



**Title of Project : Oxygen biology: a new criterion
for integrated understanding of life**

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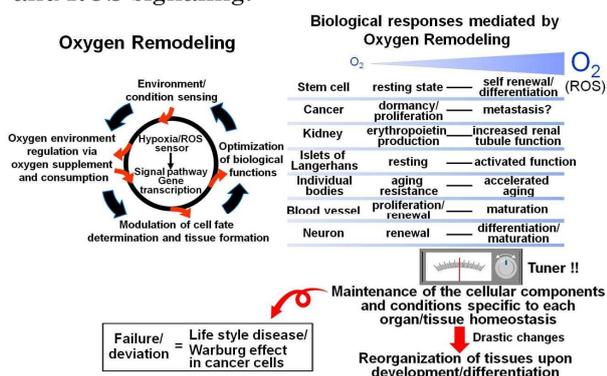
Research Project Number : 26111001 Researcher Number : 80212265

【Purpose of the Research Project】

Molecular oxygen (O₂) is indispensable for aerobic organisms. From the perspective beyond the classical understanding of O₂, a new biology field “oxygen biology” is emerging.

The first novel point of view in oxygen biology is the significance of the different levels of hypoxia inside the bodies. It is known that O₂ supply is increased under hypoxic conditions to prevent damages. However, recent studies show that the internal hypoxic environment has physiological significance, overturning the preconceptions of O₂. The second point is the role of O₂ and reactive oxygen species (ROS) and electrophiles as signaling molecules. New O₂-originating species have been identified, but their biological insights are still limited and not investigated for systems as a whole within a specific internal O₂ environment.

Based on our unprecedented concept “oxygen remodeling” that cells actively regulate O₂ concentration to the optimal range according to their needs, this project will aim to unveil how cells sense, respond and utilize the O₂ environment, by focusing on energy metabolism and ROS signaling.



Nobel concept of oxygen biology: “Oxygen Remodeling”
【Content of the Research Project】

This research project will be coordinated and conducted based on the specific aims A01-A03.

A01 aims to clarify the mechanisms by which hypoxic environments *in vivo* are detected and formed from the perspective of energy metabolism. Specifically, hypoxia effectors such as Hypoxia-inducible factors regulated by prolyl

hydroxylases/unknown hydroxylases will be identified, to reveal the acute and chronic regulatory systems in the cells and tissues.

A02 studies the mechanism of how ROS, reactive nitrogen/sulfur species (RNS/RSS) mediate and confer reversibility to elementary processes in the signaling pathways evoked by O₂, to elucidate active utilization of hypoxic environments in oxygen remodeling for the optimization of functions of tissues and cells.

A03 will develop novel *in vivo* imaging techniques to visualize hypoxia and electrophilic reactive species, to secure the methodological basis to conduct A01 and A02.

【Expected Research Achievements and Scientific Significance】

The new field “oxygen biology” established by the fusion of leading-edge researches will bring forth world-leading achievements. Also, this project will integrate and restructure different research fields to significantly improve the overall levels of academia. Furthermore, scientists from various generations gathering at the common platform of oxygen biology will facilitate cultivation of the next generation.

This project will help to prevent and develop treatments of lifestyle-related diseases, cancer, aging, inflammation, caused by the deviation of O₂ and ROS signals. These developments will contribute to solving critical social problems in super-aging society and adaptation of our life to the changes of global environment.

【Key Words】

Oxygen remodeling: the concept that the cells actively control O₂ concentration to be in the optimal range according to their needs.

【Term of Project】 FY2014-2018

【Budget Allocation】 1,176,200 Thousand Yen

【Homepage Address and Other Contact Information】

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