Published in final edited form as:

Dig Dis Sci. 2009 December ; 54(12): 2561–2567. doi:10.1007/s10620-008-0673-4.

Pattern Recognition Scavenger Receptors, SR-A and CD36, Have an Additive Role in the Development of Colitis in Mice

Helieh S. Oz,

Center for Oral Health Research, College of Dentistry, University of Kentucky Medical Center, 800 Rose Street, Lexington, KY 40536, USA. Department of Internal Medicine, University of Kentucky Medical Center, Lexington, KY, USA

Jian Zhong, and

Department of Internal Medicine, University of Kentucky Medical Center, Lexington, KY, USA. Division of Digestive Diseases, University of Kentucky Medical Center, Lexington, KY, USA

Willem J. S. de Villiers

Department of Internal Medicine, University of Kentucky Medical Center, Lexington, KY, USA. Division of Digestive Diseases, University of Kentucky Medical Center, Lexington, KY, USA

Helieh S. Oz: Helieh.oz@uky.edu

Abstract

The multifunctional pattern recognition scavenger receptors, SR-A and CD36, are predominantly expressed by lamina propria macrophages and considered important in innate immunity. We examined the role of these receptors in the pathophysiology of inflammatory bowel disease. Colitis was induced in wild type (WT), SR-A^{-/-}, CD36^{-/-}, and SR-A/CD36 double deficient mice by administering DSS. DSS-induced moderately severe colitis in WT mice was manifested by weight loss, reduced hematocrit, and pathology. SR-A/CD36 double deficient mice developed significantly more severe colitis as indicated by anemia ($P < 0.01$), decreased colonic length due to inflammation ($P < 0.01$), and lesions when compared with WT and single deficient animals. Serum amyloid A was significantly more elevated in SR-A/CD36^{-/-} mice ($P < 0.01$) compared with WT and single deficient animals. However, the spleens of WT mice ($P < 0.05$) were significantly enlarged. Inflammatory cytokine levels were considerably increased in WT mice (IL-6 $P < 0.001$, TNF α $P < 0.01$). In contrast, SR-A deficient mice maintained more normal body and splenic weight and developed less severe colonic lesions compared to other groups. In conclusion, our data indicate that SR-A/CD36 double deficiency leads to more severe colonic lesions and dys-regulated inflammatory response as compared with single SR-A or CD36 deficiency in colitis, suggesting additive effects between these two receptors in this model.

Keywords

Scavenger receptors; Macrophages; SR-A; CD36; Colitis

Introduction

Animal models of inflammatory bowel disease (IBD) play a major role in elucidating the pathophysiology of the human disease and are valuable in testing potential therapeutic

Correspondence to: Helieh S. Oz, Helieh.oz@uky.edu.

H. S. Oz and J. Zhong contributed equally to this work.

targets. Transgenic technology and gene targeting have significantly increased the variety of available models to provide insight into the possible role of the defined genes in the pathogenesis of IBD.

IBD is associated with an increased number of macrophages (MΦ) in colonic mucosa. Scavenger receptors, expressed primarily on the MΦ surface (e.g., SR-A, CD36, TLR), form the first line of body defense and play a pivotal role in innate immunity [1]. The scavenger receptors known as “pattern recognition receptors” identify the conserved structure of the pathogen ligand and mediate the binding and uptake of antigens including microorganisms [2].

Scavenger receptor A (SR-A) was originally identified by its ability to uptake and bind to modified low-density lipoprotein (LDL). Studies revealed that certain molecules such as lipopolysaccharide (LPS) of gram-negative bacteria and lipoteichoic acid (LTA) of Gram-positive bacteria, compete for binding to these receptors [3]. The expression of SR-A on MΦ is influenced by different cytokines. For instance, TNFα and IFN-γ mainly inhibit SR-A activity by transcriptional and posttranscriptional regulation [4,5]. On the other hand, MΦ colony stimulating factor (M-CSF) and granulocyte MΦ colony stimulating factor (GM-CSF) upregulate the expression of murine SR-A [6–8]. In contrast, PPAR-γ agonists inhibit expression of SR-A and regulate MΦ activation [9].

