Profiles of the mRNA Expression by Macrophages Infected with *Mycobacterium leprae* and *Mycobacterium avium* Complex

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Profiles of cytokine (CK) expression in the hosts infected with *Mycobacterium leprae* have been actively investigated. In particular, Modlin and his colleagues demonstrated that mRNA encoding Th1 CKs, including IL-2, IFN-γ, and lymphotoxin were detected at higher levels in tuberculous lesions, but virtually absent in lesions of lepromatous leprosy patients. In contrast, Th2 CKs, such as IL-4, IL-5, and IL-10 mRNAs, were present at higher levels in lepromatous than in tuberculoid lesions (15, 20, 30). IL-12 produced by macrophages (Mφs) infected with *M. leprae* facilitates a Th1 response, which is closely associated with cell-mediated immunity against *M. leprae* antigens, acts by activating NK cells to release IFN-γ, which in turn activates Th1 cells in collaboration with IL-12 (10, 26, 30). In the case of the host immune response against *M. leprae*, IL-12 and IL-18 produced by *M. leprae*-infected Mφs display collaborating effects in eliciting a Th1 response (40, 41). Moreover, IL-7 and IL-15 produced by infected Mφs also facilitate T-cell activation and expansion in response to *M. leprae* antigens (11, 25). On the other hand, IL-10 produced by Mφs and IL-4 produced by Th2 cells, NK1.1+ T cells, or CD19+/B220+B cells suppress the Th1 response, but facilitate the Th2 response against *M. leprae* antigens (16, 24). Moreover, Mφ-derived IL-10 and transforming growth factor-β (TGF-β) are known to down-regulate Mφ antimycobacterial activity (7, 8). It is, thus, conceivable that Mφs determine the host immune response against *M. leprae* infection, not only by acting as antigen processing cells or bactericidal phagocytic effector cells, but also by producing various kinds of immunoregulatory CKs.

*Mycobacterium avium* complex (MAC) has been reported to resemble *M. leprae* both taxonomically and biologically as follows. First, MAC and *M. leprae* are highly related and form a phylogenically tight cluster apart from other mycobacterial species, including slow growers and rapid growers (27). Second, although most *M. leprae* antigens have close homologs in the *Mycobacterium tuberculosis* complex (2), the homolog of the 35-kDa antigen of *M. leprae* is found in MAC only (3). Third, electron microscopic studies showed that, after the entry of MAC, as well as *M. leprae* into host cells, including Mφs and epithelial cells, the electron transparent zone (ETZ) consisting of bacterial mycosides starts to form and surrounds these bacilli inside phagosomes (1, 2). The presence of an ETZ is considered to play a crucial role in bacterial resistance to the action of bactericidal effectors provided in phagolysosome vesicles (18, 30). The presence of an ETZ is considered to play a crucial role in bacterial resistance to the action of bactericidal effectors provided in phagolysosome vesicles (18, 30). The presence of an ETZ is considered to play a crucial role in bacterial resistance to the action of bactericidal effectors provided in phagolysosome vesicles (18, 30). The presence of an ETZ is considered to play a crucial role in bacterial resistance to the action of bactericidal effectors provided in phagolysosome vesicles (18, 30). The presence of an ETZ is considered to play a crucial role in bacterial resistance to the action of bactericidal effectors provided in phagolysosome vesicles (18, 30). The presence of an ETZ is considered to play a crucial role in bacterial resistance to the action of bactericidal effectors provided in phagolysosome vesicles (18, 30).

These situations encouraged us to investigate profiles of the interaction of *M. leprae* and MAC with host Mφs in terms of CK expression by Mφs. In the present study,
we have found some differential modes of CK mRNA expression by Mφs infected with *M. leprae* or MAC.

