DELEGATES' ABSTRACTS (GENERAL)

G1 Gene-environment-lifestyle factors in breast cancer susceptibility: machine learning tools to build predictive models

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Background: Breast Cancer (BCa) predisposition has 30% genetic and 70% environmental (E), health & life style (HLS) components. Exposures to exogenous (viruses, chemicals and radiation) or endogenous (estrogen) carcinogens contribute to the etiology of BCa. Available tools offer statistical probability of risk at a population level but, not at an individual level. Our aim is to build predictive models for BCa risk for personalized screening. Hypothesis: HLS/E information collected by population biobanks could serve as surrogates to identify risk factors and help build machine learning based predictive models. Methods: We collected data (378 features related to Diet/HLS/E) from 810 healthy subjects/576 Bca cases. We divided the data into training and validation sets. We used WEKA tools for implementation and tested 13 different algorithms. Results and Conclusions: HLS/E factors as features (age, ethnicity, and type of food input, social involvement, traveling, physical activity and body measurement) produced a good predictive model; Bayes Network in the training (10-fold cross validation) and validation sets showed an accuracy of 87.65% and 95.68% respectively. Serum profiling (molecular/ metabolome) of the subjects may help to gain mechanistic insights to disease etiology. Our model will potentially aid in screening of individuals who are predisposed to breast cancer risk.

G2 Cell cycle inhibitors as checkpoints for malignant transformation of leukoplakia: An overview

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Cell cycle is a complex and coordinated process of cell progression orchestrated by cyclins and cyclin dependent kinases (CDK) and their inhibitors. The activity of cyclin D- CDK complex is positively regulated by mitogenic growth factors and negatively by CDK inhibitors (CKI's). The inhibitors may be responsible for maintainance of cell cycle and proliferation arrest once cells' development fate has been reached. CKI's belong to 2 large families namely INK4/ARF and Cip/Kip based on their structural and functional properties. Oral leukoplakia harboring histological features of hyperplasia and/or dysplasia is a frequent precursor of oral squamous cell carcinoma. Advanced oral leukoplakia has a well established rate of malignant transformation characterized by accumulation of genetic events resulting in distinct phenotypic changes that evolve into invasive cancer. Cell cycle inhibitors act as checkpoints to identify the defective components of cell and inactivation of these genes may interfere with terminal differentiation thus leading to cell proliferation and tumorigenesis. Evidence to the alterations of various cell-cycle inhibitors in oral leukoplakia and oral squamous cell carcinoma have been documented in the literature. The objective of this presentation is to provide an overview of the possible association between cell cycle inhibitors and malignant transformation of oral leukoplakia.

G3 A study on mechanism of chemosensitization of tumour cells by fish oil in experimentally induced colon carcinogenesis

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5-Fluorouracil (5-FU) is used for the treatment of colorectal cancer but has low therapeutic response rate and severe side effects. Recently fish oil (FO) rich in n-3 PUFAs has been shown to improve the efficacy of anticancer drugs. The current study is designed to understand the alteration in underlying mechanisms such as cell proliferation and apoptotic pathway on FO as an adjuvant with 5-FU in experimental colon carcinogenesis. Male Balb/c mice were divided into control and N,N'-dimethylhydrazine dihydrochloride/ dextran sodium sulphate (DMH/DSS) group and were kept for 20 wks for the development of colon cancer and further subdivided based upon the treatment with 5-FU and/or FO. FO along with 5-FU led to a significant increase in survival rate and decrease in tumor volume. Moreover, the combination dosage significantly decreased cell proliferation and ras expression. This also facilitated the process of apoptosis by activating both extrinsic and intrinsic apoptotic pathway as demonstrated by an increase in Fas, FasL, Caspase8, Bax and a decrease in Bcl-2 levels. The results of the present study demonstrated that FO as an adjuvant chemosensitizes the tumor cells through the suppression of cell proliferation and activation of apoptotic pathway and hence, abrogates the process of carcinogenesis.

