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ROLE OF HUMAN MICROBIOTA IN SKIN DERMATITIS AND ECZEMA: A SYSTEMATIC REVIEW

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Background Human gut microbiota – are normal flora living freely in the human gastrointestinal systems and this symbiotic bond begins at birth, and there are associations between human microbiota and skin allergens.

Methods This systematic review provides an insight into the role and condition of human microbiota that affects skin dermatitis and eczema. A thorough search was conducted using predefined terms in several electronic databases (PubMed, Medline, ScienceDirect), from database inception to March 2018. Studies must involve human microbiota, dermatitis, eczema, and full texts needed to be available. A total of 20 eligible articles were identified.

Abstract IDDF2018-ABS-0240 Figure 1

Results Based on the literature, several factors involving gut microbiota were identified that could affect skin dermatitis and eczema. Findings suggest that the dysbiosis of allergy in adults develops postnatally. At infancy stage, colonisation of the gut microbiota takes place and affects the immune development into the adolescence and adulthood. Hence, maternal milk represents a key factor to build and modulate establishment of infant gut microbiota. Low level of IgA and IgE secretion in the gut system could reduce gut microbiota diversity. These antibody levels could be used to determine the establishment of a healthy symbiosis with gut microbiota.

Interactions between dysbiosis in *Faecalibacterium prausnitzii* and gut epithelial is noted as underlie cause for the progression of dermatitis. In addition, studies reported a reduction of the abundance of *Bifidobacterium* in the gut microbiota had been seen in infants with eczema. A variation of *Bifidobacterium* colonisation patterns in early life is said to be associated with later development of eczema or dermatitis. Figure 1 illustrates what happens when an alteration takes action to the normal microbiome flora such as *Bifidobacterial*, *Escherichia coli* and *Lactobacilli*. This leads to the development of dermatitis and eczema.

Conclusions In summary, probiotics can enhance and maintain a healthy gut microbiota. Studies also suggested prenatal and postnatal supplementation of bifidobacterial may be effective in the primary prevention of allergy diseases. These findings provide vital insight and knowledge that could enhance the potential for future microbial-based therapies to improve the clinical outcome of dermatitis and eczema.

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EPIGENETICS OF MUCINOUS COLORECTAL ADENOCARCINOMA THROUGH INTEGRATED TRANSCRIPTOME, METHYLOME AND MIRNOME ANALYSIS

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Background Mucinous cancer (MC) is a distinctive subtype of colorectal cancer (CRC) identified in 10%–15% of patients. It has long been associated with poor response to treatment, low survival rates, worse prognosis and present at more advanced stage than non-mucinous adenocarcinoma. Yet, the knowledge on the molecular mechanisms associated with this type of malignancy is lacking. This study aims to elucidate the transcriptome, methylome and miRnome landscape of MC for a better understanding of the disease and to find the potential target of therapy.

Methods We obtained the TCGA-generated methylation data based on Illumina Methylation 450 beadchip, level 3 micro-RNA expression and RNA sequencing dataset from Firebrowse. Gene expression data from 41 normal colons and methylation data from 45 normal colons were included for comparisons. Unpaired t-test with multiple testing corrections was performed using Bioconductor in R version 3.4.3.

Results Despite originating from the similar organ, MC and AC have distinct molecular profiles as shown by a high number of differentially methylated and expressed genes. We identified 2420 significant demethylated genes, and 3899 differentially expressed genes in MC. *LY6G6D* is the most downregulated gene while *MUC2*, the commonly discussed gene in MC, is the most upregulated. There were only four significant differentially expressed microRNAs with modest fold change, suggesting that DNA methylation is a more dominant epigenetic event in gene regulation of MC. *EIF6* is the most significantly hypermethylated (25.6% hypermethylation; $p=4.18E-10$) in MC versus AC and its expression was downregulated -0.57 fold ($p=4.89E-07$). On the other hand, *BAG3* is the most significantly hypomethylated (22.1%

hypomethylation, $p=0.009$) despite modest but significant upregulation of expression (0.24, $p=8.20E-03$).

Conclusions Our findings could be the first to suggest that the up- and downregulation of *BAG3* and *EIF6* expression in MC could be due to hypo- and hypermethylation, however, their specific roles in MC tumorigenesis remains to be elucidated. Beyond mucin genes, upregulation of genes rarely associated with CRC was also observed, suggesting new insight into the aetiology of MC resistance to therapies and their roles as a potential target for MC treatment may be worth investigating.