A prominent member of the class B scavenger receptors, CD36, is similarly involved with innate immunity [10]. CD36 is an 88 kDa cell surface glycoprotein expressed on a variety of cell types including MΦ, adipocytes, and endothelial cells. CD36 is pivotal in antigen presentation, clearance of apoptotic cells, and lipid transportation [11–15]. These two major scavenger receptors (SR-A and CD36) are involved in macrophage foam cell formation and development of atherosclerosis. Currently, the role of these receptors in the pathophysiology of IBD is not defined. The objective of this investigation was to evaluate the role of these receptors in the development of colitis in the DSS-induced murine model.

Methods

Animals

C57BL/6 wild type mice (WT) were obtained from Sprague Dawley Laboratories (Harlan Laboratories, Indianapolis, IN). Scavenger receptor A deficient mice (SR-A^{-/-}) were kindly provided by Dr. M. F. Linton, Vanderbilt University Medical Center, Nashville, Tennessee. CD36 deficient mice (CD36^{-/-}) were donated by Dr. R. L. Silverstein, Weill Medical College of Cornell University, New York, New York. SR-A/CD36 double deficient mice were crossbred in our animal facility. The SR-A/CD36 double deficient as well as SR-A^{-/-} and CD36^{-/-} mice were developed on a C57BL/6 background. Animals were maintained in the pathogen-free facility under equal light/dark cycles with free access to water and food at the Veterans Administration (VA) Medical Center Animal Facility and UK Medical Center. All procedures were approved by the IACUC/VA institutional animal use and care committee.

Animals were divided into eight per group. Colitis was induced in mice by the addition of 3% dextran sodium sulfate (DSS, mol wt, 50,000) into drinking water for 8 days. Mice were euthanized at day 8, and blood was collected by cardiac puncture. Spleens were removed and weight and length were measured. Colons were removed, washed with sterile phosphate-buffered saline (PBS pH 7.2), and the length and weight were measured as a parameter to evaluate the colonic inflammatory response. The experiment was independently repeated twice.

Colonic Cytokine Secretion

Proximal and distal sections (~1 cm) of cleansed colons were excised, opened longitudinally, and attached to pieces of sterile silicon paper, with the mucosa exposed. Sections were washed twice with culture media RPMI (GIBCO BRL, Grand Island, NY) supplemented with 5% (v/v) endotoxin-free fetal calf serum, 2 mmol/l glutamine, and 1×10^5 U/ml of penicillin/streptomycin. Samples of similar weight were then plated into 0.5 ml supplemented media in a 24-well cell culture plate. The cultures were incubated for 24 h at 37°C in an atmosphere with 10% CO₂ and 95% relative humidity. Each culture supernatant was collected separately and stored at -70°C.

Histology

The colonic tissues were cleaned with PBS and cut in half longitudinally. One portion of each colon was Swiss rolled and fixed in 10% formalin for histological examination. The remainder was snap-frozen in liquid nitrogen and stored at -80°C. The formalin fixed sections were processed for histology slides, and stained with hematoxylin and eosin (H & E). Each slide was provided with an encrypted label, and evaluated by light microscopy by two of the investigators (Oz and de Villiers). The severity of colitis was assessed with a validated histological semi-quantitative grading score as described previously [16]. The scores were based on histological features with a numeric value (0–4) assigned according to the % of tissue that corresponded to either of following criteria:

Grade 0: No detectable lesions, no inflammatory cells, normal mucosal appearance.

~~Grade 1~~ **Grade 1** inflammatory infiltrate in the mucosa, crypt epithelium involved less than 25% of the total colon.

~~Grade 2~~ **Grade 2** multi-focal inflammation with moderate expansion of the mucosa; crypt epithelium involved more than 26% of the colon.

