Chlamydia pneumoniae Induces Interleukin-10 Production that Down-Regulates Major Histocompatibility Complex Class I Expression

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Recently, it was demonstrated that CD8+ T cells are important for the response against Chlamydia pneumoniae. By use of the human monocytic cell line U937 and human monocytes taken from peripheral blood, we investigated the effect of infection on various molecules critical for CD8+ T cell function. A strong secretion of interleukin (IL)–10 by infected cells was observed, together with an inhibited expression of major histocompatibility complex (MHC) class I antigens, but without significant alteration of tumor growth factor–β secretion or MHC class II expression. Recombinant IL-10 added to uninfected U937 cells decreased the expression of MHC class I, whereas blocking antibodies to IL-10 and its receptor abolished the C. pneumoniae–induced inhibition of MHC class I expression. Analysis of our data provides evidence that IL-10 secretion induced by C. pneumoniae infection of monocytes cells down-regulates the expression of MHC class I molecules and thereby might reduce the presentation of bacterial epitopes by MHC. This would decrease the ability of CD8+ T cells to eliminate infected cells.

Chlamydia pneumoniae is a gram-negative bacterium that has recently emerged as a pathogen with a potential causal role in atherosclerosis [1–4]. Like other species of the genus Chlamydia, it is an obligate intracellular microorganism. The main bases to support its role in atherosclerosis are as follows: (1) the correlation between elevated titers of antibodies to C. pneumoniae in patients and atherosclerotic disease [2, 5], (2) the presence of the bacterium in atheromatous lesions [1, 3], (3) the formation of foam cells in the presence of low-density lipoproteins after infection of monocytes or macrophages with C. pneumoniae [6, 7], and (4) the accelerated atherogenesis in hypercholesterolemic apolipoprotein E–deficient mice after infection with C. pneumoniae [8, 9].

In vitro studies have demonstrated that C. pneumoniae can infect human endothelial cells, smooth-muscle cells, and macrophages and that they can multiply within these cells [10]. Infection results in production of proinflammatory cytokines and expression of cell surface molecules that may contribute to local inflammation, worsening and accelerating the atherogenesis. Thus, C. pneumoniae infection of endothelial cells increases the secretion of monocyte chemoattractant protein 1 and interleukin (IL)–8 and –1β, as well as the expression of adhesion molecules such as E selectin, intercellular adhesion molecule 1 (CD54), and vascular cell adhesion molecule 1 [11–13]. The infection of monocytes or macrophages also induces the production of cytokines (tumor necrosis factor [TNF]–α and IL-1β, -6, and -8) and up-regulates the expression of CD14, known to be a lipopolysaccharide (LPS) receptor [14–17].

Monocytes and macrophages are likely to play a central role in atherosclerosis—for instance, in foam cell formation and as putative target cells for C. pneumoniae. Because of the possible intracellular survival of the pathogen, the monocytes cells may represent a reservoir for persistent infection [4, 9, 10]. Survival of the pathogen in the body must involve mechanisms that enable chlamydiae to evade the host defense. However, almost nothing is known about the diverse protection mechanisms that C. pneumoniae could use against host immune responses. Although it has been shown recently that Chlamydia-infected monocytic cells can resist apoptosis induced by TNF–α, Fas antibody, and granzyme B/perforin [18], other mechanisms may be proposed. For instance, C. pneumoniae might alter the cytokine network or the expression of membrane molecules used by monocytes and macrophages to cooperate with other cells, particularly with lymphocytes involved in intracellular pathogen elimination (e.g., interferon-γ–secreting Th1 lymphocytes or cytotoxic CD8+ T lymphocytes) [19]. Among the numerous cytokines, IL-10 is known to have anti-inflammatory properties and to play a significant role in the regulation of immune responses [20].

The functions of lymphocytes and monocytes/macrophages appear to be particularly susceptible to alteration mediated by IL-10 [21, 22]. For example, IL-10 can inhibit the responses of Th1 and cytotoxic T lymphocytes toward viruses [22–24]. On
the other hand, the adhesion molecules, such as CD54 and integrins, are necessary for the cooperation between T cells and macrophages and for the efficacy of the immune response against intracellular pathogens. The triggering of cell-mediated immunity against intracellular microorganisms depends also on a sufficient presentation of antigenic peptides by major histocompatibility complex (MHC) class I molecules [25, 26]. In this work, we investigated the effects of *C. pneumoniae* infection of monocytes on IL-6, transforming growth factor (TGF)-β, and IL-10 secretion and on CD54, CD18 (integrin b2 subunit), and MHC class I and class II expression.

