cirrhosis only one showed intense staining. In HBV and HCV, 5/26 were positive and 0/9 in normal [p<0.001]. In rat tissues, TLR7 was found in all HCC tumour cells only while the background either normal, dysplastic or cirrhotic was negative. Study 2. Using confocal microscopy, TLR7 was found in the cytoplasm and the nucleus of both HepG2 and Huh7 and with stimulation of TLR7 agonist the cellular proliferation significantly increased compared to control p<0.05.

Conclusion The data show that TLR7 is highly expressed in human HCC's, animal model of HCC and in cell lines. Importantly, the background cirrhotic liver does not express TLR7. Their stimulation is associated with marked increase in proliferation. These data suggest that TLR7 may be a future target of therapy in HCC.

Competing interests None declared.

PMO-093 MRNA PROFILING OF THE CANCER DEGRADOME IN OESOPHAGO-GASTRIC ADENOCARCINOMA

doi:10.1136/gutjnl-2012-302514b.93

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Introduction Degradation of the extracellular matrix is fundamental to tumour development, invasion and metastasis. Several protease families have been implicated in the development of a broad range of tumour types, including oesophago-gastric (OG) adenocarcinoma. The aim of this study was to analyse expression levels of all core members of the cancer degradome in OG adenocarcinoma, and to investigate the relationship between expression levels and tumour/patient variables associated with poor prognosis.

Methods Comprehensive expression profiling of the protease families [matrix metalloproteinases (MMPs), members of the ADAM metalloproteinase-disintegrin family (ADAMs)], their inhibitors [tissue inhibitors of metalloproteinase (TIMPs)], and molecules involved in the c-Met signalling pathway, was performed using quantitative real-time reverse transcription PCR in a cohort of matched malignant and benign peri-tumoural OG tissue (n=25 patients). Data were analysed with respect to clinico-pathological variables (tumour stage and grade, age, sex and pre-operative plasma C-reactive protein level).

Results Gene expression of MMP1, 3, 7, 9, 10, 11, 12, 16 and 24 was upregulated by factors greater than fourfold in OG adenocarcinoma samples compared with matched benign tissue (p<0.01). Expression of ADAM8 and ADAM15 correlated significantly with tumour stage (p=0.048 and p=0.044), and ADAM12 expression correlated with tumour grade (p=0.011).

Conclusion This study represents the first comprehensive quantitative analysis of the expression of proteases and their inhibitors in human OG adenocarcinoma. These findings implicate elevated ADAM8, 12 and 15 mRNA expression as potential prognostic molecular markers.

Competing interests None declared.

PMO-094 SUPPRESSION OF SULF2, AN EXTRACELLULAR ENDOSULFATASE UP-REGULATED IN HEPATOCELLULAR CANCERS, MODULATES WNT SIGNALLING AND INHIBITS CELL GROWTH

doi:10.1136/gutjnl-2012-302514b.94

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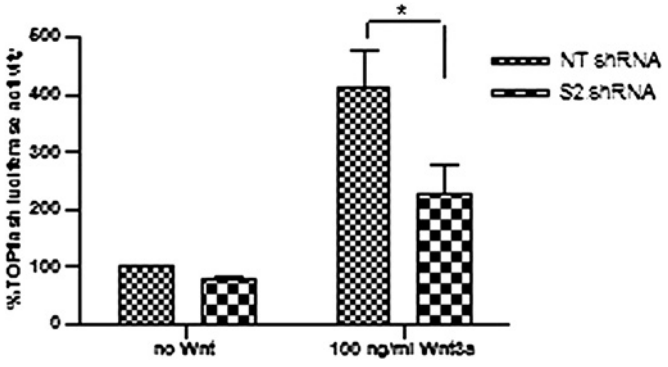
Introduction Hepatocellular carcinoma (HCC) is the 3rd most common cause of cancer death globally and effective systemic treatments for the disease are limited. HCC complicates chronic liver disease and its incidence is increasing dramatically in the UK. Sulfatase 2 (SULF2) is one of two extracellular heparan sulphate 6-*O*-endosulfatase and one of 17 human sulfatases. It reportedly modulates ligand activated FGF and Wnt signalling and is up-regulated in 57% of HCC. We aim to explore the potential of SULF2 as a therapeutic target for HCC treatment and have characterised its biology in HCC cell lines.

