

The Human Glycome Atlas Project: Initiating and Envisioning the Future

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Research System, Nagoya, Japan**



MAKE NEW STANDARDS.

東海国立
大学機構



名古屋大学



岐阜大学



iGCORE

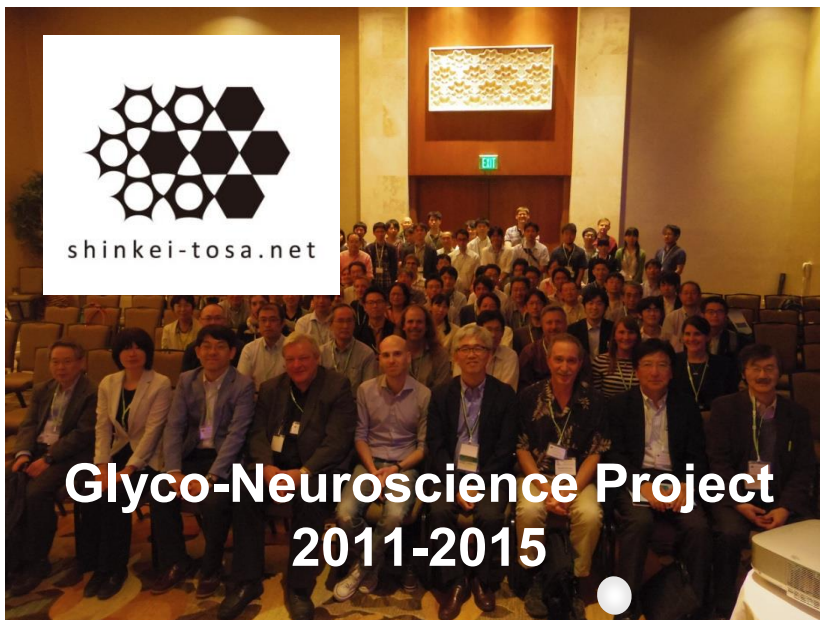
Institute for Glyco-core Research
Tokai National Higher Education and Research System



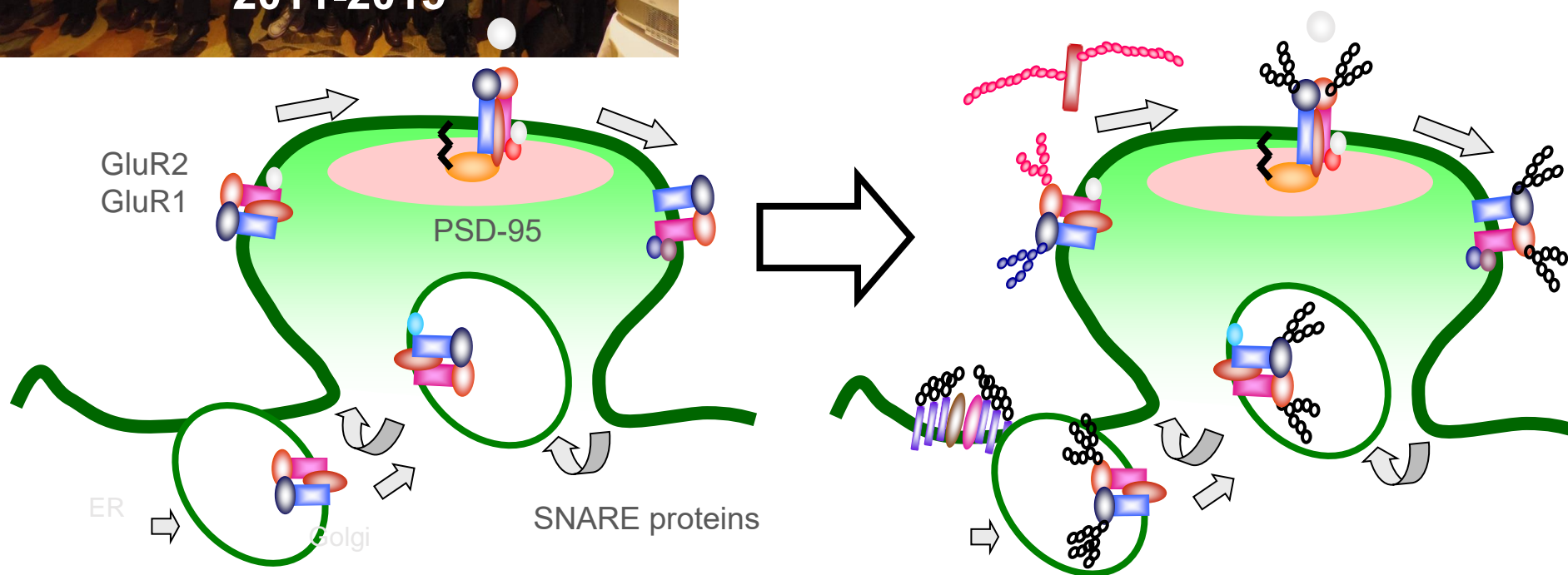
J-GlycoNet



Curiosity with a slightly broader perspective



Infrastructure Development Project ~Curiosity with a slightly broader perspective~ Human Glycome Atlas Project (HGA)





