Rapamycin as a potential agent against oral cancer: Mechanisms of action

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Treatment of oral cancer is based exclusively on surgery combined with or without chemotherapy. However, this treatment has several side effects. Targeting a new, more effective therapy has become an urgent matter. The literature shows that inhibition of the mTOR pathway could be a potential therapeutic target. This pathway has been identified as the target of rapamycin; hence the objective of this project is to study the therapeutic effect of rapamycin in oral cancer. Epithelial gingival cancer cells (Ca9-22) and epithelial normal gingival cells (GMSM-K) were stimulated with different concentrations of rapamycin to assess proliferation by MTT assay, cytotoxicity by LDH assay, colony formation with crystal violet, Ca9-22 cell migration by the scratch method as well as apoptosis and autophagy by flow cytometry. The expression of proteins involved in the cell cycle (cyclin D1, p15, p21, p27) and autophagy (LC3B, p62) as well as the expression of oncogenic genes (Bcl-2, ERBB2, RET and JND) and tumor suppressor genes (ACTB and HPRT1) were determined by quantitative PCR. The cancer signaling pathways were evaluated by western blot. Our results showed that rapamycin decreases cell proliferation and colony formation in a dose-dependent matter only in cancer cells and induces cytotoxicity as well as apoptosis, autophagy and cell migration. The effects of rapamycin pass primarily through the MAPKase, Wnt and NF-κB signaling pathways. Finally, rapamycin reduces the expression of certain oncogenic genes and stimulates the expression of tumor suppressor genes. These results indicate that rapamycin could be a potential agent for the treatment of oral cancer and for a prevention strategy. This research is funded by the Émile Beaulieu Foundation.

Keywords: Rapamycin; oral cancer; apoptosis; autophagy; oxidative stress

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Biography:

Sofia Lappas is a student at the Faculty of Dental Medicine at Laval University. She works under the supervision of Dr Abdelhabib Semlali from the Oral Ecology Research Center on a theme based on the use of natural products or their derivatives in the therapy of oral cancer. Sofia Lappas greatly contributes to the use of rapamycin as an inhibitor of the mTOR pathway as an alternative or complementary treatment to chemotherapy to fight this type of cancer.