CD14 Impairs Host Defense against Gram-Negative Sepsis Caused by *Burkholderia pseudomallei* in Mice

W. Joost Wiersinga,1,2 Alex F. de Vos,1,2 Catharina W. Wieland,1,2 Masja Leendertse,1,2 Joris J. T. H. Roelofs,3 and Tom van der Poll1,2

Centers for 1Infection and Immunity Amsterdam and 2Experimental and Molecular Medicine and 3Department of Pathology, Academic Medical Center, Amsterdam, the Netherlands

**Background.** CD14 is a pattern-recognition receptor that can facilitate the presentation of bacterial components to either Toll-like receptor 2 (TLR2) or TLR4. We have recently shown that during melioidosis, a severe infection caused by the gram-negative bacterium *Burkholderia pseudomallei*, TLR2 but not TLR4 impacts the immune response of the intact host in vivo.

**Methods.** The function of CD14 in melioidosis was analyzed by means of in vitro and in vivo approaches, using wild-type (WT) and CD14 knockout (KO) mice.

**Results.** CD14-deficient macrophages and whole blood leukocytes released less tumor necrosis factor (TNF)–α on stimulation with *B. pseudomallei* or *B. pseudomallei* lipopolysaccharide in vitro, compared with WT cells. Strikingly, CD14 KO mice intranasally inoculated with *B. pseudomallei* demonstrated reduced lethality and significantly decreased bacterial outgrowth, compared with WT mice. Administration of recombinant soluble CD14 to CD14 KO mice partially reversed their phenotype to that of WT mice. Lastly, CD14 deficiency did not alter the capacity of macrophages or neutrophils to phagocytose or kill *B. pseudomallei*.

**Conclusion.** CD14 is crucially involved in the recognition of *B. pseudomallei* by innate immune cells but plays a remarkable detrimental role in the host response against *B. pseudomallei*. Inhibition of CD14 may be a novel treatment strategy in melioidosis.

Melioidosis, a recognized biological threat caused by the soil-dwelling gram-negative bacillus *Burkholderia pseudomallei*, is an important cause of community-acquired sepsis in Southeast Asia [1, 2]. Eradication of the organism following infection is difficult because of the slow fever-clearance time, the need for prolonged antibiotic therapy, and the high rate of relapse if therapy is not completed. The mortality of primary disease varies from 20% to 50% [6, 7]. Patients habitually present with pneumonia with bacterial dissemination to distant sites [3]. We previously developed a mouse model in which *B. pseudomallei* is administered via the airways, because this route may be more clinically relevant than the intraperitoneal route used in several previous studies [4–6].

CD14 and Toll-like receptors (TLRs) are key pattern-recognition receptors of the innate immune system. These receptors are known to collaborate in order to detect host invasion by pathogens, and they form the crucial link between innate and adaptive immunity [7–9]. The surface-anchored glycosylphosphatidylinositol CD14 acts as the ligand-binding portion of the lipopolysaccharide (LPS)–receptor complex, further consisting of TLR4 and the extracellular protein myeloid differentiation factor–2 (MD-2) [7, 10]. On monocyte activation, membrane-bound CD14 can be shed as a soluble form [11, 12]. Both membrane-bound and soluble CD14 (sCD14) can interact with a variety of bacterial ligands from gram-negative bacteria (e.g., LPS) and gram-positive bacteria (e.g., peptoglycan and lipoteichoic acid) [7, 12–15].

Numerous studies have established the essential role of CD14 in systemic and pulmonary inflammation induced by LPS [16–20]. Furthermore, CD14 has been found to play a key role in mounting an adequate innate...
immune response during gram-negative bacterial infection [21]. Indeed, in in vivo models of infection, inhibition or elimination of CD14 resulted in an increased outgrowth of different gram-negative bacterial species [20, 22–25]. We have previously documented a clear role for CD14 in improving the pulmonary clearance of clinically relevant gram-negative respiratory pathogens such as Haemophilus influenzae and Acinetobacter baumanii [24, 25]. In contrast, during murine pulmonary infection with the gram-positive pathogen Streptococcus pneumoniae, it was shown that CD14 facilitates the dissemination of this pathogen from the respiratory tract, as reflected by the fact that CD14 knockout (KO) mice—in contrast to wild-type (WT) control mice—did not become bacteremic after intranasal infection [26].

