Introduction Oral iron supplementation is given in a broad range of conditions such as iron-deficiency anaemia but can cause significant gastrointestinal side effects in up to 70% of patients. Constipation and bloating are amongst the commonest side effects. Recent research has shown that increased methane production by archaea in the gut microbiome is related to the slowing of gut transit and constipation, via inhibition of smooth muscle contractility (1). Geobiological research has shown that iron is the most abundantly required metal in the archaeal enzymatic pathway for methanogenesis (2). We hypothesized that oral iron consumption resulted in increased methane production.  

Methods A retrospective study of 396 patients who attended The Functional Gut Clinic for a lactulose or glucose hydrogen and methane breath test between June 2018 and January 2019 was carried out. Prior to the test, patients followed a 24hr low fermentable diet and 12hr fast. After providing a baseline breath sample, 10g lactulose or 75g glucose was ingested with 200mL water. Breath samples were taken every 15-minute for 135 minutes. Methane was detected using a sensitive gas chromatography technique and methane producers defined as those producing >10ppm at any point during the study. The relationship between iron supplementation and the prevalence of breath methane was analysed via a Chi-squared test and cumulative methane production was analysed via a two-tailed T-test. Due to lack of information about iron supplementation, 59 patients were excluded.  

Results Of the patients that took iron supplements, 32% produced methane, versus 17.3% of non-iron takers. A significant relationship was identified between iron supplementation and breath methane \( \chi^2 (1, N=337) = 4.3885, p < 0.05 \). Mean cumulative methane production between iron and non-iron takers (536ppm and 376ppm respectively) was statistically significant (\( p < 0.05 \)). No adverse events were reported during the test.  

Conclusions This preliminary, observational study provides the basis for a new model linking a dietary intervention (ingestion of oral iron supplementation) to a gut microbiome metabolic process (methanogenesis) and a clinical outcome (constipation) which is a common, unexplained side effect of the intervention. This model can be used in prospective studies to determine risk factors for developing GI side effects and test potential therapeutic interventions aimed at disrupting methanogenesis and improving tolerability. These advances would have significant clinical and cost saving potential in a broad group of patients.

REFERENCES

PWE-057 COLON CANCER CELLS INDUCE 3T3-L1 ADIPOCYTES DE-DIFFERENTIATION THROUGH DOWN REGULATION OF PPARG

1Maria Tabuso*, 2Raghu Adya, 3Mark Christian, 1,2Ramesh P Arasaradnam. 1UHW, Coventry, UK; 2University of Warwick, Warwick, UK

Introduction Adipocyte de-differentiation at the tumour invasive front has been demonstrated in breast, ovarian and colon cancers, although signalling mechanisms are not known. Aim of this study was to evaluate the effect of colon cancer cells on adipocyte de-differentiation.  

Methods We investigated interactions between HCT 116 colon cancer cells and murine 3T3-L1 adipocytes as a co-culture system. HCT-116 colon cancer cells were co-cultured with 3T3-L1 adipocytes with and without 1 nM Rosiglitazone, a potent peroxisome proliferator-activated receptor gamma (PPARG) agonist known to have anti fibrogenic properties, on COL1A1, FGF7 and SFRP2.

Results Both COL1A1 and SFRP2 was evaluated employing in vitro co-culture systems. 3T3 L1 murine adipocytes were co-cultured with HCT 116 colon cancer cells with and without 1 nM Rosiglitazone for 72 hours. COL1A1, FGF7 and SFRP2 expression was evaluated using quantitative real-time polymerase chain reaction (qRT-PCR). Statistical analysis was performed using paired Student’s t-test with a cut-off of p-value <0.05.

Conclusion Our results have demonstrated significant down-regulation of pro-fibrotic genes COL1A1 and SFRP2 in mature adipocytes induced by Rosiglitazone. Rosiglitazone may represent a novel therapeutic agent in stromal targeted therapy in colon cancer.

PWE-056 ROSIGLITAZONE: A POTENTIAL NEW STROMA TARGETED THERAPEUTIC AGENT IN COLON CANCER

1Maria Tabuso, 2Raghu Adya, 3Mark Christian, 1,2Ramesh P Arasaradnam. 1UHCW, Coventry, UK; 2University of Warwick, Warwick, UK

Introduction The impact of tumour associated stroma on cancer cell invasion and metastasis is an attractive emerging field. Using Nanostring Pancancer pathway we have previously identified pro-fibrotic genes collagen type 1, alpha 1 (COL1A1), fibroblast growth factor 7 (FGF7) and secreted frizzled related protein 2 (SFRP2) significantly up regulated in human colon cancer peritumour adipose tissue compared to distal adipose tissue. Aim of this study was to evaluate the effect of Rosiglitazone, a peroxisome proliferator-activated receptor gamma (PPARG) agonist known to have anti fibrogenic properties, on COL1A1, FGF7 and SFRP2.

Methods The effect of Rosiglitazone on COL1A1 and SFRP2 was evaluated employing in vitro co-culture systems. 3T3 L1 murine adipocytes were co-cultured with HCT 116 colon cancer cells with and without 1 nM Rosiglitazone for 72 hours. COL1A1, FGF7 and SFRP2 expression was evaluated using quantitative real-time polymerase chain reaction (qRT-PCR). Statistical analysis was performed using paired Student’s t-test with a cut-off of p-value <0.05.

Conclusion Treatment with Rosiglitazone of 3T3-L1 adipocytes compared to untreated co-cultured 3T3 L1 adipocytes (20 fold change, p=0.02; 3 fold change, p=0.01 respectively). We did not observe any significant effect of Rosiglitazone on FGF7 expression in treated 3T3 L1 adipocytes compared to untreated adipocytes.

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Results Both COL1A1 and SFRP2 resulted significantly down regulated in co-cultured 3T3 L1 adipocytes treated with Rosiglitazone compared to untreated co-cultured 3T3 L1 adipocytes (20 fold change, p=0.02; 3 fold change, p=0.01 respectively). We did not observe any significant effect of Rosiglitazone on FGF7 expression in treated 3T3 L1 adipocytes compared to untreated adipocytes.

Conclusion Our results have demonstrated significant down-regulation of pro-fibrotic genes COL1A1 and SFRP2 in mature adipocytes induced by Rosiglitazone. Rosiglitazone may represent a novel therapeutic agent in stromal targeted therapy in colon cancer.

REFERENCES