Introduction Eicosapentaenoic acid (EPA) is an omega-3 polyunsaturated fatty acid which has anti-colorectal cancer (CRC) activity. The molecular mechanism (s) underlying the anti-neoplastic activity of EPA are not understood. Trihydroxy-EPA, also known as Resolvin E1 (RvE1), is an oxygenated derivative of EPA, that has been shown to inhibit NK-κB signalling, which is implicated in colorectal carcinogenesis. RvE1 has been shown to bind to two G-protein coupled receptors, ChemR23 and BLT1. We investigated whether ChemR23 and BLT1 receptors are expressed in human CRC.

Methods Seven human CRC cell lines (HCA7, LoVo, T84, HRT18, HT29, Caco2 and HCT116) were characterised for ChemR23 and BLT1 expression by quantitative real-time polymerase chain reaction, western blotting and immunofluorescence. Jurkat and THP-1 cells were used as positive controls for ChemR23 and BLT1, respectively. Membrane protein fraction analysis was carried out using a transmembrane protein extraction kit. Densitometric analysis was performed using BIO-RAD Quantity One Software. Human CRC tissue was examined for ChemR23 expression by immunohistochemistry on formalin-fixed, paraffin-embedded tissue blocks.

Results ChemR23 and BLT1 messenger RNA expression was detected in all seven human CRC cell lines. ChemR23 protein (45kDa) expression was also observed in all human CRC cell lines, with Caco2 cells expressing around two-fold more ChemR23 receptor protein relative to a-tubulin than other CRC cell lines. However, BLT1 receptor protein was not detected in any of the human CRC cell lines, but was confirmed in monocytic THP-1 cells (38kDa). ChemR23 protein was enriched in the membrane protein fraction of Caco2 cells. ChemR23 protein levels increased with confluency in Caco2 cells. There was a three-fold increase in ChemR23 protein expression in 100% confluent Caco2 cells compared with less confluent cell cultures. In contrast, HCA-7 cells did not display confluence-dependent changes in ChemR23 protein expression. Immunofluorescence demonstrated predominant cytoplasmic localisation of ChemR23 with a heterogeneous population of ChemR23-expressing and negative cells. ChemR23 immunohistochemistry on primary CRC tissue demonstrated homogeneous ChemR23 immunoreactivity in CRC cells with some stromal cell staining, including endothelial cells.

Conclusion ChemR23 (but not BLT1) protein is expressed by human CRC cells (particularly Caco2) *in vitro* and in cancer cells in human primary CRCs. ChemR23 protein expression varies *in vitro* in a confluence-dependent manner, with heterogeneous expression by Caco2 cells. ChemR23 is localised predominantly in cancer cells in human CRC. Investigation of ChemR23-dependent anti-CRC activity of RvE1 is warranted.

Disclosure of Interest None Declared.

PWE-164 UTILIZING INTEGRATIVE GENOMIC ANALYSIS AND PROTEOMICS TO DECIPHER THE BIOLOGY AND THERAPEUTIC POTENTIAL OF TRIM44 IN OESOPHAGEAL ADENOCARCINOMA AND BREAST CANCER

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Introduction The incidence of oesophageal adenocarcinoma (OAC) has quadrupled in the last 30 years and outcomes remain poor. We have previously identified TRIM44 as an independent prognostic gene commonly amplified in OAC and breast cancer. However, the exact biology of TRIM44 and its role in epithelial cancers remain unclear

Methods Gene set enrichment analysis (GSEA) was performed on gene expression microarray data of oesophageal (n = 146) and breast cancers (METABRIC, n = 1980) to identify signalling pathways activated by TRIM44 amplification and overexpression. Mass spectrometry was used to identify binding partners of TRIM44 in both endogenous and overexpression settings. Validation of the mass spectrometry results were performed using reciprocal co-immunoprecipitations experiments

Results GSEA performed on OAC samples identified 14 pathway signatures that were significantly enriched with TRIM44 overexpression. To validate these results, GSEA was performed on the METABRIC dataset and this revealed that the PI3K-AKT-mTOR signalling was the only pathway out of the 14 identified signatures to be significantly overenriched in samples with TRIM44 amplification in OAC and breast cancer ($p < 0.05$). Mass spectrometry of immunoprecipitated TRIM44 identified 2 novel binding partners of TRIM44 -- a ring finger protein associated with activation of c-jun and a tumour metastatic gene shown to directly activate the PI3K-AKT-mTOR signalling pathway. Validation of these two binding partners was successfully performed with endogenous co-immunoprecipitation of TRIM44 in HSC-39, a cell line with high level amplifications of TRIM44; demonstrating that both binding partners associate with TRIM44 in the endogenous setting.

