

Oral squamous cell carcinoma (OSCC) tumors from heavy alcohol consumers are associated with higher levels of TLR9 and a particular immunophenotype: Impact on patient survival

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Resumen

Oral squamous cell carcinoma (OSCC) is one of the most frequent types of oral cancer in developing countries and its burden correlates with exposure to tobacco and excessive alcohol consumption. Toll like receptors (TLRs) are major sensors of inflammatory stimuli, from both microbial and sterile causes and as such, they have been related to tumor progression and metastasis. Here, we evaluated the expression of TLR2, 4 and 9 as well as CD3+, CD8+ and Granzyme B+ cell infiltration by immunohistochemistry in

oral samples of 30 patients with OSCC, classified according to their consumption of alcohol. Our findings indicate that there is a significant association between heavy alcohol consumption and tumors with higher expression levels of TLR9. Moreover, patients with TLR9high tumors, as well as those who indicated high consumption of alcohol exhibited a diminished overall survival. TCGA data analysis indicated that TLR9high tumors express a significant increase in some genes related with the oral cavity itself, inflammation and tumor promotion. Our analysis of tumor infiltrating leukocytes demonstrated that the major differences perceived in heavy alcohol consumers was the location of CD8+ T cells infiltrating the tumor, which showed lower numbers intratumorally. Our data suggest the existence of a pathogenic loop that involves alcohol consumption, high TLR9 expression and the immunophenotype, which might have a profound impact on the progression of the disease. Copyright

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