Background: Inflammatory bowel disease (IBD) is an idiopathic disease caused by a dysregulated immune response to intestinal microbes in an individual with a genetic predisposition. Therefore, alleviation of inflammation is very important to treat IBD. Mesenchymal stem cells (MSCs) have been highlighted as new candidates for treating autoimmune disease based on their immunomodulatory properties.
Methods: In this study, we investigated the anti-inflammatory mechanism and therapeutic effects of adipose tissue-derived MSCs (ASCs) using THP-1 macrophages and dextran sodium sulphate (DSS)-induced mice with chronic colitis.
Results: LPS-treated THP-1 cells expressed mRNA of CD11b, an M1 macrophage marker, at Day 2. However, THP-1 co-cultured with ASCs expressed mRNA of CD206, CD68, CCL18, legumain, and IL-10, markers of M2 macrophages. In THP-1 cells co-cultured with ASCs, precursor (pro)-IL-1β, Cox-2, and NLRP3 increased dramatically compared with LPS-treated THP-1 cells. Secretion of IL-1β and IL-18 was significantly inhibited by ASCs, but PGE2 production was highly increased in co-culture conditions of THP-1 and ASCs. IL-18 secretion was inhibited by PGE2 treatment, and PGE2 inhibited inflammasome complex (ASC/Cas-1/NLRP3) formation in THP-1 cells. In the DSS-induced chronic colitis model, ASCs ameliorated colitis by decreasing the total number of macrophages and the M1 macrophage population.
Conclusions: Our results suggest that ASCs can suppress the inflammatory response by controlling the macrophage population, and ASCs may be therapeutically useful for the treatment of IBD.

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CD103+SIRPα+ DC are specifically decreased in the inflamed colon from patients with ulcerative colitis but not with Crohn's disease

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Background: Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a chronic inflammation of the human gastrointestinal (GI) tract. Intestinal dendritic cells (DC) are essential to maintain the balance between immunity against pathogens and tolerance towards nutrients and commensals. However, there is not much information about DC composition in the human GI tract both in health and IBD.
Methods: Human GI biopsies were obtained from healthy controls and IBD patients (including UC and CD; both active and quiescent). Tissue was disaggregated and lamina propria mononuclear cells (LPMC) characterised by flow cytometry.
Results: Human intestinal DC were identified within singlet viable leucocytes as CD14-CD64-HLA-DR+CD11c+. Type 1 DC were defined as CD103+SIRPα- while type 2 DC were identified as SIRPα+ and further divided into subsets based on the expression of CD103. The proportion of total DC displayed a gradient throughout the healthy human gut as it was higher in the colon (either distal or proximal) compared with the ileum. DC proportion was further decreased in the duodenum. Type 1 (minority) and type 2 (majority) conventional DC did not change their proportion throughout the healthy gut. However, CD103+SIRPα+ DC were the main subset in the duodenum as opposed to CD103-SIRPα+ DC which were predominant in the colon and the ileum. Compared with their CD103-SIRPα+ type 2 counterparts, CD103+SIRPα+ had higher levels of HLA-DR, CD40, CD86, CCR7, CD137L, ICOSL and PD-L1. CD103+SIRPα+ were also more phagocytic and had lower expression of blood-related markers like CLA and CCR2, suggesting that they are derived from CD103-SIRPα+ DC following mucosal conditioning. Indeed, CD103+SIRPα+ numbers were increased following LPMC culture, although this process was reverted in the presence of pro-inflammatory LPS. CD103+SIRPα+ DC displayed an enhanced production of IL-10, both in resting conditions and in the presence of LPS. In IBD, type 2 DC constitutively displayed lower expression of SIRPα irrespectively of IBD-type (CD or UC) or condition (active or quiescent). Nevertheless, the inflamed colon from UC patients, but not from CD, specifically displayed lower numbers of tolerogenic CD103+SIRPα+ DC. These results were in agreement with the colonic cytokine milieu, which was much more pro-inflammatory in UC patients compared with CD.
Conclusions: Tolerogenic PD-L1 expression and IL-10 production was associated with CD103+SIRPα+ DC, confirming therefore their tolerogenic phenotype. Human colonic DC from IBD patients constitutively display lower levels of SIRPα. The specific reduction of CD103+SIRPα+ DC in the inflamed mucosa from UC, but not CD, suggests the presence of different pathogenic mechanisms occurring in IBD.

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Transcriptional profiling of ulcerative colitis in remission

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Background: This study addresses whether existing transcriptional profiles can improve and support the current definition of UC in remission apart from the today existing endoscopic, histological and laboratory scoring systems.
Methods: Mucosal biopsies from treatment-naïve UC patients (n = 14), healthy controls (n = 16), and UC patients in remission (n = 14) underwent RNA-Seq using the Next Seq550 instrument from Illumina. The algorithm package STAR-2.5.2b was used for downstream analysis. Principal component analysis (PCA), Limma, and p-value adjustment methods were used to obtain a dataset of significantly differentially expressed genes (DEGs). Gene annotations were performed by using the PANTHER classification system (http://pantherdb.org/), and KEGG (www.genome.jp/kegg/). For functional enrichment the clusterProfiler package and REACTOME database (https://reactome.org/) was used. Fractions of specific cell populations in samples were estimated by applying the R/Bioconductor CellMix manual (http://web.cbio.uct.ac.za/~renaud/CRAN/web/CellMix/). TNF-α levels in biopsies were estimated by qPCR and values <7000 copies/µg protein are considered as non-inflamed tissues.
Results: Analyses revealed 927 significantly DEGs in remission when compared with UC and normal samples. PCA showed a clear distinction between remission-, normal and UC samples along the first principal component 1 (PC1) with 45.7%, and second principal component (PC2) with 9.3% of the total variance. Cell fractions of