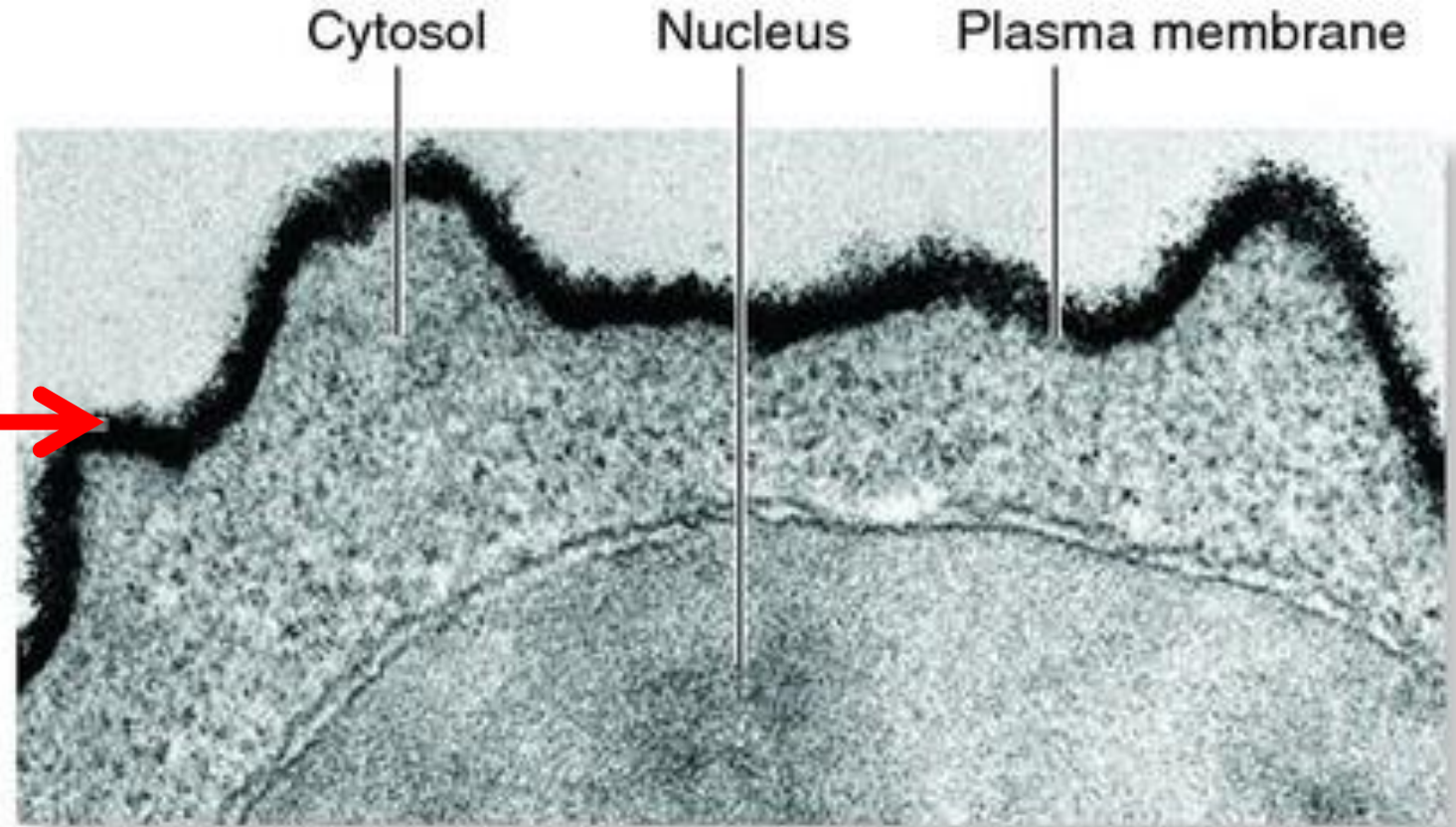
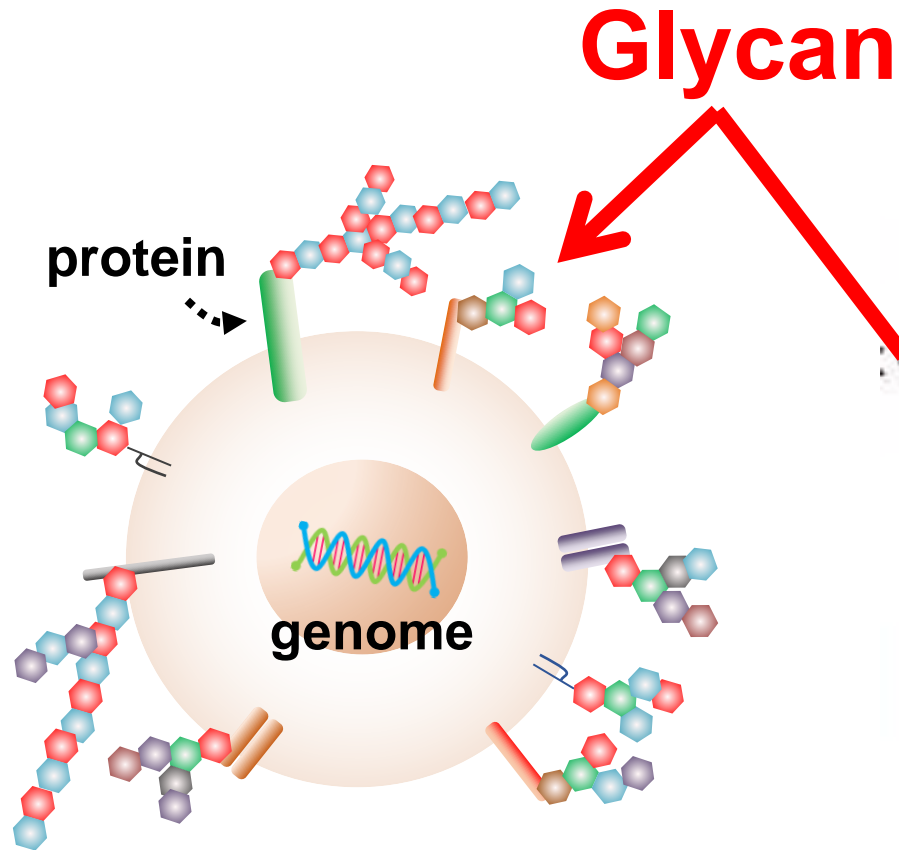
The Human Glycome Atlas Project (HGA)

The First Life Science Project in Large-Scale Academic Frontier Promotion Project “MEXT Frontier Project”

- ✓ **A project to develop the infrastructure for the future of life science**
- ✓ **A project in which Japan can lead the way**
- ✓ **A project that is expected to return benefits to the public, such as the prediction and prevention of disease**