~~Grade 3~~ **Grade 3** moderate multi-focal inflammation with moderate expansion of the mucosa, crypt epithelium disruption involved more than 50% of the colon.

~~Grade 4~~ **Grade 4** severe diffuse inflammation with crypt epithelium disruption and ulceration involved more than 75% of the colon.

Immunohistochemistry Assay

To detect CD68 expression in the colonic tissue, 5 µm in diameter paraffin-embedded sections were sequentially deparaffinized with hexane. The slides were rehydrated in alcohol baths, washed in PBS, microwaved in high pH antigen retrieval solution (DAKOcytation, Carpinteria, CA) for 5 min, again washed with PBS, incubated in 0.3% H₂O₂-methanol for 10 min, and then rinsed with distilled water. The slides were then incubated at room temperature for 1.5 h in a blocking solution consisting of normal horse serum, rinsed with PBS, and incubated with primary antibody at 4°C overnight. Rabbit polyclonal IgG against CD68 was obtained from Zymed/Invitrogen (Catalog no. 1076154; San Francisco, CA). The “Elite ABC” kit from Vector (Burlingame, CA) was used with biotinylated secondary antibodies and biotin-conjugated horseradish peroxidase, and developed with a 3,3'-diaminobenzidine solution per the manufacturer's instructions. The slides were subsequently counter-stained with Methyl Green (DAKOcytation, Carpinteria, CA).

Immunoassay for Cytokines and Serum Amyloid A

To assess systemic inflammation, levels of SAA were determined by an ELISA kit from BioSource International. TNFα, IL-1β, IL-6, and IL-12/p40 levels in colonic explant culture supernatant and plasma were measured by ELISA kits purchased from R and D Systems (Minneapolis, MN).

Statistical Analysis

The data were expressed as the mean $\pm$ SEM and analyzed using repeated ANOVA followed by the post hoc analysis of variance. A P value less than 0.05 was considered to be significant.

Results

Administration of DSS in daily drinking water induced moderately severe colitis in WT mice. This was manifested by weight loss (Fig. 1) and reduced hematocrit value (WT 36.2 ± 3.8 vs. control 43.4 ± 0.7 ; $P < 0.05$) (Table 1). Colon length was significantly decreased in WT mice due to inflammatory responses (WT 4.2 ± 0.3 cm vs. control 5.6 ± 0.1 cm; $P < 0.01$). DSS-induced elevated acute protein, serum amyloid A (SAA) (WT 336 ± 60 μ g/ml vs. control 20 ± 3 ; $P < 0.001$, Fig. 2), and a moderately severe colonic histopathological score (WT 2.6 ± 0.2 vs. 0 normal control). Amongst different groups of mice investigated in this study, SR-A/CD36 double deficient mice (SR-A/CD36^{-/-}) developed significantly more severe colitis as indicated with severe anemia (compared to WT $P < 0.01$, Table 1) and decreased colonic length (WT 4.2 ± 0.3 cm, SR-A/CD36^{-/-} 3.37 ± 0.15 , control 5.6 ± 0.1 ; $P < 0.01$). Similarly SR-A/CD36 double deficient mice showed significantly more elevated SAA level ($P < 0.01$, Fig. 2) and colonic pathological lesions when compared with WT or single deficient animals ($P < 0.05$, Figs. 3 and 4). This illustrates an additive effect of both SR-A/CD36 in regulating SAA secretion and histopathology. However, the spleen was significantly enlarged in WT mice (compared to SR-A/CD36^{-/-} $P < 0.05$, Table 1), and concentration of plasma proinflammatory cytokines, IL-6 ($P < 0.001$), and TNF α ($P < 0.01$) were mainly elevated in WT more than deficient animals (Figs. 5 and 6). In contrast, SR-A deficient mice maintained more normal body (Fig. 1), colonic, and splenic weight and colonic length (Table 1) and developed less severe colonic lesions (Fig. 3) compared to other deficient or WT mice (compared to WT $P < 0.05$ and SR-A/CD36^{-/-} $P < 0.01$). CD36 deficiency correlated with significant increases of ex vivo secretion of IL-12 in supernatant from colonic explants when stimulated with exogenous LPS (CD36^{-/-} vs. WT or SR-A $P < 0.01$, CD36^{-/-} vs. SR-A/CD36^{-/-} $P < 0.05$), while it had a negative effect in levels of serum IL-12 ($P < 0.05$) when compared with WT or SR-A^{-/-} mice (Table 1). There was no significant difference between serum levels of IL-1 β amongst groups. These data are summarized in Table 1.

