Ifi202, an IFN-inducible candidate gene for lupus susceptibility in NZB/W F1 mice, is a positive regulator for NF-κB activation in dendritic cells

Moriyasu Yamauchi¹,², Masayuki Hashimoto¹, Kenji Ichiyama¹, Ryoko Yoshida¹, Toshikatsu Hanada¹, Tatsushi Muta³, Shizuo Komune², Takashi Kobayashi¹ and Akihiko Yoshimura¹

¹Division of Molecular and Cellular Immunology, Medical Institute of Bioregulation
²Department of Otorhinolaryngology, Graduate School of Medical Science, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan
³Laboratory of Cell Recognition and Response, Graduate School of Life Science, Tohoku University, Aoba, Aramaki, Aoba-ku, Sendai 980-8578, Japan

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Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the presence of autoantibodies and lupus nephritis. The [New Zealand black (NZB) × New Zealand white (NZW)]F1 (BWF1) mouse has been recognized as an important animal model of human SLE. The Th1-prone phenotype of BWF1 mice has been shown to contribute to the development of the lupus. However, the molecular basis for Th1 skewing in BWF1 mice has not been clarified. We noticed that IL-6, IL-12 and other proinflammatory cytokines as well as IκB-ζ induction were higher in mature bone marrow-derived dendritic cells (BMDCs) from NZB and BWF1 mice than those from NZW mice. The expression of an IFN-inducible gene Ifi202, a candidate gene for lupus, was almost undetectable in NZW BMDCs. Thus, we hypothesized that Ifi202 is involved in elevated IL-12 production from BWF1 BMDCs. Overexpression of Ifi202 enhanced the LPS-induced IκB-ζ, IL-12p40 and NF-κB promoter activities, while anti-sense (AS) RNA against Ifi202 strongly suppressed them in a monocytic cell line, RAW 264.7. Furthermore, overexpression of Ifi202 enhanced LPS-induced IL-12p40 and IκB-ζ mRNA induction while Ifi202 AS RNA suppressed these in RAW 264.7 cells. In addition, forced expression of Ifi202 enhanced IL-12p40 mRNA induction in NZW BMDCs. Thus, Ifi202 is an important NF-κB activator in DCs and involved in IL-12 production, which may account for a Th1-prone phenotype of BWF1 mice.

Introduction

Systemic lupus erythematosus (SLE) is considered to be the prototypic systemic autoimmune disease. The common denominator among SLE patients is IgG autoantibody production, and the hallmark of this disease is elevated serum levels of anti-nuclear antibodies (1). SLE is considered to be a complex of genetic trait with contributions from MHC genes and multiple non-MHC genes. Hybrids of New Zealand black (NZB) and New Zealand white (NZW) mice (BWF1) develop a severe immune complex-mediated glomerulonephritis associated with high serum levels of IgG anti-nuclear autoantibodies, and these mice are considered to be an excellent model for human SLE (2–5). Since neither NZB nor NZW mice develop severe lupus-like renal disease, genes from both parents must be involved in the full expression of F1 disease.

Contributions of several cytokines, such as IFN-γ, IFN-α/β, IL-6, IL-10 and IL-12, to development of lupus in the BWF1 mice have been reported (6–12). Administration of rIL-6 accelerated the disease and blockade of IL-6R inhibited the onset of kidney disease in BWF1 mice (10, 13). IL-6 affects a variety of biological functions, such as Ig production, the acute phase inflammatory response and plasmacytoma generation by regulating cell growth, differentiation and survival (14). In addition, high levels of IFNγ have been implicated in the disease progression in BWF1 mice because IFNγ-treated animals have accelerated development of a fatal immune complex glomerulonephritis, while administration of mAbs specific for IFNγ resulted in significant remission (7). These evidences suggest that a Th1/Th2 balance, especially the IFNγ levels, is critical for the development of autoimmune diseases, but the molecular basis for the Th1-prone phenotype of BWF1 mice has not been clarified.

An IFN-inducible gene, Ifi202 (encoding the protein Ifi202), has been identified as a susceptible gene for lupus...
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(15). Ifi202 is a member of IFN-inducible p200 family of proteins. Generation of B6.Nba2 mice congenic for the Nba2 interval, which contains NZB allele of the Ifi202 gene on the C57BL/6 background, has identified Ifi202 as a major candidate gene for lupus susceptibility (15). But the molecular mechanisms by which increased levels of Ifi202 enhance the development of autoimmunity are currently unknown.

