

Review of: "Current Novel Concept of Carcinogenesis to Combat Oral Cancer"

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Potential competing interests: No potential competing interests to declare.

Dear authors,

Your manuscript is very good.

I was reading about risk factors and I didn't see anything or almost nothing about HPV, just one sentence and there are countless works referring to HPV not only as a risk factor but as a prognostic factor. HPV has triggered changes in the epidemiology of oropharyngeal and oral cavity cancer (OPC/OCC) in Asia, Europe, North America and Oceania. Thus, the incidence of cancer in HPV-related subsites is increasing, while in other non-HPV-related subsites it is decreasing. as I consider this topic very relevant for a review article, I suggest you read it and add it to your article:

- Christianto S, Li KY, Huang TH, Su YX. The Prognostic Value of Human Papilloma Virus Infection in Oral Cavity Squamous Cell Carcinoma: A Meta-Analysis. *Laryngoscope*. 2022 Sep;132(9):1760-1770.
- Menezes FDS, Latorre MDRDO, Conceição GMS, Curado MP, Antunes JLF, Toporcov TN. The emerging risk of oropharyngeal and oral cavity cancer in HPV-related subsites in young people in Brazil. *PLoS One*. 2020 May 14;15(5):e0232871.

I didn't see any discussion about the important role of HPV and what has been researched in current times. Writing about this is very important when doing an oral cancer review.

I would also like to see something related to the use of marijuana and HPV as a risk factor for oral cancer and head and neck. I recently read an interesting publication

Although there are some inconclusive studies evaluating the relationship between marijuana cancer in general and oral cancer, we then looked a little further and there is a publication worthy of being referenced in a review:

- Chao Liu, *et al.*: Cannabinoids promote progression of HPV positive head and neck squamous cell carcinoma via p38 MAPK activation, show in the Journal: *Clinical Cancer Research*. 2020 Jun 1; 26(11): 2693–2703.

("TRANSLATIONAL RELEVANCE... HPV positive carcinoma espinocelular de cabeça e pescoço (HNSCC) represents a distinct clinical and molecular entity associated with daily marijuana use. However, the functional role of the cannabinoid receptor pathway in HPV positive HNSCC is undescribed. In this study, we demonstrated that cannabinoids promote progression of HPV positive HNSCC via p38 MAPK activation using in vitro and animal models, as well as in patient cohorts, which is consistent with epidemiologic data that daily marijuana use may serve as a biologic cofactor role in

development of HPV positive HNSCC. This expands the understanding of HPV positive HNSCC carcinogenesis and may also have broader public health implications in marijuana use in the US.”)

Congratulations,

Prof. Dr. Conceição Aparecida Dornelas