Every cell is covered with a forest of glycans



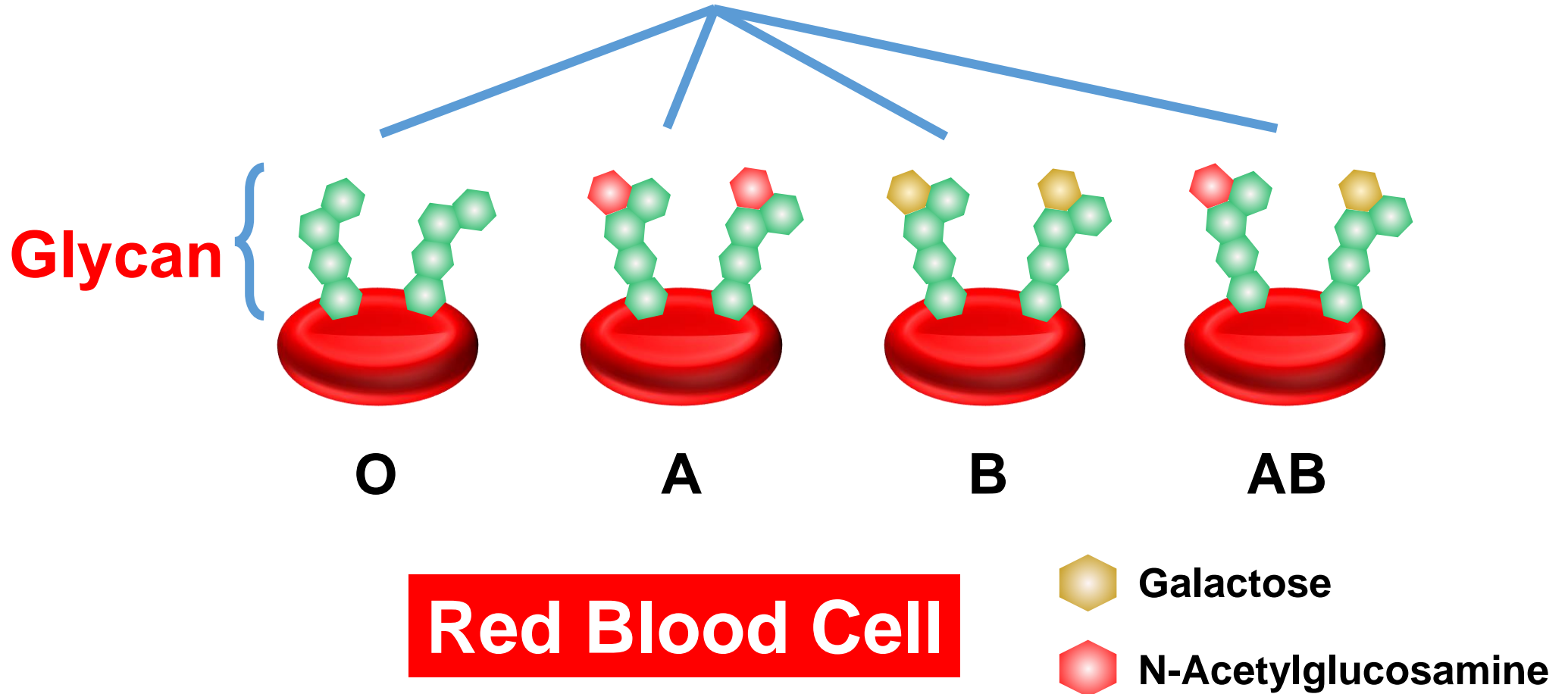
Molecular Biology of the Cell, 4th edition
Alberts Bruce et al., Garland Science, 2002

