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ABSTRACT BOOK

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Dual-stage AI system for Tumor Detection and subtyping in Oral Squamous Cell Carcinoma

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Purpose: Accurate histological grading of oral squamous cell carcinoma (OSCC) is essential for determining prognosis and guiding therapeutic strategies. This study introduces a clinically motivated and technically novel framework for the automated grading of oral squamous cell carcinoma (OSCC) from whole-slide histopathology images (WSIs). However the manual review of whole-slide images (WSIs) remains subjective, labor-intensive, and susceptible to inter-observer variability, We aimed to evaluate the feasibility and limitations of a weakly supervised deep learning pipeline for multiclass classification of OSCC grades using attention-based multiple instance learning (MIL).

Method: We curated a multi-institutional dataset comprising 1,586 OSCC WSIs stratified into well-differentiated (WD), moderately-differentiated (MD), and poorly-differentiated (PD) subtypes and 330 normal slides. A two-stage deep learning pipeline termed 'ORALPATHO' was developed in which stage one performed binary classification (normal vs OSCC) using attention-based MIL, and stage two employed gated attention with top-K patch selection for grading OSCC subtypes. Model performance was evaluated via 3-fold cross-validation and independent external validation. Attention heatmaps and UMAP projections were used for spatial interpretability and feature space analysis.

Results: The binary classifier achieved a mean F1-score greater than 0.93 across folds. The multiclass model achieved macro-F1 scores of 0.72, 0.70, and 0.68 across folds, with AUCs of 0.79 (WD), 0.71 (MD), and 0.61 (PD). Model generalizability was confirmed on external datasets. PD samples, underrepresented in training (7.4%), were most frequently misclassified, highlighting the limitations of the current approach in capturing highly heterogeneous histological features. Attention maps localized clinically relevant regions but showed reduced precision in ambiguous or borderline cases.

Conclusions: Our study demonstrates the feasibility of attention-based weakly supervised learning for OSCC grading from WSIs while identifying key limitations in classifying underrepresented and morphologically diverse subtypes. ORALPATHO offers a clinically interpretable benchmarking framework that supports reproducibility, transparency, and future model development for AI-assisted oral cancer diagnostics.

OMC-Atlas : A harmonize single-cell transcriptomic reference atlas of human oral carcinogenesis

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Purpose: Oral squamous cell carcinoma (OSCC) represents 90% of oral cancer, whose prognosis remains poor due to late-stage diagnosis and frequent relapse leading resistance to immunotherapies. Dysplasia, the precursor stage of OSCC, is clinically observed as oral lesions like leukoplakia, encompassed within oral potentially malignant disorders (OPMD). Tumor progression is driven by gradual remodeling of the tumor microenvironment (TME) and the establishment of local immunosuppression.
Despite increasing interest, the immune mechanisms driving the malignant transformation of OPMD remain poorly understood. High-resolution tools such as single-cell RNA sequencing offer a huge potential to delineate these oncogenic events. However, current studies are limited by the lack of innate immune compartment and the scarcity of preneoplastic sampling, underlining the need of a framework to map oral mucosal transformation at cellular and molecular levels.

Method: To bridge this gap, we developed the Oral Mucosa Cell Atlas (OMC-Atlas), integrating five publicly available single cell datasets (GSE139324, GSE163633, GSE164690, GSE181919, GSE188737) together with Centre Léon Bérard in-house data. The atlas includes 656,019 cells from 202 samples, across healthy, preneoplastic and tumor stages in several tissue sites including both oral cavity subsites as well as blood, tonsils, and other anatomical locations of the head and neck.

Results: This comprehensive resource reveals transcriptional dynamics of the oral tumorigenesis and highlights TME heterogeneity, especially in the myeloid compartment, exploring the progressive loss of innate surveillance functions. Findings were compared with those obtained from 66,089 cells from a public dataset of esophageal 4-NQO murine carcinogenesis model, which recapitulates a developmental trajectory similar to OSCC in mice. This preclinical model allowed cross-species comparison of conserved transcriptional programs, tumorigenic mechanisms, and immunoregulatory targets.

Conclusions: In conclusion, our work demonstrates the utility of the atlas as a reference resource by expanding it with additional datasets and applying it for cell-type annotation. This human–mouse integrative framework provides a robust foundation for developing future immuno-interception or strategies in oral cancer.

Refining Risk Stratification in Oral Leukoplakia: Oral Epithelial Dysplasia WHO 2024 Criteria and an Optimized Cut-Off for Predicting Malignant Transformation

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Purpose: Oral Leukoplakia (OL) has a variable risk of malignant transformation (MT). The presence and grade of oral epithelial dysplasia (OED) still remains the best predictor of MT. The aim of this study is to evaluate the predictive value of OED assessed according to the WHO 2024 criteria in distinguishing between high-risk and low-risk lesions.

Method: We analyzed a cohort of 133 patients previously enrolled in a prospective study with a mean follow-up of X years. The cohort included OL with no dysplasia, as well as mild, moderate, and severe dysplasia, originally diagnosed by two pathologists. All cases were re-evaluated by a third pathologist using the three-grade classification and the binary system, applying both the 2017 and 2024 WHO criteria.

Results: Malignant transformation occurred in 6 out of 133 cases.
Using the WHO 2024 binary system and the originally proposed cut-off (≥4 architectural and ≥4 cytological alterations), 7 lesions were classified as high-risk (AUC = 0.734), among which 3 progressed to malignancy. The 2017 criteria showed a lower predictive value (AUC = 0.496). In our cohort, logistic regression identified an optimal cut-off of ≥2 architectural and ≥4 cytological alterations, resulting in a ROC curve AUC of 0.976. This threshold classified 12 lesions as high-risk and correctly identified all the 6 cases that underwent MT.

Conclusions: In our cohort, the three-grade system remains the most accurate predictor. When applying a binary system based on the proposed cut-offs, the WHO 2024 criteria outperformed the 2017 classification. The cut-off identified in the present study offers an optimal AUC to be validated in larger cohorts.
Due to the small sample size and the assessment being performed by a single pathologist, this study can serve as a test set, but further validation is required.

Two Samples, One Signal: Raman Spectroscopic Study to Identify High Risk Oral Leukoplakia (OLK)

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Purpose: Effective clinical management of oral potentially malignant disorders (OPMDs) depends on accurately identifying those at greatest risk of malignant transformation. Currently, the histopathological grading of epithelial dysplasia is the most reliable predictor, with high-risk dysplasia often warranting surgical excision. However, histological evaluation is inherently invasive and subject to inter-observer variability. As a less-invasive and more patient-friendly alternative, brush biopsy cytology and saliva sampling have shown promise. In this study, we explored the potential of Raman spectroscopy—a sensitive, label-free optical technique—for distinguishing high-risk from low-risk oral leukoplakias (OLKs).

Method: OLK brush biopsy and stimulated whole saliva samples were collected from the same 31 patients with histologically confirmed high (moderate/severe dysplasia) and low-risk (no/ mild dysplasia) OLKs. Raman spectra were acquired from both sample types and analysed using partial least squares-discriminant analysis (PLS-DA). To improve diagnostic performance, spectral data from oral cells and saliva were combined using two approaches: simple data concatenation (fusion) and multiblock analysis.

Results: When analyzed separately, OLK cell samples demonstrated a sensitivity of 81% and specificity of 86%, while saliva samples showed 81% sensitivity but only 53% specificity in discriminating high-risk from low-risk OLKs. Data fusion of the two sample types improved diagnostic performance, achieving 87% sensitivity and 76% specificity. Notably, multiblock analysis yielded the best results, with 97% sensitivity and 100% specificity.

Conclusions: This study highlights the potential of Raman spectroscopy applied to minimally invasive brush biopsy and saliva samples in differentiating high and low-risk OLKs. Data fusion and multiblock strategies significantly enhanced classification performance, indicating a promising route toward non-invasive risk stratification of OPMDs.

Clinical and Histological Characteristics, Progression and Malignant Transformation Rates of Oral Leukoplakia and Oral Erythroplakia in a Large Cohort of Irish Patients

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Purpose: To establish clinical and histological characteristics, and malignant transformation and progression rates of oral leukoplakia(OLK)/oral erythroplakia(OE) in an Irish cohort.

Method: Following ethical approval, a retrospective review of attendees at the national Oral Mucosal Dysplasia Clinic between 2008-2024 was completed. Demographic details, OLK/OE characteristics, immunosuppression, previous head/neck cancer (HNC), follow-up period, dysplasia progression and oral squamous cell carcinoma (OSCC) development were retrieved.

Results: 849 patients with 1272 OLK/OE were identified (M:F=1:1; average age 56.5 years). 75.8% were homogenous OLK, 21.5% non-homogenous OLK, and 2.6% OE. Degree of dysplasia on initial biopsy was: none 8%, mild 28.5%, moderate 42.5%, severe 20.9%. There were significant associations between dysplasia degree and non-homogeneity (p=0.0005), ulceration (p=2.7x10-12), OLK/OE site (p=0.0005), and previous HNC (p=2.6x10-12).
Follow-up ranged from 134-9683 days (mean 3846). The malignant transformation rate (MTR) of OLK/OE was 4.5%, with 57 OSCCs developing in 5.3% of patients, and a highly significant association between dysplasia degree on initial biopsy and MTR (p=2x10-8). Gingival/alveolar sites had the greatest MTR with OSCC developing in 7.1% of these 198 OLK/OE. 45.7% of OSCCs were in never smokers; current smokers presented odds of 0.24 for MT (95%CI 0.12, 0.47) versus never smokers (p<0.0005). Drinking 1-20units of alcohol/week, but not >20units/week, was associated with significantly reduced MTR v non-drinkers.
6.8% of sites in 8.8% of patients progressed to severe dysplasia, mostly from moderately dysplastic sites. Progression was more likely in females (p<0.005), never v current smokers (p<0.005) and >60 years v <40 years (p<0.05).

Conclusions: This large study is the first on the characteristics and behaviour of OLK/OE in the Republic of Ireland. Never smoking was associated with increased MTR and progression to severe dysplasia. Non-drinkers had increased MTR compared to those drinking 1-20units/week. OLK/OE in females did not have increased MTR, but were more likely to progress to severe dysplasia.

Development of Novel Animal and Cellular Models of FA-Associated OSCC via 4NQO-Induced Carcinogenesis

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Purpose: Fanconi Anemia (FA) patients have a 500–700 fold higher risk of developing oral squamous cell carcinoma (OSCC) than the general population. Due to the lack of fresh FA tumor specimens and limited treatment options, there is an urgent need for reliable in vivo and in vitro models to study OSCC in the context of FA.

