AWARD NOMINATIONS

B. Poster Presentations - SHRI RAJNIKANT BAXI AWARD

PA-1
Immuono-Cytokine Gene Therapy for Head and Neck Cancer

Aditya Ambade* and Rita Mulherkar

Genetic Engineering, Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Kharghar, Navi Mumbai - 410208, India. *adiambade@indiainfo.com

Introduction: Head and neck squamous cell carcinoma (HNSCC) is the dominant cancer among males in India due to tobacco chewing habits. A large number of patients report to the clinic at a very advanced stage wherein the conventional therapies fail. Gene therapy is an alternate treatment modality, which has shown promising results in recent past. We are working on immuno-cytokine gene therapy using interleukin 2 in a xenograft nude mouse model for HNSCC. Objectives: We propose to bring about effective tumor cell kill using direct injection of IL-2 plasmid DNA in a xenograft nude mouse model for HNSCC. Methods: The plasmid DNA pCMV IL-2 IRES Neo, was transfected into 293 cells and clones were selected on G418. IL-2 secreted in culture supernatants was quantified by ELISA. Biological activity of secreted IL-2 was confirmed on murine splenocytes and human PBLs by [3H] thymidine assay. In vivo expression of the transgene was checked in immuno-competent and nude mice. Mice were injected 50 µg of DNA intramuscularly. Blood was collected from retro orbital plexus before injection and for next 7 days. The serum was checked for secreted IL-2 protein by ELISA. Presence of IL-2 transcripts in muscles was confirmed by RT PCR. Results: The stable transfectants secreted 3.7 to 4.3 ng/mL IL-2 protein. The bioassay showed stimulation index of 10 to 23. Expression of IL-2 in vivo was seen up to 7 days with IL-2 levels reaching a peak by day 3. RT-PCR confirmed the presence of IL-2 transcripts in muscle. The data suggest that this construct is producing biologically active IL-2 and can be safely used for further in vivo gene therapy studies.

PA-2
Radiation Therapy Induced Changes in Apoptosis and its Major Regulatory Proteins, Bcl-2, Bcl-XL, and Bax in Locally Advanced Invasive Squamous Cell Carcinoma of the Cervix

1Amit K Adhya*, 1Radika Srinivasan, 2Firuza D Patel

1Departments of Cytology & Gynaecologic Pathology and 2Radiotherapy, Postgraduate Institute of Medical Education and Research, Chandigarh-12. *amitadhya2003@yahoo.com

Introduction and Aims of The Study: Radiation therapy (RT) for cancer induces cell death by apoptosis. The major apoptotic regulatory molecules induce Bcl-2, Bcl-XL (anti-apoptotic) and Bax (pro-apoptotic) proteins. Invasive cancer cervix is treated mainly by radiation and hence our aim was to evaluate the changes induced by radiotherapy in the apoptotic index and correlate this to the levels of the major pro- and anti-apoptotic molecules in invasive squamous cell carcinoma of the cervix. Methods: Paired biopsies were obtained in 30 cases of invasive carcinoma cervix before and after 10Gy radiotherapy. The TUNEL [Tdt-mediated deoxy-Uridine Nick End Labelling] assay was performed to detect apoptotic nuclei and Bcl-2, Bcl-XL and Bax proteins detected by immunohistochemistry.
(IHC) using specific monoclonal antibodies. Statistical analysis was performed using the Spearman's Rank correlation Co-efficient test. Results: Following RT there was a significant increase in the mean apoptotic index (AI) [2.25 (± 2.28) in the post-RT group vs. 0.90 (±0.53) in the pre-RT group]. Bax, a major pro-apoptotic protein also showed a significant increase following RT (p<0.05) whereas there was no significant change in the levels of the Bcl-2 protein in the two groups. Bcl-XL showed a significant decrease in expression following RT (p=0.006). The Bcl-2 and Bax IHC scores and the Bcl-2/Bax ratio did not correlate with the AI in the two groups. There was an inverse correlation of Bcl-XL to the AI in the pre-RT group (p=0.003) but not in the post-RT group. There was no significant interrelationship in the expression of these proteins. Conclusions: Radiation therapy for invasive squamous cell carcinoma of cervix results in increased apoptotic cell death with up-regulation of Bax and down-regulation of Bcl-XL without any significant change in the levels of Bcl-2 protein.