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TSG-6 RELEASED BY MESENCHYMAL STEM CELLS DERIVED FROM HUMAN INDUCED PLURIPOTENT STEM CELLS ALLEVIATE COLITIS THROUGH THE REGULATION OF CD44

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Background Mesenchymal stem cells (MSCs) have become a promising approach for inflammatory bowel disease (IBD). MSCs derived from human induced pluripotent stem cells (iPSC-MSCs) have increased expandability and prolonged stemness, but the therapeutic effects need to be further investigated. Tumour Necrosis Factor-stimulated Gene-6 (TSG6) released from MSCs have been shown to accelerate intestinal repair in IBD. And only CD44 acts as a TSG6 receptor. Therefore, we want to investigate the potential role and mechanism of the iPSC-MSCs on murine colitis via the regulation of TSG-6 and CD44.

Methods Murine colitis was induced by intrarectal TNBS administration. The expression of TSG6 in iPSC-MSCs was assayed with immunocytochemistry and Western blot. To study the role of TSG-6 secreted by iPSC-MSCs in alleviating murine colitis, iPSC-MSCs (2×10^6 cells/mouse) transfected with or without siRNA targeting TSG6 were injected intraperitoneally on the next day after TNBS administration. Body weight and disease activity index were recorded daily. Cell proliferation, apoptosis and the expression of CD44 were analysed by immunohistochemistry or qRT-PCR. In addition, the role of CD44 was studied by applying either control peptide or CD44 signalling inhibitor, PEP-1 to TNBS-induced murine colitis. Mice symptoms and mucosal healing were analysed as also.

Results iPSC-MSC produced and released TSG6. And the injection of iPS-MSC intraperitoneally attenuated murine colitis accompanied by increasing body weight and reducing the size of the ulcer. However, the therapeutic effects were largely decreased by knockdown of TSG6 in iPSC-MSC. In addition, iPS-MSC accelerated the ulcer healing by promoting the proliferation (Ki67) of colonic epithelial cells and increasing expression of CD44, but not in mice given iPSC-MCS with TSG-6 knockdown. And then we assessed the possible mechanism of TSG6 in promoting mucosal healing by CD44, and we found that the therapeutic effects of TSG-6 itself were similar to iPS-MSC. But the protecting effects of TSG-6 were diminished by inhibition of CD44 via injection of PEP-1 to TNBS induced colitis mice.

Conclusions iPSC-MSCs alleviate murine colitis by releasing TSG-6 and then activating CD44.

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SCREENING OF CHROMOSOMAL ALTERATIONS, K-RAS MUTATIONS AND DNA METHYLATION STATUS IN APC PROMOTER OF FAMILIAL AND SPORADIC CASES WITH CARCINOMA OF THE AMPULLA OF VATER IN TAMIL NADU POPULATION

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Background Carcinoma of the ampulla of Vater is a rare malignant tumour arising from the precancerous lesions, which accounts for 6%–7% of periampullary tumours and 0.2% of gastrointestinal tract malignancies. The aim of the study was to identify the chromosomal alterations and K-ras mutations and to check the methylation status in Adenomatous polyposis coli (APC) promoter region in the familial and sporadic carcinomas of the ampulla of Vater.

Methods A total of 42 samples of carcinoma of the ampulla of Vater (included 31 familial and 11 sporadic cases) and equal numbers of controls were selected which were categorised based on their age (group I <50 years; group II >50 years). Techniques including GTG-banding and PCR-RFLP were used to identify the genetic alterations. DNA methylation in APC promoter region was analysed for methylation status at the CpG regions.

Results The result revealed a high frequency of chromosomes 1p- and 12p+involved in the poorly differentiated (PD) tumour grade and an increased prevalence of the K-ras mutations at the codon 12 associated with >2 cm tumour size in the familial carcinomas of the ampulla of Vater. The APC promoter region showed hypermethylation in the CpG islands of carcinoma patients compared to controls.

Conclusions The results concluded that the chromosomes 1p- and 12p+region might play a vital role for the development of a high grade tumour and the K-ras gene mutation is an early molecular event leading to an abnormal proliferation of the cells. Methylation profiling showed that APC gene has a key role in stabilising b-catenin pathway, in which hypermethylation in APC promoter region could lead to proteasome degradation of b-catenin suggesting that APC methylation may be the potential testing for Carcinoma of the ampulla of Vater diagnosis and provide a new viewpoint in the treatment.

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SPONTANEOUS CHOLECYSTOCOLONIC FISTULA IN AN ELDERLY MALE: A RARE CAUSE OF MASSIVE LOWER GI BLEEDING

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Background Biliary enteric fistulas are often incidental findings. When asymptomatic usually no treatment is necessary