Method: We treated Control, Fanca-/- and K14cre;p53loxP/loxP mice with the oral carcinogen 4 nitroquinoline 1 oxide (4NQO). To reduce early toxicity in Fanca-/- mice, we implemented an adjusted 2 (2) 14 dosing protocol. Induced tumors were used to derive OSCC cell lines in culture. These lines were then evaluated for growth capacity, sensitivity to mitomycin C (MMC), genomic alterations via whole-exome sequencing (WES), and their ability to engraft when reintroduced into mice.

Results: All derived Fanca-/- OSCC cell lines exhibited increased MMC sensitivity and varied proliferation rates compared to Fanca competent cells. WES showed that their mutation profiles closely resemble those of human oral cancers. In “in vivo” assays, engraftment rates differed by genotype, and through serial passaging we adapted one Fanca-/- cell line to form tumors consistently in immunocompetent mice. A running follow-up 4NQO study with the adapted 2-(2)-14 protocol, focusing on Control versus Fanca-/- mice, will provide clear comparisons of tumor latency, size, grade, and location under the same dosing regimen.

Conclusions: These newly established FA associated OSCC models—both in mice and cell culture—capture key hallmarks of human disease. They constitute powerful tools for unraveling FA driven cancer mechanisms and for preclinical testing of targeted therapies.

POSTER SESSION 2

1_Siren Fromreide_Patient-Derived Oral Mucosal Cells for Functional Studies of Oral Potentially Malignant Disorders and Oral Squamous Cell Carcinoma
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11_Jan Hirsch_Integrating Molecular Profiling and AI for Early Diagnosis and Prevention of Oral Cancer
12_(remote)_Dawn C Walker_Electrical Impedance Spectroscopy and machine learning-based decision support system for early diagnosis of oral cancer
13_(remote)_Neetu Sinha_From Prevention to Precision - An App-based risk stratification with epigenomic profiling in understanding malignant transforma...
14_(remote)_SEVAL AĞAÇDİKEN ALKAN_The Use of Artificial Intelligence-Based Clinical Decision Support Systems in the Care of Individuals with Oral Poten...

Patient-Derived Oral Mucosal Cells for Functional Studies of Oral Potentially Malignant Disorders and Oral Squamous Cell Carcinoma

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Purpose: Oral squamous cell carcinoma (OSCC) arises from the oral mucosal epithelium and represents a major global health burden with significant morbidity. Previous studies indicate that between 6% to 30% of OSCC cases are associated with pre-existing oral potentially malignant disorders (OPMDs). The lack of robust, patient-derived experimental models of OPMDs and OSCC hampers progress in understanding oral carcinogenesis and developing preventive and therapeutic strategies.

Method: In this study, we aimed to establish and characterize in vitro models using primary cells derived from oral mucosa, including normal, dysplastic, and tumor tissue, to serve as platforms for functional assays.

Results: Tissue samples were harvested from patients undergoing surgery for primary OSCC and matched adjacent oral mucosa (n = 14). We successfully isolated and propagated epithelial tumor cells in 33% of OSCC lesions. Cancer-associated fibroblasts (CAFs) were isolated from 71% of OSCC lesions. Fibroblasts from oral mucosa adjacent to OSCC lesions were successfully cultured in 75% of cases, and exhibited elongated, spindle-like shapes with high αSMA expression. In 3D organotypic models, tumor epithelial cells retained key histopathological features of the primary tumor, and cells derived from adjacent mucosa reflected their respective tissue of origin.

Conclusions: In conclusion, our study demonstrates the feasibility and value of establishing patient-derived in vitro models from OSCC and adjacent oral mucosal tissues. These models provide a biologically relevant platform to study epithelial–stromal interactions and to test individualized therapeutic approaches in OSCC and OPMDs.

Buccal Micronucleus Cytome Assay in Human Oral Precancerous and Cancerous Lesions

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Purpose: Oral cancer is a malignant disease associated with lifestyle, primarily caused by tobacco chewing, smoking and excessive alcohol use. It develops over several years as a result of the progression of various precancerous conditions.

Method: Micronuclei (MN) are formed due to structural and numerical chromosomal aberrations. The measurement of MN in human cells has become one of the most widely used methods for assessing chromosomal instability and DNA damage caused by genotoxic agents. For the first time in Armenia, we applied the MN assay to exfoliated buccal cells to study genetic instability in treatment-naive patients with primary oral cancer. In this study, buccal cells from 32 patients with oral cancer, 12 patients with a precancerous condition—leukoplakia, and 30 healthy individuals (control group) were analyzed for the presence of MN and other nuclear abnormalities associated with cytotoxic effects. The cells were collected from surrounding tissue located a few centimeters away from the tumor/lesion site.

Results: The results revealed an almost twofold increase in the frequency of MN in patients with leukoplakia and a 4.5-fold increase in cancer patients compared to the control group. The results for all other nuclear abnormalities showed a similar pattern and were significantly elevated in patients compared to healthy individuals.

Conclusions: These preliminary findings demonstrate a substantial increase in MN (chromosomal instability) and other nuclear abnormalities (cytotoxic effects) in the buccal cells of oral cancer/precancer patients compared to the control group, supporting the potential use of the buccal MN cytome assay as a biomarker of genetic damage in oral carcinogenesis.

The use of 3D models in decoding the role of Hedgehog-GLI signaling in tumor-stroma communication in head and neck squamous cell carcinomas

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Purpose: This research aims to unravel the role of Hedgehog-GLI signaling, which is upregulated in HNSCC, in tumor-stroma communication. In recent years, the role of stromal cells and tumor extracellular matrix has been highlighted as crucial, and their effect on disease outcome is becoming increasingly investigated. But, in order to investigate the tumor microenvironment, better models are required. So this research aimed to create 3D mono- and coculture models for HNSCC. This research aims to unravel the role of Hedgehog-GLI signaling, which is upregulated in HNSCC, in tumor-stroma communication. In recent years, the role of stromal cells and tumor extracellular matrix has been highlighted as crucial, and their effect on disease outcome is becoming increasingly investigated. But, in order to investigate the tumor microenvironment, better models are required. So this research aimed to create 3D mono- and coculture models for HNSCC.

Method: We optimized 2D and 3D mono- and coculture models by the number of cells and the time period. On the 3D coculture models with overexpressed Hedgehog-GLI pathway, we performed a protein array on cells overexpressing GLI2 to detect potential transcriptional targets of this pathway. These results were validated in 2D and 3D settings via qPCR.
We also tracked the localization of different cell types in 3D coculture models by labeling them with membrane fluorescent dyes and tracking them on the fluorescent microscope during 8 days.

Results: Our analysis uncovered 10 commonly expressed proteins between fibroblasts and cancer cells, with 9 exclusive to fibroblasts and 1 to cancer cells. Notably, GLI2 activation reshaped fibroblast secretomes by upregulating 6 proteins and downregulating 12, while cancer cells exhibited 1 novel protein induction alongside 6 upregulated and 3 downregulated proteins. In our 3D co-culture spheroid model, fibroblasts consistently localized to the spheroid core, while cancer cells formed an outer layer, indicating self-organized spatial compartmentalization.

Conclusions: These findings highlight context-dependent molecular shifts driven by Hedgehog-GLI signaling and underscore the importance of tumor-stroma interactions in shaping HNSCC biology. Our 3D model offers a robust platform to dissect the spatial and molecular intricacies of the TME, paving the way for discovering novel therapeutic targets.

Salivary oxidative stress markers in the progression of OPMDs – a pilot study

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Purpose: This pilot study aimed to compare the salivary levels of ferric reducing ability of saliva (FRAS), advanced oxidation protein products (AOPP), and uric acid among healthy individuals, patients with oral potentially malignant disorders (OPMDs), and patients with oral squamous cell carcinoma (OSCC), and to explore their potential as biomarkers of disease progression.

Method: Unstimulated saliva was collected from 10 healthy controls, 10 patients with OPMDs (7 oral lichen planus, 3 oral leukoplakia), and 10 patients OSCC. The saliva samples were stored at –80°C until analysis. FRAS was measured using a modified version of Benzie and Strain's method, AOPP levels were determined following the method by Witko-Sarsat et al., and uric acid concentrations were measured using the URIC ACID MR CromaTest kit.

Results: FRAS values (mean ± SD) were 161.39 ± 44.99 µmol/L (healthy controls), 176.01 ± 26.47 µmol/L (OPMDs), and 179.83 ± 65.33 µmol/L (OSCC), with no significant differences. AOPP values were 5.07 ± 1.94 µmol/L (healthy controls), 10.10 ± 2.92 µmol/L (OPMDs), and 12.87 ± 3.67 µmol/L (OSCC), with significant differences between controls and both OPMDs and OSCC ($p<0.001$), but not between OPMDs and OSCC ($p=0.079$). Salivary uric acid levels were 4.79 ± 0.97 mg/dL (healthy controls), 2.67 ± 1.68 mg/dL (OPMDs), and 2.70 ± 1.38 mg/dL (OSCC), with significant differences between controls and both OPMDs ($p=0.003$) and OSCC ($p=0.001$), but not between OPMDs and OSCC ($p=0.965$).

Conclusions: Our results demonstrate that salivary AOPP and uric acid levels are significantly altered in patients with OPMDs and OSCC compared to healthy controls, which was not registered in the FRAS values. These alterations suggest a possible involvement of oxidative stress in the development of OPMDs and OSCC. However, the absence of significant differences between OPMDs and OSCC limits the utility of salivary AOPP and uric acid as markers of malignant progression. Larger, longitudinal studies are necessary to validate these preliminary findings and to identify more specific biomarkers for disease staging.

Immune Mechanisms Driving Clinical Heterogeneity in Oral Lichen Planus

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Purpose: To study the role of T cell subsets, natural killer (NK) cells, and B lymphocytes—along with their cytokine profiles—in oral lichen planus (OLP) pathogenesis, aiming to uncover immune mechanisms underlying different clinical presentations (reticular [OLP-R] and erosive [OLP-E] forms).

Method: A cross-sectional study was conducted involving 61 OLP patients (31 OLP-R , 30 OLP-E) and 30 healthy controls. Peripheral blood mononuclear cells were analyzed using 24-color flow cytometry to assess immune cell populations and activation markers. Cytokine secretion profiles (IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-17A, IL-22, IL-23, IFN-γ, TNF-α, TGF-β1) were measured via Luminex following CD3/CD28 stimulation. Statistical comparisons for categorical variables were conducted using Fisher's exact test, while the Mann-Whitney U test or Kruskal-Wallis's test were applied for continuous variables.

