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Dextran sulphate sodium increases splenic Gr1$^+$CD11b$^+$ cells which accelerate recovery from colitis following intravenous transplantation

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Summary

While Gr1$^+$CD11b$^+$ cells are known to regulate immune responses and accumulate in most cancer tissues, the function of Gr1$^+$CD11b$^+$ cells in inflammation is poorly understood. We investigated the role of Gr1$^+$CD11b$^+$ cells in a dextran sulphate sodium (DSS)-treated mouse model of ulcerative colitis (UC). C57BL/6 mice were treated with 2% DSS in drinking water for 5 days. Disease progression and recovery were assessed by body weight, disease activity index score (DAI) score and colon length. Splenic Gr1$^+$CD11b$^+$ cell number was greatly increased during the recovery phase of DSS-induced colitis. DSS-derived splenic Gr1$^+$CD11b$^+$ cells were administered intravenously to recipient (C57BL/6) mice during the early phase of DSS treatment. The transplanted splenic DSS-induced Gr1$^+$CD11b$^+$ cells improved DSS-induced colitis and promoted efficient colonic mucosal healing. We found that the CD11b$^+$ single positive cells increased in the course of DSS-induced colitis in lamina propria. The transplantation of splenic Gr1$^+$CD11b$^+$ cells induced feedback suppression of myeloid-lineage cell development. Namely, the transplantation of splenic Gr1$^+$CD11b$^+$ cells greatly suppressed the migration of CD11b$^+$ single positive cells to the lamina propria. Further, transplantation of Gr-1$^+$CD11b$^+$ cells greatly suppressed the increase of the same population, especially during the late phase of DSS colitis both in spleen and bone marrow.

Keywords: CD11b, DSS, Gr-1, myeloid-lineage, ulcerative colitis

Introduction

Inflammatory bowel disease (IBD) is a chronic and relapsing inflammation of the gastrointestinal tract that affects millions of people worldwide. The major forms of idiopathic IBD are ulcerative colitis (UC) and Crohn's disease (CD), and occur typically in the second and third decades of life, with the majority of affected individuals progressing to a relapsing and chronic disease [1]. Although the causes of IBD are still unknown, recent advances in the understanding of the molecular pathogenesis of IBD have been made owing to three related lines of investigation. First, in contrast to some other complex disorders, IBD has been amenable to the discovery of susceptibility genes. Secondly, it appears that commensal bacteria (or their products), rather than conventional pathogens, are the drivers for the dysregulated immunity observed typically in IBD cases. Thirdly, murine models that exhibit many of the features of UC seem to be driven bacterially and have helped to unravel the pathogenesis and/or mucosal immunopathology of IBD. Overall, it appears that an imbalance of the mucosal immune system leads to the overproduction of inflammatory cytokines, release of reactive oxygen metabolites and the infiltration of neutrophils into the intestine, resulting in uncontrolled intestinal inflammation and tissue damage [2–4].

Thus, neutrophils and macrophages may play important roles in disease progression and/or host defence. Both neutrophils and macrophages belong to the myeloid lineage, and multiply and differentiate in the bone marrow. In mice, surface expression of Gr-1 and CD11b defines granulocytes, macrophages and dendritic cells (DC), as well as immature myeloid cells (IMCs) having a marker of Gr1$^+$CD11b$^+$ phenotype. In normal mouse bone marrow 20–30% of the cells possess this phenotype, but these cells constitute only a small proportion (2–4%) of spleen cells and are absent from the lymph nodes. Myeloid-derived suppressor cells (MDSCs), which are also Gr1$^+$CD11b$^+$, have been shown to be up-regulated in several pathological conditions, including cancer [5,6] and infection [7–10].

Dextran sulphate sodium (DSS) is used commonly in rodent IBD models to induce acute intestinal inflammation chemically. DSS-induced colitis is characterized by weight loss, bloody diarrhoea, epithelial cell damage and immune cell infiltration. The DSS model faithfully reproduces many of the immunological disturbances observed in human IBD [11,12]. Here we asked whether DSS administration induces $Gr1^+CD11b^+$ myeloid cells in spleen and bone marrow.

Materials and methods

Experimental animals

All experiments used C57BL/6NCrSlc (C57BL/6) mice, 8–12 weeks old, purchased from SLC (Japan SLC Inc., Shizuoka, Japan) and maintained at the Animal Research Facility at Nagoya University Graduate School of Medicine under specific pathogen-free conditions. This work was approved by the ethical committee of Nagoya University.

Induction of DSS colitis

Colitis was induced by oral administration of DSS (ICN Biomedical, molecular weight (MW) = 36 000–50 000 Da) at 2% (w/v) in drinking water *ad libitum* for 5 days followed by normal drinking water. Mice were checked each day for morbidity and weights were recorded. After the mice were killed, colons were dissected, and colon length and spleen weight were measured. Day 0 represents the last day of DSS administration.

Colon histology

At autopsy, 1-cm sections of colon were fixed with octreotide (OCT) compound. Colon sections (5 μm) were stained with haematoxylin and eosin (H&E) according to standard protocol and sections were graded in a blinded fashion according to a scoring system based on a previous study [13,14]. Briefly, a combined score of inflammatory cell infiltration and tissue damage was determined as follows: normal colonic mucosa was considered zero, loss of the bottom one-third of the crypts was graded as one, loss of the bottom two-thirds of the crypts was scored as two, loss of the entire crypt area while retaining an intact surface epithelium was graded as three and loss of both the entire crypt area and surface epithelium (i.e. erosion) was graded as four.

Disease activity index (DAI) scores

To reflect the general condition of the mice, DAI scores were determined by an investigator blinded to the protocol, and based on the extent of body weight loss, stool guaiac positivity or gross bleeding and stool consistency, according to the method of Murthy *et al.* [13,14]. For each parameter a score of 0 to 4 was attributed, giving rise to a maximal DAI score of 12.

Flow cytometric analysis

Bone marrow and spleen tissues were homogenized to give single cell preparations, which were then isolated, counted and stained with antibodies against myeloid cell markers. All antibodies were purchased from Pharmingen (San Diego, CA, USA). Data were acquired (10 000 events) and lymphocytes separately gated on a side-scatter *versus* forward-scatter cytogram using a fluorescence activated cell sorter (FACS)Calibur and analysed using FlowJo software (BD Biosciences, Franklin Lake, NJ, USA), Fluorescein isothiocyanate (FITC)-labelled anti-mouseGr-1 (clone RB6-8C5, recognizing both Ly-6G and Ly-6C; BD Biosciences), phycoerythrin (PE)-labelled anti-mouse CD11b (clone M1/70; BD Biosciences), FITC-labelled anti-mouse Ly6G (clone 1A8; BD Biosciences), peridinin chlorophyll-cyananin (PerCP-Cy)5·5-labelled anti-mouse Ly6C (cloneHK1·4; eBioscience) were used in these experiments.

Granulocyte–macrophage colony-stimulating factor (GM-CSF) treatment *in vivo*

GM-CSF-producing Chinese hamster ovary cells (CHO–GM-CSF) were a gift from Dr T. Sudo, Toray Silicon, Tokyo, Japan. Mice received intraperitoneal (i.p.) injections of 0·1 ml of CHO–GM-CSF supernatant daily for 7 days.

