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

Section II

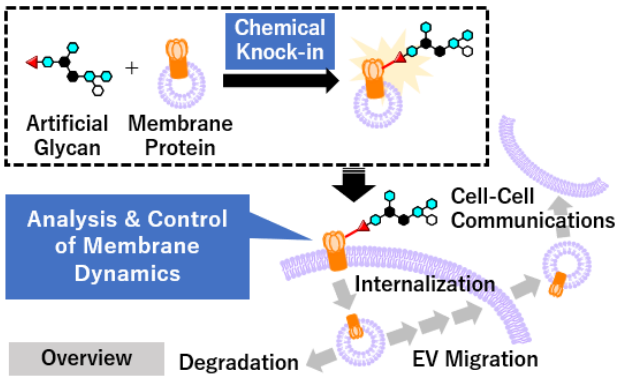
Title of Project： Regulation of membrane dynamics by glycan chemical knock-in

OISAKI Kounosuke
(The University of Tokyo, Graduate School of Pharmaceutical Sciences, Lecturer)

Number of Research Area：21B201　Researcher Number：00583999

【Purpose of the Research Project】

Cell-surface glycans are involved in membrane dynamics of biomolecules related to various functions of life, such as endocytosis, migration to rafts, and extracellular vesicle (EV) uptake. Glycans connected to membrane proteins play a central role in membrane dynamics. We hypothesize that the regulation of membrane protein dynamics by glycans may lead to new artificial methods for analysis and regulation of biological functions. We are developing technologies based on the integration of biocompatible chemistry and biological research, such as synthesis of homogeneous glycoproteins and developing a chemical labeling method to precisely track the dynamics and interactions of membrane glycoproteins. We are also pursuing "glycan chemical knock-in" as an innovative methodology to control the membrane dynamics of glycoproteins depending on the glycan structure, in which artificial glycans are modified on membrane proteins using biocompatible chemical reactions.



【Content of the Research Project】

The three research groups are organized to study corresponding sub-projects in a parallel and shared style.

[A01] "Creation" of glycoproteins on membranes

We will construct a homogeneous glycan library with a variety of structures. In parallel, we will develop a method to link glycans to membrane proteins without being restricted by glycan structures.

[A02] “Observation” of membrane dynamics of glycoproteins with chemical probes

To track the behavior and interaction mode of glycoproteins, we will establish a labeling technique using small biocompatible catalysts and ultra-small protein tags, and a tracking system for protein membrane dynamics.

[A03] "Manipulation" of membrane dynamics of glycoproteins by glycan modification and external stimuli

We will establish a catalytic methodology for precise introduction of non-natural modification groups and stimuli-responsive groups into glycans to expand the structural diversity of glycoproteins. We will prepare a comprehensive library of glycosylated membrane proteins on the exosome and investigate the correspondence with membrane dynamics. We will also demonstrate the possibility of artificial manipulation of membrane dynamics by changing the glycan structure by external stimuli.

【Expected Research Achievements and Scientific Significance】

We will advance the understanding of membrane dynamics of glycoproteins with high precision, leading to artificial control methods. This will lead to the creation of new drug delivery systems and new methods of manipulation of biological functions by biocompatible reactions (kinetic chemical perturbations).

【Key Words】

Chemical knock-in: Technologies that use biocompatible reaction chemistry to add-on/upgrade biological functions.
Membrane dynamics: The spatiotemporal behavior of biomolecules on biomembrane. Biomolecules change their localization with the membrane and perform their proper function when properly localized on the biomembrane.

【Term of Project】 FY2021-2023

【Budget Allocation】 104,800 Thousand Yen

【Homepage Address and Other Contact Information】

https://glycan-chemical-knockin.com/
glycan.chem.knockin@gmail.com