Title: Seeing is believing: Novel imaging techniques reveal the fate of viral genomes

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Date: September 21, 2016 (Wed) 18:00-19:30
Venue: Igakukei-tou Seminar Room 483 (4th floor)

Abstract:
During infection, nuclear replicating DNA viruses dynamically remodel their genomes as well as the nuclear environment of the host. Elucidating the underlying regulatory mechanisms for viral genomes in the cellular context is key to understand the dynamic nature of viral propagation. For most viruses, however, it remains unclear where and when viral genomes interact with or counteract cellular processes. Using adenoviruses (Ad) as a model, we conducted a detailed imaging analysis of viral genomes throughout the infection cycle. First we developed a live-cell imaging system for individual incoming Ad genomes by focusing on a host protein that is recruited onto viral genomes upon nuclear entry. Using this system, we found that in contrast to the anticipated view, incoming Ad genomes are not targeted by potential nuclear antiviral factors. While this system is restricted to the analysis of incoming viral genomes, we recently developed a novel viral system that enables genome visualization with ANCHOR™ technology, allowing us to visualize not only incoming but also newly replicated Ad genomes in living cells. Using this novel technology, as well as metabolic labeling of viral genomes, we identified two morphologically and functionally distinct Ad DNA replication compartments in late phases of infection. Based on our results, we believe that our imaging tools will enable us to gain the spatio-temporal information needed towards comprehensive understanding of viral genome regulations.