We recently characterized the expression and function of TLRs in septic melioidosis and found that, although both TLR2 and TLR4 contribute to the cellular responsiveness to B. pseudomallei in vitro, TLR2 detects the LPS of B. pseudomallei and only TLR2 has an impact on the immune response of the intact host in vivo [6]. In addition, increased CD14 expression was detected on circulating monocytes and granulocytes of patients with septic melioidosis [6]. In the present study, we aimed to characterize the function of CD14 in sepsis caused by B. pseudomallei, using our established mouse model of melioidosis [4–6].

MATERIALS AND METHODS

Mice. C57Bl/6 WT mice were purchased from Harlan-Sprague Dawley. CD14 KO mice, backcrossed 6 times to a C57Bl/6 genetic background, were obtained from Jackson Laboratories. All experiments involved animals matched by age (10–12 weeks) and sex. The Animal Care and Use of Committee of the University of Amsterdam approved all experiments.

Preparation and stimulation of alveolar and peritoneal macrophages. Alveolar and peritoneal macrophages were harvested from WT and CD14 KO mice by bronchoalveolar and peritoneal lavage (5–8 specimens per strain), respectively, as described elsewhere [6, 25, 27]. Adherent monolayer cells of alveolar and peritoneal macrophages and whole blood were stimulated with growth-arrested B. pseudomallei (clinical isolate strain 1026b [6, 28, 29]; 1 × 10^5 colony-forming units [CFU]/mL), LPS from Escherichia coli 055:B5 (100 ng/mL [Sigma-Aldrich]), LPS from B. pseudomallei (100 ng/mL), or RPMI 1640 for 16 h. Because of the limited number of alveolar macrophages, we chose to stimulate the alveolar macrophages only with B. pseudomallei. For in vitro experiments, we chose to use growth-arrested bacteria, for which only the bacterial replication mechanism is hampered, instead of heat-killed bacteria, for which the whole bacterial structure is lost. For the preparation of growth-arrested B. pseudomallei, B. pseudomallei strain 1026b was cultured, thoroughly washed as described elsewhere [4, 6], and dispersed in sterile PBS after the last centrifugation at a concentration of 1 × 10^8 living bacteria/mL. Concentrated B. pseudomallei preparation was treated for 90 min at 38°C with 100 μg/mL of mitomycine-C (Sigma-Aldrich) to prepare live but growth-arrested bacteria. LPS from B. pseudomallei strain 1026b was prepared as described previously [6]. Supernatants were collected and stored at −20°C until assayed for tumor necrosis factor (TNF–α).

Experimental infection and determination of bacterial outgrowth. Pneumonia was induced by intranasal inoculation with B. pseudomallei strain 1026b (1 × 10^6–3 × 10^7 CFU per 50 μL) [6, 28, 29], as described elsewhere [4–6]. The median lethal dose is 1 × 10^2 CFU per 50 μL. In some experiments, mice infected with B. pseudomallei received either saline or recombinant mouse sCD14 (1 μg [Biometec]) intranasally, 0, 24, and 48 h after infection [26]. CFUs of B. pseudomallei were determined as described elsewhere [5, 26].

Assays. Lung homogenates were prepared as described previously [4–6]. TNF–α, IL-6, IL-10, IL-12p70, interferon (IFN)–γ, and monocyte chemoattractant protein (MCP)–1 concentrations were subsequently measured by means of a cytometric bead array (CBA) multiplex assay (BD Biosciences) in accordance with the manufacturer’s recommendations. Myeloperoxidase (HyCult Biotechnology) and sCD14 levels were measured with commercially available ELISA kits. Alamine aminotransferase, creatinine, and blood urea nitrogen levels were determined with commercially available kits (Sigma-Aldrich), using a Hitachi analyzer (Roche).

Pathologic analysis. Lungs, liver, and spleen specimens obtained for histologic study were prepared and analyzed for lung inflammation, as described elsewhere [4–6]. Granulocyte staining, using fluorescein isothiocyanate–labeled rat antimouse Ly-6G mAb (BD Pharmingen), was done as described previously [30].