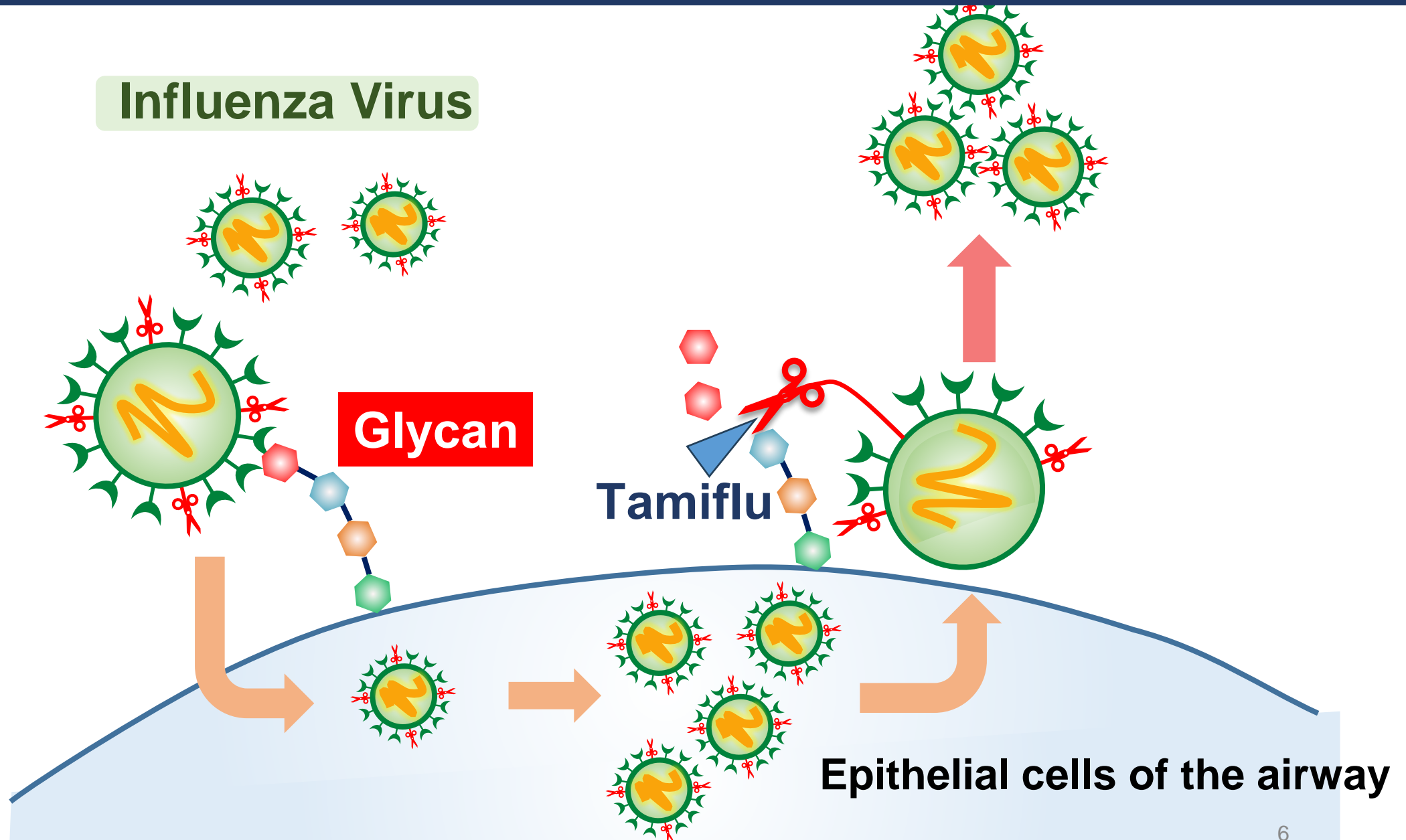
200 nm



Glycans determine blood type

Differences in glycan structure = blood type

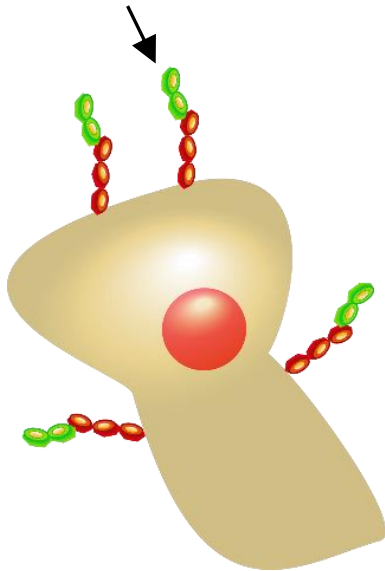




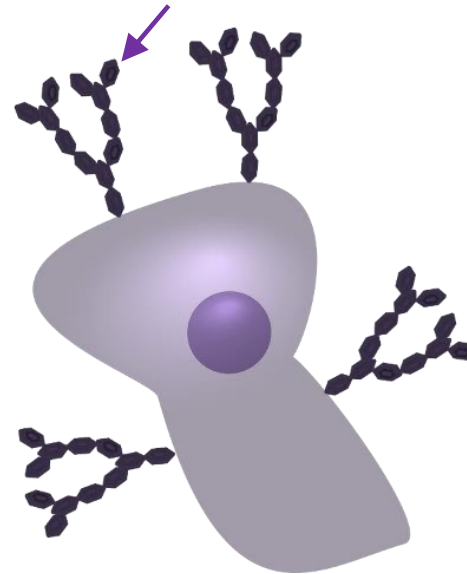


Cancer

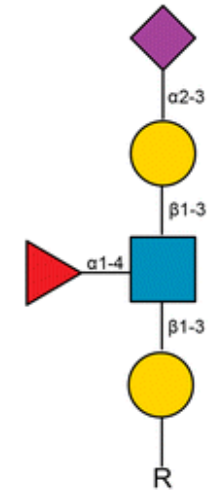
Normal cell



Cancer cell



Cancer marker

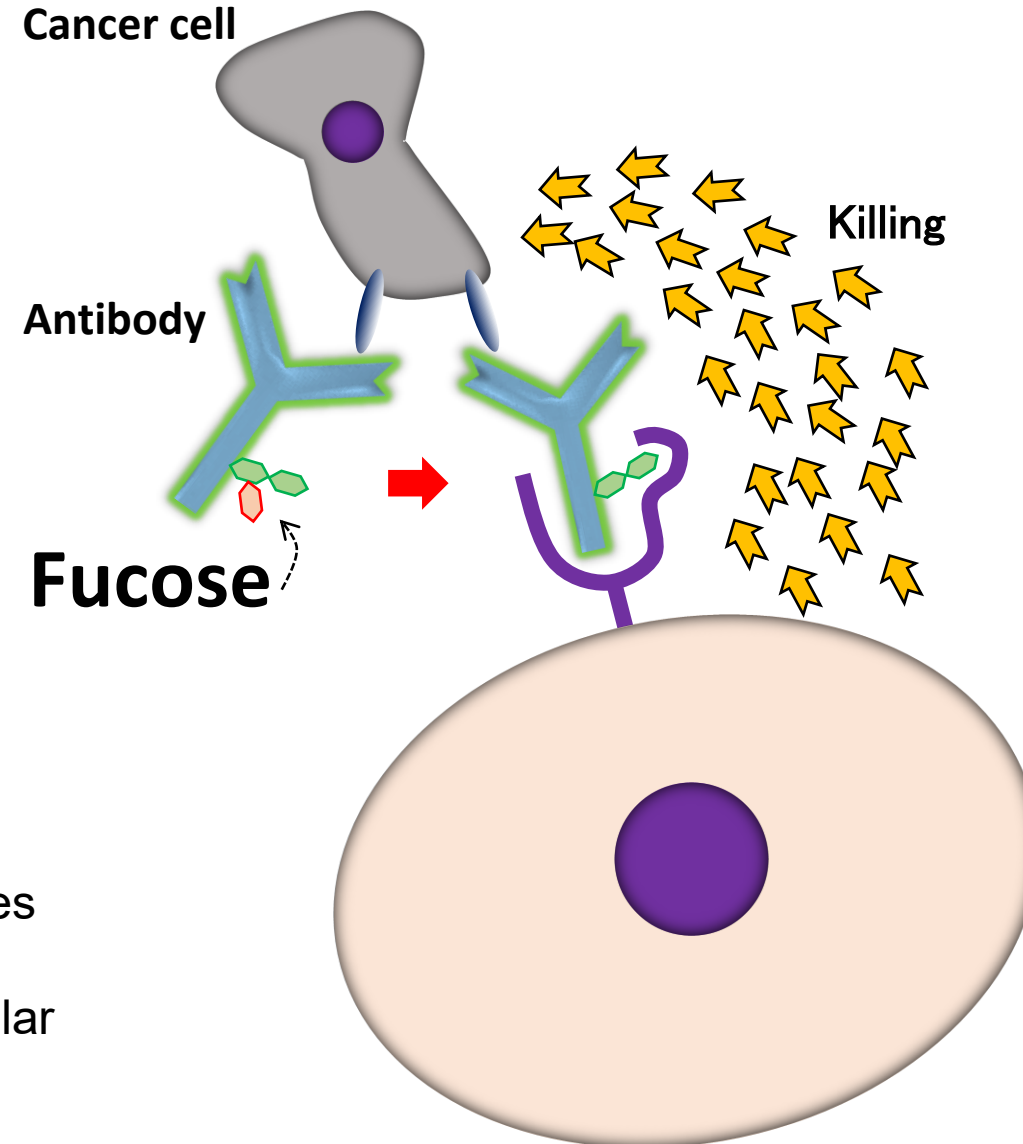


CA19-9

Pancreas cancer marker
Glycan epitope



Potelligent



Antibody drug

Potelligent

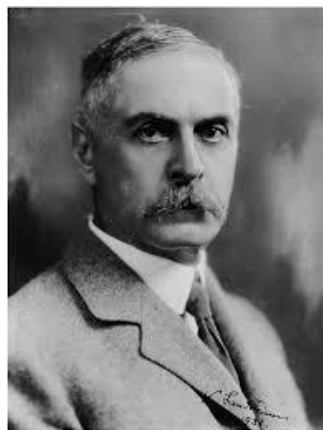
Anti-cancer effect increases
100 folds
(Antibody-dependent cellular
cytotoxicity: ADCC)