**MATERIALS AND METHODS**

**Microorganisms.** *M. leprae* Thai-53 strain was harvested from infected footpads of BALB/c nude mice, and bacterial suspensions were prepared as follows (23). The infected footpads were homogenized in Hanks’ balanced salt solution (HBSS) containing 5% fetal bovine serum (FBS) and centrifuged at 200 x g for 5 min. The upper layer was saved and the bacilli were collected by recentrifugation at 1500 x g for 15 min. The bacterial suspension was again centrifuged at 200 x g for 5 min, to remove bacterial clusters and the upper layer (about 90% volume) was harvested. The resultant bacterial suspension was then treated with 0.1 N NaOH for 1 min, neutralized with 0.1 N HCl, centrifuged at 1500 x g for 15 min. The resultant sediment was suspended into 10 ml of RPMI 1640 medium. pronase-P was added at 0.5 μg/ml, incubated at 37°C for 2 hr, and the pronase-P reaction was stopped by the addition of bovine serum albumin (BSA) at 0.7%. After washing twice with phosphate buffered saline (pH 7.2) containing 0.1% BSA, the resultant bacterial pellet was suspended into RPMI 1640 medium supplemented with 10% FBS. The viability of *M. leprae* organisms before and after pronase-P treatment was determined by the fluorescein diacetate/ethidium bromide (FDA/EB) staining according to the method of Tsukiyama, et al. (32). The percentage of green-stained viable cells in the *M. leprae* preparations before and after pronase-P treatment was estimated as 87.5 ± 1.2% and 86.2 ± 1.4% (n = 3). This indicates that pronase-P treatment did not cause severe damage in the cell surface of the *M. leprae* organisms.

Virulent SmT variant of MAC N-260 strain, showing smooth, transparent and irregularly-shaped colonies and avirulent SmD variant, showing smooth, opaque, and dome-shaped colonies (2) were used. MAC N-260 strain was identified as *M. intracellulare* by a DNA probe test, and determined to belong to serovar 16 by an agglutination test. MAC organisms were grown in Middlebrook 7H9 medium and bacterial suspensions prepared with 0.1% BSA-PBS were frozen at -80°C until use. Before use, the bacterial suspension was centrifuged at 200 x g for 5 min to remove bacterial clumps.

**Expression of cytokine mRNA by *M. leprae*- or MAC-infected Mφs.** Mφ monolayer cultures prepared by seeding 5 x 10⁶ peritoneal cells of 8- to 12-week-old male BALB/c mice on 60 mm culture dishes were incubated in 5 ml of 10% FBS-RPMI 1640 medium at 37°C for 48 hr in a CO₂ incubator (5% CO₂-95% humidified air). After washing with Hanks’ balanced salt solution (HBSS) containing 2% FBS, the Mφs were cultured in 5 ml of the medium containing 1 x 10⁹ bacilli/ml (CFU/ml for MAC) of test organisms at 37°C in a CO₂ incubator for up to 24 hr.

At intervals, cultured Mφs were harvested and reverse transcription (RT)-PCR analysis of the mRNAs expression of test CKs (IL-12 p40, TNF-α, IL-10, TGFB-β), inducible nitric oxide synthase (iNOS), and ICAM-1 in the Mφs was performed as described previously (21) with slight modifications. Total RNA was isolated from the Mφ samples using the ISOGEN kit (Nippon Gene Co., Toyama, Japan). After deoxyribonucleoside-I (DNase-I) (GIBCO BRL Co., Rockville, Maryland, U.S.A.) treatment (1 unit DNase-I/μg of RNA sample) at room temperature for 15 min, the resultant RNA samples were reverse transcribed to the first chain of cDNA using oligo dT primers (GIBCO) and 200 units Superscript II reverse transcriptase (GIBCO) with the standard reaction mixture (20 µl): 1 x reverse transcriptase (RT) buffer (pH 8.3), 1 mM each dNTP including dATP, dCTP, dGTP and dTTP (GIBCO), and 2.0 units of ribonuclease inhibitor (GIBCO). After 1 hr reaction at 42°C and subsequent heating at 72°C for 15 min, 1 μl of aliquots of resultant cDNA were amplified specifically by PCR in the standard reaction mixture (50 µl) containing 1 x PCR buffer (pH 8.3), 0.2 mM of each dNTP, 1 unit of Taq polymerase (Takara Biomedicals Co., Tokyo, Japan), and 20 pmol of sense and antisense primers for test proteins (synthesized by Greiner Labortechnik Co., Tokyo, Japan) as follows (sense/antisense): IL-12 p40 (CGT GCTCATGGCTGGTGCAAAG/CTTCATCTGCAAGTTCTTG GGC): TNF-α (AG CCCACGTCGTAGCAAACCACCAA/AC...
ACCCATTCCTTC ACAGAGCAAT); IL-10 (TGACTGGCATGAGGATC AGCAG/ATCCTGAGGGTCTTCAGCTT); TGF-β1 (AGCCTTGATACCAACTATTGCTTCA GCTCCACAG/AGGGGCGGGCGGGCGGGGCTTCAGCTGC); iNOS (CCTGC TCACCTAGCCA/AG/AGTCATGGAGGCTGCT); and ICAM-1 (CAGGAGAGCACAAACAGCAGTG/AGAGCGGCAGAGCAAAAGAAGC). Reactions were carried out in a DNA Thermal Cycler (ASTEC Corp., Fukuoka, Japan) for 25 cycles including denaturing at 94°C for 1 min, annealing at 58°C for 2 min, and extension at 72°C for 2 min for each cycle. PCR products were analyzed by electrophoresis on ethidium bromide-stained 2% agarose gels.