Discussion

Our data indicate that SR-A and CD36 (scavenger receptors) double deficiency lead to severe colonic lesions and dysregulated inflammatory response as compared with WT and single SR-A or CD36 deficiency in DSS-induced colitis, suggesting additive effects between these two receptors in this model.

The multiligand and multifunctional pattern recognition scavenger receptors, SR-A and CD36, are expressed primarily by lamina propria macrophages and play an important role in the innate immunity and defense against pathogens [1–3]. Macrophage scavenger receptors are known to facilitate the uptake of modified LDL, and formation of foam cells leading to development of atherosclerosis. Studies indicate that LPS competes for SR-A binding sites, and M Φ from SR-A deficient mice show decreased LPS binding ability as compared with the cells from WT mice [17]. This suggests that SR-A recognizes LPS and contributes to the binding and uptake of LPS. Indeed LPS or lipoteichoic acid have been suggested to act as bacterial ligands for SR-A. Recent evidence indicates that some microbial pathogens (e.g., *Streptococcus pyogenes*) may avoid recognition by SR-A and phagocytosis using their surface M protein and polysaccharide capsule [18]. In addition, SR-A deficient mice have increased susceptibility to bacterial and viral agents [19] and impaired bacterial clearance

[20]. However, the mechanism by which SR-A provides protection against diverse pathogens is not clear and may vary according to microbial strains.

Furthermore, SR-A deficient mice were more susceptible to LPS-induced endotoxic shock after inoculation with live BCG. SR-A deficient mice produced more TNF α and IL-6 and showed an increased mortality in response to LPS that was blocked by administration of anti TNF- α antibody before LPS challenge [21]. In contrast, other studies showed that peritoneal M Φ from SR-A deficient mice were more resistant to LPS treatment, bind remarkably less LPS than those from WT animals, and secrete lower levels of IL-1 β [22]. In another study, bacterial (*C. parvum*) hepatic granuloma formation was delayed and expression of certain proinflammatory cytokines down-regulated in SR-A deficient mice [23]. Taken together, these data suggest that SR-A is involved in regulating inflammatory cytokine secretion. This correlates with our findings that DSS induced more severe colitic pathology in SR-A and CD36 deficient mice; in contrast, they demonstrated a dysregulated proinflammatory cytokines profile and secreted considerably less IL-6 and TNF α than WT mice. Similarly, recent studies suggest that agents (such as antioxidants, α tocopherol) that decrease expression of scavenger receptors (SR-A and CD36) partially inhibit proinflammatory cytokines (IL-6) and chemokine (IL-8) production, and macrophage foam cell formation [24,25]. Also, TNF α release from activated macrophages is inhibited using anti-CD36 antibody, indicating that scavenger receptors may be involved in the induction of cytokine release from these cells [26].

The scavenger receptor CD36 is also important in the pathophysiology of colonic inflammation as suggested by the current results. CD36 was originally identified as a platelet membrane glycoprotein and a receptor for thrombospondin [27]. CD36 recognizes a variety of ligands including anionic phospholipids, oxidized LDL, apoptotic cells, collagen, and long-chain fatty acids [10]. It is possible that CD36 protects the colonic tissue against DSS-induced injury by its ability to clear apoptotic cells. This needs to be further investigated.

