



Analyzing glycans, the third life chain,  
and redefining life science from Japan.

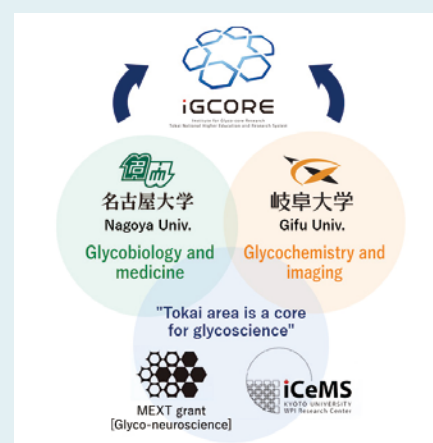
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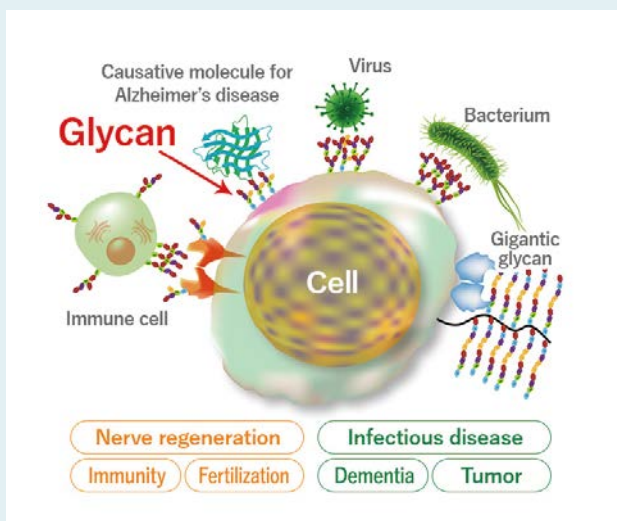
Aiming to decode all glycans and develop new diagnosis and treatment through fusion research, the first in the world.

Advancement in science and medicine is largely based on whole-genome analysis and protein research. However, many mysteries in life phenomena still remain. Glycans have gained attention as a possible key to solving those secrets. Along with genomes and proteins, glycans are considered to be essential molecular chains, and often referred to as the third life chain. Glycans cover the surface of all cells, and come in an enormous variety. Their structure and changing forms have been found to be closely related to many life phenomena and diseases, including immune and nerve function, aging, infection, cancer development and dementia. For example, differences in blood type are the result of different glycan forms, and the drug Tamiflu used to treat the flu (influenza) was born from glycan research.

Previously, life phenomena were studied mainly based of genomes and proteins. To truly understand life and see the whole picture however, glycan information is essential. Japan has taken the international lead in glycoscience research, and Nagoya University, namely the School of Medicine, was quick to focus on glycans. Many researchers, most affiliated with the Department of Biochemistry, have been studying this field for many years. Based on this tradition, the Tokai National Higher Education and Research System\*1 was established by the Institute for Glyco-core Research (iGCORE) in 2020. As a hub and base of glycoscience in Japan, world top-level researchers in glycochemistry and imaging, glycobiology, and glycomedicine have gathered to this institute from Nagoya and Gifu Universities, expanding their research activities.



For details, please refer to the Organization's website (<https://igcore.thers.ac.jp/>)



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## The established tradition of glycoscience takes the lead in next generation medicine.

In 2022, the Glyco Science Network (J-GlycoNet), which is supported by iGCORE, was designated by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) as a Joint Usage/Research Center. Not only individual research projects, but also integrative research projects that combine glycans with genomes and proteins, are underway in a nationwide system in coordination with the Exploratory Research Center on Life and Living Systems (ExCELLS) at the National Institutes of Natural Sciences (NINS) and Glycan & Life System Integration Center (GaLSIC) at Soka University.

For example, the Human Glycome Atlas Project (HGA) -From Glycome Big Data to Innovations in Life Science and Medicine- in which iGCORE plays a central role, has been chosen as a Project to Promote Large-Scale Academic Frontiers\*2 by the Japanese government in 2023. The word "glycome" is used to describe a sugar chain. This will be the first time in the world where various cutting-edge approaches are used to completely decode the vast amount of glycan structures present in humans in order to clearly understand the principles of life, and then connect this knowledge to innovative medicine.

In this project, human glycan information will be meticulously read and a precise map of the human glycan will be prepared. It is important to note that there are significant variations in glycans among individuals. For instance, blood type-specific glycans can vary depending on factors such as race, age, and other demographic variables. Consequently, information on human glycan structures must be collected from various groups, from young people to the elderly, people with diseases, etc., in order to understand the mechanisms of diseases and aging and generate a human disease-related glycan catalog. We are also working to clarify the mechanism of glycan production in the body to obtain an atlas of glycan biosynthesis pathways. Furthermore, a comprehensive knowledge base on glycan information, TOHSA, will be established, in an effort to publicize this information for use in various studies.



This project, conducted by three research institutes sharing various roles, promotes cohort studies of human populations that explore the relationship between glycans and disease through the participation of many talented resources in iGCORE, especially those in the Graduate School of Medicine of this University. Furthermore, the Brain & Mind Research Center, managed by the departments of Neurology, Psychiatry, and Neurosurgery, and in cooperation with the National Center for Geriatrics and Gerontology (NCGG) and the Tokyo Metropolitan Institute for Geriatrics and Gerontology (TMIG), will perform analysis of glycans based on blood samples from approx. 20,000 persons over 5 years, in an effort to clarify the mechanisms underlying dementia and aging. The goal is to develop biomarkers, mainly glycans, that can be used in blood tests for early diagnosis of dementia. By predicting the risk of developing various types of dementia, including Alzheimer's, the search for new treatments which have not been available up to now will be possible. Furthermore, with the collection of human glycan information of approx. 200,000 cases within the next 5 years, understanding the relationship between glycans and intractable cancers and other diseases is expected.

Trends in research themes change with the generation. However, the pioneers at this university have patiently continued their work on glycans, unphased by current popular trends. I personally have continued to pursue research in glycans, strongly aware of the many possibilities in the relationship between glycans and diseases, such as cancer, dementia, and neurologic diseases, etc. Recently, cancer has begun to be labeled as a curable disease. However, some cancers are still intractable, including pancreatic cancer. Study of glycans may contribute to future diagnosis and treatment of such cancers and other diseases. Furthermore, research in glycan age as an indicator in the maintenance of health is also being considered.

From a global standpoint, progress in the research on glycans has been slow due to their complexity and diversity, and recognition of glycans in society has yet to be established. At the same time, our goal is to map all glycans within the next 10 years and connect this to diagnosis, treatment, and the prevention of the disease based on the obtained information. This is a very lofty goal, but we hope to extensively educate society on the importance of glycans by sharing the significance of our projects and returning the research results to society, which in turn, will further promote research activities. In addition, we hope to share the attraction of glycan research to the younger generation, and promote the training of researchers who can continue to carry our role into the next generation. Integrative research centering on glycans represents an untouched field in the world. I believe this challenge will redefine our view of life science.

\*1Tokai National Higher Education and Research System / Integration of Nagoya University and Gifu University under one corporation in order to share the strengths of each university, aiming to contribute to regional development and advancement into world-leading research universities. Established in April 2020.

\*2 Project to Promote Large-Scale Academic Frontiers / A project by the Ministry of Education, Culture, Sports, Science and Technology (MEXT), combining cutting-edge technology and knowledge to meet challenges in research that have not been attempted by man up to now, and promote large-scale projects with groundbreaking results which will lead future world academic research.