PA-3
Combination Chemoprevention of Experimental Gastric Carcinogenesis by S-Allylcysteine and Lycopene

B. Velmurugan and S. Nagini

Department of Biochemistry, Faculty of Science, Annamalai University, Annamalainagar-608 002, Tamil Nadu, India. *r_kumar24@rediffmail.com

Dietary modification has emerged as a cost-effective approach to control the incidence of cancer. S-allylcysteine (SAC), an organosulphur constituent of garlic and lycopene, an antioxidant tomato carotenoid are recognized to possess anti-inflammatory, hepatoprotective, antioxidant and anticarcinogenic properties. We evaluated the combinatorial chemopreventive effects of SAC and lycopene on MNNG and S-NaCl-induced gastric carcinogenesis. The animals were divided into eight groups of six. Rats in group 1 were given MNNG (200 mg/kg body weight) by intragastric intubation on days 0 and 14 as well as S-NaCl (1 mL/rat) every three days during weeks 0 to 3 (six times; on days 3,7,10,14,17,21). Animals in groups 2-4 given MNNG and S-NaCl as in group 1, received in addition SAC (100 mg/kg bw), lycopene (1.25 mg/kg bw) and SAC + lycopene (100 mg/kg bw + 1.25 mg/kg bw) respectively three times per week starting on the day following the first exposure to MNNG. Rats in groups 5 to 7 received the test agents alone whereas group 8 served as controls. The animals were sacrificed after an experimental period of 21 weeks. Multiple markers reflecting different aspects of the carcinogenic process were used to monitor chemoprevention. These include the ability of SAC and lycopene to scavenge reactive oxygen species, enhance detoxification enzymes, and induce apoptosis. Combined administration of tomato and garlic significantly reduced the tumour incidence, modulated the extent of lipid peroxidation, enhanced activities of glutathione redox cycle enzymes, and induced apoptosis as evidenced by downregulation of Bcl2 and upregulation of Bax, Bim and caspases. These results demonstrate that combinatorial chemoprevention by SAC and lycopene on MNNG+S-NaCl-induced gastric carcinogenesis is mediated by multiple pathways.

PA-4
The Role of Estrogen Receptor Alpha and Beta and Progesterone Receptor in Endometrial Carcinogenesis

Dimple Chakravarty¹, S. Radhika¹, S. Gopalan², S. Majumdar³ and A. Rajwanshi⁴

¹Department of Cytology & Gynecologic Pathology, ²Obstetrics and Gynecology, ³Experimental Medicine &
Introduction: The endometrium is regulated by estrogen and progesterone which act through their cognate receptors, Estrogen Receptor (ER) and Progesterone Receptor (PR). There are two types of ER - a and b. The focuses of this study are ERb and ERb2/Bcx. Objectives: To determine the expression of ERa, ERb, ERbcx and PR in normal, hyperplastic and carcinoma endometrium. Methods: A total of 39 cases of normal cycling endometrium, 20 cases of endometrial hyperplasia and 26 cases of carcinoma endometrium were studied. Expression of transcripts (Erα, ERβ, ERβcx and PR) determined by RT-PCR and densitometry performed ER and PR protein expression determined immunohistochemically. Statistical tests: Mann-Whitney Test, Students t Test, Chi Square Test. Results: There was no significant difference in the levels of ERα and ERβcx among the groups. However, both ERβ and PR transcripts are downregulated in carcinoma endometrium compared to normal and hyperplastic endometrium (p<0.05). In carcinoma endometrium, there was a significant downregulation of ERβcx in the tumors with increasing myometrial invasion or higher stage (p=0.02). There was good correlation of the transcript and protein levels of ERα (P=0.01) and PR (p=0.004). PR also correlated well with the ERα transcript and protein levels. A definite relationship of the combination expression of the ER isoforms to PR expression was not discernable. Conclusion: In the endometrial carcinomas, there is a significant down regulation of ERβ and PR expression as compared to normal controls. The ER cx isoform is down regulated with increasing depth of myometrial invasion in endometrial cancers.

