【Grant-in-Aid for Transformative Research Areas（B）】

Innovative Intestinal Dialogue Research on Gut Microbe-Host Interactions Mediated by Glycans

Principal Investigator	Gifu University, Institute for Glyco-core Research (iGCORE), Professor FUJITA Morihisa　Researcher Number : 30532056
Project Information	Project Number : 25B304　Project Period (FY) : 2025-2027 Keywords : Glycans, HMOs, Gut Microbes, Intestinal Immunity, Intestinal Diseases

Purpose and Background of the Research

●Outline of the Research

The human gut contains about 40 trillion bacteria that interact with the host directly or through metabolites. Traditionally, glycans in the gut were seen as nutrients for microbes or protective barriers for the host. However, recent studies show that glycans serve as a "common language" between gut bacteria and host cells, playing key roles in immune regulation and gut homeostasis. Despite their importance, many molecular mechanisms behind interactions mediated by glycans remain unclear due to their complexity. This study pioneers "Gut Glycobiology" by investigating the roles of human milk oligosaccharides (HMOs), mucin glycans, and bacterial surface glycans in shaping the gut environment. We also explore how disruptions in these interactions contribute to diseases like necrotizing enterocolitis, inflammatory bowel disease, and cancer. Our goal is to uncover the biological significance of glycans and their potential for disease prevention and treatment.

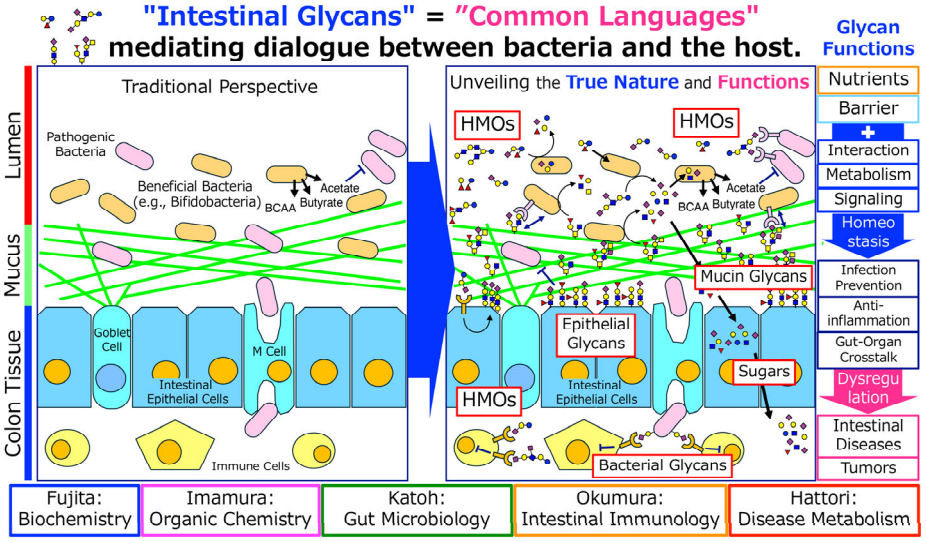

Figure 1. Establishment of Intestinal Glycan Dialogue Research

●Research Team

Our research team consists of young experts from diverse fields, including Biochemistry (Fujita), Organic Chemistry (Imamura), Gut Microbiology (Katoh), Intestinal Immunology (Okumura), and Disease Metabolism (Hattori). By integrating these disciplines, we aim to go beyond traditional academic boundaries and establish a comprehensive research domain on gut glycan dialogue.

Expected Research Achievements

●Plan and Methods for Promoting the Research Area

This research introduces the "Intestinal Glycan Dialogue" hypothesis, proposing that common structures of gut glycans, such as human milk oligosaccharides (HMOs) and mucin glycans, function as a shared biochemical language between gut microbiota and the host cells. By deciphering this language, we aim to understand its role in intestinal homeostasis and disease mechanisms and explore its potential therapeutic applications.

To achieve this, we integrate multiple research projects, each focusing on different biological contexts where gut glycans play a crucial role:

【1】HMO Biosynthesis and Roles in Gut

We will elucidate the biosynthetic pathways of HMOs, which are utilized for communication between gut microbiota and intestinal cells, and develop HMO production systems. Using Organic Chemical approaches, we will synthesize HMOs and mucin glycans to investigate their impact on gut microbiota composition, metabolome changes, and inflammatory disease prevention. Specifically, we will examine their therapeutic potential in necrotizing enterocolitis (NEC) and other inflammatory conditions.

【2】Gut Glycans and Intestinal Homeostasis

We will analyze how gut glycans contribute to microbiota stability and immune homeostasis using natural or labeled HMOs and glycosyltransferase gene-deficient mice that lack specific mucin glycan structures. Through omics analyses, we will elucidate how these glycans influence microbial dynamics, the barrier function of intestinal epithelial cells, and immune responses.

【3】Pathogen Immune Evasion via Glycans

Many pathogens evade immune surveillance by modifying their surface polysaccharides with sialic acid, mimicking host cell structures. We will investigate these immune evasion mechanisms and explore how HMOs influence pathogen-host interactions, potentially leading to new antimicrobial strategies.

【4】Gut Bacteria-Derived Metabolites and Disease

We propose that bacterially synthesized branched-chain amino acids (BCAAs) derived from glycan metabolism directly influence other organs and tumor stem cells. We will investigate their role in tissue homeostasis, stem cell function, and tumor development, providing insights into the systemic impact of gut-derived metabolites.

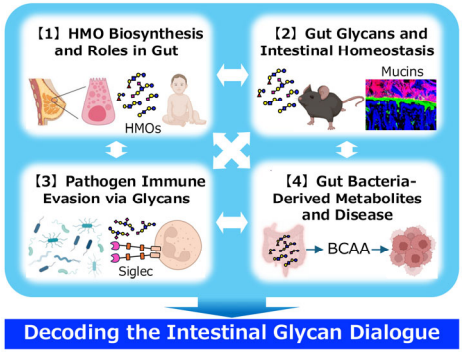

Figure 2. Research Objectives

●Potential Impact of the Research Area

Beyond gut health, this research has the potential to expand into "Extra-Gut Dialogue", exploring how gut homeostasis influences other organs, such as the brain, liver, and pancreas. Furthermore, our findings may extend to mucosal glycan interactions in the oral cavity, respiratory tract, stomach, and reproductive system, paving the way for broader applications in host-microbiome research and therapeutic development.

Homepage Address, etc.	http://intestinal-glycan-dialogue.jp/