Phagocytosis and bacterial-killing assays. Phagocytosis was evaluated as described before [27, 31]. To determine the phagocytosis capacity of neutrophils or peritoneal macrophages, whole blood (50 μL) or peritoneal macrophages (resuspended in RPMI 1640 at a final concentration of 5 × 10^5 cells/mL) were incubated with growth-arrested bacteria (1 × 10^7 CFU/mL) and carboxyfluorescein diacetate succinimidyl ester dye (Invitrogen) for 10, 60, or 120 min at 37°C. Cells were suspended in Quenching solution and incubated in FACS lysis/fix-solution (Becton Dickinson). Neutrophils were labeled using anti-Gr-1-PE (BD Pharmingen) for 10, 60, or 120 min at 37°C. Cells were suspended in Quenching solution and incubated in FACS lysis/fix-solution (Becton Dickinson). Neutrophils were labeled using anti-Gr-1-PE (BD Pharmingen). Cells were washed with ice-cold FACS buffer, after which the degree of phagocytosis was determined using FACS Calibur (Becton Dickinson). Results are expressed in terms of a phagocytosis index, defined as the percentage of cells with internalized B. pseudomallei multiplied by the mean fluorescence intensity [32, 33]. Bacterial killing was determined as described elsewhere [34]. In brief, peritoneal macrophages were harvested from WT and CD14 KO mice (5 specimens per strain).
and plated as described above. *B. pseudomallei* was added at a multiplicity of infection of 50 and spun onto cells at 400 g for 5 min, after which plates were incubated at 37°C for 10 min. Each well was then washed 5 times with ice-cold PBS to remove extra-cellular bacteria. To determine bacterial uptake after 10 min, wells were lysed with sterile dH2O at a time designated as t = 0. RPMI 1640 was added to remaining wells and plates were incubated at 37°C for 10 or 60 min, after which cells were again washed 5 times with ice-cold PBS and lysed with dH2O. Cell lysates were plated on blood-agar plates, and bacterial counts were enumerated after 16 h. Bacterial killing was expressed as the percentage of killed bacteria in relation to t = 0.

**Statistical analysis.** Values are expressed as means ± SEM. Differences between groups were analyzed by the Mann-Whitney *U* test or the Kruskal-Wallis test with the Dunn post hoc analysis performed, followed by log-rank test. All analyses were performed with GraphPad Prism 4.00 (GraphPad Software). *P* values of <.05 were considered statistically significant.

**RESULTS**

**CD14 contributes to cellular responsiveness to *B. pseudomallei* in vitro.** To obtain initial insight into the function of CD14 in melioidosis, we tested the capacity of alveolar macrophages, peritoneal macrophages, and whole blood harvested from WT and CD14 KO mice to release TNF-α on stimulation with *B. pseudomallei*-derived LPS or with intact growth-arrested *B. pseudomallei*. *E. coli* LPS was used as a control stimulus and was expected to induce CD14-dependent TNF-α release [13, 35]. Macrophages and whole-blood leukocytes obtained from CD14 KO mice released less TNF-α than macrophages and blood leukocytes from WT mice on stimulation with *B. pseudomallei* or with *B. pseudomallei* LPS in vitro, although in blood stimulated with intact *B. pseudomallei*, the difference with WT leukocytes did not reach statistical significance (figure 1). Of note, *B. pseudomallei* was more potent than LPS in inducing TNF-α release in vitro; this may have been related to the LPS dose used and/or the fact that *Burkholderia* organisms harbor other proinflammatory components in addition to LPS. These data indicate that CD14 is involved in the recognition of *B. pseudomallei* and *B. pseudomallei* LPS by innate immune cells.

**CD14 KO mice are protected against *B. pseudomallei*-induced lethality.** We next inoculated WT and CD14 KO mice with *B. pseudomallei* (1 × 10² of 3 × 10³ CFU were used in 2 independent experiments) and monitored them for 14 days (figure 2). After infection with the lower dose, 50% of the WT mice died on day 6 after inoculation, whereas in sharp contrast all CD14 KO mice remained alive throughout the experiment (*P < .005*) (figure 2A). A survival benefit for CD14 KO mice was also seen after infection with a high dose of *B. pseudomallei*. Although all WT mice in this experiment died by day 4 after inoculation, mortality was delayed and reduced among CD14 mice, of which 10% survived until the end of the 6-week observation period (*P < .005*) (figure 2B).

**CD14 KO mice show a reduced growth of *B. pseudomallei* in vivo.** To gain insight into the mechanisms underlying the reduced mortality among CD14 KO mice during experimental melioidosis, we infected WT and CD14 KO mice with 5 × 10² CFU of *B. pseudomallei* and sacrificed the animals after 24, 48, or 72 h to determine bacterial loads in lungs (the primary site of the infection) and the liver and blood (to evaluate the extent of bacterial dissemination) (figure 3). Relative to WT mice, CD14 KO mice displayed markedly reduced bacterial loads in their lungs and liver 72 h after infection. In addition, all WT mice had positive culture results ≥48 h, whereas *B. pseudomallei* could be cultured from blood at 72 h for only 3 of 8 CD14 KO mice (figure 3). Hence, the presence of CD14 remarkably facilitated the growth of this pathogen in lungs and the subsequent spread to
distant body sites. The same phenotype was seen in CD14 KO mice infected with a higher inoculum (3 × 10^3 CFU) of B. pseudomallei; in these latter experiments, we also determined the bacterial loads in spleen homogenates and observed that, similar to findings for liver specimens, CD14 KO mice had significantly lower B. pseudomallei loads than WT mice (data not shown).