Glycans and the Nobel Prize



Hermann E. Fischer
1902 Chemistry: Synthesis
of sugar/purine derivatives



Karl Landsteiner
1930 Physiology & Medicine
Discovery of Blood Type



Luis F. Leloir
1970 Chemistry: Discovery
of Sugar Nucleotides

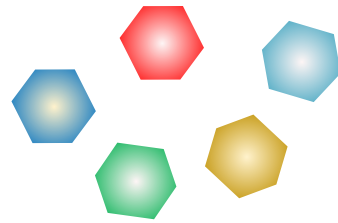


Carolyn R. Bertozzi
2022 Chemistry: Click Chemistry

<https://chemistry.stanford.edu/people/carolyn-bertozzi>
2023.2.27



Glycans are complex and diverse structures

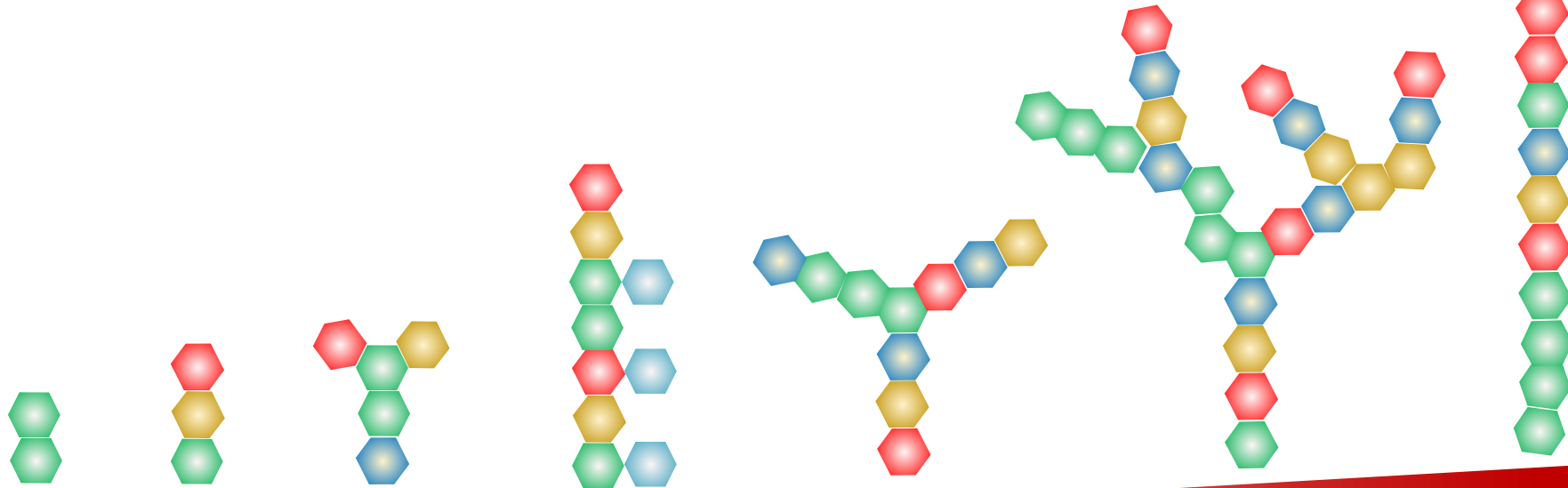


Connected
→

Component units of the chain
(Monosaccharides: members of the glucose family)
Approx. **20** types

Glycans

- ◆ Various combinations
- ◆ Diverse lengths
- ◆ Diverse branching



Short

Long



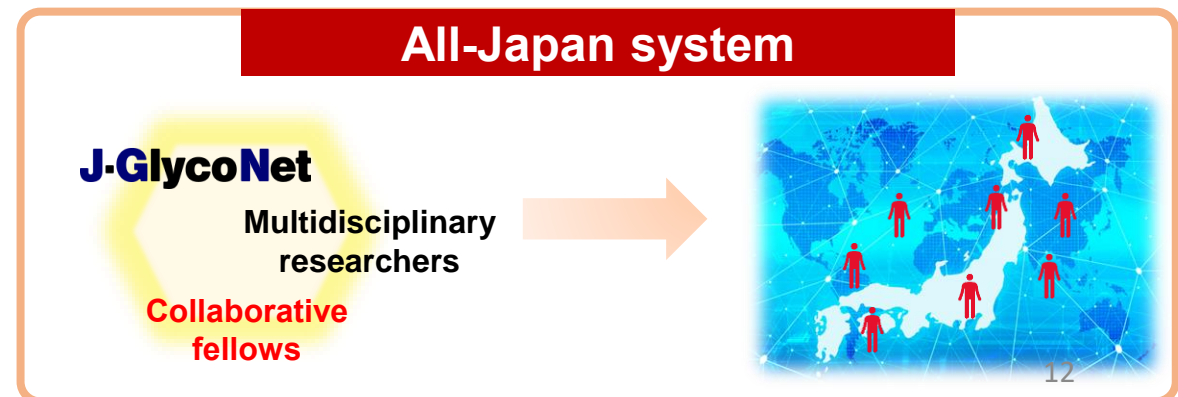
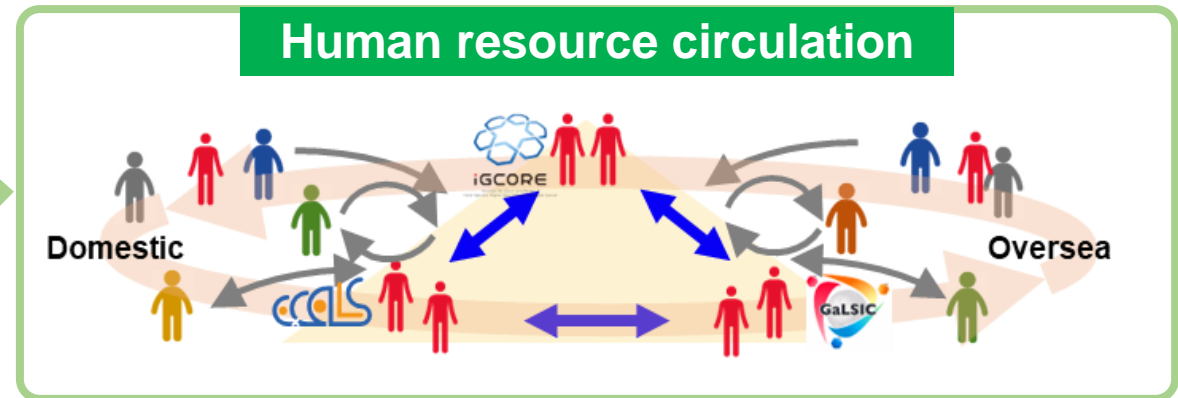
J-GlycoNet: 3 roles



