**Cell-to-cell transmission of HIV-1: role of mitochondria demonstrated by live-cell real-time imaging**

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## Abstract

HIV-1 can infect host target cells by both cell-free viral infection and cell-to-cell transmission of the virus. In cell-free viral infection, free virus is exposed to cellular, immunological, and drug barriers, so infection efficiency is low and drug sensitivity is high. In cell-to-cell transmission, virus is transmitted directly from cell to cell, shielded from most of the barriers. Thus, the infection efficiency is much higher, and drug sensitivity is lower. Importantly, HIV spreads *in vivo* mainly by cell-to-cell transmission. In contrast to cell-free viral infection, the mechanism of cell-to-cell transmission of HIV-1 is much less understood. At present, there is no drug to cure AIDS and no vaccine to prevent HIV infection. Viral mutation, viral latency, epitope specificity/accessibility, and mechanism of cell-to-cell viral transmission all contribute to difficulties in prevention and cure. Mitochondria have long been known to be essential organelles. In addition to providing metabolic energy, they are involved in many cellular signaling pathways, including host innate immunity, apoptosis, autophagy, and aging. We used live-cell, real-time fluorescence imaging of co-cultures of HIV-1-infected T cells and uninfected target cells to investigate the role of mitochondria in cell-to-cell HIV transmission. We discovered that mitochondria of HIV-infected cells carrying the virus enter uninfected target cells, mediate cell-to-cell HIV-1 transmission and viral spread. Our results show that human mitochondria serve as HIV-1 reservoirs and carriers and move from infected cells to target cells. Furthermore, we discovered for the first time that cell-free mitochondria purified from HIV-1-infected cells are infectious. These results offer new insights into the mechanisms of cell-to-cell transmission of HIV-1 as well as identify mitochondria as new host targets for viral infection and therapeutic development.

## Biography

Dr. Sylvia Lee-Huang is a Professor of Biochemistry and Molecular Pharmacology at New York University School of Medicine, in New York, New York, USA. Dr. Lee-Huang received her Ph.D. in Biophysics from the University of Pittsburgh with Professor Gary Felsenfeld. She did her post-doctoral research with Dr. Liebe Cavalieri at the Sloan-Kettering Institute for Cancer research. She started her academic research with Nobel Laurate Professor Severo Ochoa at NYU School of Medicine, Department of Biochemistry, in Molecular Biology and Biochemistry. Professor Lee-Huang has a broad background in biochemistry, biophysics, cell biology, molecular biology, molecular genetics and virology. As a graduate student, she studied the interactions of DNA, RNA and protein with Dr. Gary Felsenfeld, laying the groundwork for nucleic acid interactions. As a postdoctoral fellow, she studied the mechanism of DNA replication with Dr. Liebe Cavalieri. She proposed the first concept and provided the first experimental evidence for the reversed flow of genetic information from RNA to DNA. Her work challenged and revolutionized the “central dogma” in gene expression. As a research associate with Nobel laureate Professor Severo Ochoa, she studied the regulation of gene

expression and discovered small RNAs act as inhibitors and activators in gene expression. This work laid the concept for small regulatory RNAs including today's RNAi, miRNA, and lncRNA. As a PI on NIH-grants, her lab was the first to clone and express human erythropoietin. Recently, her lab studied the mechanism of anti-HIV compounds. Her team isolated, purified, characterized and elucidated the mechanism of anti-HIV proteins, oligopeptides, and small molecules. Her work has been published in major journals, including ***Cell, Nature, Science, PNAS, Biochemistry (JACS), BBRC*** and others.

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