Isolation of splenic $Gr\text{-}1^+/CD11b^+$ cell populations and lamina propria cells

Single splenocyte suspensions were obtained on day 11. Following red blood cell lysis, splenic $Gr\text{-}1^+/CD11b^+$ cell populations were purified and collected by flow cytometry (FACS Vantage; BD Biosciences) ($>5 \times 10^5$ cells). Cells were resuspended at a density of $2{\cdot}5 \times 10^4$ cells/ml in modified Eagle's medium (MEM) supplemented with 10% fetal bovine serum (FBS). In transplantation experiments, a total of $1{\cdot}5 \times 10^6$ $Gr1^+CD11b^+$ myeloid-derived splenocytes were administered intravenously to recipient mice (C57BL/6J mice) cytospins. Sorted splenocytes (2×10^5) were resuspended in 200 μl phosphate-buffered saline (PBS) and centrifuged onto microscope slides using a Cytospin-4 (Shandon, Life Sciences International, Astmoor, UK). Slides were then stained by May–Grünwald Giemsa according to standard protocol. Lamina propria cells were isolated as described previously [15]. Briefly, colons were opened longitudinally, digested, and epithelial cells removed and collected into 5-mM ethylenediamine tetraacetic acid (EDTA) PBS. Cells were then incubated with Hanks' balanced salt solution (HBSS) containing 4% FBS, 1 mg/ml collagenase type II, 1 mg/ml dispase and 40 μg/ml DNase, and incubated for 15 min at 37°C. The cells then washed three times and suspended in PBS.

Real-time polymerase chain reaction (PCR) analysis

Total RNA was purified from sorted cells using an RNeasy mini kit (Qiagen, Tokyo, Japan). First-strand cDNA was syn-

thesized using the high-capacity cRNA reverse transcription kit (Applied Biosystems). Real-time PCR reactions were performed using the MX3005p system (Stratagene, Santa Clara, CA, USA) using SYBR premix EX Taq II (Takara, Otsu, Japan). The expression of the β-actin gene was used to normalize the amount of the investigated transcript.

The following primers were used: β-actin (forward) 5′-AGTGTGACGTTGACATCCGT-3′, β-actin (reverse), 5′-GCAGCTCAGTAACAGTCCGC-3′, interleukin (IL)-1β (forward), 5′-GCCCATCCTCTGTGACTCAT-3′, IL-1β (reverse), 5′-AAGGCCAGGTATTTTGTCG-3′, transforming growth factor (TGF)-β (forward), 5′-AAGTGGATCCAC GAGCCCAA-3′, TGF-β (reverse), 5′-CTGCACTTGCAGG AGCGCAC-3′, monocyte chemoattractant protein (MCP)-1 (forward), 5′-TGAATGTGAAGTTGACCCGT-3′, MCP-1 (reverse), 5′-AAGGCATCACAGTCCGAGTC-3′, M-CSF receptor (forward), 5′-GACCTGCTCCACTTCTCCAG-3′, M-CSF receptor (reverse), 5′-GGGTTCAGACCAAGC GAGAAG-3′, GM-CSF (forward), 5′-ATGCCTGTCACGT TGAATGA-3′, GM-CSF (reverse), 5′-CCGTAGACCCTGC TCGAATA-3′ and GM-CSF receptor (forward), 5′-ACGGAG GTCACAAGGTCAAG-3′, GM-CSF receptor (reverse), 5′-TGAGGGTCTCAGGGTTCACT-3′.

Results were evaluated on a Lumi Vision Analyzer (Aisin-seiki Co., Ltd, Aichi, Japan).

Statistical analysis

Differences were analysed statistically by Student's *t*-test using StatView5·0 for Windows (SAS Institute, Cary, NC, USA). A *P*-value of <0·05 was considered to be statistically significant.