Dendritic cells (DCs) include a heterogeneous family of professional antigen-presenting cells involved in the initiation of immunity and in immunological tolerance. Ishikawa et al. (16) found that CD11b+CD11c+ cells were markedly increased in the thymus, spleen and peripheral blood in aged BWF1 mice. DCs in the thymus produce high levels of B lymphocyte chemoattractant (BLC/CXCL13) and recruit B cells into the thymus, which has been shown to be linked to breaking immune tolerance in the thymus (17). We have also reported that SOCS1-deficient mice developed SLE-like autoimmune diseases and that DCs and B cells were accumulated in the thymus. SOCS1-deficient DCs induce stronger T,1 responses, including higher IFNγ production from T cells (18, 19).

We suspected that DCs in BWF1 mice might play a critical role in the increased production of proinflammatory cytokines and the induction of enhanced Th1-type responses as SOCS1-deficient DCs. IL-6, IL-12 and other proinflammatory cytokine levels were higher in mature bone marrow-derived dendritic cells (BMDCs) from NZB and BWF1 mice than from NZW mice. Consistent with previous findings, Ifi202 was rapidly induced in NZB- and BWF1-BMDCs but not in NZW-BMDCs in response to LPS. Therefore, we hypothesized that Ifi202 protein positively regulates proinflammatory gene expression. Overexpression of Ifi202 enhanced the LPS-induced IL-12p40 and IFN-γ promoter activities, while knockdown of Ifi202 reduced them in a monocytic cell line RAW 264.7 cells. Ifi202 also enhanced NF-κB promoter activity, suggesting that Ifi202 protein directly enhances transcriptional activity of the NF-κB in monocytes DCs. Taken together, we propose that Ifi202 positively regulates production of IL-12 from DCs, which contributes to the progression of lupus in BWF1 mice.

Methods

Mice

NZB, BWF1, NZW and C57BL/6 mice, originally obtained from the Nippon SLC Corporation (Shizuoka, Japan), were maintained in our animal facility at Kyushu University. Female mice aged 2 months were used.

Cell culture

RAW 264.7 cells were maintained in DMEM (Sigma) containing 10% FBS, antibiotics and nonessential amino acids (GIBCO). BMDCs were generated from bone marrow according to the method described by Inaba et al. (20) with modifications. Briefly, bone marrow samples from the femurs and tibiae of mice were cultured in RPMI 1640 with 10% FBS, antibiotics and 10 mM HEPES (Sigma) containing 20 ng ml⁻¹ granulocyte macrophage colony-stimulating factor (GM-CSF) (Pepro Tech) or the culture supernatant from a J558L cell line transfected with the murine GM-CSF cDNA for 7 days with replenishment of the medium every other day.

Plasmids

cDNA fragment encoding Ifi202 was obtained from RAW 264.7 cell RNA by reverse transcription (RT)-PCR and cloned into pCMV14 (Sigma) and pRcCMV (Invitrogen) in the appropriate (sense) and inverted (anti-sense (AS)) orientation, respectively (21). The IFN-γ promoter reporter plasmid was described previously (22). IL-12p40 promoter region (about 700 bp) was isolated by genomic PCR using primers 5’-GAGCTCAATGTTAGCTTATCCAAAAAGTGG-3’ and 5’-CCGGGATCCGGTACCGTAGAGCTTATCCAAAAAGTGG-3’ and sub-cloned into the pGVB-luciferase reporter vector.

Luciferase reporter assay

Reporter plasmids and control lacZ plasmid were transiently co-transfected into RAW 264.7 cells with either control, Ifi202, or AS-Ifi202 expression vectors using FuGENE HD transfection reagent (Roche). After stimulation with 10 ng ml⁻¹ LPS for 6 h, luciferase activities and β-galactosidase were measured. Relative luciferase activities normalized with lacZ activity are shown.

Retroviral constructs and transfection to RAW 264.7 cells

The sense Ifi202 was sub-cloned into pGCDΔNSamI/E retroviral vector, and the transfection was performed as described previously (24). RAW 264.7 cells were retrovirally transduced with the virus supernatants. GFP-positive cells were sorted by a cell sorter, FACSaria (BD Biosciences), and used for the assays.