Conclusion Integrative genomic analysis and GSEA provided an insight into the pathways activated by TRIM44. The mTOR pathway was consistently associated with TRIM44 amplification and overexpression. A proteomics approach identified two potential mechanistic explanations how TRIM44 activates the mTOR pathway. Clinically, these findings open up the possibilities of using mTOR inhibitors or peptides disrupting TRIM44 protein interactions to treat TRIM44 amplified tumours.

Disclosure of Interest None Declared.

PWE-165 CERVICAL NEOPLASIA IN LOW RISK WOMEN WITH INFLAMMATORY BOWEL DISEASE ON COMBINATION OF INFLIXIMAB AND THIOPURINES

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Introduction Women with inflammatory bowel diseases (IBD) may have increased rates of pre-malignant lesions in the uterine cervix compared to age and sex matched controls (1.2). European guidelines recommend regular gynaecological screening for women with IBD, especially if they are on immunomodulators (3). However protocols in the UK are lacking and cervical screening is often underutilised by gastroenterologists. We describe 3 cases of cervical neoplasia in patients who had none of the usual risk factors other than prior use of Infliximab (IFX) and azathioprine.

Methods Three patients on maintenance treatment with IFX for IBD have recently presented unexpectedly with high grade cervical dysplasia or cancer to the gynaecologists. We have summarised their clinical history and reviewed their risk factors for development of cervical neoplasia.

Results Case 1: 31-year-old lady with extensive small bowel Crohns disease on azathioprine received IFX for 11 months and developed adenocarcinoma of the cervix 8 months after stopping IFX. She required a radical hysterectomy. Case 2: 30-year-old lady with ileocolonic Crohn's disease on azathioprine received IFX for 3 years and developed high grade cervical intra-epithelial neoplasia 2 months after stopping IFX. She required a large loop excision of the transformation zone (LLETZ). Case 3: 32-year-old lady with colonic and perianal Crohn's disease on azathioprine received IFX for 1 year and then developed high grade cervical intra-epithelial neoplasia 1 month later. She also required a LLETZ procedure. All three patients had also previously been steroid dependent. They were all in long-standing monogamous relationships, were non-smokers and had one or no pregnancies.

Conclusion It is suggested in the literature that women with IBD have an increased risk of cervical neoplasia. It is possible that

immunosupressants and biological therapies prevent clearing of the Human Papilloma Virus that predisposes to cervical dysplasia. These three cases remind us that women with none of the classical risk factors other having used a combination of biologic and immunomodulator therapies should have enhanced screening for cervical neoplasia prior to and during treatment with those drugs.

Disclosure of Interest None Declared.

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PWE-166 HEPATIC ARTERY EMBOLISATION IN NEUROENDOCRINE TUMORS; OUTCOMES FROM A SERIES OF 50 PATIENTS

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Introduction Transarterial embolisation (TAE) and transarterial chemoembolisation (TACE) are established treatments, mainly for symptom control, in patients with advanced NETs with predominantly hepatic tumour burden. The aim was to assess efficacy, toxicity, overall survival and predictive factors in patients undergoing TAE and TACE.

Methods We carried out a retrospective analysis of 50 patients with NETs who underwent a total of 67 embolisation procedures in a period of nine years. All patients had either symptomatic and/or radiological progression despite previous treatments.