In some experiments, CK mRNA expression by Møs was measured by the ribonuclease (RNase) protection assay using Ribonuclease Protection Assay System (Pharmingen Co., San Diego, California, U.S.A.) according to the manufacturer’s instruction manual. In this study, mCK-2b and mCK-3 mouse cytokine multiprobe template sets were used for measurement of cytokine mRNAs as follows: mCK-2b: IL-10 and IL-12 p40 mRNAs; mCK-3: TNF-α and TGF-β mRNAs.

RESULTS

Expression of CK mRNAs by *M. leprae*-infected Møs. The time-course of the expression of IL-12, a proinflammatory CK TNF-α, and immunosuppressive CKs (IL-10, TGF-β) in Møs stimulated with *M. leprae* infection was examined by the RT-PCR assay. Fig. 1 shows the profiles of the mRNA expression of these CKs by Møs during chase cultivation after *M. leprae* infection. IL-12 p40 mRNA expression was not observed for Møs at least during 24-hr cultivation after infection. Second, TNF-α mRNA expression was remarkably increased at 3 hr after infection, and thereafter, gradually declined until 24 hr. The intensities of TNF-α mRNA expression of *M. leprae*-infected Møs were nearly identical. Notably, intense expression was still seen for the TNF-α mRNA at 24 hr.

The IFN-γ (500 units/ml) treatment yielded no obvious change in the modes of CK mRNA expression of *M. leprae*-infected Møs (unpublished observation).

Expression of CK mRNAs by MAC-infected Møs. Fig. 2 shows Mø mRNA expression profiles measured by the RT-PCR assay of IL-12, TNF-α, IL-10, and TGF-β after infection with MAC organisms with different levels of virulence, a virulent SmT variant and an avirulent SmD variant. The mRNA expression of IL-12 p40 was increased in Møs infected with MAC SmT variant as well as in those infected with MAC SmD variant at 3 hr after infection. The mRNA expression, thereafter, gradually decreased, and almost disappeared at 24 hr. Second, TNF-α mRNA expression was markedly increased at 2 hr after MAC SmT as well as MAC SmD infection, and, thereafter, gradually declined until 24 hr. The intensities of TNF-α mRNA expression of MAC SmT- and MAC SmD-infected Møs were nearly identical. Notably, intense expression was still seen for the TNF-α mRNA at 24 hr.
**Shimizu, et al.: mRNA Expression by Mφ**

**THE TABLE.** Expression of IL-12 p40, TNF-α, IL-10, and TGF-β mRNAs by Mφs infected with MAC N-260 or M. leprae alone or co-infected with both organisms.

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Time after infection (hr)</th>
<th>Relative intensity of mRNA expression of Mφs infected with:</th>
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<tr>
<td></td>
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<td>M. leprae</td>
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<tr>
<td>IL-12 p40</td>
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<tr>
<td></td>
<td>3</td>
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<td></td>
<td>24</td>
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<td>TNF-α</td>
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<td>0.58</td>
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<td></td>
<td>3</td>
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<td>IL-10</td>
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<td></td>
<td>48</td>
<td>0.12</td>
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</table>

*The relative intensity of each CK mRNA expression in terms of CK/L32 band ratios were estimated from the data indicated in Fig. 4.*

*Undetectable.*

mRNA even at 24 hr. Third, IL-10 mRNA expression was increased at 3 hr after MAC SmT and MAC SmD infection. The mRNA expression was retained at the same levels during 3 to 6 hr, and, thereafter, gradually declined until 24 hr. Notably, IL-10 mRNA expression during 3 to 6 hr was much stronger in MAC SmD-infected Mφs than in MAC SmT-infected Mφs. Fourth, TGF-β mRNA was constitutively expressed by uninfected Mφs. Both MAC SmT and MAC SmD infections caused a moderate increase in TGF-β mRNA expression at 3 hr, and the increased level of TGF-β mRNA expression was retained until 24 hr. In separate experiments, the increase in TGF-β mRNA expression lasted at least for 48 hr (data not shown). Similar levels of TGF-β mRNA expression were seen for Mφs infected with MAC SmT and those infected with MAC SmD. Notably, the IFN-γ (500 units/ml) treatment yielded no obvious change in the modes of CK mRNA expression of MAC N-260-infected Mφs (unpublished observation).

