Austin Virology and Retro Virology

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Short Communication

# Interdisciplinary Research of Virology and Nanobiology

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**Received:** October 10, 2014; **Accepted:** November 13, 2014; **Published:** November 15, 2014

## Short Communication

The intersection of virology and nanoscience provides new views and technologies for virology and nanobiotechnology. On one hand, the development of nanotechnology provides new techniques and concepts for the biological/medical fields including virology research. On the other hand, as a kind of nanoscale bio-organism, viruses are also natural nano-materials and provide good ideas and strategies for construction of nano-machines. Aiming to open a new field in the intersection of Virology and Nanotechnology, we carry out this interdisciplinary research on two major directions. One is using advanced nano/molecular fluorescence technology to image virus-host interactions in live cells and animals, and the other is developing functional nano-structures with viral elements.

Live cell imaging can provide direct, instantaneous, and dynamic information of the virus infection and replication processes in real-time. Many important molecular events of viral RNA/DNA, protein-protein interactions, and RNA-protein interactions, virus particles, etc., need to be uncovered in live host cells or animals in real-time. However, the methodology to image these molecular events, such as image viral RNA and RNA-protein interactions in live cells, remains challenging. And most of the dynamic processes were not seen in live host cells and animals. The development of new nano/molecular optical probes and techniques may provide new tools for imaging of virus–host interactions. With the newly constructed optical imaging techniques, the infection and pathogenic mechanism of human virus will be revealed or given a new view.

A virus is a small infectious agent with nano size (generally from 20 to 400 nm in diameter). For human beings, some viruses can cause horrible diseases and pandemics. On the other hand, the nano size, the symmetry, and the easiness of structural manipulation make viruses as good nano platforms bridging biology and nanotechnology. The natural structure and character of viruses also provide good ideas and strategies for construction of nano-machines. A very interesting character for some viruses is self-assembly. Based on the self-assembly mechanisms and the delicate structure, new functional nano-structures and nano-machines with viral elements, such as virus capsid encapsulating inorganic nanoparticles, will be constructed, which is helpful for the nanotechnology, virology and biomedical applications.

## Major Research Progresses

Over the last few years, we have made progresses mainly in two aspects. Firstly, with nano/molecular fluorescent probes and techniques such as molecular beacons, quantum dots, FRET imaging, etc, we have developed a series of methods for visualizing viral nucleic acids, proteins and virus particles in living cells by using some viruses as models including influenza virus, SV40 virus, etc. We have visualized dynamic behaviors for some viral nucleic acids, viral proteins and virus particles in living cells, and demonstrated their molecular mechanisms.

For example, by using molecular beacon technology we have realized direct visualization of poliovirus plus-strand RNA [1] and several kinds of mRNAs of influenza A virus in live host cells [2] and uncovered their dynamic behaviors in live cells. We have developed aptamer beacons, aptamer-QDs probes, and dual-fluorescent reporter systems to label and study the viral proteins, viral particles and viral miRNAs for HIV and influenza A virus [3-5]. We have also developed new red and far-red protein fragment complementation systems for imaging protein-protein and RNA-protein interactions in live cells and in live mice [6-8]. Some of new important viral protein-protein interactions were revealed by FRET imaging and analysis [9,10].

Another aspect of the progress is that we have developed the new methodology for construction of hybrid nanostructures of virus assembly with inorganic nanoparticles. New nanoelements including hybrid nanoparticles and nanowires were built for multifunctional biosensing. And pathogen detection assays were carried out with high sensitivity.

For example, we have constructed virus-like-particles SV40 VLPs-QDs. This virus-like-particles encapsulated quantum dots (VLPs-QDs) could infect live cells showing fluorescence and would be very useful for virus imaging [11] and biosensing [12]. This QD-encapsulation-based virus imaging strategy has been highlighted in *Nature China*: "A sheep in wolf's clothing". Gold nanoparticles (AuNPs) were also encapsulated into SV40 capsids and SV40 capsids are able to carry AuNPs into living Vero cells [13]. Multifunctional protein nanowires based on the self-assembly of a yeast amyloid protein, Sup35 were also constructed for ultra-sensitive molecular biosensors. These protein nanowires can transfer hundreds of signal ligands with small number of specific binding molecules which gives protein nanowire a strong signal amplification ability in pathogen detection [14-17].

## Current Research and Future Directions

Currently, our research programs still include molecular imaging of virus-host interactions and developing functional virus-based nano-structures. Our scientific objective is to real-time image the key processes of virus (HIV, Influenza virus) infection and pathogenesis, and to construct virus-enabled nano-devices for important biomedical applications.




**Citation:** Cui Z. Interdisciplinary Research of Virology and Nanobiology. Austin Virol and Retrovirology. 2014;1(1): 2.

Future research will focus on the nanoscopic virus imaging and functional virus nanoapparatus. Nanoscopic virus imaging mainly includes imaging of virus-host interactions at the nanometer scale in live cells by single-molecular or single virus imaging. This will be reached by SIM, STORM and PALM optical microscopy with super resolution and sensitivity. With the nanoscopic imaging techniques, we will image HIV infection in primary CD4 T cells and macrophages. Functional virus nanoapparatus includes new virus-based self-assembly nanostructures helpful for understanding and controlling virus infections.

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Austin Virol and Retrovirology - Volume 1 Issue 1 - 2014
**ISSN: 2472-3517** | www.austinpublishinggroup.com


**Citation:** Cui Z. Interdisciplinary Research of Virology and Nanobiology. Austin Virol and Retrovirology. 2014;1(1): 2.