Visualization of individual living cell reactions by means of surface plasmon resonance imaging sensor

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A technique to visualize individual living cell activation in a real time manner without any labeling is required in the fields of life sciences and medicine. Surface plasmon resonance (SPR) sensors detect the refractive index (RI) changes on the surface of sensor chips in label-free and on a real-time basis. We previously reported that SPR sensors could detect real-time large changes of RI in response to activation of living cells, such as mast cells, keratinocytes, basophils and B lymphocytes on a sensor chip without labeling, suggesting the potential of SPR as a new method for clinical diagnosis and drug screening. Thus, SPR sensor possesses great potential to reveal nano-scale living cell actions in evanescent field. However, conventional SPR sensors detect only an average RI changes in the presence of thousands of cells in an area of the sensor chip, and could offer only small number of sensing channels. Therefore, we developed SPR imaging (SPRI) sensor with a CMOS camera and an objective lens in order to visualize RI distribution of individual living cells and their changes upon stimuli.

The sensor we developed is composed of a light source (LED), an achromatic lens, a P-polarizer, a prism (RI=1.72), an objective lens and a CMOS camera. The SPRI sensor chips (RI=1.72, 20 mm × 20 mm × 1 mm) coated with gold thin film (1 nm Cr layer and 49 nm gold layer) by means of vapor deposition. The SPRI sensor we developed could detect reactions of individual rat basophilic leukemia (RBL-2H3) cells and mouse keratinocyte cells in response to specific or nonspecific stimuli. Moreover, the sensor could detect the reactions of individual human basophils isolated from patients in response to antigens. Furthermore, we also succeeded in distinguishing reactions of basophils activated by antigens from those of non-activated basophils spotted on an area.

The technique can visualize the effect of various stimuli, inhibitors and/or conditions on cell reactions as change of intracellular RI distribution at single cell levels [1-3]. Establishment of the technique to rapidly isolate cells from patient blood should enable us to utilize SPRI system as a high throughput screening system in clinical diagnosis, such as type I allergy and drug hypersensitivity, and as a tool to reveal novel phenomena in evanescent fields around plasma membrane.

References