Expression of CK mRNA by Mφs co-infected with M. leprae and MAC. It has been reported that co-infection of MAC with M. leprae increases the pathogenicity of leprosy bacilli and facilitates the progression of the disease in vivo (14). Thus, it is of interest to examine the mode of CK mRNA expression by Mφs co-infected with M. leprae and MAC. For this purpose, we measured the expression of IL-12, TNF-α, IL-10 and TGF-β mRNAs by Mφs co-infected with both organisms by the RNase protection assay. As shown in Fig. 3 and The Table, Mφs co-infected with both organisms showed the mRNA expression of IL-12, TNF-α, and IL-10 in an intermediate mode for those of Mφs infected with either M. leprae or MAC alone. The levels of IL-12 and IL-10 mRNA expression seen in Mφs infected with M. leprae alone were decreased due to co-infection with MAC, while the opposite phenomenon was observed for TNF-α mRNA expression. On the other hand, the level of TGF-β mRNA expression was somewhat decreased in Mφs.
FIG. 2. Expression of IL-12 p40, TNF-α, IL-10, and TGF-β mRNAs by Møs infected with MAC SmT or SmD colonial variant. The other details are the same as those described in the legend of Fig. 1.

FIG. 3. Expression of IL-12 p40, TNF-α, IL-10, and TGF-β mRNAs by Møs infected with M. leprae or MAC alone or co-infected with both organisms. CK mRNA expression by Møs was measured by the RNase protection assay. The mRNA expression of L32, a housekeeping gene, was measured as the positive control of constitutive mRNA expression.
Expression of iNOS and ICAM-1 mRNA by M. leprae- and MAC-infected Møs. Fig. 4 shows Mø mRNA expression profiles of iNOS and an adhesion molecule ICAM-1 measured by the RT-PCR assay, when Møs were infected with either M. leprae or MAC. MAC infection caused a marked increase in the iNOS mRNA expression by Møs at 3 hr post infection, whereas M. leprae infection failed to show such an effect. The increase in iNOS mRNA expression in MAC-infected Møs lasted at least for 24 hr. Notably, MAC SmT-infected Møs expression stronger mRNA during 3 hr to 24 hr than did MAC SmD-infected Møs. Second, ICAM-1 mRNA was constitutively expressed by uninfected Møs. The mRNA expression of ICAM-1 was increased in Møs at 3 hr after infection with M. leprae, as well as MAC SmT or MAC SmD, and, thereafter, gradually decreased until 24 hr. Similar levels of ICAM-1 mRNA expression were noted for MAC SmT- and MAC SmD-infected Møs. These results on ICAM-1 mRNA expression are consistent with our previous findings concerning ICAM-1 expression in a protein level by M. leprae- and MAC-infected Møs (23, 24).

**DISCUSSION**

The present study revealed some differences in the profiles of Mø expression of CK and other protein genes between M. leprae- and MAC-infected Møs, as follows.

Although weak but significant increase in the IL-12 p40 mRNA expression was noted for MAC-infected Møs in the early-phase (3 hr) after infection, such a phenomenon was not observed for M. leprae-infected Møs. The latter finding is enigmatic, since the important role of Mø-derived IL-12 in the establishment of Th1 response in M. leprae-infected hosts has been well documented (14, 16, 26, 29). Moreover, in the case of M. leprae infection in mice without immunodeficiency, bacterial growth at the sites of infection is well controlled due to strong expression of anti-M. leprae cellular immunity that is mediated by host Th1 cells in humans (14, 16, 29) and in mice (12, 13). It appears that this strange situation may be attributable to our experimental conditions, particularly that we used marine resident peritoneal Møs. That is, efficient production of anti-M. leprae cellular immunity that is mediated by host Th1 cells in mice requires additional stimulatory signals other than phagocytosis of the organisms. It is likely that priming of Møs with certain stimulants, that is deficient in resident Møs, may be prerequisite for the gene expression of IL-12 induced by engulfment of M. leprae organisms. Concerning this point, further studies are needed.