Results The patients' median age was 62 years (30 males/20 females). Thirty two had TAE and 19 had TACE. The majority of them had midgut (53%) followed by pancreatic NETs (27%). Symptomatic response was observed in 46 patients (69%), and radiological response (either disease stabilisation or partial response) in 51 (76%). There was no significant association between the type of procedure and symptomatic relief ($p = 0.36$) or radiological response rates ($p = 0.23$). Urinary 5HIAA and plasma CgA levels were reduced in 50% and 65% patients respectively, post procedures. Increase of plasma CgA levels post procedures was significantly associated with reduced OS ($p = 0.0001$). The median PFS for the whole group was 19.0 months (95% CI 13.2–24.8), whilst the median OS was 65.0 months (95% CI 22.7–107.3). High grade (G3) NETs were associated with significantly reduced OS ($p = 0.002$) and PFS ($p = 0.043$). There was no survival advantage on OS ($p = 0.21$) and PFS ($p = 0.19$) comparing TAE to TACE treatment. The presence of extra-hepatic metastases at the time of diagnosis was not associated with reduced survival ($p = 0.72$). Patients already on somatostatin analogues (38/50.76%), at the time of procedures, survived 46 months longer than those off analogues ($p = 0.013$), but somatostatin analogues did not affect PFS ($p = 0.216$). The commonest complication observed was post embolisation syndrome (22/50.44%), whilst mortality rate was 4%. Overall, the complication rate was not significantly different between TAE and TACE ($p = 0.4$).

Conclusion TAE/TACE are beneficial treatments for control symptoms' as well as tumour growth with acceptable morbidity and mortality rates. No significant efficacy and survival differences were shown between TAE and TACE. Extra-hepatic metastases at the time of treatment did not affect survival. Increase of plasma CgA levels, post-treatment, was associated with worse prognosis. The use of Somatostatin analogues at the time of treatment improved OS but not PFS.

Abbreviations 5HIAA = 5-hydroxyindoleacetic acid, PFS = Progression-Free Survival, OS = Overall Survival, CgA = Chromogranin

Disclosure of Interest None Declared.

PWE-167 IDENTIFICATION OF ALTERED KERATIN LEVEL IN CANCERIZED COLONIC FIELDS USING ISOBARIC TAGS FOR RELATIVE AND ABSOLUTE QUANTIFICATION (ITRAQ) FOR PROTEIN PROFILING

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Introduction A cancerized field is an area of abnormal tissue in the vicinity of a cancer that macroscopically appears normal, and which may be responsible for neoplastic recurrence. Evidence from keratin-8-deficient mice suggests that it is important for colonic mucosa stability. Keratin 8 (K8) levels are also up-regulated in the immediate area around colorectal carcinomas. Moreover, the anti-colorectal cancer action of butyrate may, at least in part, be mediated by K8. Therefore we investigated levels of K8, and its association with butyrate levels, in human sporadic colorectal adenomas.

Methods Patients (n = 8) with an adenoma detected on routine colonoscopy had biopsies taken from three sites (adenoma [AD], bowel wall opposite adenoma [CO] and mid-sigmoid colon [MS]). Mid-sigmoid biopsies were also taken from patients (n = 8) with no colonic pathology (N). Intermediate filaments from the biopsies were extracted and solubilised, prior to pooling according to site and exposure to high (H) or low (L) butyrate within the colonic lumen (determined via faecal sampling). K8 levels were then determined using iTRAQ. GeneBio Phenyx software and the UniProt protein knowledgebase were used for protein identification. iTRAQ results were validated using Western immunoblot analysis.

Results Independent of the butyrate level, K8 was increased in pathological tissue (AD, CO and MS) when compared to non-pathological tissue (figure 1). A high butyrate environment was associated with increased K8 levels compared to low butyrate samples (figure 1). Adenoma samples from both butyrate groups demonstrated a lower molecular weight form of K8 (figure 2; red arrows).

Conclusion Increased K8 may represent a response to malignant transformation to stabilise colonic mucosa. Human colonic adenomas exhibit a lower molecular weight form of K8 not seen in normal colorectal mucosa, possibly associated with the degradome. The anti-neoplastic action of butyrate may be mediated via up-regulation or altered solubility of K8.

Disclosure of Interest None Declared.

PWE-168 CRYPT CELL DYSPLASIA WITH MATURATION IN BARRETT'S ESOPHAGUS SHOWS CLONAL IDENTITY BETWEEN THE CRYPT AND SURFACE CELLS

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Introduction Dysplasia in epithelia is an important histological diagnosis although the specific genetic changes which are responsible for this phenotypic change are unknown. Recent reports indicate that the dysplastic phenotype may not be immutable: in basal crypt dysplasia like atypia (BCDA), unequivocal dysplasia is seen in the crypts in Barrett›s oesophagus and other pre-invasive lesions in the gastrointestinal tract, but the upper crypts and surface epithelium