CD36 is required for the phagocytosis of apoptotic cells by human M Φ [28]. M Φ treated with anti-CD36 antibodies or those that harbor a mutated form of CD36 have been shown to block the uptake of apoptotic materials [29]. Furthermore, CD36 gene transfer confers the ability to ingest apoptotic cells by non-activated phagocytes [30].

Our data indicate that SR-A and CD36 double deficiency can lead to more severe colonic damage and dysregulated inflammatory response as compared to WT, SR-A, or CD36 single deficiency, suggesting an additive effect between these two receptors. It is possible that these receptors function at alternative pathways to protect the host against inflammatory responses, indicating that the innate immune system has evolved overlapping mechanisms to combat pathogens as well as inflammation.

Conclusion

Our data indicate that scavenger receptors SR-A and CD36 together exert protective effects in the progression of colitis against dysregulated inflammatory response and colonic damage in this model. This protective effect appears to be additive and associated with the relative roles of these receptors in regulating signaling pathways in intestinal M Φ infiltration in lamina propria.

Acknowledgments

This study was partially supported by the National Institutes of Health grant NCCAM-AT1490 and NCRR P20RR020145, COHR-Pilot Project (H. S. Oz).

Abbreviations

DSS	Dextran sodium sulphate
INF-γ	Interferon gamma
IL-6	Interleukin-6
LDL	Low-density lipoprotein
LPS	Lipopolysaccharide
LTA	Lipoteichoic acid
MΦ	Macrophage
SR-A	Scavenger receptor A
TNFα	Tumor necrosis factor
WT	Wildtype

References

1. Gordon S. The macrophage scavenger receptor type A is expressed by activated macrophages and protects the host against lethal endotoxic shock. *J Exp Med.* 1997; 186:1431–1439.10.1084/jem.186.9.1431 [PubMed: 9348300]
2. Gordon S. Pattern recognition receptors: doubling up for the innate immune response. *Cell.* 2002; 111:927–930.10.1016/S0092-8674(02)01201-1 [PubMed: 12507420]
3. Platt N, Gordon S. Is the class A macrophage scavenger receptor (SR-A) multifunctional?—The mouse's tale. *J Clin Invest.* 2001; 108:649–654. [PubMed: 11544267]
4. Geng YJ, Hansson GK. Interferon-gamma inhibits scavenger receptor expression and foam cell formation in human monocyte-derived macrophages. *J Clin Invest.* 1992; 89:1322–1330.10.1172/JCI115718 [PubMed: 1556191]
5. Hsu HY, Nicholson AC, Hajjar DP. Inhibition of macrophage scavenger receptor activity by tumor necrosis factor- α is transcriptionally and post-transcriptionally regulated. *J Biol Chem.* 1996; 271:7767–7773.10.1074/jbc.271.13.7767 [PubMed: 8631819]
6. De Villiers WJS, Fraser IP, Hughes DA, Doyle AG, Gordon S. Macrophage-colony-stimulating factor selectively enhances macrophage scavenger receptor expression and function. *J Exp Med.* 1994; 180:705–709.10.1084/jem.180.2.705 [PubMed: 8046345]
7. De Villiers WJS, Fraser IP, Gordon S. Cytokine and growth factor regulation of macrophage scavenger receptor expression and function. *Immunol Lett.* 1994; 43:73–79.10.1016/0165-2478(94)00148-0 [PubMed: 7737693]
8. Guidez F, Li AC, Horvai A, Welch JS, Glass CK. Differential utilization of Ras signaling pathways by macrophage colony-stimulating factor (CSF) and granulocyte-macrophage CSF receptors during macrophage differentiation. *Mol Cell Biol.* 1998; 18:3851–3861. [PubMed: 9632769]
9. Ricote M, Li AC, Willson TM, Kelly CJ, Glass CK. The peroxisome proliferator-activated receptor- γ is a negative regulator of macrophage activation. *Nature.* 1998; 391:79–82.10.1038/34178 [PubMed: 9422508]
10. Febbraio M, Hajjar DP, Silverstein RL. CD36: a class B scavenger receptor involved in angiogenesis, atherosclerosis, inflammation, and lipid metabolism. *J Clin Invest.* 2001; 108:785–791. [PubMed: 11560944]
11. Ockenhouse CF, Chulay JD. *Plasmodium falciparum* sequestration: OKM5 antigen (CD36) mediates cytoadherence of parasitized erythrocytes to a myelomonocytic cell line. *J Infect Dis.* 1988; 157:584–588. [PubMed: 2449507]
12. Oquendo P, Hundt E, Lawler J, Seed B. CD36 directly mediates cytoadherence of *Plasmodium falciparum* parasitized erythrocytes. *Cell.* 1989; 58:95–101.10.1016/0092-8674(89)90406-6 [PubMed: 2473841]

