

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

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## Carcinogenesis in oral cancer

This paper discuses oral cancer development. The author emphasizes that understanding of the oral cancer biology is critically important for making further advances in treatment and prevention of oral cancer. The author summarizes the recent progress in studies of genetic and molecular alterations that take place during oral carcinogenesis. The "field cancerization" in the oral cavity has been talked about for years, yet the author does not provide any in depth insights into its origin, role and contribution to oral carcinogenesis in molecular/genetic/functional terms. Despite advances in treatment, oral cancer is associated with high morbidity and long-term survival rates that hover around 50%. An increased risk for development of second primary malignancy exists, and early detection as well as prevention are essential. Thus, search for biomarkers of oral carcinoma in various body fluids, including saliva, special attention to oral pre-malignant lesions and novel state-of-the art methodologies (the omics approach) provide hope for earlier diagnosis and the use of personalized thrapies resulting in improved disease outcome.

Studies of oral carcinogenesis in animal models, including immunocompetent mouse models such as 4-NQO mice, have proven to be very useful in investigating oral carcinogenesis and in identifying cancer chemopreventive drugs. The current emphasis has been almost entirely on chemoprevention of oral cancer. A variety of agents that have been evaluated as chempreventive agents for oral carcinogenesis, including retinoids and many others, have been promising, but accompanying toxicity remains a significant and a persistent downside effect. Newer combinations of drugs that target COX2 and EGFR appear to be effective in treatment of pre-malignant lesions, but their efficacy remains to be confirmed in clinical trials.

The author presents a rather dismal picture for prevention and treatment of oral cancer. It seems we have been arrested in exploratory stages, with some promising insights into the biology of oral carcinogenesis (exosomes?? cytokines??) without making much progress in therapy. While a search for early diagnostic markers and of prognostic indicators for oral carcinogenesis goes on, has there been an attempt to turn to immunotherapy as an alternative strategy? Clearly, immune suppression is a hallmark of carcinogenesis in oral cancer. ICI therapies applied locally or systemically and designed to restore immune functions, especially early in carcinogenesis. might be effective on oral cancer, Can the author comment on this aspect of oral cancer development and therapy.

