Laboratory of Nanobiology

Institute for Protein Research

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Our body is made up of many cells. The proper functioning of each cell allows us to live in good health. Knowing the state inside a cell and knowing what is happening inside a cell is very important for understanding life. Therefore, we are developing methods to measure the environment of the nano region inside the cell using small fluorescent diamond particles, measuring the local temperature inside the cell, and investigating how the temperature change affects the cell function. We also provide a fluorescence microscope that can image protein secretion from individual cells in real time, and are conducting collaborative research with multiple laboratories.

Developing techniques for intracellular temperature measurement

The temperature is a fundamental parameter in biology and affects metabolism and biorhythm. However, temperature fluctuations in space and time in individual cells has been largely unknown. We develop methods to quantitatively image the temperature using the fluorescence microscopy and various types of fluorescent “nanothermometers” that are based on fluorescent polymers (Fig. 1), fluorescent nanodiamonds, fluorescent nanoparticles or fluorescent molecules. In this research topic, we are studying the biological relevance of the thermal fluctuation. We also aim to apply our methods to issues in biomedical studies.

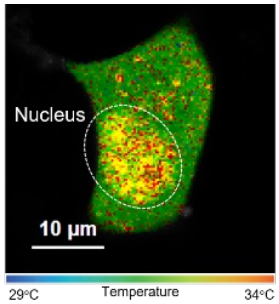

Figure 1. Intracellular temperature imaging

Quantum biosensing using fluorescent nanodiamond

It is necessary to develop a nano-sized sensor to investigate how nanometric environments (e.g. temperature, magnetic and electric fields) affect the biochemical reactions inside single cells. Fluorescent nanodiamonds (FNDs) containing nitrogen-vacancy centers (NVCs) are emerging as a novel type of fluorescent probe due to the stable fluorescence showing no photo-bleaching (Fig. 2). Besides, their unique quantum properties lender them as a promising nanometric biological sensor.

Our group has developed an ODMR microscope enabling the optical read-out of the quantum states of FNDs. Using the ODMR microscope, we have demonstrated temperature and thermal conductivity measurements of living single cells. We currently investigate the mechanism how cells sense temperature by using chemically controlled FND composites.

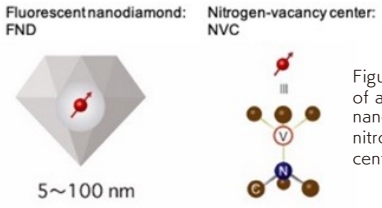

Figure 2. Illustration of a fluorescent nanodiamond and a nitrogen-vacancy center

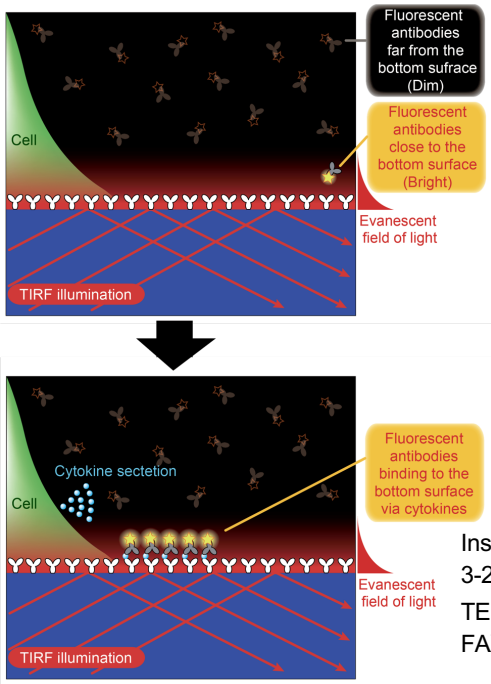

Figure 3. Schema of LCI-S: live-cell imaging of secretion activity

Analysis of immune responses using live-cell imaging of secretion activity

Intercellular messengers such as hormones, cytokines, and extracellular vesicles play an important role in the information exchange between cells and the collaborative regulation of the biological systems that organize human body. We have developed "live-cell imaging of secretion activity (LCI-S)" to visualize the true state of cell secretion by combining fluorescence sandwich immunostaining and total internal reflection fluorescence microscopy (TIRFM) techniques (Fig. 3). Since LCI-S is suitable for primary cultured mouse cells, human clinical biopsied cells, ES cells, iPS cells, etc., it is expected to be used for various applications such as functional hematology in precision medicine, phenotypic screening and toxicity evaluation in drug discovery, quality control of cell therapy and evaluation of efficient control of differentiation in regenerative medicine. We are also working on a social implementation of our technology (Live Cell Diagnosis, Inc.).

Looking inside the cells that make up our body, various protein molecules are working there. In order to know about organisms, it is very important to investigate how protein molecules work. So far, we have developed a method for directly observing how protein molecules work using a microscope, and have investigated how proteins work well. Recently, we are also observing cells in order to understand the cells where proteins work. Little by little, we want to approach the wonders of life.

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