13. Endemann G, Stanton LW, Madden KS, Bryant CM, White RT, Protter AA. CD36 is a receptor for oxidized low density lipoprotein. *J Biol Chem.* 1993; 268:11811–11816. [PubMed: 7685021]
14. Moore KJ, El Khoury J, Medeiros LA, et al. CD36-initiated signaling cascade mediates inflammatory effects of beta-amyloid. *J Biol Chem.* 2002; 277:47373–47379.10.1074/jbc.M208788200 [PubMed: 12239221]
15. Medeiros LA, Khan T, El Khoury JB, et al. Fibrillar amyloid protein present in atheroma activates CD36 signal transduction. *J Biol Chem.* 2004; 279:10643–10648.10.1074/jbc.M311735200 [PubMed: 14699114]
16. Zhong J, Eckhart E, Oz HS, Bruemmer D, de Villiers W. Osteopontin deficiency protects mice from DSS-induced colitis. *Inflamm Bowel Dis.* 2006; 12:790–796.10.1097/00054725-200608000-00015 [PubMed: 16917234]
17. Van Lenten BJ, Fogelman AM. Lipopolysaccharide-induced inhibition of scavenger receptor expression in human monocyte-macrophages is mediated through tumor necrosis factor-alpha. *J Immunol.* 1992; 148:112–116. [PubMed: 1727858]
18. Areschoug T, Waldemarsson J, Gordon S. Evasion of macrophage scavenger receptor A-mediated recognition by pathogenic streptococci. *Eur J Immunol.* 2008; 38:3068–3079. [PubMed: 18924218]
19. Suzuki H, Kurihara Y, Takeya M, Kamada N, Kodama T, et al. A role for macrophage scavenger receptors in atherosclerosis and susceptibility to infection. *Nature.* 1997; 386:292–296.10.1038/386292a0 [PubMed: 9069289]
20. Thomas CA, Li Y, Kodama T, Suzuki H, Silverstein SC, El Khoury J. Protection from lethal gram-positive infection by macrophage scavenger receptor-dependent phagocytosis. *J Exp Med.* 2000; 191:147–156. [PubMed: 10620613]
21. Haworth R, Platt N, Keshav S, et al. The macrophage scavenger receptor type A is expressed by activated macrophages and protects the host against lethal endotoxic shock. *J Exp Med.* 1997; 186:1431–1439. [PubMed: 9348300]
22. Kobayashi Y, Miyaji C, Watanabe H, et al. Role of macrophage scavenger receptor in endotoxin shock. *J Pathol.* 2000; 192:263–272. [PubMed: 11004705]
23. Hagiwara S, Takeya M, Suzuki H, et al. Role of macrophage scavenger receptors in hepatic granuloma formation in mice. *Am J Pathol.* 1999; 154:705–720. [PubMed: 10079248]
24. Singh U, Devaraj S, Jialal I. Vitamin E, oxidative stress, and inflammation. *Annu Rev Nutr.* 2005; 25:151–174. [PubMed: 16011463]
25. Takeda N, Manabe I, Shindo T, et al. Synthetic retinoid Am80 reduces scavenger receptor expression and atherosclerosis in mice by inhibiting IL-6. *Arterioscler Thromb Vasc Biol.* 2006; 26:1177–1183. [PubMed: 16484594]
26. Mytar B, Woloszyn M, Macura-Biegun A, et al. Involvement of pattern recognition receptors in the induction of cytokines and reactive oxygen intermediates production by human monocytes/macrophages stimulated with tumour cells. *Anticancer Res.* 2004; 24:2287–2293. [PubMed: 15330174]
27. Li WX, Howard RJ, Leung LL. Identification of SVTCG in thrombospondin as the conformation-dependent, high affinity binding site for its receptor, CD36. *J Biol Chem.* 1993; 268:16179–16184. [PubMed: 7688364]
28. Fadok VA, Warner ML, Bratton DL, Henson PM. CD36 is required for phagocytosis of apoptotic cells by human macrophages that use either a phosphatidylserine receptor or the vitronectin receptor (alpha vs. beta 3). *J Immunol.* 1998; 161:6250–6257. [PubMed: 9834113]
29. Stolzing A, Grune T. Neuronal apoptotic bodies: phagocytosis and degradation by primary microglial cells. *FASEB J.* 2004; 18:743–745. [PubMed: 14766802]
30. Ren Y, Silverstein RL, Allen J, Savill J. CD36 gene transfer confers capacity for phagocytosis of cells undergoing apoptosis. *J Exp Med.* 1995; 181:1857–1862. [PubMed: 7536797]

