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Human papilloma virus (HPV) 18 proteins E6 and E7 up-regulate ABC transporters in oropharyngeal carcinoma. Involvement of the nonsense-mediated decay (NMD) pathway

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Abstract

Oropharyngeal cancer incidence increased dramatically in the last decades, being infection with human papillomaviruses (HPV) a determinant of this trend. Concerning etiology, treatment response and prognosis, HPV^+ and HPV^- oropharyngeal cancers constitute different disease entities. The underlying molecular background is not completely understood. ATP-binding cassette (ABC) transporters mediate the efflux of anticancer drugs and are regulated by changes in the intracellular milieu. Furthermore, a role in cancer pathogenesis besides drug transport was reported. We evaluated the effect of transfection with E6 and E7 oncogenes from HPV16 and HPV18 on ABC transporters in oropharyngeal cancer cells. HPV18E6/E7 up-regulated P-glycoprotein (P-gp), multidrug resistance-associated protein 1 (MRP1) and MRP2 expression in HNO206 cells and breast cancer resistance protein (BCRP) in HNO206 and HNO413 cells. While P-gp was regulated translationally, MRP1, MRP2 and BCRP up-regulation resulted from mRNA stabilization. For MRP1 and MRP2, the nonsense-mediated decay pathway was involved. In general, resistance to substrates of up-regulated transporters was increased. Transfection with oncogenes individually indicated a major role of HPV18E7. Our findings suggest ABC transporters as molecular players leading to differences in the pathogenesis of HPV^+ and HPV^- oropharyngeal cancer.