Viruses customize autophagy protein for efficient viral entry

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Negative-strand RNA viruses are highly pathogenic and cause many severe diseases in humans and animals. These viruses generally use existing cellular pathways to enter cells, which involves intensive interaction with the endomembrane network, offering the endocytic pathway as an attractive scheme for therapeutic intervention. The molecular mechanisms governing virus entry remain incompletely understood. We found that UVRAG, well-known for regulating autophagy and intracellular trafficking, is a critical factor for virus entry through combinatorial interactions with a tether and endosomal SNAREs. UVRAG mediates viral endocytic transport and membrane penetration through interactions with the class C Vps complex and endosomal Q-SNAREs, leading to the assembly of a fusogenic trans-SNARE complex involving VAMP8, but not VAMP7. Indeed, UVRAG stimulates VAMP8 translocation to virus-bearing endosomes. Inhibition of VAMP8, but not VAMP7, reduces viral entry. Understanding the mechanism that allows the virus to interact with late endocytic organelles could identify the specific set of proteins that have a role in virus entry, which help us to design specific therapeutic agents against virus entries.

Biography

Chengyu Liang is an Assistant Professor (tenure-track) at the Keck School of Medicine of the University of Southern California. Research in her lab is centered on investigating the basic principle of cellular processes including apoptosis and autophagy, and genomic stability, as well as intracellular trafficking pathways in viral entry, replication, pathogenesis and cancer biology. She was the first to identify UVRAG as an autophagic tumor suppressor in cancer and dictate its important roles in synchronizing diverse cellular processes in human diseases including viral infection (Nature Cell Biology 2006, 2007, 2008, 2009, 2013; Dev Cell 2012). She achieved extensive training and accomplishments in the molecular study of KSHV and γHV68 at Harvard Medical School, and pioneered the study of structural bases and functions of vBcl-2-mediated anti-autophagy and anti-apoptosis in AIDS-associated g-herpes virus infection (PLoS pathogen 2008, 2009). Due to the remarkable nature of these findings, she has been granted the Leukemia & Lymphoma Society Fellow, the Wright Foundation Young Investigator Award, the Baxter Foundation Junior Faculty Award, and American Cancer Society Research Scholar. She successfully administered the projects, collaborated with other researchers, and produced several peer-reviewed high-profile publications from each project. She also serves as the Director of confocal imaging core of the department.

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