Transfection into RAW 264.7 cells and BMDCs by electroporation

The expression vectors for control empty or ASIfi202 were co-transfected with pEGFP vector into RAW 264.7 cells by MicroPorator (Digital Bio Technology) according to the manufacturer’s instructions. GFP-positive cells were sorted by a cell sorter and immediately used for gene expression analysis with RT-PCR. For NZW-BMDCs, 1.8 × 10⁷ cells were mixed with 18 µg of empty or Ifi202/pCMV14 plasmid together with 18 µg of GFP plasmid, then pulsed twice at 2000 V for 10 ms. After 6 h incubation in the presence of GM-CSF, GFP-positive cells were sorted by FACSaria, and then collected cells were stimulated with 100 ng ml⁻¹ LPS for 3 h. Transfection efficiency was >60% judged by GFP fluorescence.

Western blot

Total cells were lysed in lysis buffer A [20 mM HEPES (pH 7.3), 150 mM NaCl, 0.5% Nonidet P-40, 50 mM NaF, 10 mM sodium pyrophosphate, 1 mM dithiothreitol, 1 mM sodium vanadate, 1 mM phenylmethylsulphonyl fluoride and 1% aprotinin]. The total cell extracts were resolved by SDS-PAGE, and the proteins were detected by immunoblotting as described (25, 26).

RNA isolation and gene expression analysis

Total cellular RNA was isolated from RAW 264.7 cells and BMDCs using TRIzol Reagent (Invitrogen) according to the manufacturer’s instructions. RT-PCR was carried out using the one-step RT-PCR kit (Applied Biosystems) according to
the manufacturer’s instructions. The following primers were used: Ifi202 (exon)(F: cca acc gta act taa ggt cat c, R: cta gga gga cac ctc tgg tcg gc), Ifi202 (3’UTR)(F: ggt atg tat ggg tct ctt gc, R: gga aat ttc cac cat tga att ggg gt), tumor necrosis (TNF)α (F: tga act tgg gta tcc gtc, R: acc ctt gcc cct tga aga gga c), IL-12p35 (F: gac cac cag tga cat ggt gaa gac, R: gga gct cag ata gcc cat ca), IL-12p40 (F: gta gaa gct gtc gag tgg gcc gct ac, R: act cct tct gtc act cca gca), G3PDH (F: acc aca ggt gtc cat gcc atc ac, R: tcc acc acc ctt tgt ctg ta). The PCR products were visualized in ethidium-bromide-stained agarose gels.

Antibodies and reagents

The anti-ERK2 (C-14), anti-IkBα (C-21), anti-Stat1 (E-23) and anti-Stat3 (C-20) antibodies were purchased from Santa Cruz Biotechnology. The anti-phospho-ERK1/2 (9106), anti-phospho-JNK (9255), anti-phospho-p38 (9216), anti-JNK (9252), anti-phospho-p38 (9212), anti-phospho IκBα (9246), anti-phospho Akt (2087) and anti-Akt (9272) antibodies were obtained from Cell signaling. The LPS (Escherichia coli serotype 055:B5) was from Sigma Chemical.

High-density oligonucleotide microarray analysis

Total RNA was extracted by standard methods using a TRizol reagent. cRNA preparation and microarray hybridization were carried out according to the instructions from the supplier (Affymetrix) using Genechip HG-U95Av2. Scanned output files were analyzed using the probe level analysis package, Microarray Suite MAS 5.0 (Affymetrix).

Statistical analysis

For statistical analysis, we performed the Student’s t test, and a 95% confidence limit was taken to be significant, defined as P < 0.05.

Results

Higher IL-12 production from NZB- and BWF1-BMDCs than from NZW-BMDCs

Previous observations suggest a T1,1-prone condition of BWF1 mice (6, 7, 27). To define the molecular basis for this, we first examined the phenotypes of matured BMDCs from New Zealand mice. Bone marrow cells were prepared from mice and cultured in the presence of GM-CSF for 6 days, and maturation was induced by incubation with LPS for 24 h. The number, morphology and CD11c expression of BMDCs from BWF1 mice did not differ from those from parental mice (data not shown). In response to LPS, the expressions of CD40, CD80 and CD86 on BMDCs were equally enhanced among these three strains (data not shown).

