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To study the BRCA1 and BRCA2 mutations in Chinese patients with early onset breast cancer and affected relatives, 489 high-risk breast cancer patients from five breast clinical centers in China, were analyzed by using PCR-DHPLC or SSCP-DNA sequencing analysis. Allelotype analysis was done at five short tandem repeat (STR) markers in or adjacent to BRCA1 on the recurrent mutation carriers. In the 489 patients, 447 patients received mutation detection in both genes and 41 cases were analyzed only in BRCA1 gene. Twenty-three BRCA1 mutations and 21 BRCA2 ones were detected in our study. Two recurrent mutations in BRCA1, 1100delAT and 5589del8, were identified. The recurrent mutations account for 34.8% BRCA1 mutations in our series. Furthermore, 2 cases of BRCA1 5589del8 (0.5%) and one case of BRCA1 1100delAT (0.2%) was detected in 426 sporadic breast cancer patients and 564 healthy controls, respectively. Similar allelotypes were detected in most STR status for those harboring the same mutations. The frequency of BRCA1 and BRCA2 mutation in our study was both 4.7%. For those analyzed both genes, 8.7% of early-onset breast cancer cases and 12.9% of familial breast cancer cases had a BRCA1 or BRCA2 mutation, as compared with the 26.1% of cases with both early-onset breast cancer and affected relatives. When we stratified with number of breast cancer patients in family, the frequency had no statistical significance. However, the average age of disease onset in the families carrying BRCA1/2 mutations was significantly younger than the families without mutations ($P=0.003$), and more the younger patients in family, higher the mutation frequency was. For those reporting malignancy family history other than breast/ovarian cancer, the prevalence of BRCA1/2 mutation is about 20.5%, and it was significantly higher than the patients only with family history of breast/ovarian cancer ($P=0.02$). The family history of ovarian cancer (26.7% vs. 11.9%) and stomach cancer (23.8% vs. 11.8%) doubled the incidence of BRCA1/2, but the difference did not reach the statistical significance. We recommended the BRCA1 and BRCA2 genetic analysis could be done for high-risk breast cancer patient in Chinese population, especially for those with both early-onset breast cancer and affected relatives.

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Toremifene as a reference drug in the treatment of breast cancer

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Tamoxifen has opened the era of oestrogen receptor blockers. However, Tamoxifen has turned out to be a genotoxic and teratogenic drug as it has been reported by numerous authors and mentioned in the Statements of St. Gallen Consensus Conference.

During the past 15 years, we have been administering Tamoxifen instead of Toremifene. One thousand five hundred seventy one cases of administration of the drug in postmenopausal patients with breast cancer of above 50 years of age have been analysed. No cases of cancer of the liver or endometrium have been detected. Endometrium hyperplasia eliminated by a temporal cancellation of the administration of the drug was reported in 23 % of cases.

A study of the hormonal homeostasis has shown that administration of Toremifene makes it possible to achieve a fourfold reduction of follicle-stimulating hormone levels (reduction by 1/3 is observed on administration of Tamoxifen), which is important from an etiopathogenetic point of view. Moreover, Toremifene

acts in both oestrogen-receptor-positive and oestrogen-receptor-negative patients (5 year survival is similar in both subpopulations).

Toremifene is advantageous as compared with Tamoxifen in the combined therapy of patients with advanced breast cancer: full remission has been achieved in 8.7 % of patients taking Toremifene and in 3.4 % of those taking Tamoxifen and time to progress is 5.1 months in patients on Toremifene and 3.9 months in patients on Tamoxifen.

The above data suggest that Toremifene should be a reference drug for the treatment of breast cancer.

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Multivariate discrimination functions composed with amino acid profiles (Amino Index[®]) as a novel diagnostic marker for breast and colon cancer

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Introduction: Amino acids balance is changed in patients of various diseases due to metabolic transition while it is maintained in healthy human. For example, Fisher ratio (ratio of branched amino acids to aromatic amino acids) is used as a primary index of hepatic failure. It is also known that the metabolism cancer cells are totally altered. Therefore, it is expected that the detection of metabolic transition using amino acid profiles is promising biomarker of various cancers. In this study, significant changes of plasma amino acid profiles of breast cancer and colon cancer patients were detected by discriminants (Amino Index[®]) by conducting with multivariate analysis.

Material and Methods: Blood samples were collected and cooled down from 50 colon cancer patients, 30 breast cancer patients, and age-gender adjusted healthy controls. Then, plasma samples were collected by centrifuge (3000rpm, 15min) and amino acid concentration was measured using LC/MS. The most appropriate discrimination functions for each cancer were estimated. The discrimination ability of discriminants was estimated as the area under the receiver-operator curve (ROC_AUC) of function values. The performances of the discriminants were also estimated using the test data randomly divided in advance. All the statistical and multivariate analysis was performed with MATLAB and GraphPad Prism.

Results: For discrimination of colon cancer, discriminant-1 composed with six amino acids (phenylalanine, threonine, alanine, glutamine, alpha-aminobutyric acid, and citrulline) was obtained. For breast cancer, discriminant-2 composed with composed with six amino acids (glutamine, arginine, isoleucine, alanine, ornithine, and histidine) was obtained. Both of them showed high performance for discrimination; 0.849 of ROC_AUC for discriminant-1 and 0.882 for discriminant-2, respectively. Then, the validation of performances of them using test data resulted 0.943 of ROC_AUC for discriminant-1 and 0.897 for discriminant-2, respectively, suggesting the reliability of these discriminants. Furthermore, the possibility of classification between these three groups was investigated. By conducting with discrimination analysis, it was suggested that the three statuses were