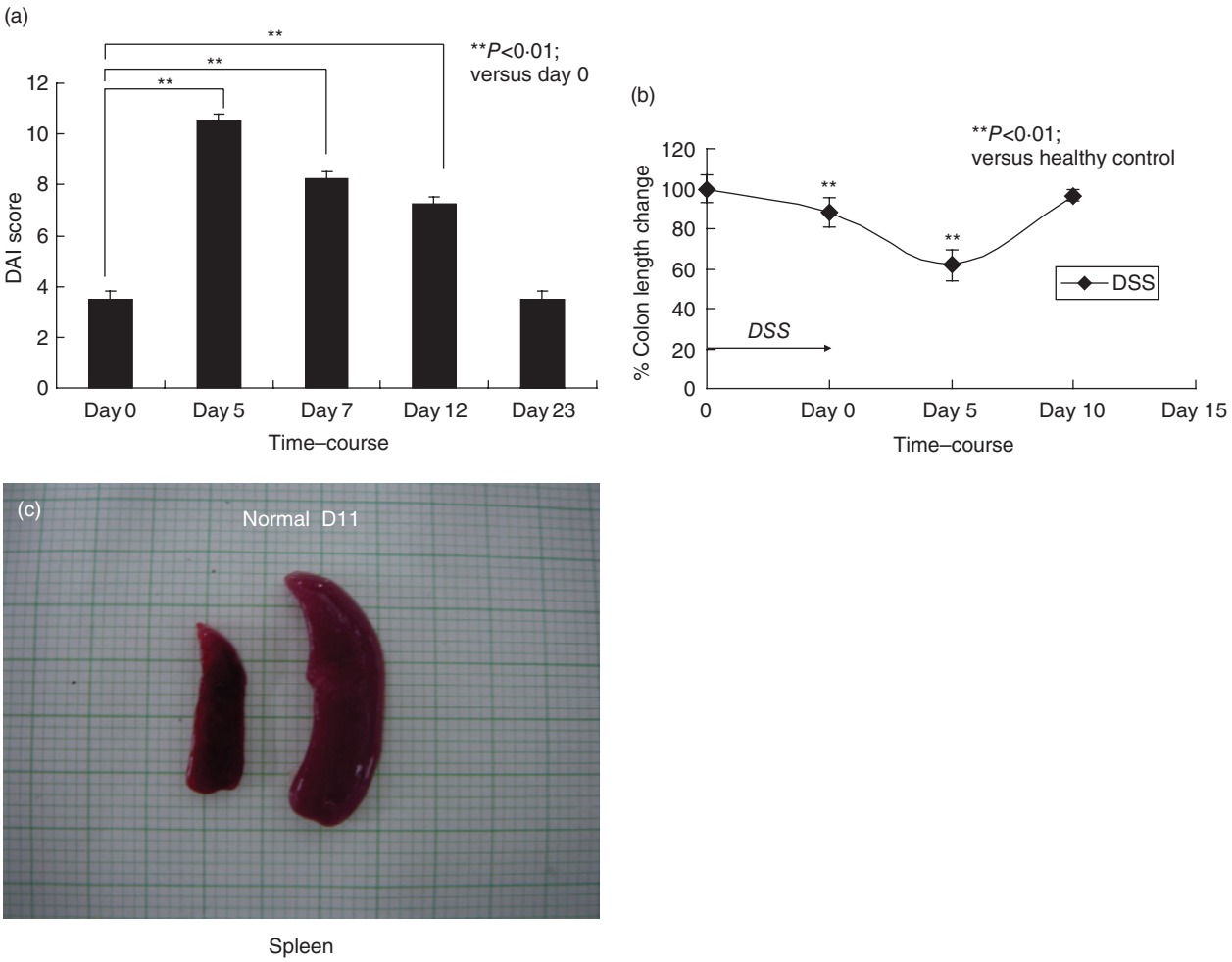

Fig. 1. Time–course of dextran sulphate sodium (DSS)-induced acute colitis. (a) Disease activity index (DAI) in C57BL/6 mice treated with 2% DSS for 5 days. DAI is determined by body weight loss, stool consistency and the crypt damage index, as described in Materials and methods. Each value represents the mean ± standard deviation (s.d.) ($n = 4$ mice). $^{**}P < 0{\cdot}01$ (day 0 *versus* days 5, 7, 12 or 23 mice). (b) Colon length was determined on days 0, 5 and 10. Each value represents the mean ± s.d. ($n = 4$ mice). $^{**}P < 0{\cdot}01$ (normal *versus* DSS-treated mice). (c) Macroscopic examination of the spleen. Normal indicates untreated control. D11 indicates day 11 after DSS treatment.

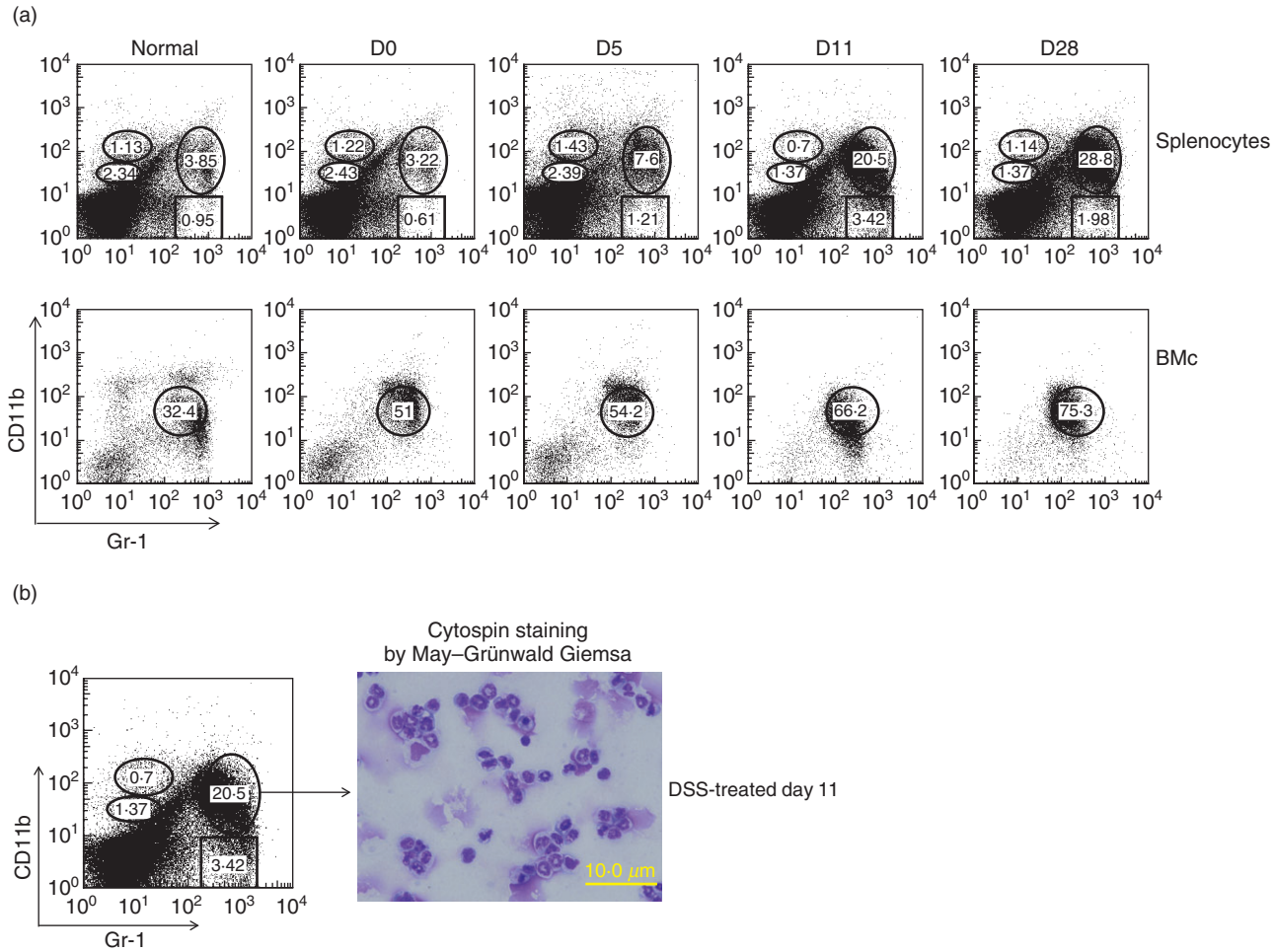

Fig. 2. Gr1$^+$CD11b$^+$ cells were markedly increased after dextran sulphate sodium (DSS) treatment. (a) Splenocytes (upper) and bone marrow cells (lower) were isolated from normal and DSS-induced C57BL/6 mice. Cells were stained with fluorescein isothiocyanate (FITC)-labelled anti-Gr1 and phycoerythrin (PE)-labelled anti-CD11b and analysed by fluorescence activated cell sorter (FACS), as described in Materials and methods. Each value represents the mean ± standard deviation (s.d.) ($n = 4$ mice). $^{**}P < 0{\cdot}01$ (day 0 mice *versus* days 5, 7, 12 or 23 mice). (b) Splenic Gr1$^+$CD11b$^+$ cells were isolated on day 11 of DSS by cell sorting. They were cytospun and stained with May–Grünwald Giemsa. Data are representative of five independent experiments.

Results

Spleen and bone marrow Gr1$^+$CD11b$^+$ cell populations are increased in the spleen and bone marrow of mice with DSS-induced colitis

To investigate DSS-induced epithelial damages and its relationship to myeloid-lineage cells during the disease progression and recovery from DSS-induced colitis, C57BL/6 mice were treated with 2% DSS for 5 days. DAI scores changed during the DSS treatment (Fig. 1a) and colon lengths were found to shorten significantly during the progression of colonic inflammation (Fig. 1b). Disease progression peaked around 5 days after completion of the 5-day DSS treatment. The mice recovered gradually and colon length was back to the starting level at day 10 (Fig. 1b). These findings were associated with marked splenomegaly on day 11 (Fig. 1c). To investigate whether DSS could induce Gr1$^+$CD11b$^+$ cells in the spleen and bone marrow, splenocytes and bone marrow cells were subjected to flow cytometric analysis. The Gr1$^+$CD11b$^+$ cell population in spleens without stimulation was less than 5%. Gr1$^+$CD11b$^+$ cells normally constitute approximately 30–40% of the cells in bone marrow without stimulation. The Gr1$^+$CD11b$^+$ cell population in both the spleen and bone marrow increased steadily from day 11 to day 28. In spleen the Gr1$^+$CD11b$^+$ cell population reached 28·8% on day 28, while the bone marrow Gr1$^+$CD11b$^+$ cell population increased to 75·3% (Fig. 2a). We performed a morphological assay by cytospin and May–Grünwald Giemsa staining, and found that the splenic Gr1$^+$CD11b$^+$ cells from DSS-treated mice had a segmented nuclear morphology characteristic of myeloid-lineage cells and were a heterogeneous population in nature (Fig. 2b).

