STAT3 and P38 MAPK. Cell proliferation was also significantly reduced in NUGC-3, AGS and MKN45 cells following treatment with either a JAK inhibitor (JAK-Inhibitor 1) or a P38 MAPK inhibitor (SB203580), however, treatment with anti-IL-6R antibody and wortmannin (PI3-K inhibitor) had no inhibitory effect on cell proliferation.
Conclusions: Our data indicates an important role for both the JAK/STAT and P38 MAPK signaling pathways (independent of IL-6) in the proliferation of gastric cancer cells and highlights a potent anti-proliferative effect of SOCS-1/-3 gene delivery *via* the suppression of these signaling pathways. SOCS-1/-3 gene delivery may thus represent a future novel therapeutic strategy for the treatment of gastric cancer.

6644 POSTER

A novel NF-kB inhibitor DHMEQ suppressed peritoneal dissemination of pancreatic cancer in mouse xenograft model

M. Sato[1], M. Ozaki[2], K. Nakanishi[1], T. Watanabe[3], K. Mino[1], H. Yokoo[1], K. Umezawa[4], Y. Ohmiya[5], T. Kamiyama[1], S. Todo[1]. [1]*Hokkaido University Graduate School of Medicine, Department of General Surgery, Sapporo Hokkaido, Japan;* [2]*Hokkaido University Graduate School of Medicine, Department of Molecular Surgery, Sapporo Hokkaido, Japan;* [3]*ATTO Corporation, R & D Division, Tokyo, Japan;* [4]*Keio University Faculty of Science and Technology, Department of Applied Chemistry, Tokyo, Japan;* [5]*National Institute of Advanced Industrial Science and Technology (AIST), Research Institute of Genome-based Biofactory, Osaka, Japan*

Background: Pancreatic cancer in advanced stage is lethal in most patients. NF-kB is frequently and constitutively activated in pancreatic cancer and well known to be involved in the biological aggressiveness of this cancer, and hence can be an attractive therapeutic target. In the present study, we studied the therapeutic potentials of a newly developed NF-kB inhibitor, dehydroxymethylepoxyquinomicin (DHMEQ), especially in pancreatic cancer metastasis.
Materials and Methods: We evaluated growth inhibitory effect of DHMEQ on AsPC-1 human pancreatic cancer cells using MTT assay. For quantitative analysis of tumor size in vivo, we applied GLuc, a secretory type of luciferase (marine copepod, *G. princeps*) to AsPC-1 cells (AsPC-1-Gluc), which enables us to monitor in living mice 1) tumor growth in mice by bio-luminescence imaging and 2) whole tumor progression by measuring bio-luminescent intensity of extracellularly secreted GLuc from cancer cells into circulating blood. 5×10^6 AsPC-1-GLuc cells were implanted subcutaneously into 6-week-old male BALB/c nu/nu mice. For evaluation of the effect of DHMEQ on pancreatic cancer metastasis, 1×10^7 AsPC-1-Gluc cells were injected intraperitoneally into mice as a peritoneal dissemination model (day 0). We administered vehicle or DHMEQ (15 mg/kg or 30 mg/kg) by i.p. injection into the mice twice a day. We monitored tumor growth by GLuc activity in plasma, and tumor metastasis by bio-imaging every 3 or 4 days. The mice were finally sacrificed on day 30 for evaluation of tumor volume and histological examination.
Results: DHMEQ inhibited proliferation of AsPC-1 cancer cells in a dose-dependent manner in vitro. 5 μg / ml of DHMEQ was enough to inhibit cell growth by 50%. In xenograft model, we firstly confirmed that GLuc activity in the blood reflects tumor mass in mice. A good correlation was observed between subcutaneous AsPC-1-GLuc tumor mass and the Gluc activity in mice plasma, indicating this method is appropriate to evaluate tumor mass. In the mouse peritoneal dissemination experiment, DHMEQ significantly reduced GLuc activity in plasma as well as tumor size and dissemination. Histological examination showed the reduced mitosis and the increased apoptosis in the DHMEQ-treated tumor cells. NF-kB activity in the tumor was also suppressed.
Conclusions: Our results indicate that DHMEQ possesses a good potential for treatment of pancreatic cancer.