**Reduced pulmonary influx of neutrophils in CD14 KO mice after infection with B. pseudomallei.** Pneumonia results in inflammatory cell recruitment and local inflammation, which are integral parts of the host immune response [36]. A total of 72 h after inoculation, both WT and CD14 KO mice showed inflammatory infiltrates, characterized by interstitial inflammation together with endothelialitis, bronchitis, pleuritis and edema (figure 4A and 4B). No differences in total lung histopathological scores between CD14 KO and WT mice were seen at any time point (figure 4C). However, the lungs of CD14 KO mice contained fewer infiltrating neutrophils, as visualized by Ly-6 staining 72 h after inoculation (figure 4D and 4E). In accordance with this finding, measurements of myeloperoxidase in lung homogenates showed reduced levels 72 h after infection in CD14 KO mice, compared with control mice (figure 4).

**Decreased systemic TNF-α levels and increased IFN-γ levels in CD14 KO mice.** Because cytokines are important regulators of the inflammatory response to bacterial pneumonia...
we measured pulmonary and systemic TNF-α, IL-6, IL-10, IL-12, IFN-γ, and MCP-1 levels (table 1): 24 h after infection, all cytokine levels were low in both lungs and plasma, after which strong increases were found. In lungs, most differences between CD14 KO and WT mice did not reach statistical significance, although the concentrations of TNF-α and IL-6 tended to be lower in the former mouse strain. The pulmonary level of IL-12 was low in both groups but significantly higher in CD14 KO mice 48 and 72 h after infection. In plasma, CD14 KO mice had decreased levels of TNF-α and IL-6, with significant differences between levels in WT mice 48 h after infection. Plasma IFN-γ and IL-12 plasma concentrations were slightly higher in CD14 KO mice at this time point (table 1).

Effect of CD14 deficiency on distant-organ injury. We next performed histopathological analyses of liver tissue and evaluated liver injury and kidney function by clinical chemistry testing 72 h after infection in both CD14 KO and WT mice. At this time point, all mice showed evidence of hepatic injury, characterized by inflammation of liver tissue, thrombi formation, and foci of liver necrosis; the mean liver histological scores were similar in CD14 KO and WT mice (data not shown). However, the mean plasma levels (±SEM) of alanine aminotransferase, indicative of hepatocellular injury, were lower in CD14 KO mice, compared with WT mice (132 ± 37 vs. 264 ± 58; P < .05). In addition, plasma creatinine and blood urea nitrogen levels appeared to be lower in CD14 KO mice than in WT mice, although these differences did not reach statistical significance because of a relatively large interindividual variation among WT mice (data not shown).

Role of sCD14 in host defense against B. pseudomallei. Having established the detrimental role of CD14 during experimental melioidosis, we next wondered whether soluble CD14 could compensate for CD14 gene deficiency during B. pseudomallei pneumonia. First, we measured sCD14 concentrations in bronchoalveolar lavage fluid (BALF) harvested from WT mice before and 24, 48, or 72 h after infection. sCD14 was detectable in BALF from healthy mice and significantly increased during the course of pneumonia (figure 5A and 5B). We next administered recombinant mouse sCD14 to CD14 KO mice intranasally, using a treatment and dosing schedule previously found to completely reverse the phenotype of CD14 KO mice in a model of S. pneumoniae pneumonia [26] (figure 5C–E). Intranasal administration of recombinant mouse sCD14 to CD14 KO mice did not change the bacterial load in lungs of CD14 KO mice during experimental melioidosis (figure 5D). However, in BALF of CD14 KO mice, sCD14 treatment resulted in enhanced bacterial growth that was indistinguishable from that in WT mice (figure 5C). Furthermore, sCD14 treatment influenced the dissemination of Burkholderia organisms: all (8 of 8) WT mice

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and only 3 of 8 CD14 KO mice had blood cultures positive for *B. pseudomallei*, whereas 6 of 8 CD14 KO mice treated with sCD14 were bacteremic. In accordance with these findings, sCD14 administration resulted in higher bacterial loads in livers of CD14 KO mice, in essence reversing the phenotype of CD14 KO mice into that of WT mice (figure 5E). In other words, sCD14 can, in part, replace cell-associated CD14 after infection with *B. pseudomallei*, because sCD14 administration resulted in enhanced bacterial growth in BALF of CD14 KO mice, which was accompanied by an increased dissemination to the circulation and liver. Together, these data suggest that sCD14 can, in part, compensate for cell-bound CD14 in impairing host defense against *B. pseudomallei*.