Results: OLP-R patients showed elevated cytokines versus controls: IL-2 (16.1 vs 10.8 pg/mL, $p < 0.05$), IL-4 (14.7 vs 10.6 pg/mL, $p < 0.05$), IL-17A (115 vs 76 pg/mL, $p < 0.05$), and TNF-α (2.8-fold higher; 397 vs 141 pg/mL, $p < 0.05$). OLP-E exhibited no significant cytokine increases. T cell analysis revealed higher CD4+Th1 frequencies in OLP-R (9.4% vs 7.0%, $p < 0.05$), while all OLP patients had upregulated TIGIT in CD4+ T cells (9.6% vs 7.8%, $p < 0.05$) and CD56dimCD16+ NK subsets ($p < 0.05$). CD19+ naïve B cells were expanded in OLP patients (12.1% vs 7.3%, $p < 0.01$).

Conclusions: Two immunological phases were identified: OLP-R displayed a Th1/Th17-driven inflammatory response with elevated IL-2, IL-17A, and TNF-α, whereas OLP-E showed attenuated cytokine production but shared dysregulation of B/NK cells and TIGIT pathways. These findings highlight distinct and common mechanisms in OLP subtypes, offering insights for targeted therapies.

Effect of Thienopyrimidines on Oral Cancer Cell Lines with Different Malignancy

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Purpose: Oral cancer, particularly Oral squamous cell carcinoma OSCC, is a significant global health concern. Treatment resistance and tumor heterogeneity pose major challenges. Recent research has focused on targeted therapies, including small molecules that modulate specific cellular pathways. Thienopyrimidines, due to their structural similarity to nucleotides, can interact with nucleic acid-processing enzymes and signaling proteins, making them promising candidates for anticancer drug development.

Method: Cell lines: HaCaT normal cell line, HSC-3 human tongue squamous carcinoma cell line is a suitable model for the study of metastatic squamous cell carcinoma, SCC-9 is a cell line squamous cell carcinoma. The synthesized thienopyrimidines (1-7) was evaluated for the cytotoxicity of the thienopyrimidines again the above mentioned human cell lines. Test for cell viability (MTT test). IC50.

Results:
• Compound 6 showed the highest selectivity for both HSC-3 (SI = 6.41) and SCC-9 (SI = 22.32), suggesting strong potential as a selective anticancer agent.
• Compound 4 also demonstrated a high SI against SCC-9 (12.8) but was less selective for HSC-3 (2.08).
• Compound 5 showed a similar selectivity to Doxorubicin, but with higher IC_{50} values, implying less potency but potentially reduced toxicity.
• Compounds 1 and 2 had low SI values (<3), suggesting limited selectivity.
• Compounds 3 and 7 had moderate selectivity, particularly toward SCC-9.

Conclusions: The evaluation of thienopyrimidine derivatives against oral squamous cell carcinoma (OSCC) cell lines of varying malignancy revealed significant differences in both potency and selectivity. These findings support the further development of compound 6, and potentially compound 4, as promising leads for selective oral cancer therapeutics, particularly due to their ability to discriminate between malignant and non-malignant cells.

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Assessing the Role of DNA Methylation in Development and Early Diagnosis of HNC

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Purpose: Head and neck cancers (HNCs) are among the deadliest cancers worldwide. The majority of patients suffer from poor prognosis, and those with a more favourable response to treatment often encounter life-long side effects as a result of surgery and radiation treatment. While premalignant lesions may precede HNC, their characteristics have not been conclusively defined, leading to a current gap in knowledge and the manifestation of delayed diagnoses. DNA methylation machinery is disrupted in several diseases, including the majority of cancers. It has been proven that DNA methylation is one of the main epigenetic modifications that can alter gene expression levels during carcinogenesis. Methyl binding domain 2 (MBD2) is an epigenetic modulator that plays a critical role in regulating the transcriptional profiles of several genes by recognizing methylated cytosines and recruiting chromatin remodeling complexes. We propose to investigate MBD2 in HNC to unveil the mechanisms of carcinogenesis and potential value in diagnosis and as a therapeutic target.

Method: We performed computational analyses to determine MBD2 expression levels in normal, premalignant, and HNC tissue. Next, we generated transient MBD2 knockdown in HPV+/- HNC cell lines, followed by downstream functional assays to assess the MBD2-controlled transcriptional program in HPV+/- HNC. Along with MBD2, we examined the impact of reduced levels of other DNA methylation elements, including TET1 and DNMT1, in HNC cell lines in vitro.

Results: Preliminary work in our lab suggests that MBD2 is expressed at higher levels in HNC and is necessary both to sustain colony formation and viability in HPV- HNC. MBD2 appears to have disparate functions in HPV- and HPV+ cancers, consistent with previous findings from our lab in cervical cancers. Initial bioinformatic analyses utilizing publicly available datasets showed increased expression of MBD2 in HNC tissue compared to normal tissue.

Conclusions: These results suggest that the potential utility of MBD2 inhibition may be specific to HPV- cancers. Recurrent and metastatic HNC represent a global health concern with resistance to therapy and thus poor survival rates. This new knowledge may have a significant impact on the landscape of oncological treatments and patient outcomes. Since MBD2 is elevated in cancers we will explore whether higher MBD2 expression and deregualted DNA methylation dynamics are an early hallmark of oral carcinogenesis which may help to better characterize OPMDs.

The Oral Carcinogenesis Evolution Analysis Network - OCEAN

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Purpose: The complex oncogenic process of oral cancer is a continuum, evolving from oral potentially malignant disorders (OPMDs) due to genetic alterations, epigenetic modifications, and a deregulated tumour microenvironment. This study's main objective is to retrospectively compare the histopathological data of OPMDs and oral squamous cell carcinoma (OSCC) in Portuguese and Indian patients, developing and training an artificial intelligence (AI) model based on those histopathological images, and establishing the trajectory of the oral cancer continuum.

Method: This retrospective and multicenter study will be conducted at the Faculty of Medicine of the University of Porto, Portugal, and RVS Dental College, India, from September 2025 to September 2026. Post-ethical approval, histopathological images of OPMDs and OSCC will be collected retrospectively. OPMDs included are leukoplakia and erythroplakia. Regarding our sample size, 20 cases of hyperkeratosis/hyperplasia, 25 cases of OPMDs and 5 cases of OSCC will be analysed from both the Portuguese and Indian cohorts.

Results: In the majority of cases, OSCC and OPMDs result from prolonged exposure to risk factors, namely tobacco consumption (smoked and smokeless), areca nut use, and chronic alcohol consumption. By involving Portuguese and Indian patients, this initiative promotes transnational collaborations, facilitating knowledge sharing between regions with different exposures to risk factors and distinct health infrastructures. In this retrospective multicentric study, clinical data and histopathological images of OPMDs and OSCC of Portuguese and Indian cohorts will be compared and an AI model will be developed.

Conclusions: This research aims to provide comprehensive data on the evolution and risk factors of oral cancer, thereby helping to develop novel diagnostic tools and personalised treatment plans. The findings of this study may also contribute to the creation of risk-adapted screening protocols, facilitating the early identification of vulnerable populations in both countries and, consequently, improving the prognosis of oral cancer.

Deep Learning Integration of Morphological and Biochemical Data for Oral Cancer and OPMD Diagnosis

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Purpose: Histopathological image analysis remains the gold standard for diagnosing suspected oral cancer or oral potentially malignant disorder (OPMD). This analysis is performed using hematoxylin and eosin (H&E) stained tissue sections that allows to reveal morphological and structural cellular changes. However, it offers limited insights into the underlying cellular processes. Infrared (IR) imaging has emerged as a supporting tool providing biochemical tissue composition and enabling a deeper understanding beyond traditional morphological analysis However, deciphering and interpreting the intricate relationships between morphological and biochemical datasets obtained from infrared imaging remains challenging, as the vast volume of generated information is not inherently human-interpretable. Deep Learning (DL) algorithms have emerged as an alternative to process, manage and learn Intrinsic and complex relationships between different data sources without requiring extensive human intervention. Here, we propose a DL workflow to integrate and correlate both morphological and biochemical information in the context of oral cancer and OPMD. As a proof of concept, a first objective will include the automatic segmentation of oral cancers in 10 classes (including cancer cells, stroma, nerve, muscle, fat and others) to prove the contribution of IR imaging in histopathological analysis. A second objective will include how to integrate biochemical information using DL for the proper diagnosis of dysplasia in patients with OPMDs.

Method: The initial phase involves evaluating different DL architectures and backbones for the automated segmentation of ten tissue types on H&E images. Subsequently, IR images will be acquired using a custom scanner developed by ADMIR and integrated into the DL pipeline to assess their contribution to the learning process. Ultimately, the objective is to investigate how this bimodal information can be added for the proper diagnosis of oral dysplasia.

Expected results: A first exploration on H&ES images using DeepLabV3 architecture and Xception backbone shows an accuracy of 92% and weighted IoU of 85.7%. An improvement in the results is expected with the inclusion of IR imaging.

Accuracy of machine learning models in predicting treatment response and flares in patients with oral lichen planus

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Purpose: The main objective of this study is to evaluate the predictive performance of machine learning (ML) models in evaluating treatment response and recurrence risk in patients with oral lichen planus (OLP). The primary goal is to validate the accuracy of ML algorithms in predicting clinical improvement and the number of annual flare-ups. A secondary objective is to determine the influence of various epidemiological and clinical variables on these outcomes.

Method: Retrospective observational study. The study included data from OLP patients treated between 2022 and 2024 at two centers: The clinic of the Postgraduate Specialization in Oral Medicine at the Complutense University of Madrid and the University of Catania. Inclusion criteria required a confirmed clinical and histopathological diagnosis of OLP and a minimum 12-month follow-up. Ethics committee approval was obtained at both centers.
Predictive variables included patient demographics, systemic diseases, medications, lifestyle factors (e.g., smoking, alcohol), lesion characteristics, treatment types (topical corticosteroids, secondary and tertiary interventions), and adverse effects. Data was anonymized and collected from clinical records using Excel.
ML models will be trained on 80% of the dataset using five-fold cross-validation and tested on the remaining 20%. Multiple classification algorithms (e.g., decision trees, Stochastic gradient descent, Random forests, Logistic regression, Linear regression, Neural networks, Gradient boosting, Support vector machine, Naïve Bayes and k-nearest neighbors) will assess treatment response (OLP signs and symptoms) and recurrence rate. Model performance will be measured using accuracy, recall, F1-score, ROC curves, and AUC values.
The sample size was estimated at 300 patients, marking this as a pilot study. If successful, it could inform future larger-scale collaborations across Europe.
Ultimately, these ML tools aim to support, not replace, clinical decision-making in the management of OLP.

