“High-risk” HPVs, HPV16 and HPV18, the major causative agent of uterine cervical carcinomas, encode E6/E7 oncoproteins, which acting in concert prevent host cell apoptotic death. Several studies provide information regarding the numerous host cell proteins whose expression is induced by E6 or are targeted by E6 for proteasome degradation in order to support cell transformation. Instead, much less is known on factors controlling the levels and stability of E6 proteins in HPV infected cells.

In the present study we demonstrate the role of co-chaperone BAG3, a component of cell anti-apoptotic machinery, in promoting survival and proliferation of HeLa cells, a HPV18+ cell line. We also show that BAG3 down-regulation leads to an increase of p53, this making HeLa cells more susceptible to p53-mediated cytotoxic/cytostatic effects of phenethylisothiocyanate (PEITC). Notably, the relationship between BAG3 down-modulation and restored p53 levels was signified by the concomitant decrease of E6 oncoprotein levels. The role of BAG3 in sustaining E6 levels was specific since no changes of E6-associated protein, the other key player in p53 degradation, were observed upon BAG3-down regulation.

These data suggest a possible role of BAG3 in drug-/radiotherapy-resistance of HPV18-bearing cervical carcinomas.