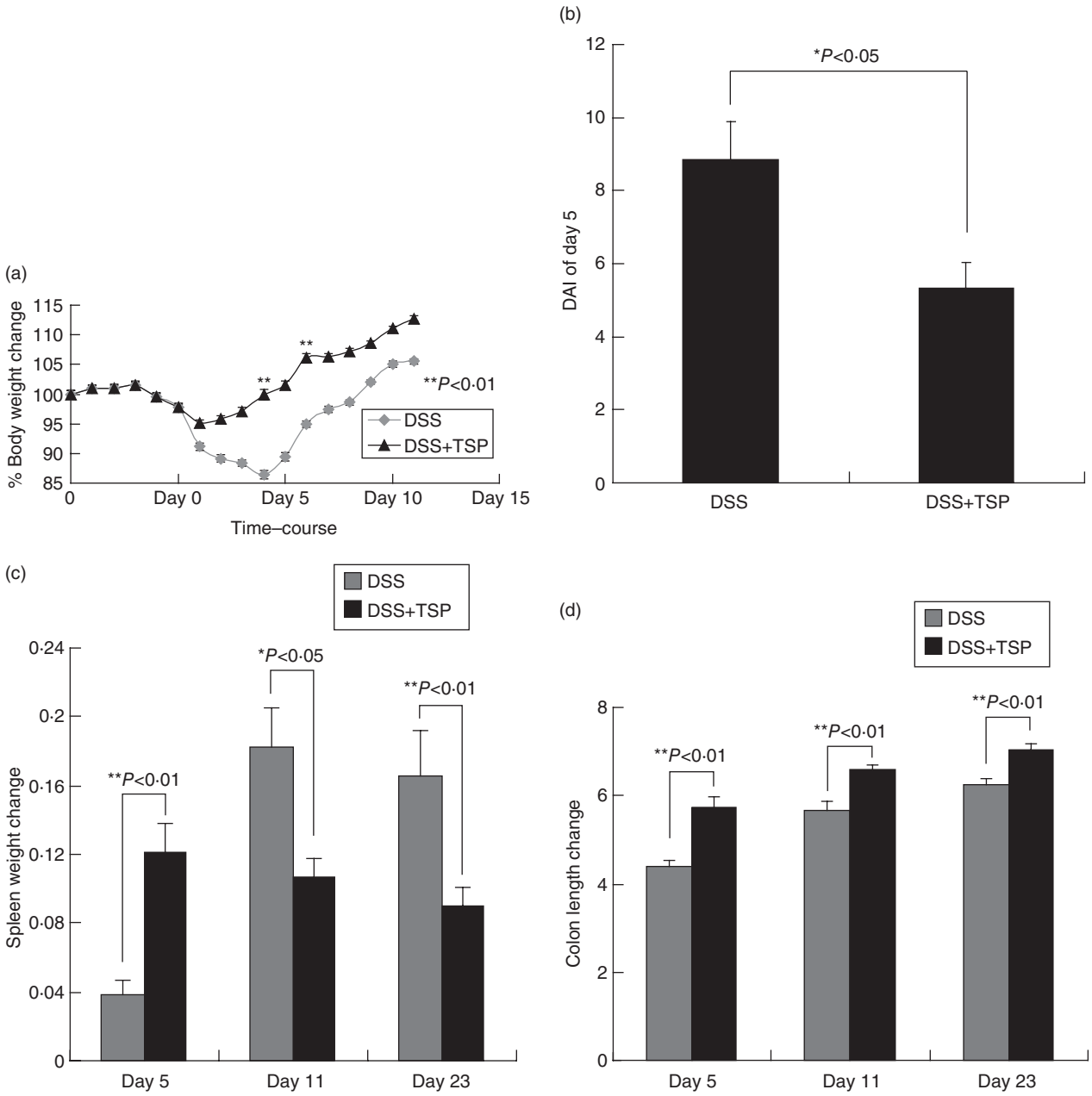

Fig. 3. Transplantation of dextran sulphate sodium (DSS)-induced splenic $Gr1^+CD11b^+$ cells ameliorated DSS-induced colitis. $Gr1^+CD11b^+$ spleen cells from DSS-treated mice were purified on day 11 by sorting. They were administered intravenously to recipient mice on the last day of DSS-treatment at a dose of $1{\cdot}5 \times 10^6$ $Gr1^+CD11b^+$ cells per mouse. (a) DAI scores, (b) body weight, (c) spleen weight (d) and colon lengths of non-transplanted and transplanted mice were measured. Each value represents the mean ± standard deviation (s.d.) ($n = 4$ animals); $^{**}P < 0{\cdot}01$; $^{*}P < 0{\cdot}05$. DSS *versus* DSS + TSP mice. (e) Haematoxylin and eosin-staining results of lower part of colon sections from non-transplanted and transplanted mice on days 7, 11 and 23. Results are representative of five independent experiments. Photographs were taken under ×40 and ×1000 magnification. DSS: 2% DSS-treated C57BL/6 mice. DSS + trimethylsilyl propionate (TSP): 2% DSS-treated C57BL/6 transplanted with $1{\cdot}5 \times 10^6$ $Gr1^+CD11b^+$ cells.

Transfer of splenic DSS-derived $Gr1^+CD11b^+$ cells into DSS-treated mice ameliorates colitis

Great increases of GR-1^+ $CD11b^+$ cells may enhance recovery from colitis. We performed a transplantation experiment whereby DSS-derived splenic $Gr1^+CD11b^+$ cells obtained at day 11 were transferred into mice at the end of DSS treatment (day 0) to investigate the function of the DSS-induced $Gr1^+CD11b^+$ cells. As shown in Fig. 3, the loss of body weight was less severe and the weight recovery faster in the transplanted mice than in the control DSS-treated mice that did not receive transplanted cells (Fig. 3a). The DAI score of the

