SEXUALLY TRANSMITTED INFECTIONS, HIV/AIDS

THE HUMAN PAPILLOMAVIRUS TYPE 11 EARLY PROTEIN E6 ACTIVATES AUTOPHAGY VIA REPRESSION OF THE MTOR PATHWAY

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Introduction: Infection with human papillomaviruses (HPVs) often causes condyloma acuminatum and cervical cancer as well as a number of other tumors. Low-risk HPV (LR-HPV) type 11 mainly causes genital warts, and its E6 gene was found to play an important role in pathogenesis. Several studies have reported that autophagy supports the viral replication cycle after infection.

Objective: Whether autophagy is altered during HPV infection is unknown, as are the effects of viral protein E6 on autophagy. So we want to explore the relationship between HPV 11E6 and autophagy.

Materials and Methods: To gain insights into the role of autophagy during HPV infection, we used gene microarrays to analyze the autophagy-related genes .We examined the expression of autophagy-related protein in HPV11 E6-expressing HaCaT stable cell line. Moreover, we analyzed autophagic flux with an mCherry-green fluorescence protein (GFP)-microtubule-associated protein 1 light chain 3B (LC3B) fusion protein via immunofluorescence assays. To elucidate how HPV11 E6 affects autophagy,the signaling pathway involved in autophagy was examined using Western blotting.

Results: We demonstrate that ATG10 mRNA increased in HPV11 E6-transfected HaCaT cells through gene microarray and the ratio of LC3B II/LC3B I was upregulated. The mTOR pathway was found to be suppressed in HPV11 E6-transfected HaCaT cells.p-AKT and p-ERK1/2 were suppressed in the presence of HPV11 E6, whereas no obvious changes were observed in AMPK and p53 signaling. The phosphorylation sites of unc-51-like autophagy activating kinase 1 (ULK1) (Ser757) were affected by mTOR signaling when nutrients were plentiful, while the ratio of p-ULK1 (Ser757)/ULK1 was reduced.

Conclusions: Our findings expand the current understanding of the relationship between HPV infection and autophagy and will help elucidate HPV pathogenic mechanisms.