PA-5
Detection of Mitochondrial DNA Mutations in Cervical Cancer Tissues

Himani Sharma*, Archna Singh, Sunesh Kumar Jain* and Neeta Singh

Department of Biochemistry and Obstetrics & Gynecology*, All India Institute of Medical Science, New Delhi 110029, India. *himanisharma@rediffmail.com

Introduction: There are approximately 1,24,000 new cases of cervical cancer being detected annually in India. Mitochondrial DNA is more susceptible to DNA damage than nuclear DNA due to continuous exposure to ROS. Tumor formation is associated with mitochondrial DNA mutations and alterations in mitochondrial genomic function. Objective: In an attempt to understand the relationship of mitochondrial DNA alterations and cervical carcinogenesis, we studied the mitochondrial DNA for mutations, if any, in cervical cancer and normal cervical samples. Methods: We have evaluated the entire mitochondrial DNA of primary cervical cancer samples for mutations, using eight different pairs of primers by multiplex polymerase chain reaction followed by cloning and sequencing. Results: A significantly higher prevalence of mitochondrial mutations, mostly deletions were seen in the cervical cancer samples (15/28; 53.5%) vs the controls (2/12; 16.6%). 25/28 (89.2%) tumors and 1/12 controls were HPV positive. The highest frequency of mutations was seen in the “D loop” region. The other mutations observed were in OXPHOS complex I (ND3, ND4 and ND5) complex III (12 s rRNA and 16 s rRNA) complex IV (CO1, CO2, CO3), complex VI (ATPase 6 & 8) and in Cyt b. Since these mutations occur in the coding region they are likely to have biological consequences and may play a role in the initiation and promotion of carcinogenesis. Conclusions: Since mitochondria is involved in apoptosis, these somatic mitochondrial mutations have potential therapeutic implications and could be useful in augmenting the definitive biological diagnosis.
PA-6
Modulation of Xenobiotic-Metabolizing Enzymes and Redox Status During Chemoprevention of Hamster Buccal Carcinogenesis by Bovine Lactoferrin

K.V.P. Chandra Mohan¹, P. Vidjaya Letchoumy¹ and S. Nagini¹

¹Department of Biochemistry, Faculty of Science, Annamalai University, Annamalainagar-608 002, Tamil Nadu, India. *r_kumar24@rediffmail.com

The present study was designed to evaluate the chemopreventive efficacy of bovine lactoferrin (bLF), an antioxidant found in milk on 7,12-dimethylbenz[a]anthracene (DMBA)-induced hamster buccal pouch (HBP) carcinogenesis. Hamsters were divided into four groups. The right buccal pouches of animals in group 1 were painted with 0.5 per cent DMBA three times a week for 14 weeks. Animals in group 2 painted with DMBA as in group 1, received in addition, basal diet containing 0.2 per cent bLF. Group 3 animals were given basal diet containing 0.2 per cent bLF alone. Group 4 animals served as untreated control. The status of phase I (cytochrome P450) and phase II (glutathione S-transferase, DT-diaphorase) carcinogen-metabolising enzymes, the extent of lipid peroxidation and glutathione-dependent antioxidants in the buccal pouch as well as the frequency of bone marrow micronuclei were used as biomarkers of chemoprevention. All the hamsters painted with DMBA alone for 14 weeks, developed HBP carcinomas that showed diminished lipid peroxidation and increased activities of carcinogen-metabolizing enzymes and antioxidants with enhanced bone marrow micronuclei. Dietary administration of bLF significantly decreased the incidence of DMBA-induced bone marrow micronuclei and HBP carcinomas. This was associated with a significant decrease in phase I enzymes, modulation of lipid peroxidation and enhanced antioxidant and phase II detoxification enzyme activities. The results of the study suggest that the chemopreventive effects of bLF is mediated by reducing DMBA-induced genotoxicity and modulating carcinogen-metabolising enzymes and the cellular redox status.