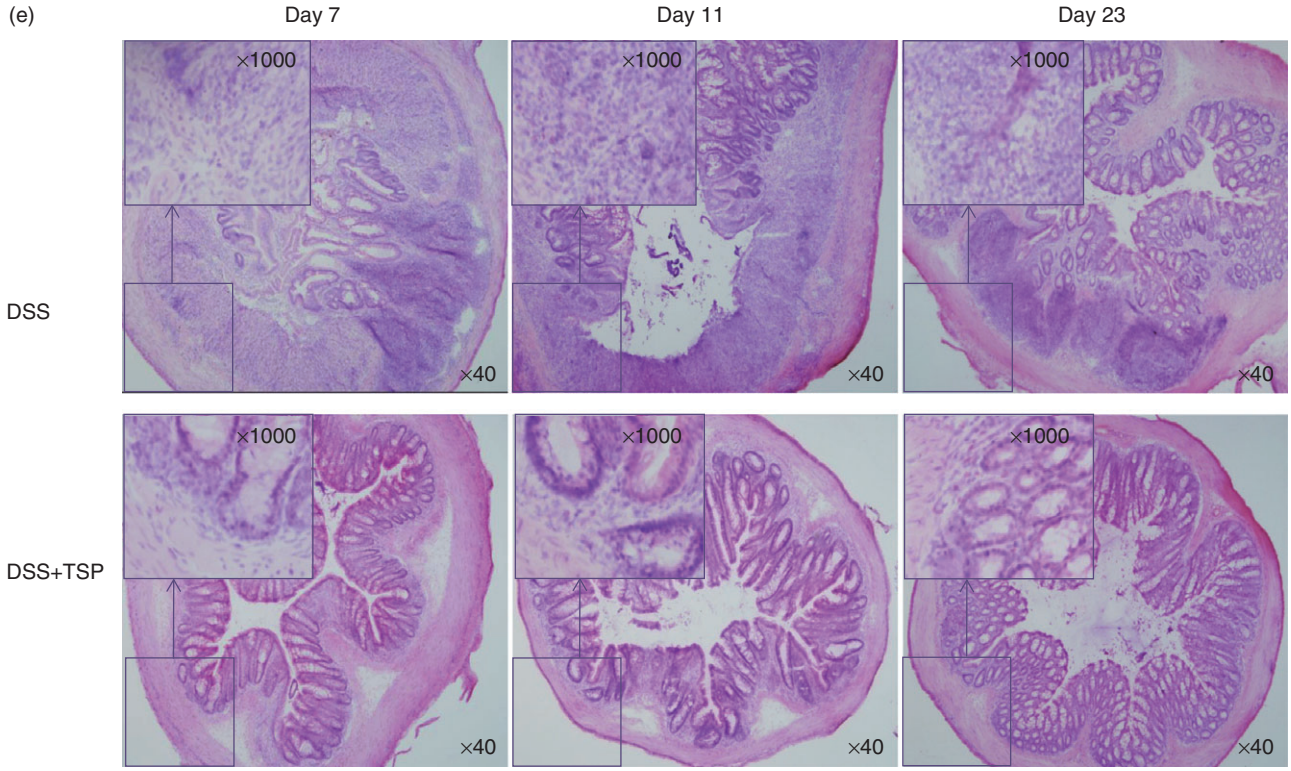

Fig. 3. *Continued*

transplantation group was significantly lower than that of the control group on day 5 (Fig. 3b). The spleen was not enlarged in the transplanted mice (Fig. 3c) and colon length did not decrease in the transplanted group (Fig. 3d). Pathological examination showed that the recovery from epithelial destruction of non-transplanted mice was delayed compared to the transplanted group. Invasion of neutrophils and macrophages to the epithelial layer and lamina propria continued later in the non-transplanted group (Fig. 3e). These results indicated that DSS-treated splenic Gr-1$^+$CD11b$^+$ cells could ameliorate DSS-induced colitis.

Increased expression of GM-CSFR in DSS-treated spleen

In order to identify the cause of the expansion of Gr-1$^+$CD11b$^+$ cells, we used real-time PCR to examine the expression of GM-CSF receptor (GM-CSFR) in DSS-treated spleen by real-time PCR. We found that the spleens of day 11 of DSS-treated mice greatly increased their levels of GM-CSFR expression. While the expression of GM-CSFR was also observed in GM-CSF-treated mice, the expression of GM-CSFR was much higher in DSS-treated mice than that of GM-CSF-treated mice. Although GM-CSFR was high, GM-CSF was low in the spleens of day 11 of DSS-treeted mice (Fig. 4). Other cytokines, including IL-1β, TGF-β, chemokine MCP-1 and cytokine receptor MCSF-R, were low in DSS-treated spleens (Fig. 4).

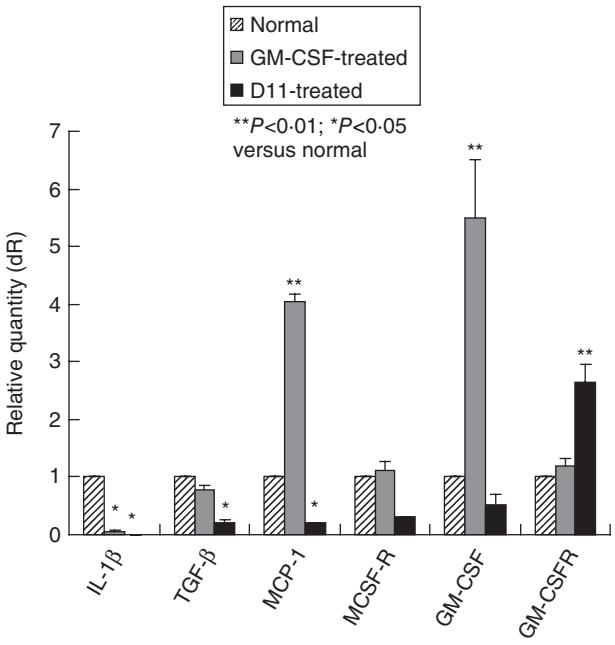

Fig. 4. Increased expression of granulocyte–macrophage colony-stimulating factor receptor (GM-CSFR) by Gr1$^+$CD11b$^+$ cells in dextran sulphate sodium (DSS)-treated spleens. Total RNA from splenic Gr1$^+$CD11b$^+$ cells isolated at day 11 was extracted, DNase-treated and converted to cDNA. Real-time polymerase chain reaction (PCR) was performed according to the Materials and methods. Bars indicate mean values of three experiments. Normal indicates untreated control.