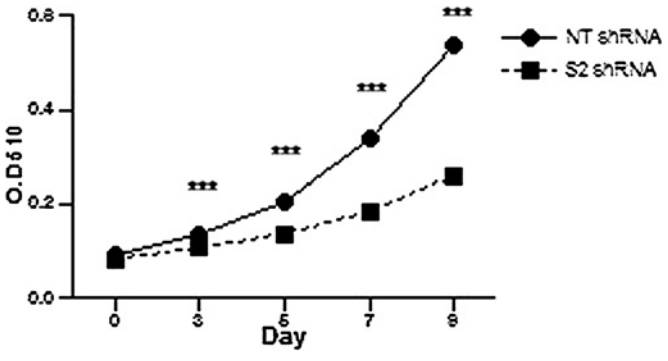
Methods Expression of SULF2 and its homologue SULF1 were assessed at RNA and protein levels in six HCC cell lines. The desulfating enzymatic activity of these cell lines were compared using the fluorogenic substrate 4-methylumbelliferyl sulphate (4-MUS). SULF2 was knocked down using short hairpin RNA lentiviral particles. SULF2 gene silencing effect on receptor tyrosine kinase signalling was investigated by phospho-ERK and phospho-AKT immunoblot and its effect on Wnt signalling by the TCF luciferase reporter assay. Cell growth was assessed by SRB assay.

Results 3 of the six tested HCC cell lines showed up-regulated SULF2 expression at the RNA and protein levels. HuH-7 cells had the highest sulfatase activity. SULF2 gene silencing in this cell line caused dramatic inhibition of Wnt3a-induced β-catenin-dependent transcriptional activity (twofold and p value = 0.03, Abstract PMO-094 figure 1), with relatively modest effects on the phosphorylation of ERK or AKT after stimulation with FGF-1, FGF-2 or IGF-I. SULF2 suppression significantly reduced cell number (twofold and p value <0.0001, Abstract PMO-094 figure 2) and enzymatic activity (p value <0.0001, Abstract PMO-094 figure 3) of HuH-7 cells.

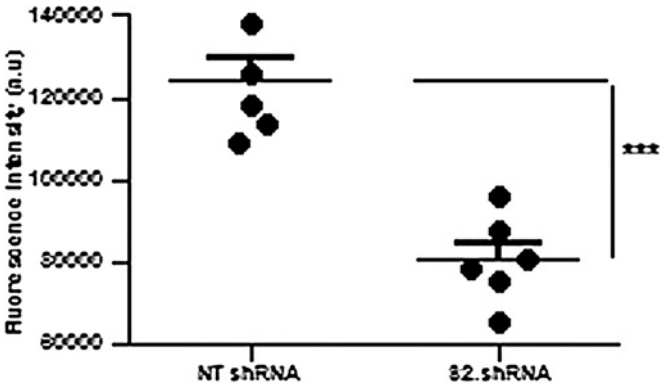
Conclusion SULF2 is over-expressed in the majority of HCCs and is catalytically active. SULF2 gene silencing in HuH-7 inhibits Wnt signalling and cell growth. These data support a key role for SULF2 in hepatocarcinogenesis, the inhibition of which offers a novel means of antagonising Wnt signalling in cancers.



Abstract PMO-094 Figure 1 SULF2 knockdown inhibits Wnt signalling.



Abstract PMO-094 Figure 2 SULF2 knockdown decreases sulfatase enzymatic activity.



Abstract PMO-094 Figure 3 SULF2 knockdown inhibits cell growth.

Competing interests None declared.

Pancreas

PMO-095 LAPAROSCOPIC VS OPEN PANCREATICODUODENECTOMY: ONCOLOGICAL OUTCOMES USING LEEDS PATHOLOGY PROTOCOL (LEEPP)—A MATCHED-PAIR ANALYSIS

doi:10.1136/gutjnl-2012-302514b.95

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Introduction Laparoscopic Pancreaticoduodenectomy (LPD) has recently been shown to be a technically safe procedure. Oncological safety of LPD is still a matter for debate. Currently, there is limited evidence for cancer outcomes following LPD, especially in comparison to Open Pancreaticoduodenectomy (OPD). The aim of this study is to compare the adequacy of cancer resection and outcome following LPD and OPD.