PA-7
Correlation of Tissue Lipid Peroxidation and Antioxidants with Clinical Stage and Menopausal Status in Patients with Adenocarcinoma of the Breast

R. Kumaraguruparan¹, J. Kabalimoorthy² and S. Nagini¹

¹Department of Biochemistry, Faculty of Science ²Department of Surgery, Faculty of Medicine, Annamalai University, Annamalainagar-608 002, Tamil Nadu, India. * r_kumar24@rediffmail.com

Breast cancer is the most common cancer in women worldwide and its incidence is increasing in most countries. The etiology of breast cancer is multifactorial. Hormonal, genetic and environmental factors appear to interplay in the pathogenesis of breast cancer. The risk factors associated with breast cancer may exert their effects via generation of reactive oxygen species (ROS). The sensitivity of the mammary epithelial cells to ROS is attenuated by an array of enzymic and nonenzymic antioxidants. The present study was designed to evaluate the extent of lipid peroxidation and the antioxidant status in breast cancer patients in relation to different clinical stages and menopausal status. Fifty newly diagnosed patients with adenocarcinoma of the breast were chosen for the study. The patients were divided into different groups based on the clinical staging and menopausal status. The extent of lipid peroxidation as evidenced by the formation of thiobarbituric acid reactive substances (TBARS), lipid hydroperoxides (LOOH) and conjugated dienes (CD) as well as the status of the antioxidants superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH) and glutathione...
peroxidase (GPx) in tumour tissues and adjacent normal tissues were estimated in these patients. Enhanced lipid peroxidation accompanied by significant elevation in enzymatic and nonenzymatic antioxidants was observed in breast tumour tissues compared to the corresponding uninvolved adjacent tissues irrespective of clinical stage and menopausal status of the patients. The magnitude of the changes in tissue oxidant-antioxidant status was however more pronounced in stage III and in premenopausal patients compared to stage I and II and postmenopausal patients respectively. The results of the present study reveal a correlation between tissue redox status and tumour progression and suggest that upregulation of antioxidants enables tumour cells to counter oxidative stress thereby conferring a selective growth advantage over corresponding normal cells.

PA-8
Molecular Insights into Apoptosis Signaling in Human Oral Tumors and Cell lines

Sanchita Mallick*, Sagar N Pawar, #Alok Pathak and Tanuja R. Teni

Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Tata Memorial Centre, Kharghar, Navi Mumbai - 410 208, India. #Tata Memorial Hospital, Tata Memorial Centre, E. Borges Marg, Parel, Mumbai-400 012. *sanchita_mallick@rediffmail.com

An altered apoptotic response represents a pivotal feature of cancer, contributing to carcinogenesis and resistance to therapy. Our earlier studies demonstrate an inhibition of cell death and enhancement of proliferation in the transition from oral lesions to oral cancer. Frequent overexpression of p53, bcl-2 and bax, members of the p53-dependent apoptotic pathway was observed in oral cancers and a subset of oral lesions. The present study proposes to identify the apoptotic molecules and pathway(s) altered in the oral cancer cell lines Dwivedi & Gurav and Immortalized fetal buccal mucosa cell line FBM as compared to that of oral tumor tissues. The ribonuclease protection assay was used to analyse the mRNA expression of apoptotic genes of Bcl-2, Fas, IAP and Caspase family members in the above samples. A high expression of anti-apoptotic Mcl-1, Bcl-xL, bclw and proapototic bad and bax genes was observed in both the cell lines and majority of tumors. The Fas pathway members were elevated in the cell lines while the TRAIL pathway molecules were high in the oral tumors. High caspase 4 and survivin expression was observed in cell lines and tumors. However the cell lines expressed high caspase 8 while the tumors expressed high caspase 1. RT-PCR assay confirmed the high mRNA expression of Mcl-1 and survivin while immunohistochemical analysis revealed expression of p53, bclxl and Mcl-1 proteins in oral cell lines. Thus altered expression of the bcl-2 related pathway, altered caspase cascade and abnormal p53 and survivin expression observed in our studies may contribute to evasion of apoptosis and the pathogenesis of oral cancers.

PA-9
Syzygium aromaticum  L. (CLOVE), a Promising Chemopreventive Agent for Lung Cancer

Sarmistha Banerjee* and Sukta Das

Dept. of Cancer Chemoprevention, Chittaranjan National Cancer Institute, Kolkata 700026, India. *rmisti@rediffmail.com