To identify the genes that would be involved in preferential T1,1 induction by BWF1-BMDCs, we compared LPS-inducible genes in BWF1-BMDCs with those in NZW-BMDCs using microarray analysis. Among LPS-inducible genes, which were >3 fold higher after 2 h LPS stimulation in BWF1-BMDCs than without LPS stimulation, several cytokines, such as TNFα, IFNβ and some chemokines were higher in BWF1-BMDCs than in NZW-BMDCs (Table 1). Attention was given to IL-12 since it is the most important cytokine secreted from DCs that induces T1,1 differentiation. We confirmed IL-12 levels by ELISA. Consistent with the result of microarray analysis, BWF1-BMDCs secrete higher levels of IL-12p70 than NZW-BMDCs in response to LPS (Fig. 1A). Interestingly, NZB-BMDCs secreted more IL-12p70 than BWF1-BMDCs, suggesting that the IL-12 levels are regulated by genes inherited in the NZB strain. The TNFα and IL-6 levels were also higher in the order of NZB-, BWF1- and NZW-BMDCs, but the differences were not as strong as with IL-12. The IL-10 levels were also higher in NZB- and BWF1-BMDCs than in NZW-BMDCs.

Ifi202 gene expression of NZB-, BWF1- and NZW-BMDCs

It has been shown that Ifi202 is the lupus susceptibility gene in the NZB strain (15), but the molecular function of Ifi202 has not been clarified. The Ifi202 gene encodes a 52 kDa protein p202, which is an inducible transcriptional modulator (28–30) belonging to the p200 protein family. The ability of p202 to modulate the transcription of genes depends on its ability to bind and inhibit the transcriptional activity of factors, such as E2Fs, NF-κB, c-Myc, AP-1 and p53 (21, 30–33).

As reported, our microarray and RT-PCR analysis also confirmed the absence of expression of Ifi202 in NZW-BMDCs (Table 1 and Fig. 1B) (15). In contrast, the expression levels of Ifi202 were highly induced by LPS in NZB-BMDCs and those in BWF1-BMDCs were intermediate between those in NZB- and NZW-BMDCs. The expression levels of Ifi202 were well correlated to the levels of the proinflammatory cytokines, such as IL-6 and IL-12p40 subunits, especially at late stage of induction (Fig. 1B). Thus, we suspected that Ifi202 is the regulator of IL-6 and IL-12 expression. In addition, we examined the expression of IκB-ζ, which has been implicated in the expression of IL-6 and IL-12p40 (34) because it was also low in NZW-BMDCs in microarray data. As shown in Fig. 1(C), IκB-ζ was induced very rapidly in NZB-BMDCs within 1 h of LPS stimulation and lasted for up to 12 h. In contrast, IκB-ζ was expressed weakly in NZW-BMDCs and decreased thereafter. BMDCs from BWF1 mice were intermediate between them. Thus, IκB-ζ expression seems to be regulated by a factor present in the NZB strain.

TLR-signal transduction of BMDCs from NZB, BWF1 and NZW mice

To examine the mechanisms by which NZB- and BWF1-BMDCs produce higher levels of IL-12 than from NZW-BMDCs, we then compared the LPS-induced intracellular signaling pathways. LPS signaling regulates gene transcription via NF-κB, AP-1 and other transcriptional factors through the activation of p42/44 ERK, JNK and the p38 Mitogen activated protein kinase (MAPK) family as well as the IκB kinase (IKK) complexes (35). STAT1 and STAT3 were also activated by LPS, but this activation is a late event, probably
due to autocrine activation by cytokines including IFNγ, IL-6 and IL-10. As shown in Fig. 2(A), no significant differences in STAT1 and STAT3 activation were observed among three strains. The phosphorylation of IkBα and degradation of IkBα were not different, suggesting that IKK activation was similar among the three strains. The phosphorylation levels of Jun kinase (JNK) and p38 were not altered either. We noticed the presence of a consistently higher activation of ERK and reduced Akt phosphorylation in NZW-BMDCs in repeated experiments. PI3K and ERK pathways have been shown to be involved in the regulation of IL-12 induction (36, 37).

