the rest were used as test data set to valid the predicted "AminoIndex".

Results: Plasma concentrations of several amino acids were significantly changed in breast cancer patients compared to control subjects in study data set. Finally, "AminoIndex" for breast cancer composed with six amino acids (Gln, Ala, ABA, Trp, Orn, and Arg) was predicted.

To evaluate the performance, the ROC curve was calculated, and this gave an AUC of ROC of 0.832 using the study data. Validation of predicted "AminoIndex" using test data set resulted same discriminating performance (AUC of ROC of 0.822), suggesting the robustness of the predicted classifier.

Furthermore, predicted "AminoIndex" showed notably features.

1. The index could discriminate breast cancer patients in early stages.
2. The index showed higher discrimination performance than those of existing tumor markers especially in stages 0, I, and II patients.
3. The index could equally discriminate breast cancer patients of any histological types.

Therefore, predicted "AminoIndex" would be suitable for screening and early detection of breast cancer patients.

Conclusion and Perspectives: In this study, we demonstrated that change of plasma amino acid profile would be a helpful tool for early detection of breast cancer patients. "AminoIndex" would be useful to concentrate and inspire the candidates for further survey such as mammography. To evaluate the efficacy of this method, cohort studies are ongoing.

P7

p63, K14 and p53 expression in epithelial layers of tumor-distant oral mucosa in patients with oral squamous cell carcinoma

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The p63 gene is highly expressed in the epithelial stem cells and progenitor cells of epithelial tissues and SCC. p63 plays an essential role in epithelial development, stem cell identity and cellular differentiation, and maintenance of proliferative potential of basal keratinocytes. K14 is major keratins of basal cells. Both protein markers p63, K14 expressed in cells of basal layer of epithelium of normal mucosa. p53 gene is the most altered gene in premalignant lesions and OSCC.

Aim: Investigation of the expression of p63, K14 and p53 in tumor-distant oral mucosa from patients with OSCC.

Material and Methods: Biopsy specimens of tumor-distant mucosa and tumors were obtained from 18 patients with OSCC. Most of the patients have the smoking-drinking status and professional contact with carcinogen. The section of tumor-distant mucosa and tumors were classified according to the UICC. Tissue sections were immunohistochemically stained using monoclonal antibodies: for p63 (clone A4A), for K14 (clone 124), for p53 (clone DO-7), "Daco", counted according to ephitelial layers as labeling index (LI, %).

Results: In tumor-distant oral mucosa revealed the progression of histopathological phenotype: from hyperplasia to high dysplasia, Ca in citu and OSCC, I degree. The analysis showed the architectural alteration of cells p63 and K14 expression in the epithelial layers of tumor-distant mucosa and distribution in suprabasal layers. The suprabasal p63, C14 and p53 expression is strongly associated with grade dysplasia and development of OSCC. IL of p63 and C14 decrease in basal layer and increase in suprabasal layers from mild dysplasia to high dysplasia, carcinoma in situ and OSCC (range, LI, p63, C14, mild dysplasia, 1/bas, 45.0–56.0, l/supr 29.0–31.0; 1/bas 24.0ndash;35.5, l/supr 16.3–27.1; high dysplasia, l/bas 11.6–23.0, l/supr 34.6–70.0; 1/bas 13.0–21.5, 1/supr 30.0–34.5, respectively). In carcinomas in tumor-distant mucosa and in primary OSCCs the p63 and K14 cells represented essential part of tumor cells population of OSCC (range, LI, p63, K14, carcinoma in situ and OSCC in tumor-distant mucosa, 15.0–45.6; 10.0–51.3, respectively; primary OSCC, 19.7–79.1; 8.4–54.3, respectively). It's proposed precipitation of stem/progenitor cells in development of transformation phenotype in oral mucosa and in biology of OSCC.

Conclusion: Immunohistochemically revelation of cells p63, K14 and p53 expression in surface suprabasal layers of oral mucosa have been used to objectify differential diagnostic and monitoring the risk after treatment for cancer prevention.

P8

Mutagen sensitivity and p53 in suprabasal layers of tumor-distant oral mucosa in patients with oral squamous cell carcinoma

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Background: The epidemiology associates OSCC with long-term smoking tobacco, being alcohol, exposure to various carcinogens and genetic predisposition. The p53-tumor-supressor gene is the most altered gene in OSCC.

Aim: Investigation of the sensitivity of lymphocytes to mutagen bleomycin and p53 immunoexpression in tumor-distant oral mucosa and tumor in patients with OSCC.

Material and Methods: Peripheral blood lymphocytes and biopsy specimens of tumor-distant oral mucosa and tumors were obtained from 18 patients with OSCC (male, age from 43 to 79 years). Most of the patients have the smoking-drinking status (15/18, >1110; 20 years >1110; 20 cigarette per day) and long-term professional contact with carcinogen. Mutagen sensitivity assays: The blood lymphocytes were cultivated by standard method. Cultures were incubated for 3 days and then exposed to bleomycin (30 mg/ml) for 5 hours. Cells were harvested by cytogenetic techniques (50–100 metaphase) and mean number of bleomycin induced of chromatid breaks (b/c) estimated. Mutagen sensitivity was determined as the level b/c > 1110; 1. The tumor-distant mucosa and tumors were classified according to the UICC criteria. The sections were immunohistochemically stained using monoclonal antibodies for p53 (clone DO-7, "Daco").

Results: All investigated patients with OSCC were mutagen sensitivity (b/c = 1, one case; b/c > 1, 16 cases) and have a permanent influence on oral mucosa of epidemiological factors of cancer risk. The positive of p53 were all OSCC. In tumor-distant mucosa revealed the progression of histopathological phenotype: from hyperplasia to high dysplasia, carcinoma in situ and OSCC, I degree. p53 was detected in 88.8% cases of tumor-distant mucosa. Negative p53 was found only in cases of hyperplasia. Mild dysplasia showed p53 cells in basal and parabasal layers. In high dysplasia and carcinoma in situ p53 cells prevalent in suprabasal layers of epithelium.

Conclusion: The investigated OSCC were developed in patients with mutagen sensitive phenotype under a permanent influence on oral mucosa of epidemiological factors of cancer risk. Suprabasal p53 expression is strongly associated with grade dysplasia. The mutagen sensitive patients with areas of p53 cells in suprabasal layers of tumor-distant mucosa represent high risk of development of second tumors and require after treatment monitoring and prevention.