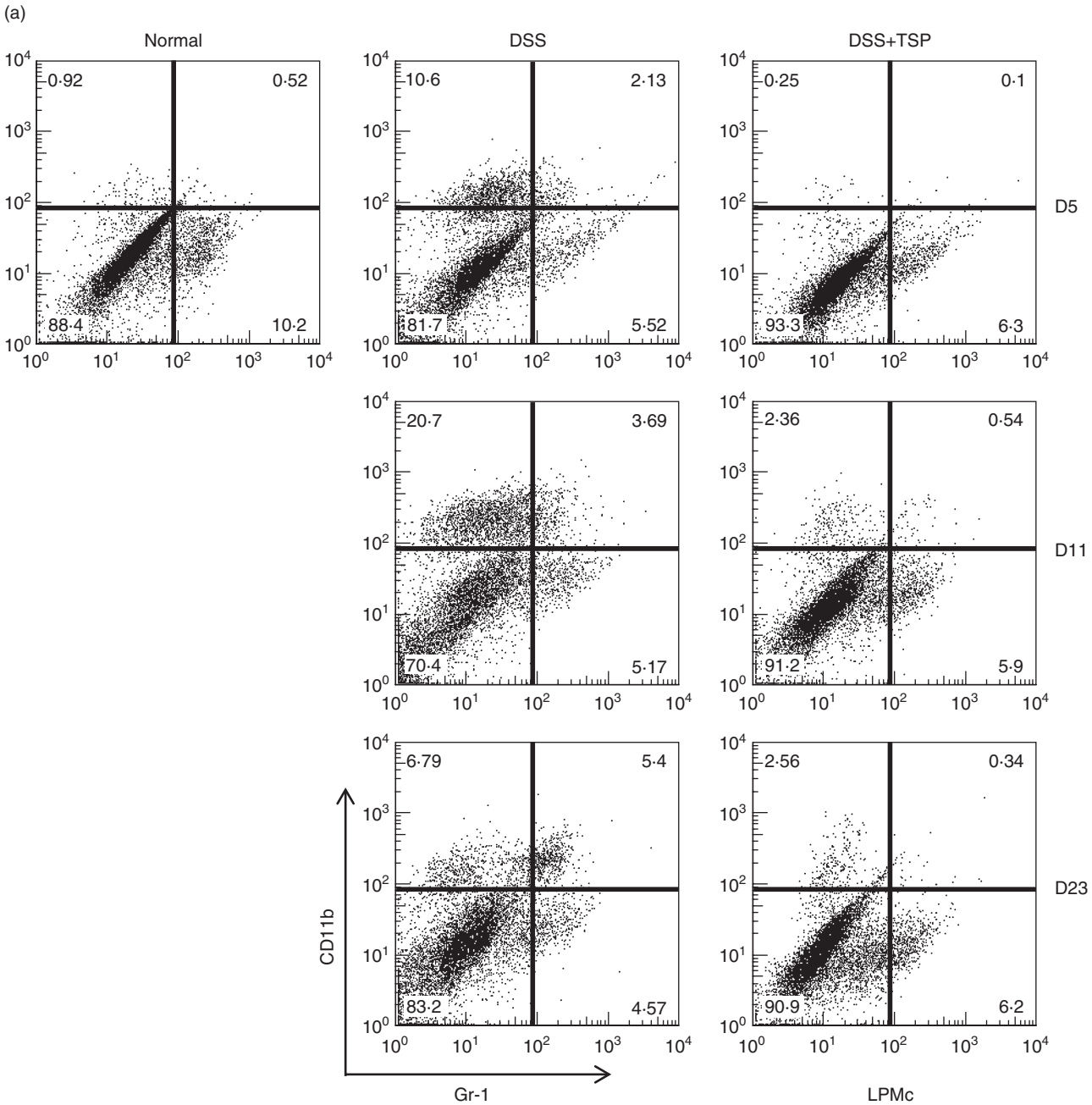

Fig. 5. Analysis of lamina propria monocytes derived from non-transplanted and transplanted mice during the experimental time–course. $Gr1^+$ and $CD11b^+$ populations (a) and the $Ly6G^+$ and $Ly6C^+$ populations (b). Frequency fluorescence activated cell sorter (FACS) data are representative of four experiments. Normal: lamina propria cells from control age-matched C57BL/6. Dextran sulphate sodium (DSS): lamina propria cells from 2% DSS-treated C57BL/6 mice. DSS+trimethylsilyl propionate (TSP): lamina propria cells from 2% DSS-treated C57BL/6 transplanted with $1{\cdot}5 \times 10^6$ $Gr1^+CD11b^+$ cells.

Possible mechanism of early recovery from colitis by $Gr1^+CD11b^+$ transplantation

We measured the myeloid cell population in the lamina propria. We found that the $CD11b^+$ single positive cells ($CD11b^+$ $Gr1^{neg}$) increased from day 5 to day 11 in DSS-treated non-transplanted mice, and decreased at day 23. Surprisingly, the transplantation of splenic $Gr1^+CD11b^+$ cells greatly suppressed the migration of $CD11b^+$ single positive cells to the lamina propria (Fig. 5a). We confirmed that the $CD11b^+$ single positive population consisted of $Ly6C^{high}$ $Ly6G^{low}$macrophages, which were down-regulated by the transplantation of $Gr1^+CD11b^+$ cells (Fig. 5b).

