S F Alhasan,* G S Beale, D R Newell, H L Reeves. suggest that TLR7 may be a future target of therapy in HCC. is associated with marked increase in proliferation. These data show that TLR7 is highly expressed in human 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
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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 ENDSULFATASE UP-REGULATED IN HEPATOCELLLAR CANCERS, MODULATES WNT SIGNALLING AND INHIBITS CELL GROWTH
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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 and AKT after stimulation with FGF-1, FGF-2 or IGF-1. 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.
Between November 2005 and April 2009, 12 LPD Methods following LPD and OPD.

The aim of this study is to compare the adequacy of cancer resection and outcome to Open Pancreaticoduodenectomy (OPD). The mean HDU stay was longer in OPD group (3.7 vs 19.2 for OPD (p = 0.534). Clavien grade I/II complications (20.7 vs 18.5, p = 0.554). Clavien grade I/II complications (5 vs 3), 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 (5.7 vs 1.4 days, p<0.001), 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.