**No role for CD14 in phagocytosis or killing of B. pseudomallei.**

The experiments described above established that CD14 KO mice display a superior antibacterial defense toward *B. pseudomallei* infection. We next wished to determine whether CD14 contributes to phagocytosis and/or killing of *B. pseudomallei*. CD14 KO neutrophils (figure 6A) and macrophages (not shown) demonstrated an unaltered capacity to phagocytose *B. pseudomallei*. In addition, no difference in the killing capacity between WT and CD14 KO cells was observed (figure 6B).

**DISCUSSION**

The primary objective of the present study was to examine the role of CD14 in the innate immune response during sepsis caused by *B. pseudomallei*. We here show that CD14 contributes to cellular responsiveness to *B. pseudomallei* in vitro. Strikingly, the lethality of *B. pseudomallei* infection was strongly reduced among CD14 KO mice and was accompanied by significantly decreased bacterial loads, compared with those in WT mice. Furthermore, the presence of sCD14 in the bronchoalveolar compartment of CD14 KO mice partially reversed the beneficial phenotype of these animals, as reflected by an increase in bacterial dissemination to the circulation and liver. These data indicate that CD14 plays a remarkable detrimental role in the host response against *B. pseudomallei*.

The essential role of CD14 in systemic and pulmonary inflammation induced by LPS is well established [16–20]. Additionally, in vivo models of infection with various gram-negative bacteria, inhibition or elimination of CD14 resulted in increased bacterial outgrowth [20, 22–25]. However, of interest, some studies have reported on the potential detrimental role of CD14 in the host defense against gram-negative bacteria: CD14 KO mice were reported to have an accelerated clearance of *E. coli* O111:B4 after intraperitoneal injection [37], although this could not be confirmed using *E. coli* O18:K1 [27]. Furthermore, in a model of chronic abscess-forming peritonitis induced by the gram-negative bacterium *Bacteroides fragilis*, reduced bacterial dissemination and liver injury was seen in CD14 KO mice, compared with control mice [38]. These studies, together with our current investigation, challenge the paradigm that CD14 is required for mounting an effective innate immune response to...
gram-negative bacteria. One should be cautious, however, in extrapolating results obtained from studying a specific cause of sepsis to the whole spectrum of sepsis. Indeed, *B. pseudomallei* is not a typical gram-negative bacteria, as illustrated by the fact that the LPS of *B. pseudomallei* is recognized by TLR2 and not by TLR4 [6]. This only adds to the increasingly accepted opinion that sepsis cannot be seen as just one disease and that, in order to really understand its pathogenesis (and evaluate new therapies), one has to investigate every individual response elicited by every single pathogen [39, 40]. Of note, our experiments are derived solely from experiments performed with mice; therefore, one should be careful when extrapolating the current results to humans.

The potential mechanism of how CD14 deficiency contributes to reduced bacterial outgrowth in experimental murine melioidosis remains to be elucidated. However, because the phenotype described here in CD14 KO mice strongly resembles the phenotype of TLR2 KO mice with melioidosis [6], we hypothesized that an interaction between CD14 and TLR2 could explain our observations. Indeed, both CD14 and TLR2 KO mice not only both display reduced mortality and decreased bacterial growth in vivo during murine melioidosis, but CD14 and TLR2