Integrating Molecular Profiling and AI for Early Diagnosis and Prevention of Oral Cancer

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Purpose: Oral leukoplakia (OL) is a potentially malignant disorder, with 3–5% of cases progressing to oral squamous cell carcinoma (OSCC)in Sweden. Early detection of dysplastic changes and recurrence is challenging due to reliance on invasive biopsies and limited follow-up strategies. This project aims to develop a non-invasive molecular diagnostic platform using self-collected brush and blood samples to enable early detection, continuous monitoring, and personalized care for patients with OL and OSCC.

Method: In 2023, a five-year longitudinal study was initiated, enrolling 1,036 individuals with OL and matched controls. Brush samples are collected for cytological and molecular analysis, supported by AI-assisted diagnostics. In situ Proximity Ligation Assay (isPLA) is used to study intracellular signaling, particularly protein interactions in the STAT pathway. Concurrently, SuperRCA technology detects circulating tumor DNA (ctDNA) in plasma at low frequencies, enabling long-term monitoring of patients after OSCC treatment. Integration with AI-driven systems enhances multi-omics profiling and biomarker discovery.

Results: Preliminary findings indicate that brush and blood sampling can effectively substitute tissue biopsies for follow-up diagnostics. AI-enhanced analysis supports early detection of malignant transformation and recurrence. IsPLA enables visualization of intracellular protein interactions, providing insights into dysplastic cell behavior. SuperRCA allows sensitive and specific detection of ctDNA in plasma, supporting ongoing surveillance and detection of recurrence. Self-sampling is being assessed for home use to reduce healthcare burden. This method presents a scalable, cost-effective solution for non-invasive monitoring with potential applications in broader cancer diagnostics.

Conclusions: This project introduces a transformative approach to cancer diagnostics, shifting from invasive, episodic testing to non-invasive, continuous monitoring. Brush sampling is simple, cost-effective, and well suited for primary care. By combining advanced molecular diagnostics with decentralized self-sampling, we aim to create a scalable framework for early detection and personalized care in oral cancer and beyond.

Towards development of an Electric Impedance Spectroscopy (EIS) and machine learning-based decision support system for early diagnosis of oral cancer

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Purpose: Electrical Impedance Spectroscopy (EIS) is a non-invasive technology exploiting the frequency-dependent electrical properties of biological tissues. Applying a small electrical current and measuring the frequency-dependent resistance (impedance spectrum) of a tissue hence allows indirect measurement of tissue structure – essentially a biomarker for cancerous changes. This study aims to use machine-learning techniques to inform an automated diagnosis system for early-stage oral cancer based on EIS measurements. Key challenges are how to deal with the structural differences of mucosal tissue and distinguish normal and diseased oral tissue at different sites.

Method: In this multidisciplinary research project, we are collecting EIS measurements from tissue-engineered constructs that closely mimic normal, OPML (oral potentially malignant lesions) and oral cancer. Authenticity of these constructs is verified by histopathology which also provides quantitative data to inform and calibrate our finite element (FE) Virtual Oral Tissue models (VOTs). These are used to augment the measured data with simulated spectra representing a realistic range of tissue structures, in order to train machine-learning models to distinguish between EIS spectra associated with healthy and dysplastic/cancerous oral tissues.

Results: Histopathological data suggests that tissue engineered constructs share characteristics with in vivo equivalents and that the EIS spectra measured in vitro show similar characteristics to those previously collected during a small in vivo study. Simulated data generated from our VOTs based on quantitative histopathology data show good agreement with the measured data. Early attempts to train machine learning models on simulated and measured in vitro EIS spectra suggest that it is possible to distinguish between normal and cancerous oral mucosa.

Conclusions: The trained machine learning models will be validated against separate sets of EIS data and will be used to generate an algorithm which will form the basis for a prototype decision support system for the diagnosis and monitoring of OPML.

From Prevention to Precision - An App-based risk stratification with epigenomic profiling in understanding malignant transformation of OPMDs.

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Purpose: Oral carcinogenesis is a complex, multistage, and multifactorial molecular process, with oral cancer being the most common cancer in men in India, accounting for approximately 24.3% of all new cases, and ranking fourth among women, with 5% of new diagnoses. While global 5-year survival rates range from 0-64%, they average around 40% in India, underscoring the need for risk stratification, early detection, and timely interception.
Oral Potentially Malignant Disorders (OPMDs) lie at the heart of this continuum, offering a crucial window for intervention. The malignant transformation rate among OPMDs varies: while the overall rate is estimated at approximately 7.9%, lesions exhibiting epithelial dysplasia show a transformation potential of 16-62%. This stratification gap highlights the urgency of integrating molecular tools into frontline screening. Hence, as precursor lesions, OPMDs enable the identification of epigenetic biomarkers predictive of malignant transformation, supporting early diagnosis and targeted management.

Method: This study aims to use the Karemitra App [Karkinos Healthcare Pvt Ltd] for risk stratification in conjunction with standard oral visual examination. We plan to enroll 20 OSCC cases from Mahavir Cancer Sansthan, Patna (India), 20 OPMDs, and 10 healthy controls. The study period is from November 2025 to April 2026. Biopsies will be evaluated for DNA hypermethylation markers: p16, MGMT, and miR-137.

Results: The epigenome acts as a physiopathological mediator and a key mechanism modulating gene expression in response to environmental or endogenous exposures. Identifying epigenetic hotspots and integrating them with digital screening tools may elucidate early-life exposure impacts and progression risk in OPMDs.

Conclusions: This study may advance the understanding of epigenetically driven plasticity and support the identification of therapeutically actionable biomarkers.

The Use of Artificial Intelligence-Based Clinical Decision Support Systems in the Care of Individuals with Oral Potentially Malignant Disorders

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Purpose: Oral malignencies is the sixth commonly reported malignant disease globally. Oral potentially malignant disorders (OPMDs) are lesions that carry a risk of progressing to oral cancer, and their early detection significantly improves treatment outcomes. However, public awareness and understanding of these conditions remain limited. Nursing plays a critical role in raising awareness, identifying at-risk individuals, providing education, and ensuring follow-up. Recently, artificial intelligence (AI)-based clinical decision support systems (CDSS) have emerged as valuable tools to assist nurses in risk assessment, decision-making, and personalized patient care. This paper explores the integration of nursing practices and AI-CDSS in the management of OPMDs and examines their impact on increasing individual awareness and improving care outcomes.

Method: This a review paper.

Results: Nurses work in primary, secondary, and tertiary health institutions that serve public health. Individuals cannot recognize the symptoms of OPMDs in the early stages.So, nurses use their roles as educators and consultants, especially in increasing society's awareness of the symptoms of OPMDs. Nurses use AI-CDDS intensively, especially in monitoring individuals, patient education material, evaluation of compliance, response to the treatment process, and determination of care needs. Also AI-CDDS can calculate the current and predicted frequency of OPMDs due to its fast data processing features. At this point, it can enable nurses to determine the care needs of the population they care for and develop strategies for these needs.

Conclusions: Considering the rapid developments in the health field and the increase in the frequency of OPMDs, nurses need to be prepared for the world of the future. The theme of 2023, determined by the International Council of Nurses as “Our Nurses, Our Future,” discussed global health issues and how nurses should be positioned in the future to improve global health for everyone. Therefore, it is anticipated that AI-CDDS will increase the provision of individual and current nursing care for OPMDs as a worldwide health issue.

POSTER SESSION 3

1_Marie Hoffner_Bridging Medical & Anthropological Perspectives: Innovative Methods for Studying Betel-Related Oral Health Risks in Contemporary India

2_(remote)_Nineta Saraci_Assesesment of Knowledge Regarding Oral Precancerous and CancerousLesiones Among Dental Professionals in Tirana, Albania

3_Damla Torul_Epidemiological and Clinical Characteristics of Oral Potentially Malignant Diseases: A Cross Sectional Study in a Turkish Population

4_Bruno Špiljak_Emergence of Papillomatous and Verrucous Lesions in a Patient with Oral Lichen Planus: Importance of Vigilant Long-Term Surveillance

5_Vlaho Brailo_Proliferative verrucousleukoplakia – management challenges.pdf

6_Tanja Boljevic _ORAL VERRUCOUS CARCINOMA OF THE ORAL CAVITY AFTER CHRONIC CANDIDIASIS – CASE REPORT

7_Loncar Brzak - Božana Lončar Brzak_SYMPTOMATIC EARLY ORAL CANCER- A CASE REPORTpdf

8_Gennaro Musella_Defining early-onset oral squamous cell carcinoma: a systematic review of age cut-offs, risk profiles, and survival

BRIDGING MEDICAL AND ANTHROPOLOGICAL PERSPECTIVES: Innovative methods for studying betel-related oral health risks in contemporary India

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Purpose: Oral Potentially Malignant Disorders (OPMDs) associated with betel chewing in India pose a major public health challenge. These lesions, resulting from prolonged betel use, significantly impact oral health and may lead to cancers. Despite increasing awareness, there is still a gap in understanding the cultural, social, and behavioral factors that sustain this practice. This study explores the intersection of oral health, cultural practices, and public health through an anthropological lens, while highlighting innovative methods for studying these issues.

Method: A multi-method anthropological approach was used to explore the cultural significance of betel chewing and its impact on oral health in India. The study combined traditional ethnographic fieldwork with innovative participatory techniques, including photo elicitation, participatory theater, and drawing exercises. These methods provided participants with an interactive platform to share experiences and perspectives on betel use and its health implications. This approach not only deepened understanding of cultural practices but also empowered participants in the research process.

Results: Preliminary findings show that betel chewing is deeply embedded in Indian social life, with significant public health implications. Despite widespread knowledge of the associated risks, cultural norms and social pressures continue to drive the practice. Innovative methods such as photo elicitation and theater offered insights into the role of betel in daily life and health decision-making, revealing the motivations behind its continued use. These methods also bridged the gap between ethnographic research and participants' lived experiences.

