were used for the production of phage displayed-antigen microarray that was applied to survey autoantibody profiles in patients with gastric cancer (n = 176), various gastrointestinal inflammatory diseases (n = 125) and healthy individuals (n = 148). The microarray data were analysed as qualitative – after normalisation the average serum antibody signal intensities in healthy donors (HD) were calculated for each antigen, and a threshold of 5 SD above the average signal intensities in HD was set to define antigens preferentially reacting with patients' sera.

Results: Serum autoantibody profiling of ~1322 element phage-displayed antigen microarray comprising all immunoselected antigens resulted in the identification of a panel of 232 antigens with potential diagnostic significance. The statistical data analysis resulted in the determination of a 60 antigen detector group that was able to discriminate between gastric cancer and healthy individuals with 81% sensitivity and 95% specificity (PPV 95%, NPV 81%), and between gastric cancer and gastrointestinal inflammatory disorders with 77% sensitivity and 90% specificity. Noteworthy, the sensitivity of the detection of stage I and II cancer was 77% and stages III and IV – 90%. Twenty-nine and 33 antigen detector groups were identified that were able to detect diffuse and intestinal type adenocarcinomas with 86% and 81% sensitivity, respectively, reaching 93% specificity in both cases, and the two groups were shown to encompass different sets of antigens.

Conclusions: Results of this study show that the serum autoantibody signatures have a potential to detect the presence of gastric cancer with significantly higher accuracy and earlier than any of the currently known serological markers and are promising candidates for the development of non-invasive serological tests.

147 Detection of circulating tumour cells in gastric cancer patients using telomerase-specific replication-competent adenoviral agent: a prospective feasibility study

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Background: Cancer of the digestive tract causes blood metastasis as well as lymphatic metastasis. Recent advanced techniques make it possible to detect circulating tumour cells (CTCs). CTCs are predicted to be involved in blood metastases. However, the relationships between CTCs and blood metastases are poorly understood.

In this study, we attempted to detect CTCs which may have potential for metastases in gastric cancer patients using telomerase-specific replication-seelctive adenovirus agent.

Material and Methods: Patients with clinical solitary gastric adenocarcinoma, underwent surgery at the Digestive Disease Center, Showa University Northern Yokohama Hospital between September, 2009 and January, 2010 were eligible for study. Patients aged over 81, those who received preoperative treatment, and those with the other organ neoplasm were excluded from this study.

Twenty-two patients (sixteen men and 6 women) fulfilled the inclusion criteria. The study was approved by the Institutional Review Board of the Showa University and each patient gave written, informed consent. The patients ranged in age from 39 to 74 years (average 55.6 years).

Peripheral blood samples (7.5 ml) were obtained from the patients before surgery, and were infected with telomerase-specific replication-competent adenovirus expressing green fluorescent protein (GFP) (OBP-401; Telome Scan) by incubation in the medium for 24 hours. Circulating tumour cells whose fluorescence can be detected were counted under fluorescence microscopy. And, it was confirmed that GFP fluorescence positive cells (GFP positive cells) were cancer cells by Immunohistochemistry staining.

The disease was pathologically staged with TNM staging system. The stage group value comparisons were performed with the Kruskal-Wallis test.

Results: Total 22 samples were examined. All values were presented as median; the value of stage IIIA group was reported as mean.

The pathological stages were IA in 12 patients, IB in 4 patients, IIIA in 2 patients, and IV in 4 patients. We detected GFP positive cells in all 22 samples. The numbers of GFP positive cells in the samples from patients at stage IA, IB, IIIA, and IV were 8.5 (range, 1–518), 3 (range, 1−10), 12.5 (range, 1−24), and 19 (range, 5−42). Although the value tended to increase with stage progression, there was no significant difference (P = 0.37).

The values in 3 patients with pathological multiple lesions at stage IA were 7, 13, and 518. On the other hand, the values in 4 patients with distant metastases were 5, 6, 32, and 42.

