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

Section III

Title of Project： Cross-scale new biology

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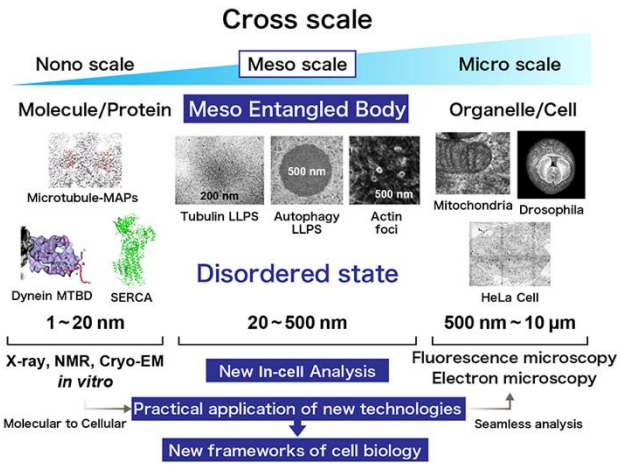
Number of Research Area：21A302　Researcher Number：80272425

【Purpose of the Research Project】

The aim of our project is to elucidate the molecular and cellular mechanisms of life phenomena and diseases by using quantitative cross-scale measurements. In particular, we focus on disordered structures of 20 to 500 nm, which we define as the "**meso-entangled bodies (MEBs)**," (see Key Words) because we think MEB is the key that determines the cell fate and organisms by transitioning from a disordered state to an ordered state.



For the cross-scale measurement, we establish a virtual "**cross-scale cell measurement center**" (see Key Words) to combine cryo-electron tomography (cryo-ET), super-resolution imaging, intracellular NMR, and intracellular atomic force microscopy (AFM). Large-scale computational science is also used to integrate and interpret experimental data. The aims of study of our biology group include the following three biological and medical areas: "The polarity of cell and development," "The shape and topology of membranes," "structural abnormalities and quality control of proteins that cause diseases." We want to create new frameworks of cell biology that answer how highly ordered, and functional structures are built from the random MEBs by analyzing these fundamental phenomena by cross-scale measurements.

【Content of the Research Project】

This Research Area consists of two groups, A01 and A02. Group A01 develops cutting-edge technologies to enable cross-scale cell measurements, and Group A02 expands new biology using cross-scale cell measurements.

To realize cross-scale observations of MEBs, the A01 technical group combines their state-of-the-art technologies, seamlessly bridging "time" and "space." For this purpose, we will carry out close collaboration based on the "cross-scale cell measurement center." For example, we will develop labeling techniques that can be used in multiple methods to enable cross-scale measurement. The labeling techniques will enable us to measure and demonstrate the same structure or phenomenon in the cell independently by multiple methods, quantifying the reproducibility of measurements.

The A02 Biology Group will apply these cross-scale cell measurement technologies to gain a deeper understanding of important cellular life phenomena from the perspective of intracellular molecular structure, localization, and dynamics, and also apply the findings to elucidate disease mechanisms from a medical perspective. The A02 group will also give feedback the needs of technological improvements that emerged through the analysis to the A01 group, leading to further technological development.

【Expected Research Achievements and Scientific Significance】

Our cross-scale cell measurement will make it possible to identify and track the MEBs precisely and observe their structure and dynamics in the cell. This will lead to the discovery of the fundamentals of life phenomena, the understanding of diseases through observing the behavior of abnormal molecules, and the creation of new functional molecular targeted therapies. Our cross-scale measurement also requires cross-disciplinary thinking, which will lead to the cultivation of young researchers who can overlook the interdisciplinary fields of biology, medicine, engineering, and chemistry.

【Key Words】

Meso-entangled body: A mesoscale structure that does not make a fixed structure within a cell (disorder) but determines the fate of a cell or organism by transitioning to an ordered state. A liquid-liquid phase separation (LLPS) condensate is one example of MEB

Cross-scale cell measurement center: A virtual center for the operation and integration of cross-scale cell measurements established in this area.

【Term of Project】

FY2021-2025

【Budget Allocation】

1,095,800 Thousand Yen

【Homepage Address and Other Contact Information】

https://structure.m.u-tokyo.ac.jp/xscalebio