BIOIMAGING

Session co-chairs: Elisa Konofagou, Columbia University, and Kazuo Kurokawa, RIKEN

Bioimaging encompasses both biological and medical imaging that are found at the intersection of physics and engineering with biology and medicine. Bioimaging relates to the structural and/or functional imaging of living organisms, thereby mapping the underlying anatomy and/or functional physiology. Such imaging has been shown feasible on multiple scales from molecules such as DNA and proteins to organelles such as nuclear and Golgi apparatus, to cells such as leukocytes in blood vessels and neurons in the brain to tissues, organ and whole body levels. The imaging scales span from a few angstroms to meters. To visualize at these distinct scales, different imaging techniques or strategies are employed. Single-molecule fluorescence imaging can be used for analyzing the dynamics of one protein molecule while positron emission tomography (PET) can trace cancer cells throughout the entire body.

The talks in this session will focus on the aforementioned broad areas of bioimaging at all different scales from molecular to tissue levels. Development of bioimaging tools and techniques will also be covered.

Topic 1: Molecular Imaging

Speaker: Kazuhiro Aoki, Graduate School of Medicine, Kyoto University
Title: *Imaging and Mathematical Modeling of Molecular Activities in Living Cells*

In multicellular organisms, cell proliferation is a highly regulated process that maintains tissue architectures and organ size. The inhibition of cell proliferation observed in cells with high cell density is referred to as contact inhibition of proliferation, or simply contact inhibition, and a defect of this process has been closely associated with uncontrolled cell proliferation, leading to cancer . We have demonstrated that the cell density-dependent control of proliferation in mammalian cells is associated with the frequency of the ERK activity pulses, which consist of pulses from both spontaneous firing and cell-to-cell propagation. An understanding of the quantitative relationship between ERK signaling and cell proliferation would provide a useful framework to predict the clinical efficacy of drugs targeting the Ras-ERK pathway to impede proliferation of cancer cells.

Speaker: Alan Jasanoff, Department of Biological Engineering, Massachusetts Institute of Technology,
Title: *New Technologies for Molecular Imaging of Brain Function*

Comprehensive analysis of brain function depends on understanding the dynamics of diverse neural signaling processes over large tissue volumes in intact animals and humans. Most existing approaches to measuring brain signaling suffer from limited tissue penetration, poor resolution, or lack of specificity for well-defined neural events. Ongoing research aims at producing analogous neurotransmitter sensors with greater target sensitivity. Our work on genetically encodable sensors revolves largely around variants of endogenous iron storage proteins, which we have modified to produce MRI changes in response to kinase activity or calcium ion concentration changes. We have applied high-throughput protein engineering approaches to

improve sensitivity of these probes, and we demonstrate results with magnetically-enhanced proteins expressed in cells.

Topic 2: Endoscopic Imaging

Speaker: Makoto Igarashi, Endoscopic Technology Olympus Medical Systems Corp.
Title: *Advanced Endoscopic Imaging Technologies*

Recently, endoscopy has been increasingly important in not only tumor detection but also differential diagnosis of lesions. However, conventional endoscopy with white light is not necessarily sufficient for effective endoscopic detection and diagnosis. We have developed the novel endoscopic imaging technologies; Narrow Band Imaging (NBI), Auto-Fluorescence Imaging (AFI), Infra-Red Imaging (IRI) and Endo-Cytoscopy System (ECS). The purpose of these technologies is to emphasize the important tissue features associated with early stages of cancer and to improve the quality of conventional endoscopy. It is our hope that advanced endoscopic imaging technologies (NBI, AFI, IRI and ECS) would greatly contribute effective endoscopic detection and diagnosis. We believe that these techniques will lead directly to further improvements in the way physicians diagnose their patients.

Speaker: Vadim Backman, Northwestern University
Title: *Photonics Meets Biology: From Nanoscale Imaging to Winning the War on Cancer*

In the past few decades, advances in optics have been translated into vital applications in biology and medicine. Nanoscale imaging is one of these emerging applications. Cellular life is fundamentally governed by physical processes at a macromolecular scale (i.e. ten to hundreds of nanometers), but observation of these scales is challenging. In particular, most of what biologists know about genome regulation comes from the view of the cell as a molecular machine. Although powerful, this prevailing approach omits an important facet: the regulatory role of nuclear nanoscale structure. This talk discusses a suite of spectroscopic imaging techniques based on the analysis of the interference of elastically scattered light, which have been recently developed to quantify the statistical properties of intra- and extracellular structure at the nanoscale. The talk also discusses the physical principles linking the nanoarchitecture with the regulation of molecular processes. Alterations in the nuclear nanoarchitecture are some of the earliest events in carcinogenesis, and optical nanoscale imaging has the potential to provide key insights into fundamental cell biology as well as lead to cancer screening.