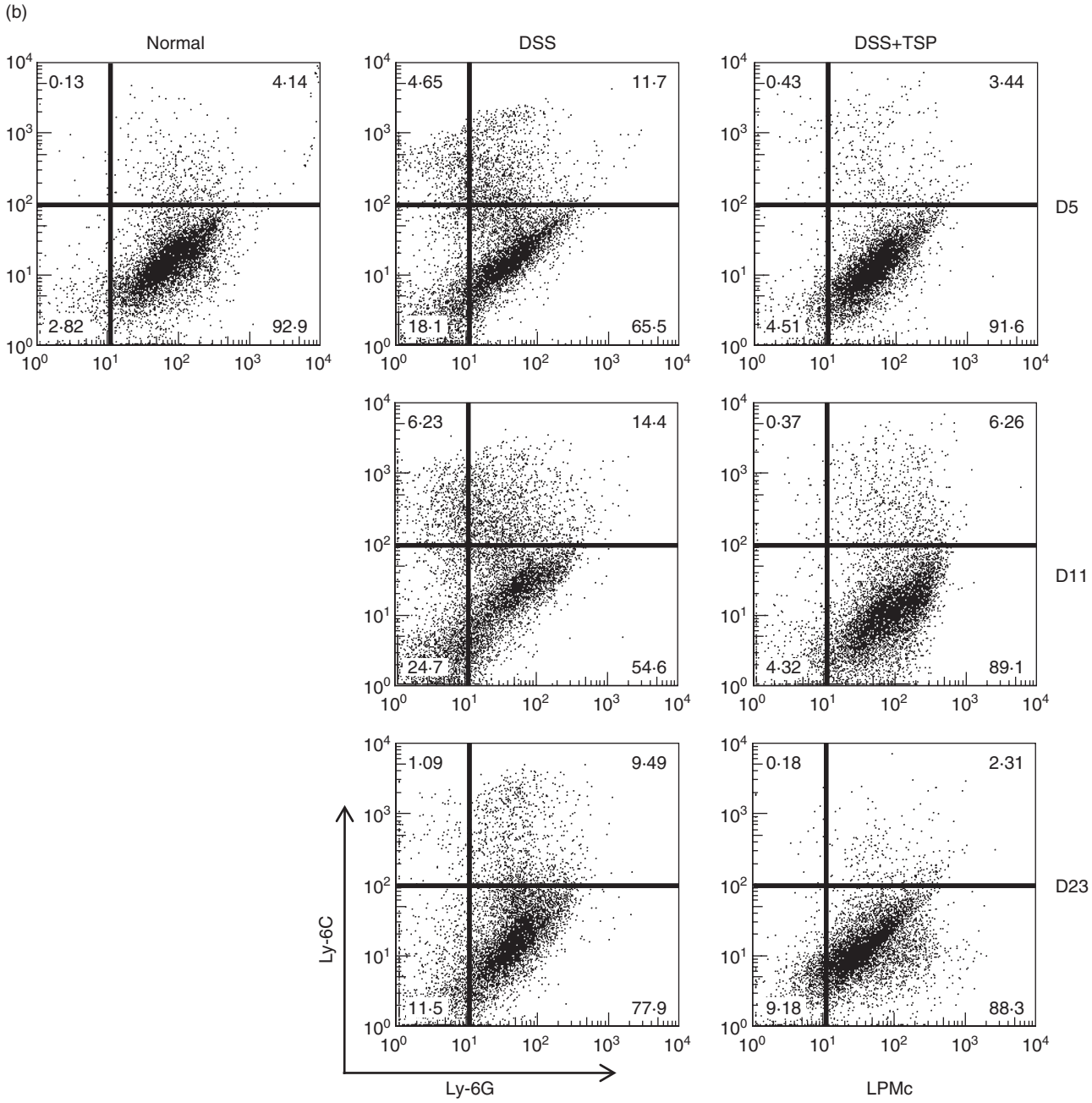

Fig. 5. *Continued*

As shown in Fig. 6a, transplantation of Gr-1$^+$CD11b$^+$ cells greatly suppressed the increase of the same population, especially during the late phase of DSS colitis both in spleen and bone marrow (Fig. 6a and b). In contrast, high levels of Gr-1$^+$CD11b$^+$ cells were maintained in both the spleen and bone marrow of non-transplanted mice after DSS treatment.

Discussion

Our results showed that the Gr1$^+$CD11b$^+$ cell population was greatly increased in the spleen and bone marrow after DSS treatment. Importantly, transplantation of splenic Gr1$^+$CD11b$^+$ cells to DSS-treated mice during the early phase of disease induction reduced inflammation and promoted efficient colonic mucosal healing. Gr1$^+$CD11b$^+$ cells constitute a heterogeneous population of myeloid-lineage cells, which include MDSC. Increased Gr1$^+$CD11b$^+$ cells in colitis has been reported by Haile *et al*. [16] in a T cell-dependent murine model of IBD. They also found an increase of CD14$^+$ human leucocyte antigen D-related (HLA-DR)$^{-/low}$ (human homologue of Gr1$^+$CD11b$^+$ cells) in patients with IBD. Haile *et al*. reported that increased

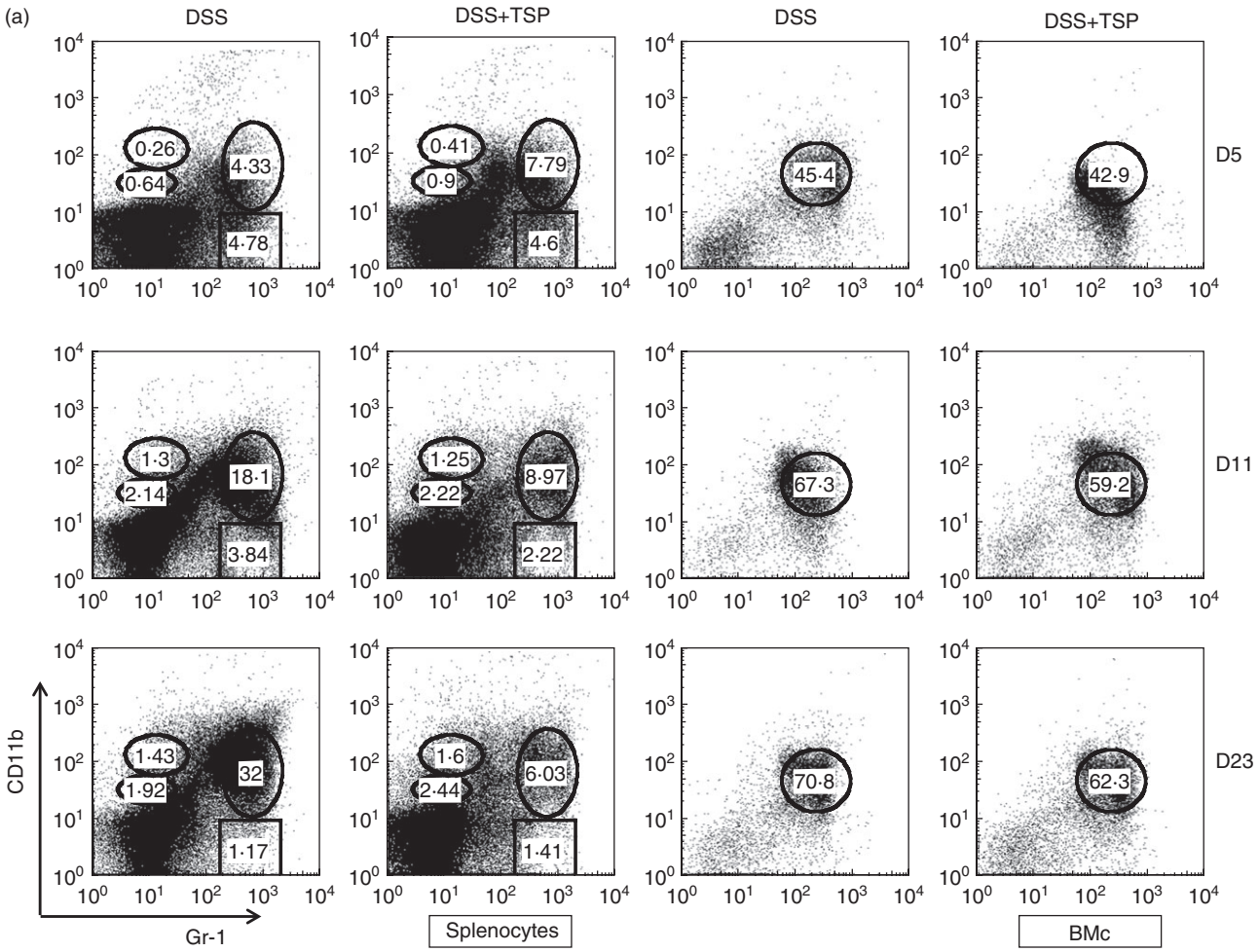

Fig. 6. Splenic and bone marrow Gr1$^+$CD11b$^+$ cells from non-transplanted and transplanted mice during the experimental period were investigated by flow cytometry to determined the percentage of Gr1$^+$CD11b$^+$ cells were measured. (a) Spleen. (b) Bone marrow. Data are representative of five independent experiments. Dextran sulphate sodium (DSS): spleen cells from 2% DSS-treated C57BL/6 mice. DSS+trimethylsilyl propionate (TSP): spleen cells from 2% DSS-treated C57BL/6 transplanted with $1{\cdot}5 \times 10^6$ Gr1$^+$CD11b$^+$ cells.