Materials and Methods

Reagents. LPS from *Escherichia coli*, glucose, and cycloheximide were supplied by Sigma-Merck (Darmstadt, Germany). RPMI 1640 medium containing Glutamax I, Eagle minimal essential medium (EMEM) modified with Earle salts, macrophage serum free medium (SFM), nonessential amino acids, and 1-glutamine were purchased from Gibco (Cergy Pontoise, France). Gentamicin was obtained from Panpharma (Fougères, France), and fetal calf serum (FCS) was obtained from Eurobio (Les Ulis, France). The fluorescein isothiocyanate (FITC)-conjugated monoclonal antibody directed against *C. pneumoniae* was supplied by Dako (Trappes, France). The FITC- or phycoerythrin-conjugated anti-CD14, anti-CD18, anti-CD54, and anti–MHC class I and class II monoclonal antibodies and the annexin V-FITC kit were supplied by Coulter-Immunotech (Marseille, France). The FITC-conjugated irrelevant mouse IgG1 was supplied by Caltag (Tebu, Le Perray en Yvelines, France). The anti–human IL-10 polyclonal antibodies were from Endogen (Perbio Science, Bezons, France). The anti–human IL-10 receptor (IL-10R) monoclonal antibody was from R&D Systems (Abingdon, UK). Recombinant human IL-10 (rhIL-10) was obtained from Pharmingen/Becton Dickinson (Le Pont de Claix, France).

Cells. The U937 monocyctic cell line and HEP-2 cells were obtained from the European Cell Collection (Salisbury, UK). The U937 cells were maintained in RPMI 1640 medium containing Glutamax I, supplemented with 10% heat-inactivated FCS and gentamicin (40 μg/mL). The U937 cells were grown routinely for 3 days, to yield between 1 × 10⁵ and 8–9 × 10⁵ cells/mL. Peripheral blood mononuclear cells (PBMC) were isolated from healthy donors by ficoll-paque centrifugation (Pharmacia Biotech, Uppsala, Sweden) and were plated for 1–3 h at 37°C, as described elsewhere [27]. After removal of nonadherent cells, the adherent PBMC were used in an infection protocol or were cultured in macrophage-SFM for 2–4 days to obtain primary monocyte-derived macrophages before infection. Adherent cells were >90%–95% positive for CD14.

The HEP-2 cells were maintained in EMEM modified with Earle salts, supplemented with 10% heat-inactivated FCS, 1% l-glutamine, 1% nonessential amino acids, and 40 μg/mL gentamicin. Cells were grown in 75-cm² culture flasks and then were transferred into 6-well plates at 3 × 10⁵ cells/mL and allowed to adhere overnight for use in propagation of *C. pneumoniae* strains.

Propagation of *C. pneumoniae*. *C. pneumoniae* strains VR1360 and TW183 were obtained from the American Type Culture Collection (Manassas, VA). *C. pneumoniae* strains were propagated in HEP-2 cell monolayers. Confluent monolayers of HEP-2 cells were infected with *C. pneumoniae* previously suspended in inoculation medium (EMEM modified with Earle salts and supplemented as described above). After centrifugation at 1500 g for 1 h at 35°C, infected cultures were incubated at 37°C in 5% CO₂ for 2 h. Supernatants were replaced with inoculation medium supplemented with glucose (5 mg/mL) and cycloheximide (0.5 μg/mL), and infected cultures were incubated for 72 h. *C. pneumoniae* were harvested by disruption of the monolayer with a pipette. All the supernatants and cells harvested were pooled, and a passage was done on a fresh HEP-2 monolayer. A second passage was done after 72 h under the same conditions. Cells and medium were pooled, suspended in saccharose-phosphate buffer, titered for infectivity, and stored at −80°C. The titers were expressed as infection-forming units (ifu; 1 ifu per cell equals 1 infectious *Chlamydia* per HEP-2 cell) per milliliter and were determined in HEP-2 cells by counting chlamydial inclusions in confluent cell monolayers with FITC-conjugated anti–*C. pneumoniae* monoclonal antibody.

Chlamydia infection of U937 cells and human monocytes. U937 cells and adherent PBMC or primary monocyte-derived macrophages were infected, as described elsewhere [6, 10, 18], with minor modifications. Briefly, after washing, cells were adjusted at 5 × 10⁴ cells/mL for U937 cells and adherent mononuclear cells or 2.5 × 10⁵ cells/mL for primary monocyte-derived macrophages and were transferred into 24-well plates (1 mL per well) or into 6-well plates (2 mL per well) for the experiments and into 96-well plates (200 μL per well) to assess infection. In some experiments, U937 cells were cultured in substationary conditions (i.e., 1–1.5 × 10⁶ cells/mL) for 24–48 h, washed, and adjusted to 10⁶ cells/mL before the infection. Monocytic cells were infected with *C. pneumoniae* suspended in RPMI 1640 (without cycloheximide) at various ifu/mL to obtain an MOI (expressed as MOI or infection-forming units per cell) of 0.001–3.

After 1 h of centrifugation and 2 h at 37°C in 5% CO₂, supernatants were replaced by fresh medium without cycloheximide. Infected cells were incubated for 6, 24, or 48 h. Supernatants were collected, to evaluate cytokines, 24 h after the infection. Cells were collected and washed twice in cold PBS for flow cytometry analysis. To assess the viability of bacteria, monocytic cells were infected, and after 72 h, cells were fixed with aceton. Chlamydial infection was evaluated with the monoclonal antibody to *C. pneumoniae*. In some experiments, an anti–human IL-10 receptor monoclonal antibody, known to neutralize the receptor bioactivity [28], or a blocking anti–human IL-10 polyclonal serum was added at different concentrations after chlamydial infection. For the anti–human IL-10R monoclonal antibody, the neutralization dose 50 was determined to be ~0.1–0.3 μg/mL on the inhibitory function of IL-10 on IL-1 production, when the antibody was added to LPS-activated human PBMC in the presence of 0.25 ng/mL of rhIL-10, as indicated by the manufacturer.