Conclusions: The study highlights the importance of incorporating innovative anthropological methods to better understand complex health behaviors, such as betel chewing, and to design more effective public health interventions. By combining cultural insights with participatory methods, this research contributes to a more holistic understanding of OPMDs and emphasizes the need for culturally sensitive public health strategies in India.

Assessment of Knowledge Regarding Oral Precancerous and Cancerous Lesions Among Dental Professionals in Tirana, Albania

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Purpose: Given their frontline role, insufficient knowledge among dental professionals can lead to missed opportunities for early diagnosis. Early detection is the most effective way for survival and reduced mortality in the case of oral cancer. The aim of this study was to assess the knowledge of dental professionals regarding early detection of OPM lesions, risk factors.

Method: A cross-sectional study was conducted by using a questionnaire among 300 dental practitioners selected randomly. The questionnaire included sections on the knowledge of risk factors, recognition of precancerous and cancerous lesions, and diagnostic approaches. It was distributed in-person and collected anonymously, between September 2023 and December 2023. At least one year of work experience as practitioners was a criterion for eligibility to be included in the study.

Results: The study shows that the information of dentists about OPM lesions is mostly based on knowledge obtained during university studies. 98% of dental proffesionals could identify smoking as a major risk. Lower percentages followed about immunity (72%) and radiation (67%). Oral Pathology , is not a specialisation chosen.
The developments of aesthetic dentistry and implantology have caused attention to be overlooked by these pathologies.

Conclusions: According to the latest WHO data published in 2020 Oral cancer Deaths in Albania reached 90 or 0,31% of total deaths. Oral cancer in Albania is often detected in the later stages. Cost limitations, inadequate technology, and insufficient training of medical personnel for widespread screening measures have severely limited OC screening in Albania. Dental proffesionals should be involved in prevention policies, diagnosis and follow -up. We recommend mandatory continuing education programs focused on oral cancer detection and the integration of regular screening protocols into routine dental practice.

Epidemiological and Clinical Characteristics of Oral Potentially Malignant Diseases: A Cross Sectional Study in a Turkish Population

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Purpose: Oral potentially malignant disorder (OPMD) is a condition that serves as a precursor to oral squamous cell carcinoma (OSCC). In order to diagnose OPMD and OSCC, skilled professionals usually use visual observation, followed by biopsy and histological investigation. The main purpose of this study was epidemiological and clinical analysis of patients with OPMD and OSCC in a Turkish patient population.

Method: Retrospective chart review research was conducted in Ordu, Turkey. OPMD and OSCC patients who visited Ordu University's Oral and Maxillofacial Surgery Clinic were included in the study. Archival records of the patients were reviewed. We gathered information on clinical features, age, sex, first diagnosis, and histological diagnosis.

Results: There were 29 patients, and the mean age of the patients was 61.71 ± 13.74 years. Females made up 58.6% (n = 17) of the cases. 21 patients (72.4%) were diagnosed with OPMD, which includes lichen planus and leukoplakia. The most often impacted area (50%) was the buccal mucosa. In 10 (34.4%) of the lesions were located bilaterally, and 6 (20.6%) of the patients pain and a burning sensation were the primary clinical complaints. The appearance of the lesion was white in 58 % (n = 14) of the patients. Six (20.6%) of the 29 individuals had OSCC, which was primarily found in the posterior region.

Conclusions: These results help to improve OSCC prevention and offer insightful information to clinicians treating OPMDs. Rising awareness regarding the risk factors and manifestations of OPMDs plays a crucial role in the prevention of malignant transformation.

Emergence of Papillomatous and Verrucous Lesions in a Patient with Oral Lichen Planus: Importance of Vigilant Long-Term Surveillance

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Purpose: Oral lichen planus (OLP) is a chronic inflammatory disorder classified as an oral potentially malignant disorder (OPMD), requiring long-term monitoring. We present a case of a patient with longstanding OLP who developed papillomatous and verrucous lesions, raising concern for malignant transformation.

Method: A female patient returned for follow-up five years after a prior diagnosis of bilateral reticular and pigmented OLP. Lesions were previously asymptomatic with occasional mild exacerbations managed by topical corticosteroids. Examination revealed a partially erythematous and hyperkeratotic sublingual mucosa without induration. The patient had a 45-year smoking history. Three months later, a papillomatous, hyperkeratotic-erythematous lesion appeared on the left sublingual mucosa, with surrounding tissue testing positive with toluidine blue. Excisional biopsy was performed. Histopathological analysis included immunohistochemical staining for p16 and C10m, considering the potential role of human papillomavirus (HPV).

Results: Histology revealed pseudo-papillary epithelial hyperplasia with focal atypia and mononuclear infiltration. HPV markers were negative, while basal proliferative activity was increased. Margins were clear, and close monitoring was advised. One month later, a 2 mm verrucous lesion was observed on the right palatal-tonsillar arch. Two months after, the sublingual lesion remained stable and toluidine-negative. However, by three months, it exhibited widespread bleeding on palpation and was toluidine-positive. The patient resumed smoking (20 cigarettes/day). She was referred to oral and maxillofacial surgery, where excision is planned due to suspicion of malignant change.

Conclusions: This case illustrates the evolving nature of OLP —or possibly proliferative verrucous leukoplakia (PVL)—and the emergence of papillary and verrucous lesions under sustained risk exposure. It emphasizes the importance of regular follow-up, adjunctive tools, and timely biopsy. The lesion's morphology and negative p16 raise the ongoing debate regarding HPV's role in oral carcinogenesis. Multidisciplinary care remains essential in OPMD management.

Proliferative verrucous leukoplakia – management challenges

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Purpose: Proliferative verrucous leukoplakia (PVL) is an oral potentially malignant disorder characterised by a significantly elevated rate of malignant transformation. PVL typically impacts middle-aged women and exhibits a clinically unpredictable progression. This study presents three cases of PVL and the associated management challenges.

Method: Three female patients were referred to the Oral Medicine Department of the University of Zagreb School of Dental Medicine for specialist evaluation due to longstanding, slowly progressing hyperkeratotic lesions. The diagnosis of PVL was established through clinical presentation, the progressive nature of the disorder, and biopsy results.

Results: The histological examination of the lesions revealed a spectrum from hyperkeratosis and dysplasia to verrucous carcinoma and carcinoma in situ. Patients underwent routine follow-up every three months. The median follow-up duration was 22 months. Toluidine blue staining served as a supplementary tool to clinical examination. Control biopsies were conducted in accordance with clinical presentation. One patient experienced a recurrence of carcinoma in situ.

Conclusions: PVL is a complex condition necessitating rigorous monitoring by an experienced oral medicine specialist. Currently, there are no available strategies for the prevention of malignant transformation.

The Development of Oral Carcinoma at the site of oral candidiasis

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Purpose: A 63-year-old male patient was referred to our hospital for evaluation of a verrucous white lesion in the oral cavity. The patient reported a four-year history of oral candidiasis treatment. A lesion on the maxillary gingiva had been present for approximately one year and had shown progressive growth in recent months.

Method: Incisional biopsy was performed under local anesthesia, histopathological examination of the analyzed material revealed the presence of cancer tissue composed of squamous epithelium with pronounced acanthosis, papillomatosis, parakeratosis, and hyperkeratosis, exhibiting a low degree of nuclear atypia and a low mitotic index, with final diagnosis of Verrucous squamous cell carcinoma - low grade (HG1; NG1).

Results: After the diagnosis of oral verrucous carcinoma (OVC) was established, patient underwent surgery under general anesthesia. The surgical procedures performed included excision of cancer en bloc with part of alveolar ridge of maxilla, part of the hard palate, along with the extraction of teeth.

Conclusions: Oral verrucous carcinoma is a uncommon, low-grade variant of squamous cell-carcinoma, which accounts for 2-12% of all primary oral malignancies. Finally, regular follow-up of patients with long-term oral candidiasis is important, as well as biopsy of suspicious areas for early detection of oral cancer.

Symptomatic early oral cancer

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Introduction: Early oral cancer usually is asymptomatic, but there are exceptions when the patient seeks help due to symptoms which allows for early diagnosis. Known risk factors include smoking and alcohol consumption, while the role of chronic mechanical irritation is still debated. Oral lichenoid lesion is a potentially malignant oral disorder which requires regular follow ups, although the patients sometimes ignore it.

Case report: A 46-year old man came to the Department of Oral Medicine, complaining of persistent burning and pain in his right posterior lateral side of the tongue. He was not a smoker and he consumed alcohol only occasionally. Two years earlier, he had a lichenoid reaction on his right buccal mucosa in contact with sharp tooth edges and old amalgam fillings on his lower right molars (46, 47, 48). He was advised to replace the amalgam fillings on these teeth and come for a check-up, which he did not do. In the meantime, a tooth 46 has been extracted, and the fillings on teeth 47 and 48 have been replaced. He reported having symptoms on the tongue for a longer period of time, but he had not come earlier. Clinical examination revealed a red-and-white ulcerated lesion with a granular texture, firm on palpation at the root area, highly suspicious for malignancy. A biopsy was done and a histopathological analysis confirmed a diagnosis of squamous cell carcinoma (T2N0M0). The patient was treated surgically, with intraoral excision and ipsilateral selective neck dissection. A follow-up examination revealed deviation of the tongue to the right side and bilateral lichenoid lesions on buccal mucosa. Further continuous follow-up of the patient is mandatory.

Conclusions: Exclusion of potential risk factors and regular follow-ups of patients with potentially malignant oral disorders are crucial for early diagnosis of oral cancer.

Defining early-onset oral squamous cell carcinoma: a systematic review of age cut-offs, risk profiles, and survival

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Purpose: This systematic review aimed to determine whether early-onset oral squamous cell carcinoma (EO-OSCC) is a biologically and clinically distinct entity. In addition to comparing EO-OSCC to conventional OSCC regarding demographics, risk factors, clinical features, and outcomes, a key objective was to assess whether a consensus definition of "early-onset" exists and whether a fixed age cut-off is clinically meaningful.

Method: A comprehensive search of MEDLINE, Embase, Scopus, and Web of Science (inception to February 2025) identified primary studies on EO-OSCC with adult comparator groups. Two reviewers independently conducted PRISMA-guided selection, quality assessment (Newcastle–Ottawa Scale), and data extraction. Random-effects meta-analyses were performed where applicable; other variables were synthesized narratively, with emphasis on the age thresholds used.