Research promotion

Human Resource Development

All-Japan System



Data from MEXT publication materials regarding R5 FY budget

世界の学術フロンティアを先導する大規模プロジェクトの推進

令和5年度予算額（案） 33,989百万円
 （前年度予算額） 33,700百万円

- 目的**
- 最先端の大型研究装置・学術研究基盤等により人類未踏の研究課題に挑み、**世界の学術研究を先導**。
 - 国内外の優れた研究者を結集し、**国際的な研究拠点を形成**するとともに、国内外の研究機関に対し**研究活動の共通基盤を提供**。

大規模学術フロンティアの促進及び学術研究基盤の構築を推進

これまで学術的価値の創出に貢献

学術研究の大型プロジェクトの例

ヒューマンライコームプロジェクト

○ **ノーベル賞受賞**につながる研究成果の創出に貢献

スーパー-Bファクトリーによる新しい物理法則の探求

H20小林誠氏・益川敏英氏
→「CP対称性の破れ」を実験的に証明
※高度化前のBファクトリーによる成果

スーパーカミオカンデによるニュートリノ研究の推進

H14小柴昌俊氏、H27梶田隆章氏
→ニュートリノの検出、質量の存在の確認

○ 年間1万人以上の国内外の研究者が集結する **国際的な研究環境で若手研究者の育成**に貢献

○ 研究成果は**産業界へも波及**

大強度陽子加速器施設（J-PARC）
 [高エネルギー加速器研究機構]
 最大級のビーム強度を持つ陽子加速器施設による2次粒子ビームを用いた物性解析

⇒リチウムイオンの動作の解析による安全かつ急速充電が可能な新型電池開発
 ⇒次世代電気自動車の実用化・カーボンニュートラルの実現へ

すばる望遠鏡
 [自然科学研究機構国立天文台]
 遠方の銀河を写すための超高感度カメラ技術
 ⇒医療用X線カメラへの応用

ハイパーカミオカンデ計画の推進
 [東京大学宇宙線研究所、高エネルギー加速器研究機構]

ハイパーカミオカンデ
 (岐阜県飛騨市神岡町)

大型検出器
 (直径74m、高さ60m、総重量26万トン)
 ⇒SKの8倍規模

ニュートリノビーム

新型光検出器
 (約4万本)
 ⇒SKの2倍の光感度

大強度陽子加速器J-PARC
 (茨城県東海村)

○ 日本が切り拓いてきたニュートリノ研究の次世代計画
 ○ 超高感度光検出器を備えた大型検出器の建設及びJ-PARCのビーム高度化により、ニュートリノの検出性能を著しく向上（スーパーカミオカンデの約10倍）

→令和9年度からの観測を目指し、**大型検出器建設のための観測装置類の製造・開発や、J-PARCのビーム性能向上**等年次計画に基づく計画を推進

ヒューマンライコームプロジェクト
 [東海国立大学機構、自然科学研究機構、創価大学]

病気で苦しむことのない未来を目指して

○ ヒトの三大生命鎖（ゲノム、タンパク質、糖鎖）の中で情報が極端に少なく、日本の研究者が国際的に先行している「糖鎖」について、**国内の糖鎖研究者を中核とする連携体制や学術研究基盤を構築し、網羅的な構造解析を目指す**

○ 糖鎖を通じたヒトの真の生命現象の統合理解とともに、**認知症等の未解決の疾患に関する治療法・予防法の開拓を目指す**

→糖鎖解析に係る**革新的技術の標準化**のもと、研究者に開かれた**糖鎖ナレッジベース「TOHSA」を構築**するとともに、国内外の多様な分野の研究者が協働する**研究の場を提供**

History of Infrastructure development for major biopolymers

1990

2000

2010

2020

2030

1953
DNA Double helix
(Watson & Crick)



Human Genome Project (1990-2003)
4320億円 (米国)

Genome Medicine



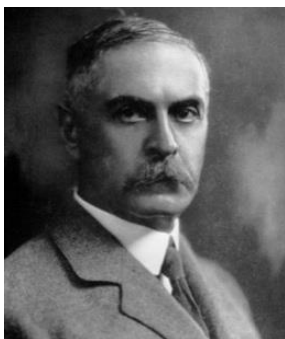
ex. Angelina Jolie



Protein3000
(2002-2006)
535億円 (日本)
300億円 (米国)

Human Protein Atlas

1901
ABO Blood type
(Karl Landsteiner)



Roadmaps for Glycoscience

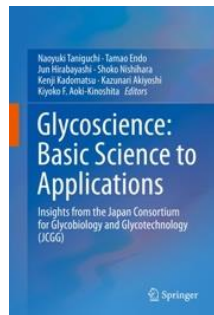
US 2012, Japan 2019, Europe 2015,2021

Glycan informatics: Glyspace Alliance

US/Japan/Europe 2018

Human Glycome Atlas Project (HGA)

Roadmap 2020, MEXT, Japan



J-GlycoNet
Joint usage/research center

"Transforming Glycoscience: A Roadmap for the Future" National Academy Press, Natl Academy Pr, 2012