MDSC (Gr1$^+$CD11b$^+$ cells) suppresses T cell responses. However, they found that Gr1$^+$CD11b$^+$ cells were not increased in DSS-treated mice. They concluded that the Gr1$^+$CD11b$^+$ population was increased only in T cell-dependent colitis. It has been shown that acute DSS-induced colitis does not require T or B cells, as it occurs in severe combine immune deficiency (SCID) mice that lack these cell types [17]. Conflicting results between our experiments and those of Haile *et al.* might be due to the amount and duration of DSS administered and the strain of mice used. We administered 2% DSS in drinking water to C57BL/6 mice for 5 days, while Haile *et al.* administered DSS on days 0 (5%), 15 (7%) and 27 (7%) to VILLIN-haemagglutinin (HA) mice. The sensitivities of the murine strains to DSS differ greatly between the two strains [18]. We showed that the Gr1$^+$CD11b$^+$ population was increased even in DSS-treated T cell-independent colitis in some condition. MDSCs, which have a Gr1$^+$CD11b$^+$ cell phenotype, are a heterogeneous population of cells that expand during cancer, inflammation and infection, and that have a remarkable ability to suppress T cell responses [19]. Various mouse and human studies have found that MDSCs emerge in the peripheral blood and tumour microenvironment and often exhibit strong immunosuppressive capabilities. The accumulation of MDSCs within either the tumour microenvironment or peripheral blood correlates with a poor prognosis [20,21]. Most studies conducted in tumour-bearing mice or human indicate that Gr1$^+$CD11b$^+$ cells are immunosuppressive. It has been reported that the accumulation of myeloid cells in tumour-bearing mice decreased anti-tumour immune responses and promoted tumour growth [22,23]. Accumulating evidence has shown that Gr1$^+$CD11b$^+$ cells also regulate immune responses during bacterial and parasitic infections, acute and chronic inflammation, traumatic stress, sepsis and transplantation [19]. In experimental autoimmune encephalomyelitis and experi-

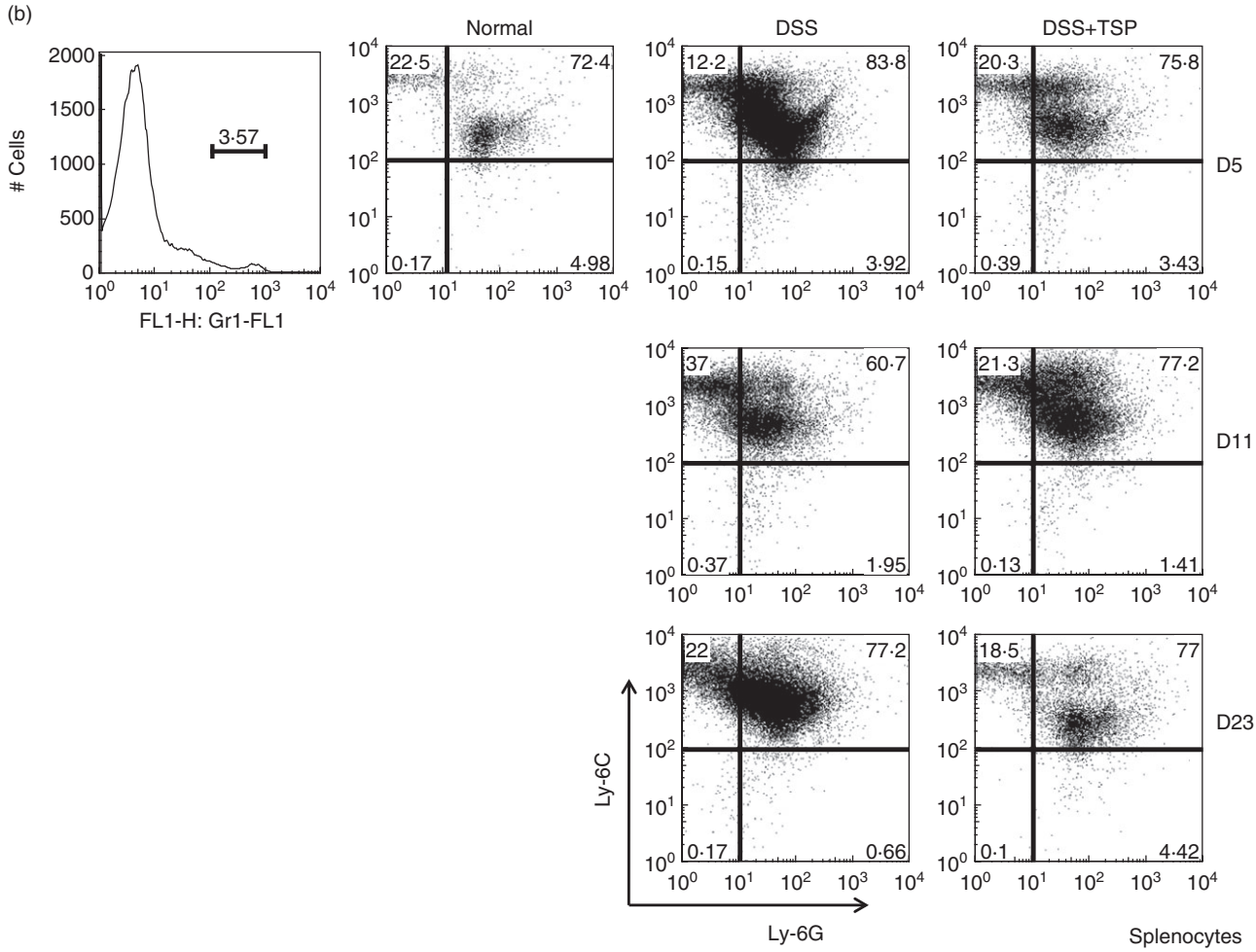

Fig. 6. *Continued*

mental autoimmune uveoretinitis, an increase in the number of MDSCs was observed in the spleen and blood [24,25]. However, the functions of $Gr1^+CD11b^+$ cells are not only immunosuppressive. It has been shown that $Gr1^+CD11b^+$ cells found in the ascites of epithelial ovarian cancer-bearing mice at advanced stages of disease are immunostimulatory rather than being immunosuppressive [26].

We showed that myeloid-lineage cells in the lamina propria in DSS-treated mice expressed consisted primarily of $CD11b^+$ ($Ly6C^+$) single positive ($Gr\text{-}1^{neg}$) macrophages and a few $Gr1^+CD11b^+$ cells. These results suggest that $Gr1^+CD11b^+$ cells may differentiate to $CD11b^+$ single positive cells and migrate to the lamina propria. In an enzyme immunoassay (EAE) model, among $Gr1^+CD11b^+$ cells only a small population of $CD11b^+Ly\text{-}6C^{high}$ inflammatory monocytes (IMC) can suppress T cell proliferation efficiently. However, in our DSS-treated colitis, transplantation of $Gr1^+CD11b^+$ cells greatly suppressed the increase of $CD11b^+$ cells in the colon. Suppression may be caused by feedback mechanism to inhibit the differentiation of myeloid-lineage cells in the bone marrow.

Splenic $Gr1^+CD11b^+$ cells express GM-CSFR during DSS-induced colitis. From these results, we speculate that the increased number of of spleenic $Gr1^+CD11b^+$ cells in immature myeloid-lineage cells may increased the number of $Gr1^+CD11b^+$ cells. Recent reports showed that GM-CSF-dependent stimulation of bone marrow-derived cells during DSS-induced colitis accelerates colonic tissue repair [27,28].

In summary, our results showed that $Gr1^+CD11b^+$ cell number was increased dramatically at the recovery phase of DSS-induced colitis. These cells accelerate the repair of colitis when transplanted at the early phase of colitis.

Acknowledgements

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Disclosure

The authors have no disclosures to declare.

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