and Her-2/neu was positive (based on IHC scores of 2–3 + and above, or FISH +) in 10 (27%) of the patients. Seven (18.9%) were ER, PR, and Her-2/neu (triple) negative. DNA was extracted from PBC then subjected to bisulfite conversion (Invitrogen, MethylCode Bisulfite Conversion kit) and the promoter region was examined using methylation specific PCR techniques (–157 to +57, +1 serving as transcription start site).

Results: We observed that 5 out of 52 (9.6%) patients with breast cancer who were negative for germline BRCA1 mutations displayed BRCA1 promoter methylation. No promoter methylation was seen in patients with breast cancer who had a deleterious BRCA1 mutation, nor in high risk women who had a deleterious BRCA1 mutation.

Conclusions: These preliminary results suggest that about 10% of sporadic breast cancers have a somatic promoter methylation in the BRCA1 gene. This finding might be important for the development of somatic BRCA1 promoter methylation assay as an assessment of breast cancer risk in women with no deleterious BRCA1 mutations. It would be interesting and important to show increased somatic promoter methylation in the BRCA1 gene in high risk women who do not have a deleterious BRCA1 germline mutation. Such analysis is currently going and will be presented.

P2

"AminoIndex" for cancer detection (1): evaluation as a novel screening tool for colorectal 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. It is also known that the metabolism of cancer cells is totally altered. Therefore, the detection of metabolic transition using amino acid profile is expected to be a promising screening marker of various cancers. We previously demonstrated that significant changes of plasma amino acid profile was observed and classifier composed of plasma amino acid concentrations as explanatory variables "AminoIndex" was high discrimination ability for colorectal cancer patients (Okamoto 2009). In this study, further possibilities of "AminoIndex" for colorectal cancer were investigated.

Subjects and Methods: Plasma samples were collected from Japanese colorectal cancer patients before any medical treatment (N = 220). Those of controls were also collected from subjects who were undergone comprehensive medical examination (N = 4,348). Plasma amino acid concentrations were measured by LC-MS. 80 patients and 400 gender- and age-matched control subjects were chosen as study data set to predict "AminoIndex". And the rest were used as test data set to valid the predicted "AminoIndex".

Results: "AminoIndex" for colorectal cancer was inferred by multivariate logistic regression analysis and classifier composed with six amino acids (Glu, Gly, ABA, His, Trp, and Arg) was predicted as the best model. The ROC curve for each predictive score was calculated, and this gave an AUC of ROC of 0.812 using the study data. Then, validation of predicted "Aminolndex" was performed using test data set and resulted equivalent discriminating performance (AUC of ROC of 0.768).

Further analysis showed that predicted "AminoIndex" for colorectal cancer had potential as a screening marker as follows:

1. The index could discriminate colorectal cancer patients in any stages equally.
2. The index showed higher discrimination performance especially in stages 0, I, and II patients while decrease of sensitivity was observed in existing tumor markers.
3. The distribution of predicted index was independent of those of tumor markers. Therefore, higher detection efficiency would be expected by combinatorial use of "AminoIndex" and tumor markers.

Conclusion and Perspectives: In this study, we demonstrated that further possibilities of "AminoIndex" for colorectal cancer based on plasma amino acid profile. For further evaluation, cohort studies are ongoing.

P3

The expression of WWOX in pancreatic adenocarcinoma

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Introduction: WWOX is a 46 kDa WW domain-containing oxidoreductase protein that has been shown in many different tumour types to have a tumour suppressor role. Few studies have investigated the expression of WWOX in small numbers of pancreatic carcinomas. The aim of this study was to assess the expression of WWOX in the normal pancreas as well as in pancreatic carcinomas and to investigate the correlation of WWOX expression in pancreatic carcinomas with tumour type, grade and stage.

Materials and Methods: WWOX expression was studied in 89 pancreatic adenocarcinomas using immunohistochemistry on formalin fixed paraffin embedded tissue. Of these cases, 76 were classical adenocarcinomas and 13 were invasive carcinomas ex intraductal papillary mucinous tumour (IPMT). The expression of WWOX was assessed in tumours and in adjacent normal pancreatic tissue. WWOX expression was assessed for staining intensity and subcellular distribution. The expression profile was correlated with tumour type, grade and stage.

Results: In the normal pancreas, WWOX was moderately/strongly expressed in the majority of the acini (98%), ductal (97%) and islet cells (91%). Localization of WWOX was only cytoplasmic in acinar and islet cells, but cytoplasmic and apical in most ductal cells (72%). The majority (62%) of classical pancreatic adenocarcinoma cases showed absent or low expression of WWOX. The ex IPMTs demonstrated absent or low expression in 46% of cases. No statistically significant correlation was found between WWOX expression and tumour type, grade or stage.

Conclusion: The results suggest that WWOX may have a physiological role in the normal pancreas, being expressed in all tissue compartments of the endocrine and exocrine pancreas. In addition, our results confirm that WWOX expression is decreased in the majority of pancreatic adenocarcinomas. Reduced WWOX expression shows no statistically significant correlation with tumour type, grade or stage suggesting that the loss of WWOX occurs as an early event in pancreatic tumorigenesis and may play a role in the initiation and progression of pancreatic carcinomas.