Results: Forty-two studies were included, covering 6,872 EO-OSCC and 28,419 conventional OSCC patients. Definitions of EO-OSCC varied: 45 years (18 studies), 40 years (14), ≤35 years (6), and others. EO-OSCC patients were more frequently female (52–60% vs. 38–45%) and less likely to use tobacco or alcohol. HPV positivity was higher (up to 25–30% vs. 10–15%), though testing methods varied. EO-OSCC presented with slightly more advanced T-stage but similar nodal involvement. Five-year survival was marginally higher (67% vs. 62%), but age was not an independent prognostic factor. Subgroup analyses showed little clinical variation by age cut-off, though lower thresholds revealed distinct etiologic patterns.

Conclusions: EO-OSCC shows a unique sociodemographic and etiologic profile, but its clinical course resembles conventional OSCC when adjusted for tumor characteristics. The lack of a standardized age definition complicates comparisons. A rigid cut-off appears clinically reductive; instead, age should be viewed along a biological and risk-based continuum. Standardized definitions and prospective studies are needed to refine classification and management.

In silico identification and characterisation of commonly deregulated microRNAs in the progression from normal oral mucosa to oral cancer

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Purpose: The development of oral cancer is a complex, multistep process involving the transformation of normal oral mucosa into premalignant lesions, such as oral leukoplakia with dysplasia, and eventually into oral cancer. A key feature of this transformation is the deregulation of small non-coding RNA molecules, microRNAs (miRNAs). The identification of miRNAs that are consistently deregulated at different stages of oral carcinogenesis is crucial to gain deeper insights into the molecular changes involved. Our aim was to identify and characterize commonly deregulated miRNAs in normal oral mucosa, oral leukoplakia, and oral cancer using publicly available databases.

Method: The National Center for Biotechnology Information Gene Expression Omnibus (NCBI GEO) was utilized to identify database containing miRNA expression data from normal oral mucosa, oral leukoplakia, and oral cancer. Data from the GSE246050 dataset were analyzed using GEO2R software. Raw fastq files were retrieved from Sequence Read Archive (SRP468035). HISAT2 and StringTie were used for identification and quantification of miRNA transcripts. A list of miRNAs commonly deregulated was further characterised by miRNet v2.0 software.

Results: In total 112 genes were identified as commonly diferentially deregulated across normal oral mucosa, leukoplakia with dysplasia and oral cancer. Among them were 6 microRNA genes: MIR429, MIR6726, MIR135B, MIR204, MIR139 and MIR211. Analysis of expression profiles of mature transcripts of these miRNA genes, revealed significant changes in expression of hsa-miR-429, hsa-miR-6726-3p, hsa-miR-135b-5p, hsa-miR-135b-3p, hsa-miR-204-5p and hsa-miR-139-5p. We have observed progressive upregulation of hsa-miR-429 and hsa-miR-135b-5p, while downregulation of hsa-miR-204-5p, and hsa-miR-139-5p. To investigate the function of all genes regulated by miRNAs, hypergeometric test and the KEGG database were used. Pathways in cancer were significantly enriched with the largest number of genes.

Conclusions: These results are good starting point for further validation of miRNA candidates in oral carcinogenesis. Further validation in a larger group of clinical samples and mechanistic studies are required.

Analyzing Raman Spectral Changes in Saliva Due to Handling and Storage

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Purpose: According to recent studies, saliva can be used for the non-invasive detection of oral cancer or oral potentially malignant disorders (OPMD) using Raman spectroscopy, which can provide a sample's biochemical fingerprint. However, prior to analysis, saliva needs to be handled, transported, and stored under the optimal conditions. This study aimed to investigate Raman spectral changes in the fingerprint region of saliva over time at room temperature, 4 degrees Celsius, and -80 degrees Celsius.

Method: Stimulated saliva samples were collected from healthy donors in accordance with a standard laboratory protocol and were divided into equal aliquots. The saliva was concentrated using ultra-filtration by centrifugation with a 3 kDa filter for 30 minutes at 4 degrees C. For the room temperature measurements, saliva was maintained at room temperature and measured as soon as centrifugation was complete and then every 15 minutes for up to an hour. For the 4 degrees C measurements, saliva was maintained at 4 degrees C and measured as soon as centrifugation was complete and then every 15 minutes for up to an hour and at 2, 4 and 6 hours. For the -80 degrees C measurements, saliva was immediately stored at -80 degrees C and measured after centrifugation at 3, 5, 7, and 10 days.

Results: Depending on storage temperature and duration, Raman spectral changes associated with molecular/structural modifications and potential protein breakdown processes was observed.

Conclusions: To preserve the integrity of saliva samples and guarantee accurate results for Raman spectroscopic analysis of oral cancer and OPMD, these findings emphasise how crucial it is to carefully regulate temperature during handling and storage of saliva samples.

Supplemental Abstracts

Prevalence of Oral Potentially Malignant Lesions and Tobacco Use Among Auto Rickshaw Drivers in Chennai: A Cross-Sectional Study

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Purpose: Tobacco use is one of the leading preventable causes of early death and disease; it is currently responsible for five million deaths worldwide, and will likely cause more than eight million by 2030. India is the second largest consumer of tobacco in the world. Tobacco use is the leading cause of death. Therefore, this study aims assess the prevalence of oral potentially malignant lesions in auto rickshaw drivers who are an important segment of the work force across the country.

Method: A cross-sectional descriptive study was done using cluster random sampling on auto rickshaw drivers working in Chennai City for more than 2 years and available for examination. A total of 400 samples were taken in 40 auto stands. A Survey Proforma was used to collect data which included a Questionnaire to evaluate tobacco use on the frequency, age of onset, amount of consumption, mental stress, economic factors, past medical history, and awareness toward oral cancer. Oral examination were done by single examiner.

Results: Auto rickshaw drivers had a very high prevalence of tobacco product consumption, which was 87%. Gutkha (72%) and bidi (40%). The most overlooked parameter was the detection of oral potentially malignant lesions, which had a 47% prevalence among subjects that were unaware of its occurrence. Most of the auto rickshaw drivers (80%) start tobacco smoking before the age of 18 years and peers influence to a great extent (78%). Seventy percent of auto rickshaw drivers have a good knowledge regarding its harmful effects; however, 60% use tobacco products due to addiction.

Conclusions: The usage of tobacco and OPM lesions were extremely on high side in auto rickshaw drivers. There were many people suffering from tobacco-related diseases like cough and oral ulcer and lung-related problems. They are in high need for tobacco cessation programs.

Prevalence of potentially malignant lesions and oral cancer awereness among seafarers in Voc Port, Tuticorin, Tamilnadu, India.

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Purpose: A sailor, seaman, mariner, or seafarer is a person who navigates waterborne vessels or assists as a crewmember in their operation and maintenance. Seafarers hold a variety of professions and ranks, each of which carries unique responsibilities which are integral to the successful operation of an ocean-going vessel. Seafarers are also frequently exposed to difficult working conditions and particular occupational risks. Seafaring is an exploratory profession with little research has been done to identify conditions that may lead to assess seafarer general health as well as oral health. Past research showed a prevalent use of tobacco and drug abuse among this population. The aim was to assess the prevalence oral potentially malignant lesions and oral cancer awareness and among seafarers in VOC port, Tamilnadu, India.

Method: A cross-sectional descriptive study was conducted among 360 seafarers in VOC port, who used tobacco on daily basis. Data was collected using a pretested Questionnaire, which included Demographic data, tobacco habits, its frequency, form and oral cancer awaareness. Oral examination was done by single examiner to evaluate and categorise the potentially malignant lesions. The data collected was analysed using SPSS version 21.

Results: Total of 360 subjects participated in the survey. Adverse habits show the overall 69.2% prevalence among the study population. The percentage of oral mucosal lesions observed were as follows: 29% leukoplakia, 35% ulceration and 3% malignant tumor. 27% of the study populations had other abnormal conditions like candidiasis and OSMF. Prevalence of oral mucosal lesions in the study population was due to high tobacco use and alcohol consumption.

Conclusions: Findings of the present study suggest that oral health condition of seafarer community was relatively poor and were characterized by a lack of awareness about oral health, deep rooted dental beliefs, high prevalence of tobacco use and limited access to health services.

Calling all INTERCEPTOR members: Let's work together on minimally invasive samples (brush biopsy and saliva) for OPMD management!

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Purpose: The gold standard method for diagnosis and monitoring of oral potentially malignant disorders (OPMD) is clinical examination and histopathology to establish a diagnosis and assess the degree of dysplasia by assessing the cell morphology and tissue architecture. Variability in the grading of dysplasia in OPMD can occur which may lead to variability in predicting malignant transformation. In addition, histopathology is an invasive procedure and cases with widespread field change or multiple lesions in the oral cavity can require multiple tissue biopsies for accurate diagnosis. Our study aims to assess new technologies and minimally invasive samples, such as brush biopsy cytology and saliva, for prediction of malignant transformation and management of OPMD.

Method: Raman spectroscopy is based on inelastic light scattering and can provide a biochemical fingerprint of a cell or tissue or biofluid and allows molecular changes to be captured in one test without the need for external dyes or labels. Biochemical changes may occur before morphological changes become apparent.

Results: In collaboration with the Dublin Dental University Hospital, our recent studies have shown differentiation of low risk (no/mild dysplasia) and high risk (moderate/severe dysplasia) oral leukoplakia using brush biopsy and saliva samples as well as detection of field cancerisation in minimally invasive brush biopsy samples.

Conclusions: We would like to expand this work on OPMD management using minimally invasive samples and we are seeking new collaborators with either (1) existing collections of brush biopsy or saliva samples together with follow up information, or (2) an interest in prospectively collecting samples and follow up information for this study.

Modulation of Drug Sensitivity Testing by Head and Neck Cancer Cell Model Systems

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Purpose: To evaluate how well two different in vitro culture systems—2D monolayers and 3D spheroids—reflect the drug response of head and neck cancer cells (HNSCC) to cisplatin, and to assess the potential of 3D models in improving preclinical drug testing accuracy.

Method: Used the LUC4 oral squamous cell carcinoma cell line and primary oral fibroblasts to develop 2D monolayers and 3D spheroid co-cultures.
• Measured cell viability using a resazurin-based assay.
• Assessed apoptotic activity using Annexin V and Zombie NIR staining.
• Distinguished cancer cells from fibroblasts by transfecting cancer cells with MitoDSRed.
• Used real-time imaging (IncuCyte system) to analyze cell invasion.
• Compared drug response in co-cultures with cancer-associated fibroblasts (CAF) vs. normal fibroblasts (NF).