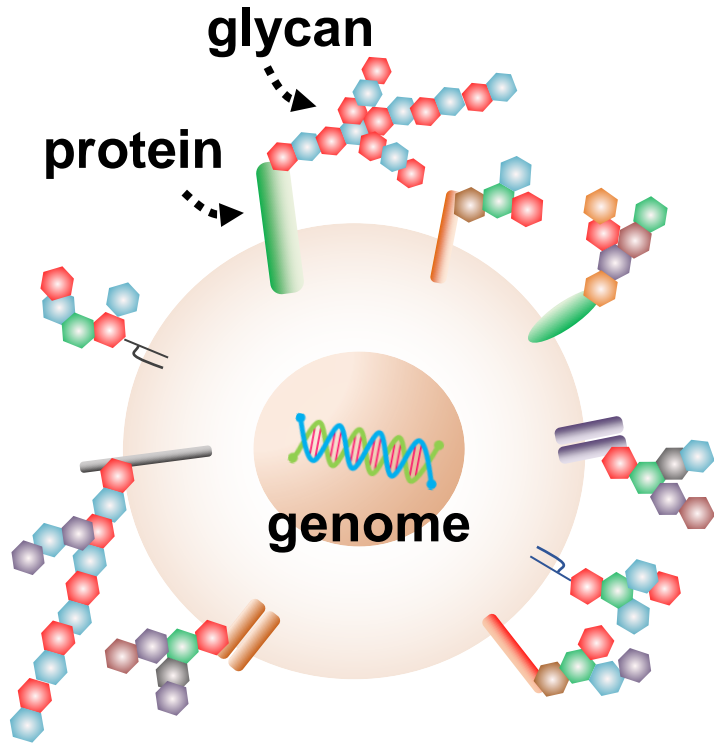
"Glycoscience: Basic Science to Applications Insights from the Japan Consortium for Glycobiology and Glycotechnology (JCGG)", Naoyuki Taniguchi et al., Springer, 2019

<https://www.ludger.com/images/news/A-roadmap-for-Glycoscience-in-Europe.pdf> 2023.3.6

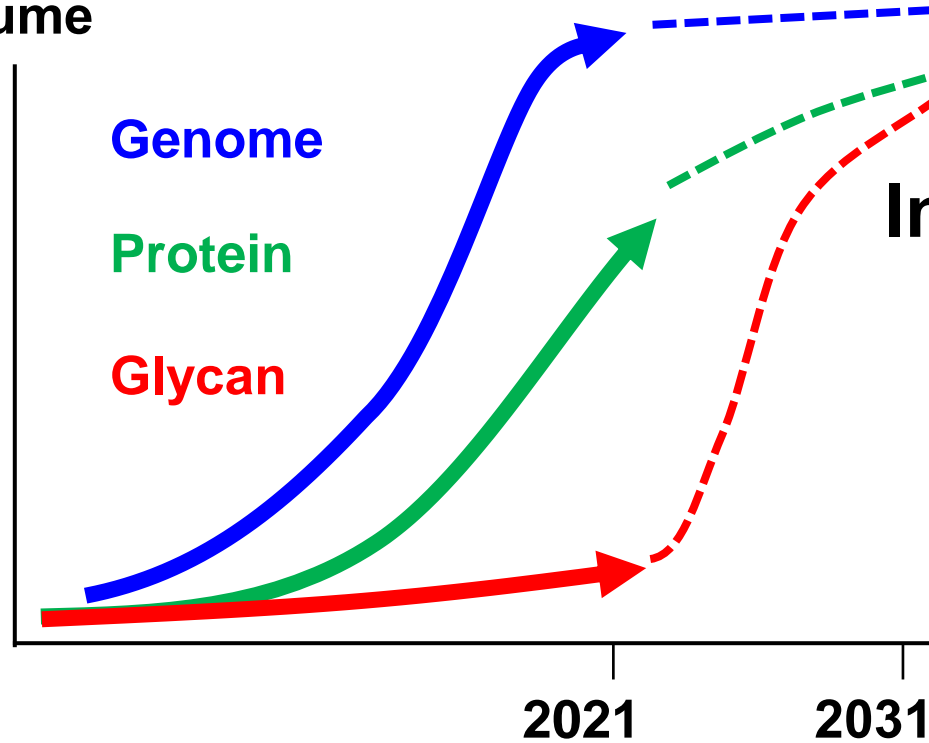
©Glyspace alliance



Increase the glycan information



Information volume



Innovation in life sciences and medicine



Increase the volume of glycan information





Contents of HGA project

Objective 1 Glycan Information Infrastructure

Construction of the knowledgebase TOHSA containing comprehensive data of human glycome

Segment 1

Human precise glycoproteome map

Segment 2

Human glycome catalog

Segment 3

Glycan biosynthesis atlas

Segment 4 Construction of the knowledgebase "TOHSA"



Planned
Fusion
Researches

Objective 3 Collaboration Infrastructure

Providing workspace and research infrastructure for cross-disciplinary researches utilizing TOHSA



All Japan
networking



Open-mix
laboratory



Global
networking

Objective 2 Equipment and Technology Infrastructure

Introduction of advanced systems necessary for construction of TOHSA and establishment of global standard technologies