G4 Prognostic value of Oct4, CD44 and c-Myc in radio-chemo resistant oral cancer patients and their tumorigenic potential in immunodeficient mice

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We have investigated the prognostic value of stem cell associated molecules in radio-chemo resistant oral cancer patients. Immunohistochemistry was performed for the expression of Oct4, CD44 and c-Myc in 87 tumour tissues and the obtained expression profile was correlated with patient's clinicopathological parameters. We observed that the expression of these markers increases with tumour progression. Keratinocytes derived from tumour tissues expressed these markers and formed biospheres. The keratinocytes enriched for these markers independently formed aggressive sarcomatoid carcinomas whereas non-enriched keratinocytes developed poorly differentiated carcinomas in immunodeficient mice. Further, we have correlated the expression of these markers individually as well as in all permutations and combinations with tumour recurrence and survival of patients after surgery and chemo/radiotherapy. All the three markers in double combinations Oct4 + CD44 (OS, p= 0.003; DFS, p=0.001), Oct4+c-Myc (OS, p= 0.0001; DFS, p=0.0001), CD44 + c-Myc (OS, p= 0.008; DFS, p=0.02) and in triple combinations Oct-4+CD44+c-Myc (OS, p= 0.0001; DFS, p=0.0001) were

also significantly correlated with overall survival and disease free survival. Our results suggest a possible use of Oct4, CD44 and c-Myc in prediction of local recurrence and poor survival of patients with oral squamous cell carcinoma. They might be used as molecular targets for effective therapy.

G5 Loss of immunohistochemical expression of p16 and its role in malignant transformation of oral submucous fibrosis

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Background: Expression of p16 has been proposed as a marker for malignant transformation. Present study aimed to evaluate the possible role of p16 expression in oral submucous fibrosis (OSF) and its malignant transformation. Material & Methods: Immunohistochemical expression of p16 was investigated in each of 20 samples of normal mucosa, OSF and oral squamous cell carcinoma (OSCC) (n=60). Using Klaes R et al. criteria, strong nuclear and /or cytoplasmic staining of the keratinocytes were considered as positive. Results: Strong and diffuse immunohistochemical expression of p16 was detected in 12/20 (60%) of normal mucosa, 4/20 (20%) of OSCC and none in 0/20 (100%) OSF. Statistically significant differences in p16 expression were found when normal mucosa, OSF and OSCC were compared. Conclusion: Loss of p16 expression in OSF may play an important role in tumor progression during malignant transformation of atrophic epithelium in OSF.

G6 The nature of tumor stroma - does preexisting premalignancy alter it? Immunohistochemical expression of myofibroblasts in OSMF, OSMF with OSCC and OSCC patients

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Oral sub mucous fibrosis (OSMF) is a well recognized potentially malignant disorder of oral mucosa. The malignant potential of OSMF was first recognized in 1956. The rate of malignant transformation is estimated to be 7-13% in recent years. It has been proposed that oral squamous cell carcinoma (OSCC) arising in preexisting OSMF constitutes a clinicopathologically distinct disease than the OSCC arising de novo. This distinction attributes to the mode of chemical carcinogen such as areca nut as compared to tobacco. The role of epithelial–mesenchymal cell interaction and tumor stroma in tumor progression is an important area of current research and has become a potential target for therapeutic intervention. Trans differentiation of a fibroblast to a myofibroblast is a crucial and early event in tumorogenesis and its expression in aggressive and malignant lesions has been suggested to represent an important participant in invasion. It was observed that most of the patients of OSMF are younger males and with better prognostic features such as better grade of tumor differentiation, lesser incidence of nodal metastases, and extra capsular spread. This raises the question, whether the extra cellular matrix in a subset of OSMF, contributes to a certain extent to make it more resistant to normal invasive mechanisms.