Results: Cell viability assays showed that IC_{50} values for cisplatin in 3D cultures were about twice as high as in 2D cultures, indicating greater resistance to the drug in 3D models.
- Apoptotic activity was slightly reduced in 3D spheroids, further supporting their increased tolerance to cisplatin-induced cell death.
- In 2D cultures, cancer cells and fibroblasts were more spatially separated, while in 3D spheroids, they showed increased physical interaction and integration.
- Real-time imaging demonstrated that cisplatin effectively inhibited cancer cell invasion, maintaining anti-metastatic potential, even in the more resistant 3D setting.
- There were no significant differences in drug response between models co-cultured with cancer-associated fibroblasts (CAF) and those with normal fibroblasts (NF).

Conclusions: 3D culture models more accurately reflect the drug resistance and cell behavior of head and neck cancer cells compared to 2D systems. Despite increased resistance, cisplatin retains anti-invasive effects, highlighting the value of 3D models for improving preclinical drug evaluation in precision oncology.

Oral lichen planus – an extrahepatic manifestation of hepatitis B, C virus and digital oral medicine

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Purpose: To investigate the relationship between hepatitis B, C virus infection and oral lichen planus, analyze the involved pathogenic mechanisms, and explore the clinical implications of this association.

Method: To investigate the relationship between hepatitis B, C virus infection and oral lichen planus, analyze the involved pathogenic mechanisms, and explore the clinical implications of this association.

Results: Oral lichen planus is one of the most common extrahepatic manifestations of hepatitis B, C virus infection. The study revealed a higher prevalence and more severe forms of oral lichen planus in patients infected with hepatitis B, C virus, confirming international epidemiological data. Pathogenetic mechanisms include the activation of cellular immune responses, molecular mimicry, and T-cell dysfunction. Furthermore, oral lichen planus lesions present an increased risk of malignant transformation, emphasizing the need for a rigorous monitoring protocol for affected patients.

Conclusions: The study supports the hypothesis of a close association between hepatitis B, C virus infection and oral lichen planus, underlining the importance of hepatitis screening in patients with oral lichen planus of unknown etiology. Early diagnosis and interdisciplinary management are essential for preventing complications, including malignant transformation.

Evaluation of Awareness and Knowledge Levels of Dentists, Dentistry Students and Dental Patients on Prevention and Early Diagnosis of Oral Cancers

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Purpose: Evaluation of Oral Cancer Awareness and Knowledge Levels of Dentists, Dental Students and Dental Patients in Terms of Prevention and Early Diagnosis of Oral Cancers
Dentists have a key role in the early diagnosis and prevention of oral potentially malignant disorders (OPMD) as they are the first-line physicians in oral examination. The fact that patients first apply to dentists for another oral complaint or routine oral check-ups places a great responsibility on dentists in the early diagnosis or prevention of oral malignant/premalignant lesions. This study aims to measure the knowledge level of dentists, dentistry students and patients in Türkiye regarding OPMD and to evaluate the level of their knowledge and awareness in the early diagnosis and prevention of oral malignant/premalignant lesions.

Method: In the study, in order to evaluate the oral cancer awareness and knowledge levels of dentists and dental students in terms of prevention and early diagnosis of oral cancer, a questionnaire form developed by Horowitz et al. and translated into Turkish by Eroğlu et al. will be applied. In the study, in order to evaluate the oral cancer awareness and knowledge levels of dental patients in terms of prevention and early diagnosis of oral cancer, questions developed by Rogers et al. and adapted to Turkish by Öçbe et al. will be asked. The study will be administered to a group of individuals who meet the inclusion criteria for the study within a certain period (April 2025- May 2025). Statistically; frequency/ratio distributions and cross variables will be examined from descriptive statistics.

Results: According to the results of this study, it is expected that dentists in Turkey do not have sufficient knowledge about OPMD and do not give it sufficient importance, and that their awareness levels are insufficient regarding the early diagnosis of OPMD and their responsibilities in the examination of patients. In addition, insufficient oral pathology education of dentistry students regarding premalignant and malignant lesions and low oral cancer awareness of patients applying to dentists are other expected results.

Conclusions: The first step in early diagnosis and prevention of OPMD is to cooperate with dentists. Education programs for dentists and dentistry students should be organized continuously. Oral malignant/premalignant lesions should be given a wider area in dental oral pathology curriculum. Authorities should be more effective in improving oral health screenings of dentists and patients. Patients need more public information about OPMD.

Can cell cycle-regulating proteins predict recurrence of oral leukoplakia?

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Purpose: The risk of recurrence and malignant transformation (MT) of oral leukoplakia (OL) has been suggested to be positively associated with large and non-homogenous OL, and the histological finding of epithelial dysplasia. However, because of poor objectivity, sensitivity and specificity, their clinical utility in predicting the recurrence or MT is limited. Therefore, identification of robust biomarkers capable of accurately predicting recurrence or MT is urgently needed. Given that aberrations in the cell cycle are among the earliest events in multistep tumorigenesis and recurrent OLs possess a higher risk for MT, we investigated whether cell cycle-regulating proteins, including p21, p27, p14INK4a, cyclin D1, and cyclin E1, could hold prognostic significance in OL recurrence.

Method: Thirty-four OL tissue samples (16 recurrent, 18 non-recurrent) were obtained from a prospective study in which patients were meticulously followed for at least five years. The expression of p21, p27, p14INK4a, cyclin D1, and cyclin E1 was examined by immunohistochemical method. Positive cell staining was quantified using QuPath digital image analysis software. Statistical comparisons were made between the recurrent and non-recurrent groups based on the percentage of positively stained cells. Kaplan-Meier analysis was used to calculate recurrence probabilities, using the median staining percentage as the stratification threshold for each biomarker.

Results: Apart from p16INK4a, non-recurrent OL showed a higher mean percentage of positive cells than recurrent OL. For each biomarker, neither the percentage of positive cells differed significantly between the two groups, nor were the recurrence probabilities significantly different when comparing samples stratified by the median percentage of positive cells.

Conclusions: None of the biomarkers showed prognostic significance for OL recurrence in the present study. However, future studies with larger samples are warranted before concluding that the cell cycle-regulating proteins cannot predict OL recurrence.

Oral cancer perceptions amongst adult attendees

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Purpose: This study aimed to assess (i) awareness of the signs and symptoms of oral cancer and its risk factors and (ii) awareness and attitudes towards oral cancer screening, in an Irish cohort.

Method: A cross-sectional self-administered survey was used in a convenience sample of patients > 18 years with no cancer history attending the Dublin Dental University Hospital. The data were analysed using descriptive statistics, Pearson's Chi-squared and Fisher's exact tests.

Results: 124 responses were received. 83.7% reported knowing little/nothing about oral cancer risk factors. 12.8% did not identify smoking, 35.3% alcohol consumption, 90.5% betel nut, 35.3% age and 80.2% male gender, as risk factors. 46% were unaware that a dentist is trained to check for oral cancer. Participants were more likely to seek advice regarding a persistent oral white or red patch from their doctor than their dentist but were more likely to attend their dentist in relation to a persistent ulcer, swelling or pain. The study did not find any statistically significant relationship between gender, age, educational level and either awareness of the signs and symptoms of oral cancer and its risk factors, or with experiences and attitudes towards oral cancer screening.

Conclusions: The study demonstrated a lack of knowledge of the risk factors, signs and symptoms of oral cancer, and of awareness of the role of dentists in screening for oral cancer. It should be repeated in a larger cohort in non-dental settings to inform the development of oral cancer awareness programmes that address those areas where awareness is lacking.

The Relevance of Architectural Dysplasia in Oral Leukoplakia and Oral Squamous Cell Carcinoma

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Oral epithelial dysplasia (OED) is the most important prediction marker for the development of oral squamous cell carcinoma (OSCC). The most recent WHO classification (2022) appoints architectural features next to the 'classical' cytonuclear atypia in the assessment of OED. "Architectural features without pronounced cytological atypia may in themselves signify dysplasia". This pure architectural pattern of dysplasia is also coined as "differentiated dysplasia".
We showed in a consecutive cohort of 176 oral leukoplakia (OL) patients, the most important clinically recognizable precursor of OSCC , that 33/176 patients developed OSCC during follow-up. Presence of classic OED increased cancer risk two-fold (HR = 2.18, p = 0.026). Lesions without classic OED could be further risk-stratified by the presence of architectural dysplasia (HR = 7.36, p < 0.001). Combined classic OED and architectural dysplasia imparted a seven-fold increased risk of malignant transformation (7.34, p = 0.001).
Besides, a cohort of 311 surgical treated OSCC patients displayed architectural dysplasia in the surgical margins of 92 specimens (29,6%). Its presence was associated with a higher risk of local relapse, indicating its clinical relevance.
Recognizing and classifying OED is difficult in practice, substantiated by a poor inter- and intra-observer agreement, however, it is still the best predictor and golden standard for prediction of malignant transformation of OL and relapse of OSCC. It is important to recognize architectural dysplasia as a separate entity and to incorporate it in daily clinical and histopathological diagnostics, because it is of great added value for the clinic.

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"The oral microbiome and OPMDs: driver or bystander?"

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Purpose: Oral leukoplakia (OLK) is a potentially malignant mucosal condition associated with an increased risk of transformation to cancer. Malignant transformation of OLK is difficult to predict and our research aims to determine if microbiome changes could be linked to the aetiology of this condition or the risk of malignant progression. We have completed microbiome analysis of 216 histologically-proven oral leukoplakias. Compared to healthy controls these patients exhibited a dysbiotic microbiome enriched for acetaldehyde generating bacteria.

Method: We have completed microbiome analysis of 216 histologically-proven oral leukoplakias. Compared to healthy controls these patients exhibited a dysbiotic microbiome enriched for acetaldehyde generating bacteria.

Results: We have isolated some of these organisms by direct culture and have shown that smokers have a higher risk of harbouring strains of R. mucilaginosa that can generated acetaldehyde from alcohol. The OLK microbiome was also influenced by the degree of epithelial dysplasia. Low risk OLK (no or mild dysplasia) was characterised by reduced abundance of specific taxa relative to high-risk (moderate or severe dysplasia). Using machine learning techniques, clinical and microbiome data could effectively discriminate high-risk and low-risk dysplasia (sensitivity 87.4%; specificity 76.5%). Follow-up swabs (n=107) were recovered from 58 patients twelve months after the initial swab. Eight of these OLKs progressed to a higher grade of dysplasia or to OSCC and these patients exhibited significantly higher levels of Fusobacterium species at initial presentation compared to those who did not progress. We have also cultured Fusobacterium nucleatum from these sites and have demonstrated in vitro that the bacterium can induce keratinocyte invasion and promote angiogenesis in HUVEC cell cultures.