Fig. 1.
Normalized body weight loss in dextran sodium sulphate (DSS)-treated mice

Fig. 2.

Concentration of serum amyloid A protein (SAA) is significantly more increased in SR-A/CD36 double deficient dextran sodium sulphate (DSS)-treated animals (ELISA, µg/ml) and illustrates additive effects between two receptors

Fig. 3. Colonic lesions score (0–4) is most severe in SR-A/CD36 double deficient dextran sodium sulphate (DSS)-treated mice

Fig. 4. Colonic sections slide representative from normal (Co) and DSS-colitis mice stained hematoxylin and eosin (H & E). Dextran sodium sulphate (DSS)-treated SR-A/CD36^{-/-} display more severe pathology compared to wild type (WT) colitic mice

Fig. 5.
Plasma concentration of TNFα is significantly increased in dextran sodium sulphate (DSS)-treated wild type (WT) mice

Fig. 6. Plasma concentration of IL-6 is significantly increased in dextran sodium sulphate (DSS)-treated wild type (WT) mice

Table 1

Comparison between dextran sodium sulphate (DSS)-treated groups

Parameter	WT	SR-A ^{-/-}	CD36 ^{-/-}	SR-A/CD36 ^{-/-}
Colon length ^a normalized (%)	75 ^{**}	75 ^{**}	69	60 ^{**}
Colon weight/g	389 ± 45 ^{*, **}	252 ± 18 [*]	263 ± 19 [*]	219 ± 20 ^{**}
Hematocrit	36 ± 3.8 ^{*, **}	28.6 ± 2.5 [*]	34 ± 2	22 ± 2.6 ^{**}
Splenic weight (mg)	153 ± 0.15 ^{*, ***}	83 ± 0.06 ^{***}	131 ± 0.9 [*]	117 ± 0.08 [*]
IL-12 ^b (pg/ml)	178 ± 20 [*]	139 ± 12	102 ± 15 [*]	180 ± 22
IL-12 ^c (pg/ml)	31 ± 8 ^{*, **}	39 ± 4.6	102 ± 14 ^{**}	63.3 ± 6 [*]
IL-1β ^d (pg/ml)	21 ± 2.3	18 ± 0.4	17.2 ± 0.4	17 ± 0.2

^a Colonic length normalized according the normal controls^b Serum IL-12^c IL-12 secretion in the ex vivo supernatant from colonic explant stimulated with LPS^d Serum IL-1β

DSS dextran sodium sulphate, NS not significant

^{*} $P < 0.05$,^{**} $P < 0.01$,^{***} $P < 0.001$