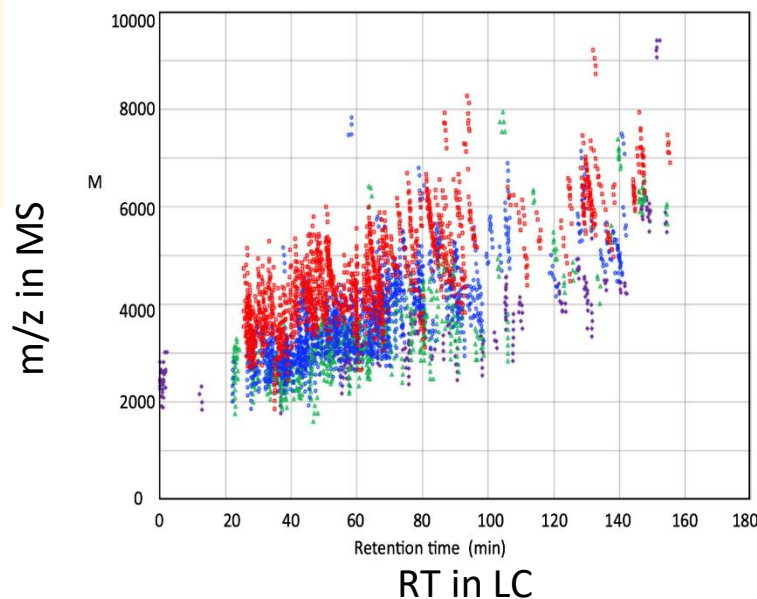


Objective 1 : Construction of the knowledgebase TOHSA

Segment 1

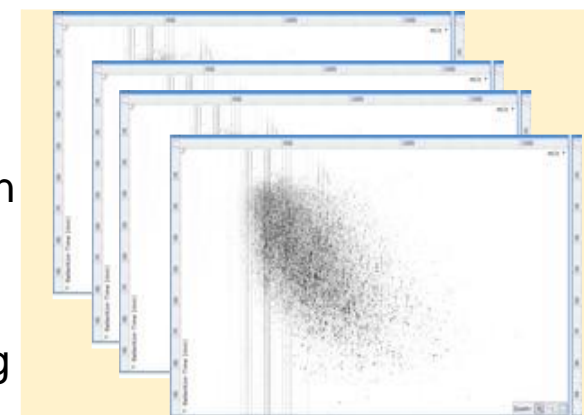
Human precise glycoproteome map

MS1: Glyco-RIDGE & IGOT
MS2: Byonic, Glyco-Decipher



Segment 2

Glycoproteome catalog



Identification



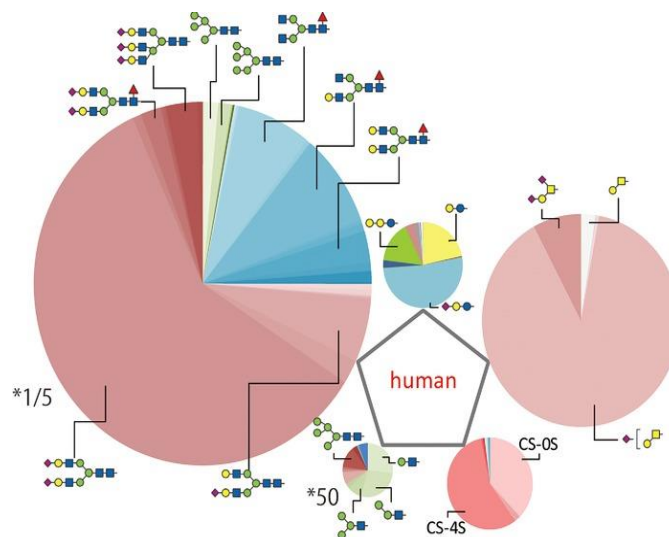
Referencing

Rapid/HTP Glycoproteomics

Large-scale comparison
(e.g., Healthy vs Disease)

Segment 2
Glycome catalog

Total Glycomics



Human glycome catalog

Segment 4

The knowledgebase TOHSA



Annual plan for HGA, a decade-long endeavor

2023

2028

2032

Comprehensive acquisition of glycome information

Objective 1

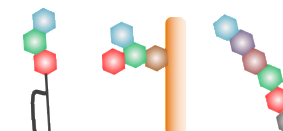
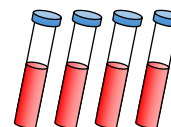
**Blood
Dementia and aged patients**

Tokyo Metropolitan Institute for Geriatrics and Gerontology

Nagoya University Brain & Mind Research Center

National Center for Geriatrics and Gerontology

**Tissue/organs/blood
Other diseases: cancer, DM etc**

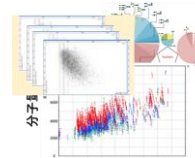
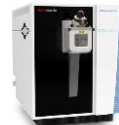
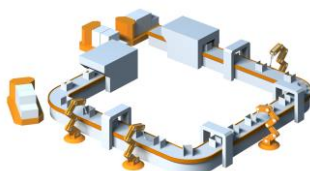


Acquisition of comprehensive data of human glycome

Acceleration and high-throughput glycomics

Objectives 1,2,3

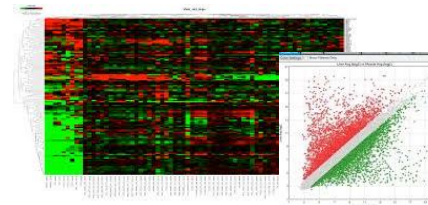
Automatization/robotics



<https://www.injection-molding.jp/blog/unmanned-driving-at-night> 2023.2.27

<https://www.thermofisher.com/jp/ja/home/industrial/mass-spectrometry/liquid-chromatography-mass-spectrometry-lc-ms/lc-ms-systems/orbitrap-lc-ms.html> 2023.2.27

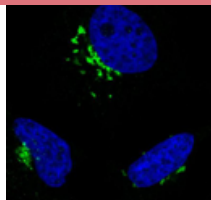
Informatics/big data analysis



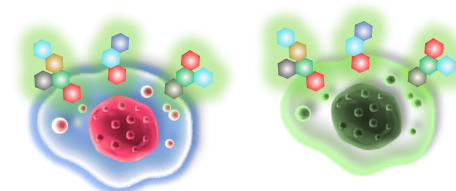
Editing of glycan structures

Objectives 1,2,3

Visualization of the biosynthetic mechanism of glycans



Development of glycan-engineered neo-cells



Toward cell therapy



Global supports for HGA

◆ **Human Glycome Atlas project**
 ◆ **J-GlycoNet**

University of Zagreb
Harvard University
Université de Lille
中央研究院 ACADEMIA SINICA
Griffith University
MACQUARIE University

January 12, 2021	
 Hirohisa Ando Director Institute for Glyco-core Research Tokyo National Higher Education and Resea	 Mark von Heijstern Director Institute for Glycomics Griffith University, Australia
 Yann Guennou Director Institute for Structural and Functional Glycobiology (USG) UMR 8576 CNRS Lille University, France	 Sheng-Cheng Hung Director Genomics Research Center Academia Sinica, Taiwan
 Ross McLennan Executive Director Research Services Macquarie University, Australia	 Gordon Luce Director Genes Glycomics Research Institute Osnite
 Richard D. Cummings Director National Center for Functional Glycomics Harvard University, USA	MOU



Global collaboration in glyco-informatics

Glycomics Informatics Integration "GlySpace" in Japan, US, and Europe in 2018