Conclusions: The GFP positive cells were detected in all blood samples from 22 gastric cancer patients, independently of cancer stage. There is possibility of early exact diagnosis of gastric cancer from only blood samples. In contrast, the numbers of GFP positive cells did not clearly show cancer stage. Therefore, the next study to investigate changes in numbers of GFP positive cells through a treatment is designed. Furthermore, we will analyze individual CTCs function after GFP positive cell separation.

148 In vivo preclinical evaluation of the topoisomerase I inhibitor camptothecin in human triple negative breast cancer xenografts

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Background: Triple negative breast cancers (TNBC) have a poor outcome and harbor early relapses despite a high chemosensitivity. New treatments are therefore warranted to improve the prognosis of TNBC.

Material and Methods: Using well characterized human primary TNBC xenografts (1), we have investigated the efficacy of the toposisomerase I inhibitor camptothecin (CPT11). CPT11 was intraperitonealy administered at a dosage of 50 mg/kg at day 1 every 3 weeks for 2 to 3 cycles. Tumour volume was measured twice a week and Relative Tumour Volumes (RTVs) from start of treatment were then calculated.

Results: The four human TNBC HBCx-4B, HBCx-11, HBCx-15, and HBCx-12B xenografts have been treated by CPT11, with an optimal tumour growth inhibition (TGI) of 100%, 91%, 100%, and 90%, respectively. In two models, HBCx-4B and HBCx-15, 100% and 87% of complete remission (CR) have been observed. As shown in the Table, CPT11 was as or more efficient than standard chemotherapies [doxorubicin + cyclophosphamide (AC), docetaxel (D), capecitabin (Cap.), or cisplatin (CDDP)], particularly in the HBCx-4B resistant xenograft.

	HBCx-4B		HBCx-11		HBCx-15		HBCx-12B	
	TGI	CR	TGI	CR	TGI	CR	TGI	CR
CPT11	100	100	91	0	100	87	90	0
AC	40	0	75	0	100	100	35	0
D	20	0	40	0	42	0	32	0
Cap.	45	0	57	0	71	0	55	0
CDDP	34	0	/	/	96	93	51	0

Spontaneous lung metastases occurrence is ongoing histopathological assessment in the spontaneously metastatic BC174 xenograft.

Conclusions: Altogether, these results suggest that topoisomerase I inhibitors could be efficiently used in TNBC. Further clinical trials are therefore warranted to confirm in cancer patients the efficacy of these cytotoxic agents.

Reference(s)

[1] Marangoni E, et al. A new model of patient tumour-derived breast cancer xenografts for preclinical assays. Clin Cancer Res 2007;13:3989−98.

149 Prediction of response to cancer therapy from functional magnetic resonance image parameters – an artificial neural network approach

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Background: In modern cancer medicine, anatomical magnetic resonance imaging (MRI) is routinely used in diagnostics, treatment planning and assessment of therapeutic efficacy. During the past decade, functional imaging techniques like diffusion-weighted (DW) MRI and dynamic contrast-enhanced (DCE) MRI have increasingly been included into imaging protocols, allowing intratumoural information about underlying vascular, molecular and physiological mechanisms, not available in structural images, to be extracted. Separately, pre-treatment and early changes in functional parameters obtained from DWMRI and DCEMRI have shown potential in prediction of ultimate therapy response. We hypothesized that the combined use of several functional parameters may increase the predictive power.

Material and Methods: We challenged this hypothesis by using an artificial neural network (ANN) approach, exploiting nonlinear relationships between individual variables, which is particularly suitable in treatment response prediction involving complex cancer data. A clinical scenario was elicited by human prostate cancer xenografts treated with combinations of androgen-deprivation therapy and radiotherapy. DWMRI and DCEMRI from pre-radiation and on days 1 and 9 following radiation, in addition to tumour volumes and the established biomarker prostate specific antigen (PSA), were used as inputs to a back propagation neural network (BPNN), both separately and combined.

Results: The use of DWMRI parameters together with tumour volumes and PSA as inputs to the BPNN model revealed a correlation coefficient