Introduction: In recent time, one of the most promising strategies for cancer prevention is chemoprevention by phytochemicals through intake of vegetables, fruits, herbs and spices in daily diet. Among spices, Syzygium
Aromaticum L. (clove) family Myrtaceae, has drawn much attention due to its health promoting properties including radical scavenging effect, antimutagenic effect. Lung cancer is one of the most a common cause of cancer death of which about 85% is associated with tobacco use. Benzo (a) Pyrene, a polycyclic aromatic hydrocarbon present in tobacco smoke is a major risk factor for lung cancer. **Objectives:** The present investigation was an endeavor to assess the anticarcinogenic potential of an aqueous infusion of clove during BP induced lung carcinogenesis in mice. **Methods:** To assess the anticarcinogenic potentiality of clove, histopathological evaluation was carried out both in carcinogen control and treated lung of mouse. To confirm histopathological study, immunohistochemistry were undertaken to detect proliferating cells and apoptotic cells and expression of COX-2, caspase-3 were analyzed by western blotting technique. **Results:** Hyperplasia, dysplasia and carcinoma in situ evident in lung of carcinogen control group after 8th week, 17th week and 26th week respectively, were effectively reduced after treatment with clove infusion. Significant reduction in number of proliferating cells and increased number of apoptotic cells was found on 8th week, 17th week and 26th week of treatment with clove. A reduced expression of COX-2 and increased expression of caspase-3 protein were also observed on 8th week, 17th week and 26th week of BP exposure in treatment group in respect to carcinogen control group. **Conclusion:** Our observation suggests a promising role of clove in prevention of lung cancer.

**PA-10**

**BAG-1 Expression in Premalignant and Malignant Tongue Lesions: A Preliminary Study**

Shalvi V. Mehta¹, Hemangini H. Vora¹, Kruti N. Shah¹, Nilima S. Desai¹, Birva V. Brahmbhatt¹, Shilin N. Shukla², Pankaj M. Shah¹

¹Immunohistochemistry Division, ²Hon. Deputy Director Research, ³The Gujarat Cancer & Research Institute and The Gujarat Cancer Society, Asarwa, Ahmedabad, India. *ihcgeri@hotmail.com

BAG-1 (Bcl-2 associated athanogene 1) is a multifunctional anti-apoptotic gene localised on chromosome 9p12 and it represents a link between growth factor receptors and anti-apoptotic mechanisms. The present study evaluated clinical significance of BAG-1 in tongue carcinogenesis. BAG-1 expression was studied in 12 patients with leukoplakia and in 61 patients with tongue cancer by immunohistochemistry. All leukoplakia patients exhibited BAG-1 expression. However, in tongue cancer, BAG-1 expression was noted in 70% patients whereas no expression was seen in 30% of the patients. BAG-1 expression when correlated with clinicopathological parameters, it was found that the expression was significantly lower in tobacco users (63%) as compared to tobacco non-users (93%; P=0.025). Further, patients with stage IV disease and patients with histological grade III tumors had low expression of BAG-1 as compared to their respective counterparts. BAG-1 expression when correlated with other biomarkers, showed a significant inverse correlation with p53 and cerbB2. Further, with overall survival significant association was not observed. Hence, in a preliminary study, down regulation BAG-1 is seen in tongue carcinoma.

**PA-11**

**Immunostimulatory Activity of Herbal Preparations - NCV I and AC II and Their Usefulness in HIV**

¹Sheeja. T. Tharakan*, ¹Girija Kuttan, ¹Ramadasan Kuttan, ²Kesavan. M, ³Sr. Austin and ³Rajagopalan. K

¹Amala Cancer Research Centre, Amala Nagar, Thrissur, 680555, Kerala, India. ²Amala Ayurvedic Hospital, Thrissur, Kerala, India.*amalaresearch@rediffmail.com
**Introduction:** Immunosuppression is a major problem in cancer and AIDS. Hence worldwide, there is an increase in demand for compounds that can stimulate immunity. **Objective:** NCV I and AC II, which were formulated at Amala Ayurvedic Research Centre contain plant materials with known immunostimulatory activity. Objectives of the study is to find out the immunopotentiating activity of these preparations in immunosuppressed animals as well as to determine the effect of these preparations on total viral load, CD4/CD8+ lymphocytes in HIV infected persons.