G7 Association of socio-economic risk factor with oral squamous cell carcinoma and its correlation with delay in diagnosis: a pilot study

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Background: Greatest burden of oral cancer falls upon people from most deprived communities but its relation to socio-economic status (SES) has not been studied extensively and is poorly understood. Objectives: To evaluate association of socio-economic risk factor with Oral squamous cell carcinoma and its correlation with delay in diagnosis. Materials & Methods: 60 histopathologically confirmed oral squamous cell carcinoma patients were included and their thorough case history was taken. SES was assessed by scale given by Kuppuswamy. Observations and Results: Out of 60 patients: One was of stage II, moderately differentiated with SES upper middle; reported between 1-3 months. Fifteen were of stage III, 3 well, 11 moderately, 1 poorly differentiated with SES, 3 upper middle,9 lower middle, 3 poorly differentiated; reported 2 between 4-6, 5 between 7-9, 7 between 10-12 months and 1 above 1 year. Fortyfour were of stage IV, 12 well, 21 moderately, 11 poorly differentiated with SES, 3 upper middle, 24 lower middle, 17 poorly differentiated; reported 4 between 4-6, 9 between 7-9, 28 between 10-12 months and 1 above 1 year. Chi-square test was significant. Conclusions: Socio-economic perspective is often ignored but can be potentially a major risk factor in the etiology of oral cancer.

G8 A clinicopathologic review of oral squamous cell carcinoma in tertiary care hospital in central India: an institutional study

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Central India is considered as a developing society characterized by Low socioeconomic status and cultural background enhances the habit of tobacco chewing, betel nut chewing more amongst men as compared to women. The purpose of this study was to present the clinicopathologic characteristics of histologically diagnosed squamous cell carcinoma (SCC) of the oral cavity in Central India, with a view toward analyzing the age, gender, site distribution and histological differentiation. All cases that were histologically diagnosed as SCC of the oral cavity between January 2009 and December 2014 were retrieved from the records of the Department of Oral Pathology and Biology, Sharad Pawar Dental College and Hospital, Sawangi (M), Wardha. All the cases were subjected to analysis of age, gender, site of occurrence, symptoms at presentation, and histological differentiation of tumors. The study revealed a male to female ratio of 1.6:1 with the largest number of OSCCs developing in the fourth and fifth decades of life. Overall, the most common site was the buccal mucosa (75.75%), followed by retromolar area (10%), floor of the mouth (4.25%), lateral border of the tongue (3.75%), labial mucosa (4.75%), and palate (1.5%). Smokeless tobacco and betel nut chewing habit was more prevalent than smoking tobacco in both men as well as women. Well differentiated SCC was the most common subtype (56.81%), followed by moderately differentiated (32.6%) and poorly differentiated (1.67%) subtypes.

G9 *In vivo* toxicity and efficacy assessment of *Anacyclus pyrethrum* and *Glycyrrhiza glabra*

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Root extracts of *Anacyclus pyrethrum* (AP, Akarkara) and *Glycyrrhiza glabra* (GG, Licorice) have been used extensively in traditional and Ayurveda

medicine for treating various diseases like paralysis, headache, rheumatism, inflammation, allergy etc. AP is also known to enhance virility and vitality in males. Anticancer activity of these extracts has not been evaluated in depth. Our prior *in vitro* studies using ethanolic extracts of AP and GG showed potent anticancer activity against carcinomas of lung (A549) and breast (MDA-MB-231). So, we tested the efficacy of these preparations invivo for inhibiting the growth of Ehrlich Ascites Carcinoma (EAC) model. Oral administration of ethanolic extracts of AP and GG at 250 mg/kg and 500 mg/kg body weight have shown no toxic side effects, as evidenced by uniform body weight, blood parameters compared to control animals. Analysis of anti-tumor effects showed a significant cancer cell growth inhibitory property. For example at 500 mg/kg AP and GG reduced the body weight of EAC tumor bearing mice by 85% and 56% respectively at day 15. In conclusion our data showed the ability of AP and GG extracts in inhibiting the growth of cancer cells in mice. Further studies are underway to elucidate the mechanism of anti-cancer activity.

