Frontier Bioscience Seminar at Osaka University, Suita Campus

Investigating Muscular Dystrophy Diseases by Single Molecule Imaging in Live Animal Models and Human Cells

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Date: December 10, 2019 (Tue)
Time: 16:30-17:30
Place: Seminar room (3rd floor) in Nanobiology Building, Suita Campus

Abstract:
Muscular dystrophy is a diverse group of disorders characterized by mutations in genes encoding key sarcolemmal, nucleoskeletal or nuclear envelope proteins. To gain new insights into the pathogenesis of Duchenne muscular dystrophy (DMD) and Emery-Dreifuss muscular dystrophy (EDMD) at the nanoscale we use single molecule optical microscopy in human cells and *C. elegans* animal models.

We have characterized the *in situ* biomolecular properties of dystrophin, a key structural protein of muscle cells that is mutated in DMD patients. Using split-fluorescent proteins and a single molecule imaging technique called Complementation Activated Light Microscopy (CALM), we imaged individual Ca^{2+} channels at the muscle surface of live *C. elegans* worm models for DMD. I will discuss how diffusion measurements on single Ca^{2+} channels and spatial pattern analyses of their nanoscale distribution *in vivo* have allowed us to demonstrate that dystrophin acts as a load-bearing apparatus and a tension transducer that modulate the nanoconfinement of Ca^{2+}channels in response to varying muscle tonus.

We have also studied the diffusional mobility and the spatial distribution of the nuclear envelope protein emerin and a variety of EDMD-associated emerin mutants by sptPALM and dSTORM super-resolution imaging in cells from EDMD patients. We started to define the nanoscale structural organization and the molecular functions of emerin that guaranty proper responses of cell nuclei to forces and I will discuss some of the mechanisms by which emerin mutations result in abnormal nuclear envelope mechanics in cells, in the context of EDMD.

These single molecule imaging approaches not only provide new means to explore the basic principles of cellular homeostatic controls for tissues under mechanical strains, but also to understand the molecular basis of diseases at the nanoscale, both in cells and in intact animals.

Host: Nobuhiko Yamamoto, PhD
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