To test the possibility that Ifi202 is such a regulator of IkB-ζ, we examined the effects of forced expression of Ifi202 on IkB-ζ levels. We used a monocytic cell line RAW 264.7 cells because gene transfer efficiency in BMDCs was too low to detect reporter activity and mRNA levels. To analyze the transcriptional regulation of the IkB-ζ gene, we used reporter plasmids containing mouse IkB-ζ promoter fused to a luciferase reporter gene (22). Overexpression of Ifi202 enhanced the IkB-ζ promoter-reporter activity in a dose-dependent manner (Fig. 3A). Furthermore, the similar effect of Ifi202 was observed in the experiments of IL-12p40 promoter-reporter activity (Fig. 3A). It has been reported that IkB-ζ- and IL-12p40 promoter activations are dependent on NF-kB and type I IFN, respectively in BMDCs (22, 23). Thus, we examined the effect of Ifi202 on NF-kB transcriptional activity. As shown in Fig. 3(A), Ifi202 enhanced LPS-mediated NF-kB transcriptional activity, but not IFNγ-mediated STAT1 transcriptional activity (Fig. 3A). Then to validate the effect of Ifi202, we stably expressed Ifi202 in RAW 264.7 cells and examined the LPS-induced gene expression by RT-PCR (Fig. 3C). TNFα levels were constantly high probably because we used retrovirus to introduce Ifi202 gene. Overexpression of Ifi202 resulted in hyperinduction of IkB-ζ and slightly higher induction of IL-12p40 mRNAs in response to LPS stimulation (Fig. 3C). Then we transiently expressed Ifi202 in NZW-BMDCs and examined the LPS-induced IL-12p40 and TNFα expression (Fig. 3D). Overexpression of Ifi202 caused the hyperinduction.

**Ifi202 enhanced the LPS-induced IkB-ζ and IL-12p40 expression**

To test the possibility that Ifi202 is such a regulator of IkB-ζ, we examined the effects of forced expression of Ifi202 on IkB-ζ levels. We used a monocytic cell line RAW 264.7 cells because gene transfer efficiency in BMDCs was too low to detect reporter activity and mRNA levels. To analyze the transcriptional regulation of the IkB-ζ gene, we used reporter plasmids containing mouse IkB-ζ promoter fused to a luciferase reporter gene (22). Overexpression of Ifi202 enhanced the IkB-ζ promoter-reporter activity in a dose-dependent manner (Fig. 3A). Furthermore, the similar effect of Ifi202 was observed in the experiments of IL-12p40 promoter-reporter activity (Fig. 3A). It has been reported that IkB-ζ- and IL-12p40 promoter activations are dependent on NF-kB and type I IFN, respectively in BMDCs (22, 23). Thus, we examined the effect of Ifi202 on NF-kB transcriptional activity. As shown in Fig. 3(A), Ifi202 enhanced LPS-mediated NF-kB transcriptional activity, but not IFNγ-mediated STAT1 transcriptional activity (Fig. 3A). Then to validate the effect of Ifi202, we stably expressed Ifi202 in RAW 264.7 cells and examined the LPS-induced gene expression by RT-PCR (Fig. 3C). TNFα levels were constantly high probably because we used retrovirus to introduce Ifi202 gene. Overexpression of Ifi202 resulted in hyperinduction of IkB-ζ and slightly higher induction of IL-12p40 mRNAs in response to LPS stimulation (Fig. 3C). Then we transiently expressed Ifi202 in NZW-BMDCs and examined the LPS-induced IL-12p40 and TNFα expression (Fig. 3D). Overexpression of Ifi202 caused the hyperinduction.

**Table 1.** List of LPS-inducible genes whose expression levels were more than two times higher in BWF1-BMDC than NZW-BMDC.

<table>
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<th>ID no.</th>
<th>Gene name</th>
<th>NZW</th>
<th>BWF1</th>
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<td>Y15163</td>
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<td>25.4</td>
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<td>Mouse strain non-obese diabetic tumor necrosis factor alpha gene</td>
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<td>2889</td>
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Total RNA was extracted by standard methods using a TRIzol reagent. cRNA preparation and microarray hybridization were carried out according to the instructions from the supplier (Affymetrix) using Genechip HG-U95Av2. Scanned output files were analyzed using the probe level analysis package, Microarray Suite MAS 5.0 (Affymetrix).
of IL-12p40 mRNAs in NZW-BMDCs in response to LPS stimulation, while TNFα levels were not strongly affected. These data suggest that the expression of IκB-ζ and IL-12p40 is positively regulated by Iffi202.

Suppression of Iffi202 reduced IκB-ζ and IL-12 expression
To verify the effect of Iffi202, we knocked down the expression of Iffi202 using ASIffi202 (32) (Fig. 4). ASIffi202 expectedly suppressed the IκB-ζ and IL-12p40 as well as NF-κB reporter activities (Fig. 4A). Overexpression of ASIffi202 reduced the TRAF6 and p65-mediated activation of NF-κB transcriptional activities (Fig. 4B). Furthermore, knockdown of Iffi202 expression down-regulated the IκB-ζ mRNA expression in RAW 264.7 cells (Fig. 4C). IL-6 and IL-12p40 mRNA levels were also suppressed by ASIffi202. Taken together, these observations indicate that Iffi202 positively regulates LPS-induced expression of IκB-ζ, and IL-12p40 expression, through the enhanced NF-κB transcriptional activities.