G10 Iron induced oxidative DNA damage in oral cancer

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Oral cancer is one of the most common cancers all over the world having multi-factorial aetiology including nutritional deficiency as one of the factor. Fe deficiency is one of them. However, literature suggests that iron deficiency as well as excess body iron, both may cause carcinogenesis. Iron deficiency may cause oral cancer via the induction of oxidative stress. Iron deficiency produces free radicals and reactive oxygen species that potentially cause cellular injury. Severe iron deficiency compromises immunity of the host as well as integrity of epithelium, which in turn may cause cancer. Iron is physiologically essential and biochemically dangerous. It is an essential component in DNA synthesis and in respiratory and oxidative metabolism. But, this causes unremitting proliferation and a more anaerobic metabolism that may contribute to a formation of neoplasm. The reaction of iron with reactive oxygen species like hydrogen peroxide produces highly reactive hydroxyl radical (OH-) and interaction of this radical with cellular components may result in damage to bio-molecules including DNA. Iron induced free radical damage to DNA seems to be important for the development of cancer. This review explains the role of iron in carcinogenesis by oxidative DNA damage.

G11 Immunohistochemical analysis of p53, Ki 67 and vascular endothelial growth factor in oral squamous cell carcinoma associated with oral submucous fibrosis

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Introduction: Oral submucous fibrosis (OSMF) is a potentially malignant disorder with malignant transformation rate of upto 7.6%. Areca nut, a causative factor for OSMF, is identified as group 1 human carcinogen. Oral squamous cell carcinoma (OSCC) patients with OSMF show distinct pattern of disease presentation with better grade of tumor differentiation. In view of this, with the aim to study this particular oral carcinogenesis, expression of Ki-67, a proliferative marker, p53, an apoptotic marker and VEGF, vascular endothelial growth factor were studied. **Materials and Method:** 10 clinically diagnosed cases of OSCC associated with OSMF were compared immunohistochemically against 10 clinically diagnosed cases of OSCC not associated with OSMF and without areca nut habit. Histopathological examination for grading of OSCC and immunohistochemistry for p53, Ki-67 and VEGF, using positive controls were done. Semi-quantitative analysis was done using morphometric image analyzer software and data was analyzed. **Results:** Difference in histopathological presentation and expression of p53, Ki-67, and VEGF in OSCC with OSMF and OSCC not associated with OSMF was observed. **Conclusion:** Findings of the study suggest that OSCC with OSMF constitute a pathologically distinct disease. Difference in expression of molecular markers between two groups suggests differential mechanisms of areca nut carcinogenesis.

G12 The journey of 'plakias' to carcinoma: Bridging the current clinical practice and basic biology

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Oral squamous cell carcinoma (OSCC) comprises 92–95% of all oral cancers. It is noteworthy that many oral squamous cell carcinomas develop from oral potentially malignant disorders (OPMDs). These include leukoplakia, erythroplakia, oral lichen planus(OLP), oral submucous fibrosis, which are found in association with and or preceding OSCC. Prevention and early detection of such oral potentially malignant disorders (OPMDs) have the potential of not only decreasing the incidence but also improving the survival of those who develop oral cancer. Leukoplakia is the most common OPMD associated with the development of OSCC. In clinical practice various clinical parameters along with subjective analysis of the histopathological severity are the main factors in predicting the malignant potential & treatment planning of these lesions. Great advances are made in understanding the molecular alterations such as dysregulation of oncogenes and tumor suppressor genes, cytogenetic changes, epigenetic changes, and mitochondrial mutations which are reFLected in these lesions. Translation of these findings into effective patient care has been a challenging issue. This paper aims to review the clinical utility of the molecular markers in risk assessment of leukoplakia and objectively stratify the patients into treatment and follow up groups.

G13 Xerostomia - an oral physician's perspective

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Xerostomia, dryness of mouth is a symptom of the underlying pathology. In almost all patients who undergo radiotherapy and in few cases of chemotherapy patient have suffered with xerostomia. I being in the speciality of oral diagnosis, medicine and radiology more concern regarding the oral microflora, hygiene, discomfort, pain, difficulty in deglutition in patient as the aftereffect of cancer therapy. This poster reviews how frequently the patients are affected with xerostomia. Here I will discuss the various clinical oral features and the management available. Special mention will there regarding the prevention and newer management approaches.

