Introduction The prognosis of oesophageal cancer remains poor with < 10% 5-year survival. Delineating the molecular pathogenesis of oesophageal cancer could inform future research into targeted therapies and may uncover novel biomarkers to aid management decisions. As a transcription factor with important roles in the control of cell cycle transcription, FOXM1 regulates cellular proliferation and chromosome stability. FOXM1 is frequently overexpressed in human cancers and this aberrant expression has been implicated in cancer initiation, progression and resistance to chemotherapy. Overexpression of FOXM1 mRNA and protein has recently been described in oesophageal adenocarcinoma (OAC) tissues. We aim to identify novel gene targets of FOXM1 to better understand the molecular pathogenesis of OAC.

Methods Chromatin immunoprecipitation (ChIP) followed by deep sequencing (ChIP-seq) of FOXM1 binding sites was performed in OE33 OAC cells. FOXM1 binding at target gene promoters was confirmed with ChIP-qPCR studies. Target gene expression in OE33 cells after siRNA-mediated FOXM1 depletion was examined using qRT-PCR and western blotting. Target gene expression in OAC tissues was examined by analysis of microarray gene expression data. Statistical significance (p) in knockdown studies was calculated by Student's t -test. The Pearson correlation coefficient (r) was used to measure strength of correlation of gene expression.

Results Putative novel FOXM1 targets identified from an existing FOXM1 ChIP-seq dataset in U2OS osteosarcoma cells were validated by ChIP-seq in OE33 cells. A large overlap between the genes bound by FOXM1 in both cell types was observed. Genes with FOXM1 binding in both cell types whose expression was highly correlated with FOXM1 in OAC tissues such as *ETV4*, *SKA2* and *NUCKS1* ($r = 0.83, 0.84$ and 0.72) were analysed further with ChIP-qPCR and FOXM1 knockdown gene expression studies. OE33 cells demonstrated significant FOXM1 binding at the *ETV4* promoter and a reduction in *ETV4* mRNA in FOXM1 depleted cells was observed compared to control ($p = 0.0006$). However, despite highly significant FOXM1 binding at the *SKA2* and *NUCKS1* promoters the reduction in *SKA2/NUCKS1* mRNA following FOXM1 knockdown was modest and not significant.

Conclusion We have identified *ETV4* as a novel FOXM1 target in oesophageal cancer. We found strong correlation with FOXM1 expression in clinical tissues, *in vivo* FOXM1 binding to its regulatory regions and evidence of regulation by FOXM1 in OE33 cells. Our studies also highlight the importance of validating ChIP-seq data with gene expression analysis since transcription factor binding at gene promoters does not always correlate with transcriptional regulation by that transcription factor.

Disclosure of Interest None Declared

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OC-032 A NEW VALIDATED WHOLE GUT TRANSIT TIME (WGTT) MEASUREMENT USING MAGNETIC RESONANCE IMAGING (MRI-WGTT) TECHNIQUE

doi:10.1136/gutjnl-2013-304907.032

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Introduction Disorders of gut transit are very common in gastroenterology clinics. Objective assessment may be useful for targeting and monitoring treatment. Current scintigraphic or radio-opaque marker techniques involve undesirable ionising radiation.

Aims

1. To validate a new MRI method for measuring WGTT against the current gold standard in which 20 radio-opaque markers (ROMs) are ingested per day on 3 consecutive days and the number retained assessed from a single abdominal x-ray on day 4.

2. To assess reproducibility of MRI-WGTT.

Methods 20 healthy volunteers (HV) ages 21–70 (12 males and 8 females) participated in the study involving 2 visits a week apart (test-retest). On each visit, each HV underwent 2 tests: (A) MRI-WGTT test for which HV swallow 5 pills, each filled with a MRI contrast agent diluted with water, 24 hours before undergoing MRI scans which precisely locate the pills in the colon. Transit of the markers was assessed by scoring each pill from its position in the colon (7 = small bowel, 6 = lower ascending 5 = upper AC, 4 = right transverse (TC), 3 = left TC, 2 = descending, 1 = rectosigmoid, 0 = expelled) and calculating an average score (Transit score TS) using an algorithm which gives a weighting inversely related to the distance from the median. (B) ROM test: the number of ROM was counted and multiplied by 1.2 to give a WGTT in hours. Spearman's correlation was used to assess the correlation between the two measurements and intra-class correlation coefficient (ICC) was used to assess the variability of each test when repeated twice.

Results The MRI images provided excellent 3D spatial resolution, allowing the gut to be viewed from all angles, hence allowing accurate location of the pills within the colon especially the sigmoid region (Figure 1). WGTT using ROM was median (SD), 27.6 (20.8) and TS was 0.9 (0.8). WGTT using ROM and TS were well correlated, Spearman's $r = 0.85$, $p < 0.01$. Using this we converted TS to MRI-WGTT in hours. Mean calculated MRI-WGTT was 27.6 (24.7) hours. The mean absolute difference in the MRI-WGTT on 2 separate visits was 15.3 hours (SD, 15.8) with an ICC of 0.62 ($p < 0.01$). The mean absolute difference in the WGTT for ROMs on 2 separate visits was 11.3 hours (SD, 9.7) with and ICC of 0.69 ($p < 0.01$).

Abstract OC-032 Figure 1 Maximum intensity projection, T1 weighted MRI image showing the MRI transit pills in descending and sigmoid colon.

Conclusion MRI-WGTT correlated well with the gold standard ROM WGTT but was more convenient, involving only one day of marker ingestion and no exposure to ionising radiation. This technique could be implemented easily in most NHS hospitals. Funded by: Medical Research Council and NIHR UK.

Disclosure of Interest None Declared

OC-033 IS LYMPHOCYTIC DUODENOSIS A MARKER FOR IRRITABLE BOWEL SYNDROME?

doi:10.1136/gutjnl-2013-304907.033

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