in OLP and supports our suggestion that molecular mimicry is involved in the pathogenesis of OLP as CYP2D6*4 has a sequence homology with human herpes virus type 1 and *Candida albicans*.
Relevance: The CYP2D6*4-genotype and environmental factors, here reflected as low or high CYP1A2 activity, may influence the progression and malignant potential of OLP however, prospective studies are needed.

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Are p75NTR and CD44 potential markers of oral cancer stem cells?

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Objective: The p75 Neurotrophine Receptor (NTR), a potential marker of keratinocyte stem/progenitor cells, is expressed by undifferentiated cells in oral squamous cell carcinoma (OSCC). The CD44, has been found as a surface marker in cancer stem cells (CSCs) of head and neck SCC. The aim of this study was to evaluate the immunohistochemical expression of p75NTFR and CD44(v6) as markers for the putative CSC population in OSCC.
Methods: Forty four tissue specimens of OSCC located in tongue (n = 22), gingiva (n = 12), floor of the mouth (n = 5), lip (n = 3) and buccal mucosa (n = 2) were collected from archived material. A standard immunohistochemical method using monoclonal antibodies against p75NTFR and CD44(v6) was performed on formalin fixed paraffin embedded tissue sections. Both the staining intensity and the percentage of the immunoreactive cells were evaluated.
Results: p75NTR was expressed by the most peripheral cells of neoplastic islands in only 4/9 well-differentiated, and in more than 50% of the cells in 5/20 moderately-differentiated and in 1/5 poorly-differentiated OSCCs respectively. Clinicopathologic parameters including site, TNM classification, tumor invasion front and perineural invasion were not significantly associated with the p75NTR expression. A decreased or negative immunohistochemical expression for CD44(v6) was observed in the more undifferentiated tumour islands compared to the neighboring oral epithelium. The decreased CD44(v6) immunoreactivity was correlated with the tumor size, lymph node metastasis and clinical stage.
Conclusion: The subpopulation of neoplastic cells demonstrating a phenotype of low or negative CD44(v6) immunoreactivity in OSCC may be considered of prognostic significance. Further investigations would be necessary to confirm the hypothesis that this subpopulation are putative CSCs or that the p75NTR positive cells have properties equal to those of CSCs.
Relevance: The immunophenotype identification of the CSCs in OSCC may be useful to determine their significance as biomarkers and targets for the therapy of this neoplasm.

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3D OSCC model: effects following topical 5-FU delivery by drug-loaded tablets

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Since the activity of several conventional anticancer drugs is restricted by resistance mechanisms and dose-limiting side-effects, the design of formulations for local application on malignant oral lesions seems to be an efficient and promising drug delivery approach.
Objectives: (i) To define the minimal drug dose enough to assess cytotoxic effects and (ii) to assess the effect of locally applied 5-FU on cell death both in a SCC4/HEK001 model and in a newly proposed 3D outgrowth model of oral squamous cell carcinoma (OSCC). Initially, the optimal drug dose was established by delivery of solutions containing different amounts of 5-FU. The solution containing 1% (w/v) of 5-FU effectively induced cell death with complete eradication of cell colonies.
Buccal tablets were designed to deliver 5-FU locoregionally to the cancer lesions of the oral cavity. Tablets were prepared using a drug loaded matrix of acrylic/methacrylic acid copolymer containing 1% (w/w) of 5-FU and applied on 3D outgrowths.
Results: Drug release from tablets appeared to be sufficient to induce cell death as confirmed by transmission electron microscopy and enzymatic assay (TUNEL). After 120 h of treatment, when about 90% of the drug had been discharged from the tablets into the culture environment, 5-FU caused loss of cell-cell communications and apoptotic cell death. After 192 h, a complete disaggregation of the 3D oral outgrowths and the death of all the cells was observed.
Conclusion: As our results suggest, buccal matrix tablets could be considered a promising new approach to the locoregional treatment of OSCC. Risks of systemic toxicity are avoided since very low drug doses are delivered. Furthermore, the newly proposed and developed 3D model could provide important insights into the relationship between epithelium and mesenchyme during carcinogenesis in further studies.

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NF-κB p65 expression in high-risk HPV+/- oral premalignancy and cancer

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Objectives: Detection of HPV DNA has been reported in both oral precancerous lesions and squamous cell carcinomas (SCC). Persistent activation of NF-κB, a key molecule acting as a transcription factor, is a common finding in various malignancies, including oral cancer. The purpose of this study is to evaluate the immunohistochemical expression of NF-κB in correlation with the detection of high risk (HR) HPV types in oral premalignant lesions and SCC.
Methods: Study material consisted of 50 cases of oral tissues, including 36 premalignant lesions (11 hyperplasias and 25 dysplasias – seven mild, nine moderate and nine severe), nine SCC and five control cases of normal mucosa. Immunohistochemical staining for NF-κB p65 detection was performed and evaluated according to intensity and percentage of positive epithelial cells in a semiquantitative manner. Positivity for the 13 most common HR HPV types was assessed by in-situ hybridization. Statistical analysis was performed.
Results: Positivity for HR HPV was detected in 51.11% of cases including 20% of normal tissues, 36.36% of hyperplasias, 60%, 100% and 85.71% of mild, moderate and severe dysplasias, respectively, and 62.5% of OSCCs. Total NF-κB p65 score in the aforementioned categories was 4.25, 4.55, 5, 5.33, 5.55 and 5.11, respectively. NF-κB staining percentage was higher in moderate and severe dyplasia compared to mild dysplasia ($P = 0.049$). No significant difference in NF-κB p65 levels between HPV+ and HPV- precancerous and cancerous lesions was recorded.
Conclusion: Despite the relatively high levels of HR, HPV detection and NF-κB expression in oral premalignant and malignant lesions, no correlation between these parameters seems to exist.
Relevance: Elucidation of the role of oncogenic molecules, such as NF-κB, and their correlation with HPV infection has the potential to improve diagnosis, prevention and management of oral cancer.

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The effect of low-level laser therapy on leukemic cells, in-vitro

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Background: Phototherapy with laser is used for the treatment of chemotherapy-induced oral mucositis in patients with leukemia, although there is limited data supporting the safety of this method. It has been suggested the laser can have biostimulatory effects on tumor cells. The present study provides guidance for safe use of LLLT (Low-level laser therapy) in patients with leukemia suffering from chemotherapy-induced mucositis.
Objective: The main aim of this study was to evaluate different doses of Low Level Laser on proliferation of Acute Myeloid leukemia cell lines (KG-1a) *in vitro*.
Materials and methods: KG-1a cell line was provided from the Pasteur Institute (IRAN). After completion of proliferation steps, $7 \cap 10^4$ cells were placed in 96-well tissue culture plates. All the surrounding wells were filled with a dark substance in order to prevent laser scattering to adjoining wells on the culture plate.
Laser irradiation was performed with infrared 810 nm laser, continuous wave. The procedure was done at 5, 10 and 20 J cm^{-2} energy densities for one, two and three exposures of each dose. Seven days after the beginning of experiment, the cell proliferation was evaluated by MTT method [3 (4,5, Dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide)]. Two-ways ANOVA was used for data analysis.
Result: Significant increase in cell proliferation was seen only after two exposures at energy density of 20 J cm^{-2} ($P = 0.021$).

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Saliva mRNA markers in early oral squamous cell carcinoma diagnosis

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