G14 Integrated genomic analyses of HNSCC: evaluation of HNSCC cancer cell lines as tumor models

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This talk depicts the power of genomic analysis of carcinomas and the utilization of the proper model systems for preclinical studies. Using comprehensive genomic profiles of 87 hnscc cell lines from the Broad-Novartis Cancer Cell Line Encyclopedia (CCLE), and human tumor tissue sample sequence from the Cancer Genome Atlas (TCGA), we reveal that the most frequently used cell lines in preclinical studies of oral cancer are not quite representative of the genetic characteristics of the most frequent type of oral cancer. This observation should call the attention of the scientific community and encourage being extremely careful when choosing an experimental model system.

G15 Characterization of biomarker and therapeutic target for triple negative breast cancer

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The biology and the molecular mechanisms which drive the growth and metastasis of Her-2 negative breast cancer are not understood. Accumulating evidence indicates that selective overexpression and activation of epidermal growth factor receptor (EGFR) and Src regulates oncogenesis in this phenotype. Here we show that known substrate of Src, Annexin A2 (AnxA2) expression increases with the progression of the Her-2 negative breast cancer. In cancer cells, the membrane bound AnxA2 has a major role in tumor invasion and metastasis. This glycosylated AnxA2 at the membrane surface interacts with many proteins and this interaction is critical for AnxA2 mediated EGFR downstream signaling in these cells. We have purified a plant protein, which has high affinity for membrane surface AnxA2. The treated molecule competes with other proteins for binding with AnxA2. This specific binding abrogates the downstream signaling activity of AnxA2 thereby decreasing the expression of antiapoptotic Bcl-2 family proteins and activates the apoptotic proteins. The functional relevance of this specific binding was confirmed by different proliferative and apoptotic assays in Triple Negative Breast Cancer cells. This illustrates that targeted therapy against membrane bound AnxA2 can be a novel strategy to target AnxA2/ EGFR autocrine loop in triple negative breast cancer.

G16 Differential incorporation of histone H2A isoforms in chromatin and their potential implications in development and cancer

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Histone variants, isoforms and their covalent modifications work together in establishing and maintaining chromatin organization, thus regulating a wide range of DNA-dependent cellular processes such as chromosome organization, DNA repair, and gene expression etc. Recent studies suggests role of histone variants and isoforms in tumor development and progression, and the cancer-associated alteration in H2A are rapidly being uncovered. Earlier studies from our lab have identified and shown the differential expression of two major H2A isoforms, H2A.1 and H2A.2, both in hepatocellular carcinoma and liver development. Despite the fact that the phenotypic association of H2A isoform has been elucidated in different physiological conditions nothing is known about their function at the molecular level. In the presentation, we will discuss recent advances in our understanding on the regulation of H2A.1 and H2A.2 isoforms, their effects on nucleosomal dynamics, impact on cellular proliferation and how disruptions of these chromatin-based mechanisms may contribute to development of cancer.

G17 Secretory phospholipase A2/ enhancing factor in epidermal homeostasis and stem cell regulation

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Epidermis is maintained throughout the life by stem cells that self-renew to maintain tissue homeostasis. Secretory phospholipase A2 Group IIA (sPLA2-IIA) or Enhancing factor catalyzes the hydrolysis of sn-2 position of glycerophospholipids to yield fatty acids and lysophospholipids. It has been shown to be associated in various cancers; however, its role in epidermal homeostasis and stem cell regulation is unknown. Here we investigated the role of sPLA2-IIA in mice hair follicle stem cells (HFSC). The transgenic mice overexpressing sPLA2-IIA (K14-sPLA2-IIA) in mice skin showed development defect such as thickening of interfollicular epidermis, sebaceous gland hyperplasia and increased differentiation. This eventually led to the gradual loss of hair follicle stem cell pool. BrdU pulse-chase label retaining cell (LRC) study showed decrease in slow-cycling stem cell population that demonstrated loss of their quiescence. In addition, the colony forming efficiency of keratinocytes was significantly reduced in the K14-sPLA2-IIA. Our results for the first time uncovered the sLAP2-IIA role in epidermal homeostasis and hair follicle stem cell regulation.