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Increased expression of delta Np73 correlates with short time survival in cholangiocarcinoma patients

P. Jearanaikoon[1], N. Nutthasirikul[2], C. Leelayuwat[1], T. Limpaiboon[1]. [1]*The Centre for Research and Development of Medical Diagnostic Laboratories (CMDL) Khon Kaen University, Faculty of Associated Medical Sciences, Khon Kaen, Thailand;* [2]*Liver Fluke and Cholangiocarcinoma Research Center Khon Kaen University, Faculty of Medicine, Khon Kaen, Thailand*

Background: Among p53 family members, p63 and p73 share similar structure and function in cell cycle control and apoptosis. All members can encode truncated N-terminal domain or delta-N isoforms; DNp53, DNp63 and DNp73, which can inhibit trans-activation of full length isoforms (TAp53, TAp63, TAp73). Therefore, over-expression of DN isoforms can exert as epigenetic inhibitor of full length proteins. The aim of this study was to examine expression pattern of p73 isoforms in cholangiocarcinoma(CCA) and investigate whether p73 isoforms can be used to predict cancer prognosis.
Materials and Methods: Six CCA cell lines and 34 CCA patients were used to investigate both p73 isoforms at transcriptional and protein levels using quantitative real time PCR and immunohistochemical staining. CCA patients were categorized into short and long survival group according to their median survival time. The association of expression pattern of p73 isoforms was statistical analyzed with patient survival.
Results: Among CCA cell lines, the increase of DNp73/TA p73 was observed in CCA cell lines with poor histopathological grading. In clinical samples, a significant increase of DNp73 transcripts was observed in the patients with short time survival (Mann Whitney test, $p = 0.007$) whereas, over-expression of DNp73 protein was also associated with poor survival patients (Chi'square test, $p = 0.04$).
Conclusion: The up-regulation of DNp73 might be used to predict the cancer outcome in CCA patients. More data in expression of DNp53 and DNp63 as well as more clinical samples should be included in further study.

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Correlation between FOXO1A transcription factor and cell cycle regulators in gastric cancer

B. Lee[1], H. Jung[1], J.h. Kim[2]. [1]*Seoul National University College of Medicine, Anatomy, Seoul, Korea;* [2]*Asan Medical Center University of Ulsan College of Medicine, Anatomy, Seoul, Korea*

Background: The present study investigated the relationship between the expression of phosphorylated FOXO1A (pFOXO1A) and the expressions of cell-cycle regulatory proteins in human gastric carcinoma.
Material and Methods: We used the immunohistochemical staining performed on tissue array slides containing 272 human gastric carcinoma specimens. Antibodies against cyclins D1, E and B3 as well as $p21^{Waf1/Cip1}$ (p21), $p27^{Kip1}$ (p27), p53, and retinoblastoma protein (pRB) were used. Data were analyzed with SPSS program.
Results: The expression of pFOXO1A positively correlated with that of cyclin D1 ($P = 0.014$), p21(Waf1/Cip1) ($P = 0.006$) or p27(Kip1) ($P = 0.001$), suggesting co-regulation of these proteins in gastric carcinoma. Moreover, cyclin D1 seems to determine the association between pFOXO1A and p21 or p27. The survival rate was higher in patients with both pFOXO1A-positive and cyclin D1/p21/p27-positive tumors ($P < 0.05$) than in the remainder of the population. On the other hand, the expression of cyclin E, p53 and pRb showed no association with that of pFOXO1A.
Conclusions: Our results suggest that the combined examination of FOXO1A and cyclin D1 along with p21 or p27 expression may allow a precise estimation of prognosis in patients with gastric carcinoma.

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MET amplification by qPCR predicts poor outcome in gastric cancer: a novel prognostic marker and a potential therapeutic target

S. Lee[1], J. Lee[1], S.H. Park[1], Y.S. Park[1], H.L. Lim[1], K.M. Kim[1], C. Park[1], W.K. Kang[1], J.O. Park[1]. [1]*Samsung medical center, Department hematology-oncology and pathology, Seoul, Korea*

Purpose: We undertook this study to assess the impact of c-Met overexpression, c-Met activation, and *MET* amplification on survival of gastric cancer patients.
Experimental Design: *MET* amplification and activation of c-Met were tested in various gastric cancer cell lines *in vitro*. Of the 482 tissue samples from gastric cancer patients who underwent curative surgery, *MET* amplification was tested in 472 gastric cancer patients. c-Met protein expression and c-Met activation were evaluated by immunohistochemical staining against c-Met protein and phospho-Met (pY1349), respectively.
Results: Analysis of the gastric cancer cell lines using quantitative real-time PCR (qPCR) identified the increased *MET* copy number which predicted sensitivity to PHA-665,752, a selective c-Met kinase inhibitor. Of the 472 patients who had DNA sample available for qPCR analysis, 100 (21.2%) of the patients had *MET* copy number greater than 4.0 copies. Of the 103 tumor samples with c-Met protein activation identified by staining against phospho-Met (pY1349), 30 (29.1%) had *MET* amplification ($\geqslant$4 copies) ($P = 0.026$). Gastric cancer patients with *MET* amplification demonstrated poorer survival following curative surgery with statistical significance (5-year OS; 50.0% vs 59.1%; *MET* amplification (+) vs *MET* amplification (−); $P = 0.0134$).
Conclusions: *MET* amplification measured by qPCR was associated with shorter DFS and poorer OS but not c-Met protein overexpression or c-Met protein activation.