resistance, AR) and insulin resistance (IR) could all be implicated in the failure of CD patients in remission to re-build muscle mass. We aimed to investigate the association between sarcopenia and AR and IR, and the role of physical activity in age, gender matched children with CD.
Methods: 18 fasted, male and female CD patients (on thiopurines ± anti-TNF alpha) in deep remission (16y, BMI=21) and 9 matched controls (Con) (16y, BMI=21) drank a liquid meal (Ensure plus, 44 g CHO, 14 g PRO, 11 g fat) at t = 0. Arterialised hand and venous forearm blood samples were collected concurrently and brachial artery blood flow measured at baseline and every 20 min for 2 h. Net balance of branched-chain amino acids (BCAA) and glucose were derived, providing indices of skeletal muscle protein balance and IR. Participants had a DEXA scan and handgrip dynamometer test on the day, and wore a pedometer and completed a food diary (each for 3 days) to assess physical activity and food intake. Patient-related outcome measure questionnaires (incl. IBD-fatigue) were completed.
Results: CD and Con exhibited an initial response to feeding by increasing BCAA flux: Con from 0.3 ± 0.5 μmol/min at t = 0 to 1.1 ± 0.7 μmol/min at t = 20, and CD from –0.8 ± 0.4 μmol/min at t = 0 to 0.8 ± 0.3 μmol/min at t = 20. This positive response was only sustained beyond t = 60 in Con, such that net BCAA balance across the 2 h was lower in CD (0.6 ± 0.3 vs. –0.1 ± 0.2 μmol/min, respectively, p = 0.05). IBD-fatigue scores indicated CD suffer from moderate fatigue (6.2), which had a moderate effect on daily activities (16.7). Handgrip dynamometer testing showed a trend towards greater fatigue in CD vs. Con (+8 %points) in the dominant arm (p = 0.061). A trend towards lower total body lean mass in CD (–15%, p = 0.084) was found. No differences were detected in strength, physical activity, diet or IR. In summary: despite not exhibiting AR, as they initially responded to the meal stimulus, CD could not maintain a positive protein balance post feeding compared with Con. This was associated with reduced muscle mass and function.
Conclusions: The inability to sustain a positive protein balance postprandially could provide an explanation for the reduced muscle mass seen in CD patients in remission. This could be contributing to fatigue and poor muscle function. Pharmacological interventions to reduce protein breakdown and a high-protein diet to improve the anabolic response to food could both be investigated as potential treatments.

P020

The effect of bone marrow-derived mesenchymal stem cells on expansion of colon organoids and organoid implantation

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Background: Mesenchymal stem cells (MSC) are involved in suppression or progression of intestinal diseases, such as inflammation and tumour. In addition, bone marrow (BM)-derived cells including bone marrow-derived mesenchymal stem cells (BM-MSCs) have important role in the process of mucosal repair in damaged intestine, and recently, intestinal organoid implantation has been considered as a novel tool to enhance the repair of mucosal defect. Therefore, we investigated the effect of BM-MSCs on expansion of colonic organoid.
Methods: Colon crypts were isolated from colon of EGFP-TG C57BL/6 mouse, using digestion buffer. Isolated crypts or cyptal cells were embedded in collagen, seeded on plates, and then overlaid by basal culture medium for colon organoid. BM-MSCs were isolated from EGFP-TG C57BL/6 mouse, and then cocultured with colon organoids in separated collagen matrix or mixed with colon organoids. Hepatocyte growth factor (HGF), known as a niche factor for stem cell growth, was added in organoid culture media. After 7 days, the number, size and shape of colon organoids were measured and compared according to the culture condition with or without BM-MSCs or HGF. The mixture with colon organoids and BM-MSCs were implanted after mucosal abrasion in the rectum of C57BL/6 mouse.
Results: The size and number of colon organoids were increased by addition of HGF or coculture with BM-MSCs. Compared with control, addition of HGF increased the number of organoid by two times, and coculture with BM-MSCs increased the organoid number by 4.5 times. In addition, coculture with BM-MSC induced the change of organoid shape with jagged edge in the half of colon organoids. The mixture with organoids and BM-MSCs were successfully implanted in the damaged rectum of C57BL/6 mouse.
Conclusions: The coculture with colon organoids and BM-MSCs could be helpful to expand organoids, and the additional effect of BM-MSCs like anti-inflammation and niche for organoid growth could be beneficial effect in organoid implantation on damaged mucosa.

P021

Aryl hydrocarbon receptor controls ILC3/ILC1 immunity in a colitis model of 2,4,6-trinitrobenzene sulphonic acid

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Background: Aryl hydrocarbon receptor (AHR) is a ligand-dependent transcription factor that controls the toxicity of dioxins and regulates the immune response. It has been generally established that the AHR plays an important physiological role in intestinal immuno homeostasis. It has been found that group 3 innate lymphoid cells (ILC3) are involved in safeguarding intestinal homeostasis in mice, whereas group 1 innate lymphoid cells (ILC1) are accumulated in chronic inflammation of the gut. Previous studies have shown that the abnormal differentiation of ILC3 and ILC1 exist in Crohn's disease (CD) patients, however the underlying mechanism remains unclear. We investigated the role of AHR in the aberrant alteration of ILC3/ILC1 in the colonic mucosal of active CD patients and mouse models.
Methods: The expression of AHR was detected by western blot in colon of active CD patients and 2,4,6-trinitrobenzene sulphonic acid (TNBS)-induced colitis mice. The ILC3/ILC1 were investigated in CD patients and TNBS-induced colitis mice (AHR–/–, AHR+/+).
Results: The expression of AHR protein was downregulated in colon tissue of active CD patients compared with the normal controls. And AHR protein was reduced in colon tissue of colitis mice. Meanwhile, the number of ILC3 was decreased while ILC1 increased in active CD patients and TNBS induced colitis of AHR–/– mice. The intestinal inflammation in AHR–/– mice induced by TNBS was more severe than wild-type mice.
Conclusions: Our data suggest that AHR may mediate abnormal differentiation of ILC3/ILC1 in CD patients and elucidate the molecular mechanism in the pathogenesis of CD, which provide evidence for prevention and treatment of CD.

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