

the detoxification index of NNK, ratio of NNAL-glucuronides/free NNAL, was significantly decreased in safrole-pretreated group ($p=0.024$). Conclusion: By using Q-TOF and MS/MS spectrometry, we have demonstrated safrole modulated the activation of NNK in vivo.

SY12-07

Mechanisms of Metastasis in Betel Quit (BQ)-associated Oral Squamous Cell Carcinomas

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Betel Quit (BQ)-associated oral squamous cell carcinoma (OSCC) is, in principle, a deadly oral malignancy among all head & neck cancers, but also features unique clinical characteristics with etiology that signifies its special biological & epidemiological manifestations in southern Taiwan. We addressed to investigate the unique histo-pathological and potential mechanisms of BQ-associated OSCC in human vs. animal models via the genomics and shotgun proteomics. Herein, the discussion will be focused to reveal the underlying cellular and molecular interactions associated metabolic pathways that concur during BQ-related metastatic spread locally and systemically.

SY12-08

Reduction or Block Carcinogenesis of Betel Related Oral Submucous Fibrosis and Oral Cancer

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Objective: The previous findings of toxicogenomics affirmed us with new direction in studying the pathogenesis and prevention of betel quid/areca nut-induced oral precancerous lesions and oral cancer. Here, we undertake chemopreventive research program to find out whether we can control the disease occurrence by blocking or reducing the carcinogenic effects from ready-to-use clinical drugs.

Methods: The microarray, pathway analysis, and qRT-PCR were performed to identify susceptibility genes and novel mechanisms accounting for betel quid/areca nut-induced pathogenesis. Case-control study further ascertained the candidate genes and its risk genotype in the development of betel-related oral cancer. Moreover, approaches of toxicogenomics (areca nut) and pharmacogenomics (selective COX-2 inhibitors) on oral cell lines and animal model were utilized to recognize the significance of susceptibility genes, and further to investigate preventive effects of COX-2 inhibitors on the early areca nut-induced oral pathogenesis.

Results: Our findings suggested 12 susceptibility genes related to xenobiotic metabolism (COX-2), DNA repair, inflammatory and stress response (COX-2), and

transforming growth factor-beta signaling family. These genes may serve as potential biomarkers for betel quid/areca nut-induced damage in chewers. Further, we also showed that COX-2 promoter -1195G>A genotype has an additive interaction with betel chewing habit ($aOR=79.4$) in risk of oral cancer, and the inflammatory response of A/A genotype can be highly induced by areca nut than A/G and G/G genotype. This finding indicates the important role of COX-2 on betel-related oral cancer in Taiwan. Moreover, in chemoprevention studies, two-way cluster analysis from gene expression profiling shows that areca nut-induced damage could be recovered in a suitable dosage of a selective COX-2 inhibitor.

Conclusion: Early detection and chemoprevention are crucial strategies for reducing or blocking carcinogenesis in betel-related oral lesions. Based on our knowledge, the selective COX-2 inhibitor in chemoprevention might be useful for reducing the occurrence of betel-related oral cancer.

SY12-09

New Perspectives in the pathophysiology of Oral Cancer

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(More detail will be presented during the talk)

Symposium 13- Social Determinants of Health II

SY13-01

Social Gradient of Health in Japan; Why and How Education and Income Matter to Health

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Social gradient of health attracts social and political concerns in many countries including Japan. Education and income have long been regarded as major indicators of one's socio-economic positions in the societal hierarchy. Recent research including ours, however, pointed out that simple measurement of socio-economic position through education and/or income lacks theoretical foundation to explain the mechanism of health gradient across social strata. Education may reflect one's skills and knowledge for self-care, while it may be confounded by economic and cultural affluence of one's parents. Income may reflect the degree of access to health-promoting material resources and time, while it may also bring prestige, power, and the degree of social inclusion. Many studies found that income and education distinctively and variously relate to health behaviors, physical and mental health status across genders, age cohorts, and regions, suggesting that the influence of income and education is heterogeneous and unspecified. A recently conducted cross-sectional