**Methods:** NCV I and AC II were administered 1g/kg.b.wt and 250mg/kg.b.wt orally to mice for one month. Simultaneously animals were immunosuppressed by treatment with radiation (600 rads) or with cyclophosphamide (50mg/kg.b.wt). Parameters assessed were hematological parameters, bone marrow cellularity and β-esterase positive cells. The effect of these drugs on humoral and cell-mediated responses was also analyzed in mice models. For clinical evaluation of these drugs against HIV/AIDS, 30 HIV positive patients were asked to take the medication everyday for one year. CD4/CD8+ lymphocytes and total viral load were determined before the treatment of NCV ACII preparations and I and after one-year treatment. **Results:** NCV I and AC II stimulated total WBC count, bone marrow cellularity and β-esterase positive cells in normal, radiation as well as cyclophosphamide treated animals. Administration of these drugs also enhanced total antibody production, number of antibody forming cells and cell mediated responses such as NK-cell, ADCC and ACC. Administration of NCV I and AC II significantly improved the CD4 status in HIV infected persons. Out of 21 patients 19 patients had increased the CD4 count and 17 patients had decreased total viral load. Viral load in 6 patients were reduced to undetectable range i.e. <20. **Conclusion:** NCV I and AC II possess significant immunostimulatory activity. These non-toxic, inexpensive preparation may be found to be useful in persons with HIV- infection.
**Introduction:** Angiogenesis, a process by which new blood vessels sprout from existing one, is a prerequisite for outgrowth and metastasis of tumour. Growth of solid tumours depends on the induction of angiogenesis to provide adequate oxygen and nutrients to proliferating cells. **Objectives:** The antiangiogenic activity of *Thuja occidentalis* was studied using in vivo as well as in vitro models. **Methods:** In vivo antiangiogenic activity was studied using B16F-10 melanoma cell-induced capillary formation in animals. Methanolic extract of *Thuja occidentalis* (5 mg/dose/animal) was administered intraperitoneally for 5 consecutive days. Serum was separated and used for the estimation of various cytokines such as IL-1, IL-2, IL-6, TNF-α and GM-CSF and inhibitors of metalloproteinases (TIMP-1) using ELISA kits according to the manufacturers instructions. Level of VEGF expression was analyzed by the ELISA as well as Quantikine m-RNA. The rat aortic ring assay was used as the in vitro angiogenesis study model. **Results:** Methanolic extract of *Thuja occidentalis* significantly inhibited the number of tumour directed capillaries induced by injecting B16F-10 melanoma cells on the ventral side of C57BL/6 mice. The cytokine profile in serum of angiogenesis induced animals showed a increased level of pro-inflammatory cytokines such as IL-1, IL-6, TNF-α, granulocyte monocyte-colony stimulating factor (GM-CSF) and vascular endothelial cell growth factor (VEGF). The mRNA expression of VEGF was also enhanced by the treatment with non-toxic concentration of *Thuja occidentalis* extract. Levels of IL-2 and tissue inhibitor of metalloprotease-1 (TIMP-1), which were enhanced in the animals during angiogenesis, were found to be reduced by treatment with the extract. Extract at non-toxic concentrations inhibited the production of micro vessel outgrowth from the rat aortic ring in vitro. **Conclusion:** Administration of *Thuja occidentalis* was found to regulate the cytokine levels during angiogenesis and this could be related to observed antitumour activity.

**PA-14**

**Association of Antioxidant Enzymes, GST-\textsuperscript{m} and Tobacco Habits with Oral Cancer**

*Tina K. Dave*, Beena P. Patel, Shilin N. Shukla, Prabhudas S. Patel

Biochemistry Research Division, The Gujarat Cancer & Research Institute, Ahmedabad-380 016. *richa_7cz@yahoo.com*

Tobacco is a major etiological factor resulting into "New epidemic" of oral cancer in India. The present study analyzed antioxidant enzymes, thiol and GST-M1 genotype from blood samples from oral cancer patients (OCP, n=140), healthy controls with habit of tobacco (WHT, n=25) and no habit of tobacco (NHT, n=25) to rule out tobacco associated free radical induced changes in antioxidant enzymes. Tobacco use in any form as well as duration, frequency and lifetime tobacco exposure were higher in OCP as compared to WHT. WHT with elevated levels of RBC GR, SOD, CAT, lower level of plasma thiol and higher lifetime tobacco exposure showed higher risk of oral cancer development. 63% of the OCP had GSTM1 null genotype. Data revealed that higher antioxidant enzymes, lifetime tobacco exposure and lower oxidative stress markers in WHT showed increased risk of cancer development. Individuals with GST-M1 null genotype may be at higher risk of oral cancer development.