Conclusions: Our data is providing an emerging picture of the oral microbiome as having an important role in initiation of oral dysplasia and the malignat progression of OSCC.

Towards an Oral Cancer Cell Atlas

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Purpose: Oral cancer is a significant global health challenge, and a deeper understanding of its cellular composition is essential for improving diagnostics and treatment. The aim of this study is to construct a high-resolution reference of the cellular landscape in oral tumor and non-tumor tissues using publicly available single-cell RNA sequencing (scRNA-seq) data, as a step toward developing an Oral Cancer Cell Atlas.

Method: We collected and analyzed a total of 458,434 single cells from nine publicly available 10x Genomics scRNA-seq datasets, spanning both tumor and non-tumor oral tissues. An in-house integration pipeline was used to harmonize datasets, reduce batch effects, and retain meaningful biological variability. For cell type annotation, we employed a hybrid approach, combining automated annotation tools with manual curation by domain experts, ensuring accuracy and consistency across the integrated data.

Results: The resulting dataset captures key cellular populations, including epithelial cells, fibroblasts, endothelial cells, lymphocytes, and myeloid cells. The integration enabled robust identification of shared and distinct features between tumor and non-tumor samples. Immune composition, epithelial diversity, and the presence of tumor-associated cell states were revealed across datasets, providing insights into cellular dynamics within the oral tumor microenvironment.

Conclusions: This study demonstrates the feasibility and value of integrating heterogeneous scRNA-seq datasets in oral cancer research. The resulting reference serves as a foundational resource for the Oral Cancer Cell Atlas, supporting future work in tumor biology, immune profiling, and biomarker discovery. All data and annotations will be made publicly available to support the wider research community.

ARID1A and ARID1B Deficiency Sensitizes Oral Squamous Cell Carcinoma to PD-1 Blockade Immunotherapy

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Purpose: The SWI/SNF chromatin remodeling complex plays a pivotal role in regulating gene expression by altering chromatin structure. Among its core subunits, ARID1A and ARID1B are critical for directing the complex to specific genomic regions through DNA binding. Mutations in genes encoding SWI/SNF components particularly ARID1A are frequently observed across a wide range of human cancers. This study investigates whether the loss of ARID1A and ARID1B enhances susceptibility to anti-tumor immunotherapeutic interventions in oral squamous cell carcinoma (OSCC).

Method: CRISPR-Cas9 technology was employed to generate ARID1A and ARID1B knockouts in Cal27 OSCC cells. Successful gene silencing was validated via Western blot analysis. The knockout cells were subsequently co-cultured with peripheral blood mononuclear cells (PBMCs) and T cells pre-treated with Pembrolizumab to inhibit PD-1 expression. Immune-mediated cytotoxicity was evaluated using Annexin V apoptosis assays.

Results: Efficient knockout of ARID1A and ARID1B was achieved in Cal27 cells. Co-culture experiments demonstrated that ARID1A/B-deficient cells exhibited significantly increased sensitivity to immune cell-mediated cytotoxicity, particularly in the context of PD-1 blockade. These findings indicate that the loss of ARID1A and ARID1B enhances the efficacy of immunotherapeutic targeting in OSCC.

Conclusions: Our results suggest that ARID1A and ARID1B deficiency augments tumor cell vulnerability to immune-mediated attack, thereby improving responsiveness to PD-1-targeted immunotherapy. These findings underscore the potential utility of ARID1A/B status as a predictive biomarker for immunotherapeutic outcomes in oral squamous cell carcinoma.

Comparative Analysis of Information Quality in Oral Potentially Malignant Disorders: Oral Medicine Specialists, General Dentists, Othorinolaringolostis and Large Language Models

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Purpose: Oral potentially malignant disorders (OPMDs) include complex conditions, requiring a tailored approach for patients and families. With artificial intelligence (AI) gaining traction in medical applications, this study evaluates the quality of information provided by large language models (LLMs) in comparison to clinicians, identifying strengths and limitations in the field of OPMDs.

Method: In a comparative blinded study, fifty-four items of increasing difficulty, namely 18 theoretical questions, 18 clinical scenarios, and 18 patient questions, were posed to ChatGPT-4.0, -4o, Claude-3, Gemini, Perplexity, Copilot, three undergraduate 5th dentistry student, three dentists, three otorhinolaryngologists, three pathologists and three oral medicine specialist; from different countries. The Quality Analysis of Medical Artificial Intelligence (QAMAI) tool was used for blinded evaluation of the quality of medical information by a panel of expert members.

Results: Oral medicine is an expanding branch of dentistry, requiring high specialization training and regular updates. As advancing knowledge about OPMDs, controversies arise as limited evidence-based recommendation exist, while inclusion of different entities in OPMD may lead to confusion. We expect to find difference in quality of the generated medical information based not only on the application of LLM, but also between oral medicine specialist and other medical practitioners.

Conclusions: Caution should be taken when addressing OPMDs and LLMs. LLMs could show promise as supportive resources in oral medicine, particularly in theoretical learning and standardized cases. Future developments should focus on refining AI capabilities for evidence-based and empathetic communication to support both clinicians and families.

HPV positive squamous cell carcinoma in situ in the patient with tongue piercing – multifactorial etiology?

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Case report: A 33-year-old woman presented to the Department of Oral Medicine at the School of Dental Medicine, University of Zagreb, Croatia with pain on the ventral surface of the tongue that had persisted for two months. She was otherwise healthy and reported smoking approximately 10 cigarettes per day. The patient previously had a tongue piercing, which she had removed about a year earlier after wearing it for several years.
Clinical examination revealed an erythematous lesion on the ventral surface of the tongue, with several erosions covered by a pseudomembranes. A toluidine blue staining test was positive, prompting an incisional biopsy.
Histopathological analysis revealed high-grade dysplasia. The patient was then referred to a maxillofacial surgeon, who repeated a biopsy, which confirmed the presence of the squamous cell carcinoma (SCC). Surgical excision of the lesion was performed intraorally, and the final histopathological analysis identified HPV-positive carcinoma in situ. No further treatment was necessary as decided by multidisciplinary oncological team.
This case report presents multifactorial etiology in the patient with oral SCC including smoking, trauma and HPV which cannot be clearly distinguished. It also helps shed light on the complexity of oral SCC's etiology and emphasizes the need for a comprehensive, multifaceted approach in both prevention and treatment.

Therapeutic Vulnerabilities in ARID1A Deficient Oral Squamous Cell carcinoma: Targeting EZH2, PARP and DNA damage Pathways

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Purpose: AT-rich interaction domain 1A (ARID1A), a subunit of the SWI/SNF chromatin remodeling complex, regulates chromatin accessibility and cellular processes. As a tumor suppressor, ARID1A mutations drive oncogenesis in various cancers, including oral squamous cell carcinoma (OSCC), a prevalent head and neck cancer. In OSCC, ARID1A is frequently altered (5–10% mutations, 10–20% expression loss), and its loss is associated with aggressive disease and poor prognosis. Targeting pathways linked to ARID1A deficiency, such as PARP and EZH2, may suppress tumor growth. This study investigates therapeutic vulnerabilities in ARID1A-deficient OSCC.

Method: Stable ARID1A-knockout Cal27 cells were generated using CRISPR/Cas9 via lentiviral transduction. EZH2 and PARP were inhibited with GSK126 and Olaparib, respectively, while etoposide and doxorubicin assessed chemotherapy responses. Cell viability, apoptosis, and cell cycle profiles were evaluated using MTT, Annexin V/7AAD, and flow cytometry, respectively. Protein expression of ARID1A, EZH2, and PARP was analyzed by Western blot.

Results: ARID1A-deficient Cal27 cells exhibited increased sensitivity to EZH2 and PARP inhibition, as shown by reduced cell viability and enhanced apoptosis. These cells also displayed greater sensitivity to DNA-damaging agents (etoposide, doxorubicin) and cell cycle arrest. ARID1A loss confers therapeutic vulnerabilities to chemotherapy and DNA repair-targeted therapies in ARID1A deficient OSCC.

Conclusions: ARID1A loss confers therapeutic vulnerabilities to chemotherapy and DNA repair-targeted therapies in OSCC. These findings suggest ARID1A status as a potential predictive biomarker for treatment response. Ongoing studies are exploring the molecular mechanisms underlying ARID1A loss and its therapeutic implications.

Biogenic Amine Detection in Saliva Using Color-Tunable Polymers and Crystal Violet on Laser-Printed µPADs for Oral Health Screening

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Purpose: Oral conditions, including oral potentially malignant disorders (OPMDs), are often associated with microbial degradation products such as biogenic amines in saliva. These small molecules are emerging as important biomarkers for oral health status. The present work introduces a rapid, accessible, and non-invasive method for detecting salivary biogenic amines using a laser-printed microfluidic paper-based analytical device (LP-µPAD) functionalized with novel polymer materials.

Method: This platform combines maleic anhydride-modified nonconjugated polyesters, such as poly(propylene succinate) and poly(propylene citraconic), in combination with crystal violet as a secondary chromophore to enhance colorimetric contrast. The synthesized polymers display color changes following interaction with specific salivary amines such as dopamine, histamine, and norepinephrine. Amines initiate chain-end interactions with ester groups, generating a visible emission shift dependent on amine concentration and identity. Using laser printing, hydrophobic barriers were patterned on cellulose substrates to create microfluidic zones, where polymer-dye combinations were preloaded. Samples were analyzed visually and via smartphone-assisted imaging.

Results: The µPAD demonstrated fast response times (<5 minutes), clear visible shifts in color, and a broad working pH range (5.5–8.5). The presence of crystal violet intensified differentiation of target analytes by providing a dual-color confirmation system, photoluminescent response from the polymer and absorption change from the dye. Quantitative analysis showed excellent sensitivity and reproducibility in saliva with minimal interference from other salivary components. Device fabrication was low-cost, and the approach enabled robust field-deployable analysis.

Conclusions: This work presents a flexible and user-friendly µPAD for detecting salivary amines as indicators of oral health status. The dual-confirmatory system leverages smart polymer chemistry and colorimetric amplification to enable real-time diagnostics. Its adaptability for future multiplexing and smartphone integration highlights its potential as a practical screening tool in clinical and community oral health settings.