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PRESS RELEASE

Source: Toyohashi University of Technology, Japan, Committee for Public Relations

Release Title: "Seeing" and "Manipulating" Functions of Living Cells
Release Subtitle: Aiming to create "God's eye" and "God's hand" to solve the mystery of life

Overview

A research team of the Department of Computer Science and Engineering and the Electronics-Inspired Interdisciplinary Research Institute at Toyohashi University of Technology has discovered that the difference in the ability to hear and distinguish English words including L and R, which are considered difficult for Japanese people, appears in pupillary (the so-called “black part of the eye”) responses. While the pupil has the role of adjusting the amount of light that enters the eye, it is known that the size changes reflect the cognitive state of humans. In this study, the research team conducted experiments to simultaneously measure the size of the pupil while playing English words in combinations such as “Light” and “Right”, and clarified that it is possible to objectively estimate the ability to distinguish English words from the eyes.

Details

An integrated understanding of life phenomena and the control thereof are absolutely essential for further development of the medical and pharmaceutical fields. The thesis for creating life innovation is to solve the structure and function of biomolecules such as genomes, proteins, and sugar chains and also solve the function of cells, which are the basic unit for life activity. Therefore, we aim to establish a technology for minimally invasive surgery to target living cells at a molecular level (God's hand to manipulate the function of cells) and visualizing changes in the dynamic behavior of intracellular biomolecules and the state of cell membrane protein at a single molecular level (God's eye to see the function of cells), and thus provide an innovative nanofabrication and nanomeasurement platform to solve the mystery of life.

Here, our research team has succeeded in giving two new functions to atomic force microscopy (AFM)1). The first advancement is to coat the tip apex of an AFM probe with a thin film of titanium oxide (TiO2) known as a photocatalyst. By this method, the photocatalytic reaction is localized in a nanoscale space (100 nm region) in the vicinity of the tip apex to achieve minimally invasive cell membrane perforation. As a result, the probability of cell membrane perforation reaches 100%, and a cell viability of 100% is also successfully achieved, allowing us to verify that minimally invasive surgery can be carried out. The second advancement is to insert the tip apex of an AFM probe coated with silver (Ag) nanoparticles into a living cell. We have thus succeeded in acquiring a sensitive Raman spectrum originating in protein, DNA, lipids,

etc. (Tip-Enhanced Raman Spectroscopy, TERS). By this method, a difference in the ratio of biomolecules between a cell's nucleus and cytoplasm was visualized as information inside a cell, and it was found that there is an inverse correlation (a phenomenon that as one increases, the other decreases) between proteins and glycogen (also called animal starch) as temporal changes in biomolecules inside cells.

1) Atomic Force Microscopy (AFM) is a microscope that detects the atomic force affecting the tip apex and the surface of a sample and was invented by Dr. Gerd Binning and others at IBM Zurich Laboratories in 1985. AFM is a strong tool that can directly observe atomic and molecular images and also evaluate mechanical properties such as frictional force and hardness and electric, magnetic, and thermal properties with nanoscale spatial resolution, becoming a fundamental technology leading today's nanotechnology. Furthermore, AFM can make observations not only in the atmosphere but also in liquids, and thus has been actively applied in the life science and biotechnology fields.

Future Outline

In order to simultaneously achieve nanofabrication and nanomeasurement functions, we will establish a tip-enhanced Raman spectroscopic (TERS) function by coating the surface of a TiO2-functionalized AFM probe with Ag nanoparticles in the future. This function will be able to visualize the process of degradation reactions of organic substances based on photocatalytic oxidation (changes in molecular structures) during the cell surgery process. We will also aim to achieve a means for measuring a single molecule in a target cell membrane protein using the high molecular recognition ability of an antigen-antibody reaction, and we will aim to establish a technique for selective nanofabrication for a single molecule in the target membrane protein identified by the above means. It is expected that this proposed technique could solve the mechanisms of life functions and be applied to work such as the development of novel medicines.

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Reference

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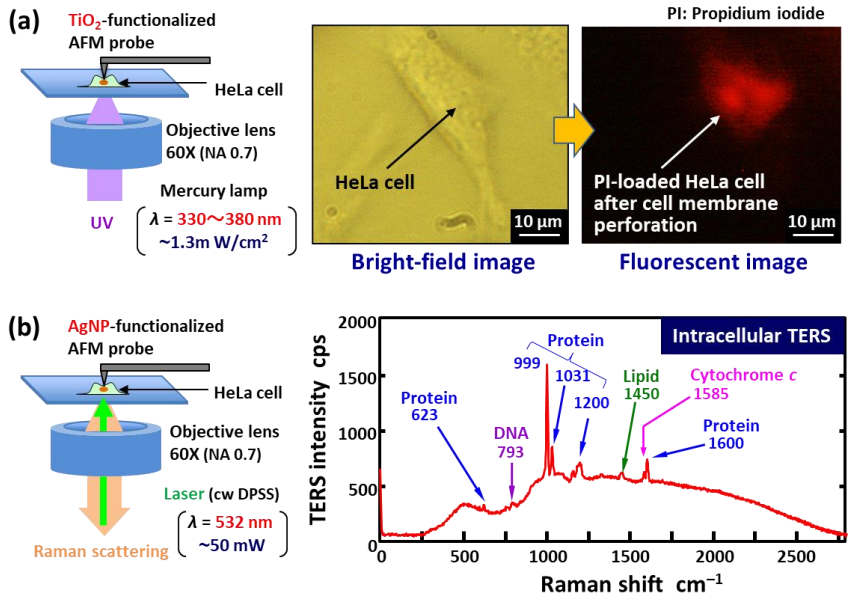
Figure:



Title: Functionalized AFM-based nanofabrication and nanomeasurement techniques for living cells

Caption: (a)Cell membrane perforation of living cells based on highly localized photochemical oxidation with a catalytic TiO2-functionalized AFM probe

(b)Intracellular tip-enhanced Raman spectroscopy (TERS) imaging of molecular dynamics in living cells using an AgNP-functionalized AFM probe

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