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

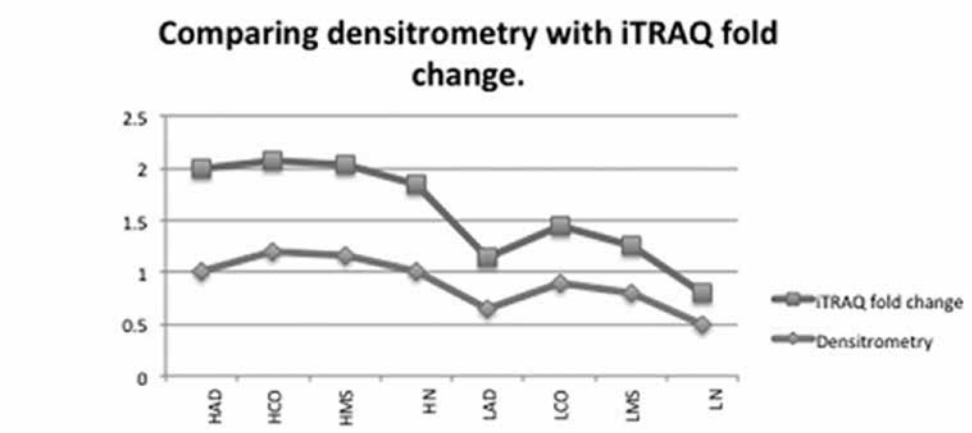

Figure 1. Graphical representation of K8 Western immunoblot densitrometry and iTRAQ fold change. H - high butyrate, L - low butyrate, AD - adenoma , CO contralateral, MS - Midsigmoid, N - normal

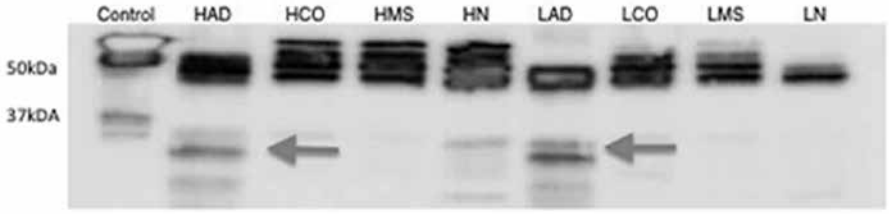

Figure 2. western immunoblot for keratin 8

Abstract PWE-167 Figure

associated with these dysplastic crypts show a differentiated epithelium. The genotypic relationship between the BCDA and the differentiated surface epithelium is unclear.

Methods We obtained 17 examples of BCDA: the lower crypts and upper crypts and surface epithelium were differentially lazer-microdissected from formalin-fixed, paraffin embedded sections and mutations were sought in tumour suppressor genes frequently associated with progression in Barrett's oesophagus.

Results Two patients showed a c.C238T mutation in the p16 (CDKN2A, p16Ink4A) gene and where the precise microanatomical relationships could be discerned: this clonal p16 mutation was present in both the BCDA at the crypt base and in the upper crypt and surface epithelium. This shows that the surface epithelium is derived from the dysplastic crypt epithelium: the dysplastic phenotype is therefore not fixed and can be reversed.

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Conclusion The mechanism of this change is unclear: dysplastic cells may, probably at an earlystage in their progression, respond to differentiation signals. We are some way from a definition of the genotypic correlates of thedysplastic phenotype, and from an understanding of its plasticity.

Disclosure of Interest None Declared.

PWE-169 DNA METHYLATION AND EXPRESSION OF TNF, IFNG AND FOXP3 IN COLORECTAL CANCER

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Introduction Colorectal cancer (CRC) progression is associated with suppression of host cell mediated immunity (CMI) and local immune escape mechanisms (1.2). The aim of the study was to assess immune function in terms of the DNA methylation and expression of TNF, IFN- γ and FOXP3 and to identify potential targets for immunotherapy in CRC.

Methods 60 CRC patients and 15 matched controls were recruited. TaqMan quantitative PCR (qRT-PCR) was performed for relative quantitation of expression of TNF, IFNG, FOXP3 in the PBMC and tumour. Methylation specific PCR was performed to determine the methylation status. MSI status was determined using microsatellite primers BAT25 and BAT26.

Results TNF expression was suppressed in CRC tumours (median fold change 0.48). IFN- γ was found to be suppressed in the PBMC (median 0.34) of CRC patients. Tumours showed enhanced expression of FOXP3 (median 2.2). Expression of FOXP3 in tumours was significantly higher when the size of the tumour was more than 50mm ($p = 0.005$). Methylated *TNFpromoter* and *FOXP3cpg* correlated significantly with suppression of TNF and FOXP3 respectively. Significant TNF suppression ($p = 0.002$) was noted in the PBMC of patients with MSI. No correlation was observed between the MSI status and DNA methylation status of our study genes.

Conclusion Our study identified changes in protein expression which correlated with the methylation status. It demonstrates the influence of DNA methylation on gene expression that could act as a biomarker for future immunotherapy with possible role for demethylating agents.

Disclosure of Interest None Declared.

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