Methods Between November 2005 and April 2009, 12 LPD's (nine ampullary and three distal Common Bile Duct tumours) were carried out in a tertiary referral centre. A cohort of 12 patients who underwent OPD from November 2003 to February 2007 were matched for age, sex, site of tumour origin and tumour size. Histology was assessed using previously validated Leeds Pathology Protocol (LEEPP) (Ref). The primary aim was to evaluate margin involvement and mean number of lymph nodes excised. The secondary endpoints were complications, high-dependency unit (HDU) stay, length of hospital stay (LOS), recurrence and mortality rate. The median follow-up was 46.8 months for LPD and 56.0 months for OPD.

Results R0 resection was achieved in 9 LPD vs 8 OPD (p=1.000). The T staging T2, T3, T4 were 6, 4, 2 for LPD vs 6, 5, 1 for OPD respectively (p=1.000). The mean tumour size was 19.8 for LPD Vs 19.2 for OPD (p=0.870). The mean number of lymph node excised for LPD vs OPD (20.7 vs 18.5, p=0.534). Clavien grade I/II complications (5 vs 8), Clavien grade III/IV complications (2 vs 6) and pancreatic leak (2 vs 1) were statistically not significant (LPD vs OPD). The mean HDU stay was longer in OPD group (3.7 vs 1.4 days, p<0.000), but LOS was no different (14.9 vs 14.9 days, p=1.000). There were two recurrences each in LPD and OPD group (p=1.000). Overall mortality for LPD vs OPD (2 vs 6, p=0.193) and recurrence-related mortality (2 vs 2, p=1.000).

Conclusion Compared to open procedure, in patients with tumour size <2 cm, laparoscopic pancreaticoduodenectomy achieves similar rate of R0 resection, lymph node harvest and long-term recurrence. LPD patients have significantly shorter high-dependency stay and lesser post-operative complications. Though technically challenging, laparoscopic pancreaticoduodenectomy is safe and does not compromise oncological outcome for tumours <2 cm.

Competing interests None declared.

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PMO-096 LAPAROSCOPIC DISTAL PANCREATECTOMY—A TERTIARY REFERRAL CENTRE EXPERIENCE

doi:10.1136/gutjnl-2012-302514b.96

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Introduction Laparoscopic distal pancreatectomy was first reported in 1996 and is increasingly employed to remove lesions from the body and tail of the pancreas. The technique has seen a slow progress due to a relatively low volume of caseload, the lack of standardisation in the management of the pancreatic stump and concerns about the ability to achieve negative surgical margins for benign or malignant pancreatic neoplasms.

Methods Data were collected by retrospective review of case notes and histopathological results. 20 patients underwent laparoscopic distal pancreatectomy from April 2009 to January 2012.

Results 20 patients were included in the study, 0.45:1 male: female ratio (nine males, 20 females), mean age 58.55 [range 25—83]. In most cases the indication for surgery was a cystic lesion in the tail of pancreas (45%). The spleen was preserved in 15 cases (75%). None of the patients in this series required conversion from laparoscopic to open surgery or blood transfusion. Four patients (20%) were transferred to HDU postoperatively for 1—5 days and the mean hospital stay was 8.5 days [range 3—23 days]. Four patients (20%) had postoperative complications: one had partial splenic infarction which was managed conservatively, one had fluid collection that was treated by percutaneous drainage, one had a pancreatic stump leak that settled conservatively and one had abscess which required surgical intervention. The latter had laparoscopic right hemicolectomy at the same time of his pancreatic resection. There was no indication of a pancreatic fistula at follow-up. Histology confirmed one chronic abscess, one congenital cyst, five cancers, six potentially malignant lesions and seven serous microcystic cystadenomas. All tumours were completely excised with clear resection margins.

Conclusion Laparoscopic resection is feasible and achieves adequate resection margins.

Competing interests None declared.

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PMO-097 SURGERY FOR PANCREATIC CANCER WITHOUT PREOPERATIVE BILIARY DRAINAGE: FICTION IN REALITY?

doi:10.1136/gutjnl-2012-302514b.97

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Introduction A recent article published in the New England Journal of Medicine describes decreased complication rate in patients who have not had preoperative biliary drainage of their obstructive jaundice caused by their pancreatic mass. Unfortunately our perception is such that the reality of early surgery without a bridging stent hangs in the realms of fantasy. Our aims were to