【Grant-in-Aid for Scientific Research (S)】

Biological role of GOMED and related diseases

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Project Information	Project Number : 23H05480 Project Period (FY) : 2023-2027 Keywords : Golgi apparatus, GOMED, proteolysis, neurodegenerative disease

Purpose and Background of the Research

●Outline of the Research

Autophagy is known as a function that controls the quality of intracellular proteins. On the other hand, the principal investigator has discovered Golgi-membrane associated degradation (GOMED) as a quality control mechanism for plasma membrane proteins and secretory proteins transported via the Golgi apparatus. We have also discovered the possibility of disease onset due to abnormalities in GOMED. This study aims to elucidate the execution mechanism of GOMED and to analyze related diseases.

1, How is GOMED executed?
2, Where and when does GOMED function in our body?
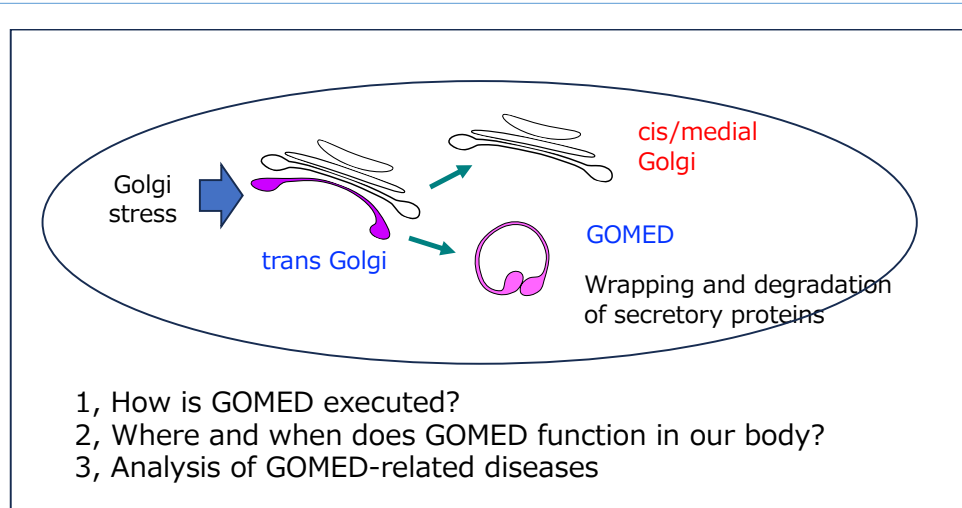3, Analysis of GOMED-related diseases

Figure 1   Purpose of this study

GOMED is formed from the trans-Golgi membranes. In this study, we will determine how GOMED is executed. We will analyze where, when, and what GOMED functions in our body. We will also identify human diseases in which GOMED abnormalities are involved.

● Analysis of GOMED-related Molecules

To date, we have identified more than 10 GOMED-related molecules, but there are several more unidentified molecules. These will be identified by yeast genetics, chemical biology, and immunoprecipitation/mass spectrometry.

●Analysis of GOMED elementary processes

GOMED is formed by deformation of the trans-Golgi membrane. We will analyze what molecules are altered in the Golgi membrane and how the membrane is deformed using high-speed super-resolution 4D microscopy (SCLIM), CLEM analysis, which combines electron microscopy and fluorescence microscopy, and SICM, which enables molecular measurement of the Golgi local area.
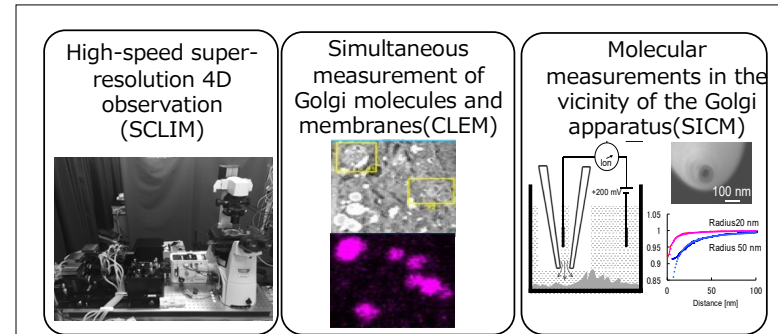

Figure 2   Analysis of the elementary process of GOMED

Analyze the linkage between structure and function of the Golgi apparatus by measuring the dynamics of Golgi molecules, the localization relationship between molecules and membranes.

Expected Research Achievements

●Analysis of GOMED-related human diseases

In mice with neuron-specific GOMED disruption, neurodegeneration with iron deposition occurs. Since diseases showing similar phenotypes have been reported, we will clarify whether modulation of GOMED is involved in these disease.

Currently, it has been suggested that GOMED is associated with a variety of diseases, including enterocolitis, and these will be proven.
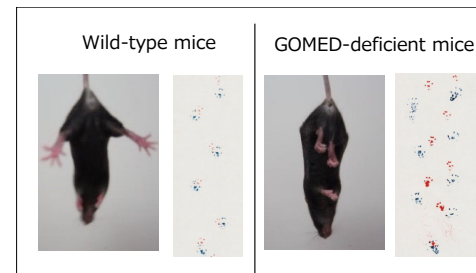

Figure 3 Mice with disrupted GOMED have impaired postural retention, gait, and neurodegenerative disease-like symptoms.
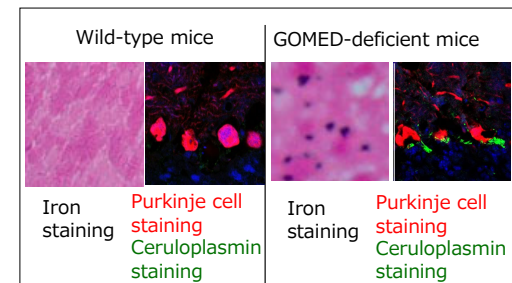
Figure 4 Iron deposition and accumulation of ceruloplasmin (an iron-metabolizing enzyme degraded by GOMED) appear in neurons of mice with disrupted GOMED

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