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

**Section III**

# Title of Project： Life Science Innovation Driven by Supersulfide Biology

MOTOHASHI Hozumi
(Tohoku University, Institute of Development, Aging and Cancer, Professor)

Number of Research Area：21A303　Researcher Number：00282351

## 【Purpose of the Research Project】

Sulfur has been an essential element for living organisms on the earth during the long history of evolution. Unique chemical properties of sulfur include redox-sensitive nature and ability to catenate only by itself. The latter allows generation of a wide variety of sulfur-containing molecules that are rather fragile due to the former. We define “supersulfides” as metabolites and proteins possessing sulfur catenation (Figure 1). Because supersulfides are so sensitive to redox perturbation and easily degraded or altered during the sample processing, their presence in biological contexts has been overlooked for a long time. Thanks to a recent technical advancement in the analytical chemistry, substantial amount of supersulfides, such as glutathione persulfide and cysteine persulfide, have been found in various organisms. Low-molecular weight supersulfides are now recognized as universal metabolites and play critical roles in energy production, antioxidant function, and anti-inflammatory function. Supersulfidated proteins are expected to be involved in the protein folding, proteostasis regulation, and regulation of protein functions. Based on these emerging biological functions of sulfur, we aim at creating and establishing innovative sulfur biology by further clarifying chemical, physical and biological characteristics of supersulfides and interdisciplinary research network among wide range of scientific fields, including chemistry, physics, geoscience, biology, mathematics and so on.

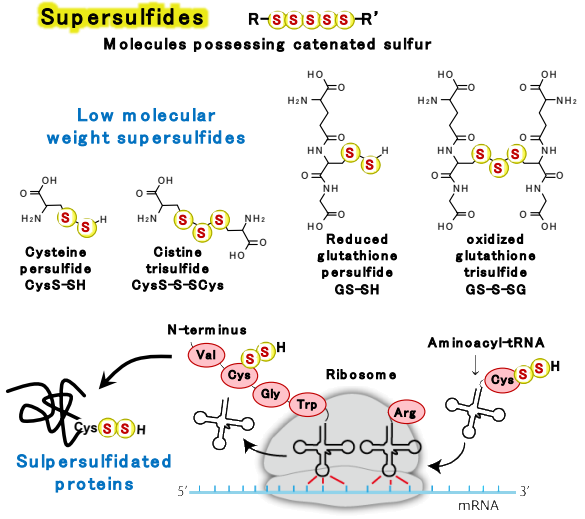


Figure 1. Supersulfides are present in the form of low molecular weight metabolites and in cysteine residue side chains of proteins.

## 【Content of the Research Project】

The most fundamental themes of our research field are clarification of chemical properties and metabolism as well as quantification and visualization of supersulifdes (Figure 2). Based on these knowledge and technology, we will clarify biological electron transfer mediated by supersulfides in various cellular compartment, such as mitochondria, chloroplast, cytoplasm, endoplasmic reticulum and plasma membrane. We will also clarify contribution of supersulfides to signal transduction and proteostasis in various organisms.

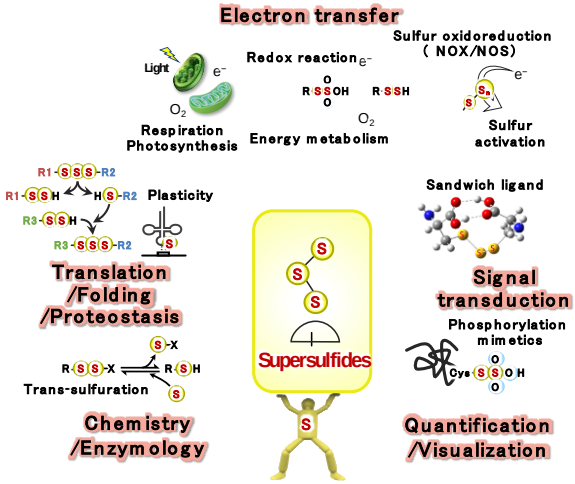


Figure 2. Multiple approaches for clarification of chemical properties, metabolism, and roles of supersulfides in various biological processes including electron transfer and signal transduction.

## 【Expected Research Achievements and Scientific Significance】

Emergence of biological supersulfides is innovating fundamental concept of life science. The impact will spread as far as medical practice by developing new diagnostics and therapeutics, food security by elevating photosynthesis efficiency, and geoengineering by modulating biogenic sulfur emission.

## 【Key Words】

Supersulfides: Molecules containing catenated sulfur atoms. Due to unique chemical properties of sulfur catenation, supersulfides play dual roles as electrophiles and nucleophiles.

**【Term of Project】** FY2021-2025

**【Budget Allocation】** 1,074,700 Thousand Yen

## 【Homepage Address and Other Contact Information】

https://www.supersulfide.proj.med.tohoku.ac.jp