G18 The advantages and disadvantages of being SLiM

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Short Linear Sequence Motifs (SLiM) of 4-8 amino acids are one of the hallmarks in biological recognition. When judiciously employed, they are invaluable tools in high throughput studies. Proteins of very different functions can be linked in a network through interactions with a single hub via a conserved SLiM. In the case of over expressed oncoproteins, such direct multiple interactions are likely to catalyze oncogenic addiction, and therefore these common motifs are invaluable for multi targeted intervention in polypharmacology.

G19 Expression of some genes in anaplastic gangliogliomas

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Objective: Anaplastic ganglioglioma is rare brain tumor. Up to now data on molecular deter-minants of tumor response to cytostatics in anaplastic gangliogliomas are limited. Our aim was to assess patterns of expression and mutational status of selected genes, which are potentially could

were analyzed. TP, β-tubulin III, Ercc1, MGMT, VEGF, TOP2α, C-Kit and PDGFRα mRNA expression was assessed by RT-PCR. Also EGFR mutation (exon19, L858R), IDH1/2 muta-tion status and 1p19q co-deletion were assessed. Results: mRNA expression of evaluated genes appeared to be differential among specimens and was classified into high, intermedi-ate and low by prespecified thresholds. No EGFR mutations were revealed. IDH1 mutation R132H was found in 2 of 9 analyzed cases. 2 of 7 tumors harboured 1p19q co-deletion. One tumor possessed both genetic alterations. Conclusions: The expression patterns of above mentioned genes is assessed in anaplastic gangliogliomas for the first time. Also for the first time IDH1 mutation and 1p/19q codeletion were revealed in this rare tumor. These molecular features should further be correlated with clinical outcomes under treatment in order to es-tablish their predictive value.

IS 20 Understanding the molecular genetics of oral cancers: role of genetic alterations in disease progression and prognosis

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The molecular mechanisms contributing to the development and progression of gingivobuccal complex (GBC) cancers - a sub-site of oral cancer, remains poorly understood. Identifying the GBC cancer-related gene expression signature and the driver genes residing on the altered chromosomal regions is crucial for understanding the molecular basis of its pathogenesis. Genome-wide expression profiling of GBC cancers with known chromosomal alterations was performed to reveal differentially expressed genes. Putative driver genes were identified by integrating copy number and gene expression data. A total of 315 genes were found differentially expressed of which 11 genes were validated by real-time quantitative reverse transcriptase-PCR (qRT-PCR) in tumors and normal GBC tissues. Overexpression of LY6K, in chromosome band 8q24.3, was validated by immunohistochemical (IHC) analysis. Array comparative genomic hybridization analysis of advanced stage oral cancers revealed gain of chromosomal region 11q22.1-q22.2 to be associated with loco-regional recurrence and shorter survival. The integrative analysis revealed BIRC3 in 11q22.2 as a candidate driver gene associated with poor clinical outcome. We are currently validating these observations by FISH and our preliminary data indicates that amplification of this locus is associated even with nodal metastasis. Furthermore, analysis of correlation between DNA copy number change and expression of protein/genes residing in this region along with its functional relevance is ongoing. Integrative analysis of DNA copy number change and gene expression data identified putative driver genes associated with oral carcinogenesis. *KRT76* was one of the differentially expressed genes implicated in the development oral pre-cancer and cancer. We observed a strong association of reduced K76 expression with increased risk of OPL and OSCC development. The buccal epithelium of DMBA treated hamsters showed a similar trend of K76 expression. Oral cavity of *KRT76*-KO mice showed pre-neoplastic changes in the gingivobuccal epithelium; however, no oral tumors were observed in these mice. Thus, our data underlines the potential of *KRT76* gene alteration being an early event although it is not sufficient to drive the development of oral cancers. Thus, our study identified previously unreported differentially expressed genes in a homogeneous subtype of oral cancer and the candidate driver genes that may contribute to the development and progression of the disease.