TITLE

TP53 gene signaling pathways and protein interactions with mdm2 and HPV in Oral Cancers: a review

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ABSTRACT

Oral cancers are a major clinical challenge in oncology and represent the sixth leading cancer worldwide, with an estimated incidence of nearly 300,000 new cases per year and a mortality rate around 60%, according to the 2018 GLOBOCAN report. They constitute a heterogeneous group of tumors in topography (they can be localized at on the lips, tongue, upper and lower gums, hard palate, floor of mouth, retromolar region, or inside of cheek), histologic forms (that can be a carcinoma, sarcoma, lymphoma, melanoma or cylindroma) and clinical outcomes (good or poor prognosis).

However, despite this phenotypic diversity, more than 50% of these cancers are associated with mutation of *TP53* gene while in the other 50%, the *p53* protein pathway is often partially inactivated. In oral cancers, the loss of function at *TP53* gene is associated with three molecular causes: (1) the genotoxic effect of risk factors such as alcohol abuse, tobacco smoking or betel nut chewing, (2) the inhibitory effect of the *TP53* antagonist gene: *MDM2*, or (3) the action of oncoprotein E6 of *high-risk* human papillomavirus (HPV).

We will summarize in one hand the complexities of *TP53* biology in normal and cancerous cells by using oral cancers model and in the other hand, we will discuss current strategies and challenges of anti-cancer therapies aiming to restore *TP53*'s tumor suppressive function.

KEYWORDS: *TP53*, Signaling pathway, *MDM2*, HPV, Oral Cancers, Cancer therapy, Review