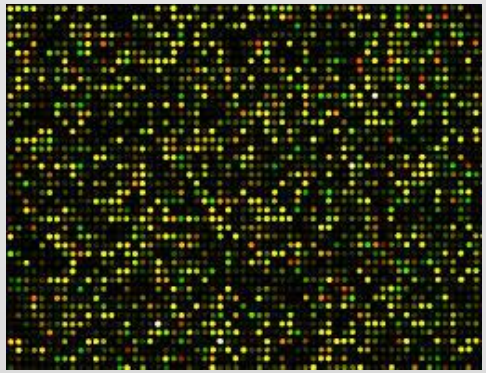
Long Term Outcomes

- **Rapid investment that will position promising tools and technologies with demonstrated proof-of-concept and public health relevance to quickly move out of CF for IC support, SBIR/STTR development and commercialization.**

- **The tools developed for studying glycans should be as straightforward and as widely used as those now available for studying DNA, RNA and proteins.**







Comments or Questions?