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**Figure 5.** Effect of soluble CD14 on bacterial growth in CD14 knockout (KO) mice. Concentrations of soluble CD14 in bronchoalveolar lavage fluid (BALF) (A) and plasma (B) from wild-type (WT) mice infected with $5 \times 10^9$ colony-forming units (CFU) of *B. pseudomallei* showed a significant increase during the course of pneumonia. Intranasal administration of recombinant mouse sCD14 (1 µg; 0, 24 and 48 h after infection) to CD14 KO mice partially reversed their phenotype to that of WT mice: 72 h after infection, CD14 KO mice treated intranasally with recombinant CD14 (black bars) displayed bacterial outgrowth in BALF (C) and liver (E) that was similar to that in WT mice (white bars). No change in the bacterial load in lungs of CD14 KO mice treated with recombinant sCD14 was seen (D). BC+ indicates the number of positive blood cultures. Data are mean values ± SEM; 5–8 specimens per strain were tested. *P < .05; **P < .01, compared with values at t = 0 or with CD14 KO mice.
are also both essential for the induction of TNF-α release by macrophages stimulated with *B. pseudomallei* LPS [6]. Because CD14 is known to be capable of facilitating the presentation of bacterial components to both TLR2 and TLR4 [7, 12–15, 41], we therefore hypothesized that an interaction between CD14 and TLR2 could explain our observations. Preliminary experiments with confocal microscopy could not, however, support any physical association between CD14 and TLR2 in cells infected with *B. pseudomallei* in vitro (unpublished data). We subsequently postulated that CD14, possibly in collaboration with TLR2, stimulates phagocytosis of the offending antigen, giving the facultative intracellular *B. pseudomallei* immediate access to a preferred environment [2, 42, 43]. Is it possible that *B. pseudomallei* deliberately uses CD14 as a cell entry receptor? Indeed, TLRs have been reported to be misused to facilitate intracellular invasion: MyD88 has been implicated in phagocytosis of *E. coli*, and TLR2 deficiency possibly delays pneumococcal phagocytosis and impairs oxidative killing by granulocytes [34, 44]. Additionally, CD14-dependent phagocytosis of gram-negative bacteria has been reported [45]. However, our current data could not demonstrate a role for CD14 in either phagocytosis or killing of *B. pseudomallei*. In accordance with these findings, our laboratory previously could not detect a role for CD14 in phagocytosis of *E. coli* [27, 46]. Of interest, recently substantive data have emerged that argue against a role of the TLRs in phagocytosis, showing among others things that TLR stimulation does not impact phagosome maturation [47, 48]. Of note, 48 h after infection, CD14 KO mice displayed modestly increased pulmonary IL-12 and plasma IL-12 and IFN-γ concentrations. Although the differences from concentration in WT mice were only small, they could have contributed to the beneficial phenotype of CD14 KO mice, considering that IFN-γ and its endogenous inducer IL-12 are known to play an essential role in the protective host defense against melioidosis [2, 49, 50]. However, more studies are warranted to dissect the exact mechanism by which CD14 facilitates the growth and spread of *B. pseudomallei* in vivo.

We recently demonstrated that CD14 can facilitate dissemination of the gram-positive pathogen *S. pneumoniae* from the respiratory tract, as reflected by the fact that CD14 KO mice did not become bacteremic after intranasal infection [26]. By using the same treatment schedule with sCD14, we here demonstrate that, similar to pneumococcal pneumonia, sCD14 can in part replace cell-associated CD14 after infection with *B. pseudomallei*: sCD14 administration resulted in an enhanced bacterial growth in BALF of CD14 KO mice, which was accompanied by an increased dissemination to the circulation system and liver. sCD14 treatment did not influence bacterial loads in homogenates of whole-lung specimens from CD14 KO mice, suggesting that cell-associated CD14 rather than sCD14 is important for transition of *B. pseudomallei* from the bronchoalveolar space into lung tissue.

A recent phase 1 clinical trial with a recombinant anti-CD14 monoclonal antibody has shown that this therapy seems to be well tolerated in patients with severe sepsis and does not increase the incidence of secondary bacterial infection [51]. We here show in mice that CD14 plays a crucial but detrimental role in the host response against gram-negative *B. pseudomallei* infection. This exceptional finding highlights the diverse nature of CD14 in the innate immune response against various pathogens.

**Figure 6.** No difference in *Burkholderia pseudomallei* phagocytosis or killing capacity between cells from wild-type (WT) mice (circles) and those from CD14 knockout (KO) mice (squares). A, Peripheral blood neutrophils were incubated at 37°C with carboxyfluorescein diacetate succinimidyl ester–labeled growth-arrested *B. pseudomallei* (1 × 10⁷ colony-forming units/mL), after which time-dependent phagocytosis was quantified as described in Materials and Methods. B, Killing capacity of peritoneal macrophages is shown as the percentage of killed *B. pseudomallei* organisms, compared with the bacterial load at t = 0. Data are mean values ± SEM; 5 specimens per strain were tested.
Inhibition of CD14 may be a novel treatment strategy in melioidosis.

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References