Discussion
Impaired T\textsubscript{h}1/T\textsubscript{h}2 balance, especially increased IFNγ levels, in BWF1 mice has been shown to be critical for the development of autoimmune diseases (6). However, the molecular basis for the T\textsubscript{h}1-prone phenotype of BWF1 mice has not been clarified. In this study, we demonstrated that DCs from NZB and BWF1 mice has a higher potential to produce IL-12, which can partly account for a T\textsubscript{h}1-prone phenotype of BWF1 mice. This enhanced IL-12 production is accompanied with up-regulated expression of IκB-ζ mRNA in response to LPS stimulation. Another IκB-ζ-dependent cytokine IL-6 was also higher in NZB- and BWF1-BMDCs. We propose that Iffi202 is deeply involved in these phenotypes.

An IFN-inducible gene, Iffi202, has been identified as a susceptible gene for lupus (15). However, molecular mechanisms by which increased levels of Iffi202 enhance the development of autoimmunity are currently unknown.
Fig. 2. TLR signaling and the effect of kinase inhibitors on IL-12 production. (A) LPS signaling in BMDCs from New Zealand mice. BMDCs from NZB, BWF1 and NZW mice were stimulated with LPS (10 ng ml$^{-1}$) for indicated periods. Whole-cell lysates were prepared and subjected to western blot analysis using antibodies specific for the indicated molecules. (B) IL-12p70 production by BMDCs in response to LPS stimulation in the presence of kinase inhibitors. BMDCs were cultured with 10 ng ml$^{-1}$ LPS for 24 h in the presence of the indicated inhibitors. The inset shows the phosphorylation of ERK and Akt to confirm the effect of inhibitors. The IL-12p70 levels in the supernatants were determined by ELISA. (C) Normalized data of IL-12p70 levels in BWF1- and NZW-BMDCs to that in NZB-BMDCs.

Fig. 3. Effect of forced expression of Ifi202 in a monocytic cell line RAW 264.7 cells. (A and B) RAW 264.7 cells were transfected with the indicated reporter plasmid and increasing amounts of an expressing vector for Ifi202 together with control lacZ plasmid. After 36 h, cells were stimulated with 10 ng ml$^{-1}$ LPS for 6 h (A) or without stimulation (B), and then luciferase activity was measured and normalized based on β-galactosidase activity. (C) GFP-positive RAW 264.7 cells infected with either control or Ifi202 retrovirus vectors were FACS sorted and stimulated with LPS (100 ng ml$^{-1}$) for the indicated periods. The levels of mRNA transcripts for indicated genes were analyzed by RT-PCR. (D) NZW-BMDCs cells (1.8 × 10$^7$) were transfected with an expressing vector for Ifi202 together with control GFP plasmid. After 6 h, GFP-positive cells were sorted and then stimulated with 100 ng ml$^{-1}$ LPS for 3 h. The levels of mRNA transcripts for indicated genes were analyzed by RT-PCR.
indicated genes were analyzed by RT-PCR.

During this period, the levels of mRNA transcripts for Ifi202 activity were measured and normalized based on β-actin expression. (C) Expression vectors for control empty or AS Ifi202 were introduced into RAW 264.7 cells by electroporation and GFP-positive cells were sorted. The cells were stimulated with LPS (100 ng/ml) for 6 h (A) or without stimulation (B), and then luciferase activity was measured and normalized based on β-galactosidase activity. (C) Expression vectors for control empty or AS Ifi202 were introduced into RAW 264.7 cells by electroporation and GFP-positive cells were sorted. The cells were stimulated with LPS (100 ng/ml) for the indicated periods, and then the levels of mRNA transcripts for Ifi202 activity were measured and normalized based on β-actin expression. Therefore, it is unlikely that IL-4 is involved in the suppression of IL-12 expression in NZW-BMDCs.

In conclusion, we found a novel function of Ifi202, which can explain a T_{h}1-prone phenotype of BWF1 mice. This study also supports that Ifi202 could be a therapeutic target in human SLE.

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Abbreviations

AS anti-sense

BMDC bone marrow-derived dendritic cell

DC dendritic cell

GM-CSF granulocyte macrophage colony-stimulating factor

NZB New Zealand black

NZW New Zealand white

RT reverse transcription

SLE systemic lupus erythematosus

TNF tumor necrosis

References


Ifi202 positively regulates NF-κB in DCs