In the case of MAC-infected Møs, the increased levels of IL-10 mRNA expression at 3 hr were maintained for long time periods after infection (at least until 24 hr). On the other hand, in the case of M. leprae-infected Møs, IL-10 mRNA expression, which was increased at 3 hr post infection, rapidly declined, reaching the undetectable level by 12 hr. However, M. leprae infection caused a...
considerably stable expression of TNF-α and ICAM-1 mRNA for 24 hr after infection. The instability of IL-10 mRNA expression in M. leprae-infected Mφs may be due to rapid down-regulation of the IL-10 mRNA transcription after 3 hr, rather than due to rapid decay of IL-10 mRNA itself.

It has been proposed that immunosuppressing cytokines, such as IL-10 and TGF-β, play important roles in the establishment of persistent infections by pathogenic mycobacteria, including MAC and M. leprae, either by down-regulating Mφ antimycobacterial functions (7, 8, 24, 25) or by attenuating mycobacteria-induced Mφ apoptosis coupled with the elimination of intramacrophage organisms (5-17). However, as indicated in Fig. 1, the mRNA expression of these cytokines was not stronger in Mφs infected with virulent MAC (SmT variant) than in those infected with avirulent MAC (SmD variant). Notably, IL-10 mRNA expression of MAC SmT-infected Mφs was conversely much weaker than that of MAC SmD-infected Mφs. These findings suggest the possibility that neither IL-10 nor TGF-β may play crucial roles in the mechanisms for bacterial escape from Mφ antimicrobial mechanisms. However, further in vivo studies are needed to reveal detailed profiles of the CK expression in granulomas of M. leprae-infected animals before such a conclusion is made.

Co-infection of MAC to M. leprae-infected mice is known to increase the pathogenicity of leprosy bacilli and facilitate the progression of the disease in mice (13). In the present study, it was found that Mφs co-infected with both M. leprae and MAC showed the CK mRNA expression (except for TGF-β) in an intermediate mode of those of Mφs infected with either M. leprae or MAC alone. This implies that the CK expression of M. leprae-infected Mφs may be modified by co-infection with MAC. Notably, the IL-12 mRNA expression of M. leprae-infected Mφs at 3 hr after infection was reduced to less than half of the original level (ca. 60% reduction) due to MAC co-infection. Moreover, Mφs co-infected with both of these organisms failed to show durable expression of IL-12 mRNA, as observed in the case of Mφs infected with MAC alone during 3 hr to 12 hr after infection. Thus, it is implicated that anti-M. leprae Th1 response of host animals may be hindered due to co-infection with MAC. This may account for the increase in the pathogenicity of M. leprae, when M. leprae-infected mice were further co-infected with MAC organisms (13).

Although MAC-infected Mφs displayed markedly increased iNOS mRNA expression during 3 hr to 24 hr after infection, such an increase in the iNOS gene expression was not noted for M. leprae-infected Mφs. Notably, reactive nitrogen intermediates, including nitric oxide radical produced by iNOS, play crucial roles in Mφ antimicrobial mechanisms against mycobacteria, including M. tuberculosis, MAC, and M. leprae (13, 9, 22, 26). It, thus, appears that the defect of M. leprae in inducing the iNOS expression by Mφs phagocytizing the organisms plays a favorable role for the organisms in escaping from Mφ antimicrobial mechanisms.

In summary, the present study revealed that there are noticeable differences in the modes of the mRNA expression of IL-12, IL-10, and iNOS in M. leprae-infected Mφs, as compared to MAC-infected Mφs. These findings may suggest differential interactions of M. leprae and MAC organisms with murine peritoneal Mφs in terms of the activation of signal transduction pathways for expression of some kinds of immunoregulatory cytokines and immunoprotective enzymes. Further investigations are needed to elucidate the precise meaning of these findings, in particular the studies using peritoneal Mφs, which are given priming with various stimulants before mycobacterial infection, or blood monocyte-derived Mφs. On this point, further studies are currently under way.

