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The pro-viral role of autophagy in coxsackievirus-induced myocarditis

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Autophagy is a cellular process by which damaged organelles/proteins are enwrapped by double membrane vesicles (autophagosomes) and degraded following fusion with lysosomes. Autophagy is traditionally considered as an anti-viral host response. We recently provide evidence that the autophagy machinery can be utilized by coxsackievirus B3 (CVB3), one of the predominant viruses causing myocarditis, to achieve successful replication. Autophagy process is activated during CVB3 infection. Inhibition of autophagosome formation significantly reduces viral replication. Conversely, induction of autophagy results in increased viral replication. Blockage of autophagosome-lysosome fusion by gene silencing of the lysosomal protein LAMP2 promotes viral replication. These results suggest that autophagosomes are likely utilized by CVB3 as sites for active viral replication. To further explore the pro-viral mechanisms of autophagy, we examined the protein levels of p62. P62 is an adaptor protein mediating selective autophagy pathway by targeting ubiquitinated proteins and invading pathogens to the autophagy pathway. We found that CVB3 infection leads to marked decreases in the protein expression of p62 (~62 kDa), accompanied by the appearance of ~30 kDa fragments. This observation was further confirmed using a flag-tagged p62 construct, suggesting that p62 is cleaved after CVB3 infection. We further demonstrated that CVB3-induced cleavage of p62 dissociates its LIR and UBA domains from PB1 domain, resulting in the loss of its function in selective autophagy. Together, our results suggest that the autophagy adaptor protein p62 is cleaved during CVB3 infection. Cleavage of p62 may be a viral strategy to establish efficient viral replication in host cells.

Biography

Dr. Honglin Luo is an Associate Professor in the Department of Pathology and Laboratory Medicine/James Hogg Research Center at the University of British Columbia, Canada. Dr. Luo completed her MSc and MD training in China. She then pursued her postdoctoral training at the University of Washington. Dr. Luo has published over 60 refereed papers and served as an editorial board member of several journals.

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