**SUMMARY**

In the present study, we examined profiles of the interaction of *Mycobacterium leprae* and *Mycobacterium avium* complex (MAC) with murine peritoneal macrophages (Mφs) in terms of up-regulation of Mφ expression of proinflammatory and immunosuppressing cytokines (CKs) after infection. First, the reverse transcription polymerase chain reaction (RT-PCR) assay revealed that both MAC and *M. leprae* infections up-regulated Mφ mRNA expression IL-12, TNF-α, IL-10, and transform-
ing growth factor-β (TGF-β), except that M. leprae-infected M0s showed no increase in the IL-12 mRNA expression. Second, the RT-PCR assay also showed some differences between M. leprae- and MAC-infected M0s with respect to the modes of IL-10 and inducible nitric oxide synthase (iNOS) mRNA expression. That is, MAC, but not M. leprae, infection caused a prolonged increase in the expression of IL-10 and iNOS mRNAs. Third, a ribonuclease protection assay revealed that M0s co-infected with MAC and M. leprae showed the IL-12, TNF-α and IL-10 mRNA expression in an intermediate mode of those of M0s infected with either M. leprae or MAC alone. This implies that the CK expression of M. leprae-infected M0s may be modified by co-infection with MAC. These findings may suggest differential interactions of M. leprae and MAC organisms with murine peritoneal M0s in terms of the activation of signal transduction pathways for expression of some kinds of immunoregulatory cytokines and immunoprotective enzymes.

RESUMEN
Se infectaron macrófagos peritoneales murinos con Mycobacterium leprae y Mycobacterium avium complejo (MAC), y se examinaron los perfiles de expresión de citocinas (CKs) proinflamatorias e inmunosupresoras consecuentes a la infección. Primero, la reacción en cadena de la transcriptasa reversa (RT-PCR) reveló que tanto la infección por MAC como por M. leprae, sobrecitaron la expresión de las mRNAs para IL-12, TNFα, IL-10, y el factor β del crecimiento transformante (TGF-β). También se observó, que a diferencia de los macrofagos infectados con MAC, los infectados con M. leprae no mostraron ningún incremento en la expresión del mRNA para IL-12. Segundo, el ensayo de RT-PCR mostró algunas diferencias entre los macrofagos infectados con M. leprae y MAC con respecto a los modos de expresión de los mRNAs para IL-10 e iNOS. Concretamente, la infección por MAC, pero no por M. leprae, causó un incremento prolongado en la expresión de los mRNAs para IL-10 e iNOS. Tercero, un ensayo de protección de la ribonuclease reveló que los macrofagos co-infectados con MAC y M. leprae, mostraron un patrón de expresión de los mRNAs para IL-12, TNFα, e IL-10, intermedio entre los patrones mostrados por los macrofagos infectados con los microorganismos por separado. Esto implica que la expresión de CKs por los macrofagos infectados con M. leprae, puede ser modificada por la co-infección con MAC. Los resultados sugieren que M. leprae y MAC interactúan de manera diferente con los macrofagos murinos y que esto se refleja en la activación de diferentes vías de señalización relacionadas con la síntesis de citocinas inmunorreguladoras e inmunoprotectoras.

RÉSUMÉ
Dans cette étude, nous avons examiné les profils d’expression des cytokines (CKs) proinflammatoires et inmunosuppressives issus de l’interaction de Mycobacterium leprae et du complexe de Mycobacterium avium (MAC) avec des macrophages murins (M0s), en terme d’augmentation de l’expression d’ARNm des CKs des macrophages après infection. Premièrement, l’étude de transcription inverse suivie de réaction de polymérase en chaîne (RT-PCR) a montré que l’infection par MAC et que par M. leprae augmentait l’expression de IL-12, TNF-α, IL-10 et du facteur de croissance induisant la transformation de type β (TGF-β), sauf que les macrophages infectés par M. leprae n’ont pas montré d’augmentation de l’expression de l’ARNm de l’IL-12. Deuxièmement, l’étude de RT-PCR a aussi montré quelques différences entre les M0s infectés par M. leprae et les M0s infectés par MAC en ce qui concerne les modes d’expression de l’ARNm de l’IL-10 et de la synthétase inductible du monoxyde d’azote (iNOS). Plus précisément, l’infection par MAC, mais pas M. leprae, provoque une augmentation prolongée des taux d’ARNm de l’IL-10 et la iNOS. Troisièmement, un essai de protection contre la digestion par les ribonucléases a révélé que les M0s co-infectés par MAC et M. leprae montraient un niveau intermédiaire d’expression des ARNm de l’IL-12, de TNF-α et de l’IL-10 par rapport à ceux observés dans les M0s infectés par M. leprae ou MAC seuls. Ceci implique que l’expression des CKs des M0s infectés par M. leprae peut être modifiée par une co-infection avec MAC. Ces données suggèrent une interaction différente de M. leprae et des microorganismes du MAC avec les M0s périnéonaux de souris au niveau des voies de transduction des signaux intracellulaires pour l’expression de certaines cytokines immunorégulatrices et d’enzymes induisant une immunoprotection.

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REFERENCES