Cytokine assay. The cytokines IL-6, IL-10, and TGF-β1 were measured in culture supernatants collected 24 h after infection. These supernatants were stored at −80°C until use. The concentrations of cytokines were determined with commercially available enzymoimmunoassay kits (Coulter-Immunotech for IL-6 and -10 and R&D Systems for TGF-β1).

Flow cyt fluorometric analysis. Control cells and infected cells
were washed with cold PBS, and cell pellets were suspended in 150 μL of PBS. In some experiments, uninfected cells were incubated for 24 and 48 h with rhIL-10 (0.05–5 ng/mL) or with E. coli LPS, after which MHC class I expression was evaluated. Cells were incubated with 2 μg/mL of fluorochrome-conjugated anti-CD18, anti-CD54, or anti-MHC class I or -class II monoclonal antibodies for 45 min, then washed twice with cold PBS. To study apoptosis and necrosis, cell pellets were suspended in binding buffer, and 5 μL of Annexin V-FITC and 5 μL of propidium iodide were added for 10 min (Coulter-Immunotech). Cells were analyzed in the FACScan flow cytometer (Becton Dickinson) or in the Beckman Coulter XL4 cytofluorimeter (Beckman Coulter, Villepinte, France), as described elsewhere [27, 29]. The expression of cell surface molecules was evaluated by the mean fluorescence intensity (MFI) of cells showing fluorescence exceeding the upper limit of fluorescence of cells incubated with an irrelevant monoclonal antibody.

Results

Effects of C. pneumoniae on expression of adhesion molecules and MHC class I antigens on U937 cells. When U937 cells in log-phase cultures were infected with C. pneumoniae (strain TW183 or VR1360) and studied by use of flow cytometry, the MHC class I molecule expression was decreased in almost the totality of the cell population 48 h after the infection, even with an MOI as low as 0.02 (figure 1A). This suggests that the modulation of class I molecules occurred not only on infected cells but also on surrounding cells. The C. pneumoniae infection induced similar results on U937 cell cultures in stationary conditions and at higher cell concentrations (data not shown), which suggests that modulation by the bacteria of MHC class I expression is independent of cellular density and cell proliferation.

The inhibitory effect on MHC class I expression, which seemed to depend on bacterial concentration, reached a maximum when the cells were infected with 1 × 10⁴ to 5 × 10⁴ ifu/mL (MOI, 0.02–0.1) and was observed as soon as 6 h after infection and up to 48 h after infection (figure 1B). In addition, the infection did not modify CD18 expression (data not shown), but it induced a moderate up-regulation of CD54 expression (figure 1B).

The decrease of MHC class I expression in infected cultures was not due to cellular death. The level of dead cells, as evaluated by the trypan blue exclusion test, was similar to that of control cultures at 48 h after infection (MOI, 0.02; 7% ± 2% for infected cells and 5% ± 1% for control cells; n = 3). Furthermore, the number of apoptotic cells was not different in control cells and infected U937 cells (MOI, 0.01–0.1) after staining with annexin V-FITC (apoptosis marker) and propidium iodide (necrosis marker) and analysis of the cells by flow cytometry (data not shown). In short, C. pneumoniae induced neither apoptosis nor necrosis in U937 cells under our experimental conditions.

In an attempt to characterize the mechanism involved in the inhibition of MHC class I antigen expression, C. pneumoniae were exposed to an elevated temperature (30 min at 90°C) before incubation with the cells. Heat-inactivated C. pneumoniae failed to grow in HEp-2 cells (indeed, there was no visible inclusion at 72 h after infection) but were still able to induce an
increase in CD54 expression (data not shown) and a decrease in MHC class I antigen expression in U937 cells (figure 2A). The viability of C. pneumoniae was not necessary to induce these effects, suggesting that a structural component of the elementary body (EB) of C. pneumoniae could be involved in the observed alteration. Similarly to C. pneumoniae infection, LPS of E. coli induced a decreased MHC class I molecule expression (figure 2B).

Effects of C. pneumoniae on IL-10 secretion and its impact on the expression of MHC class I antigens on U937 cells. IL-10 is a cytokine known for its capacity to down-regulate MHC class I and class II expression, whereas IL-6 (with TNF-α, IL-1, and IL-8) is considered to be an inflammatory cytokine. These molecules can be produced by monocytes and macrophages after LPS activation [30]. Infection of human PBMC by C. pneumoniae has recently been shown to induce production of IL-6 [15]. In the U937 cell line, infection with a low concentration of C. pneumoniae (MOI, 0.02; TW183) also induced a secretion of IL-6 and increased the basal secretion of IL-10 (51–143 pg/mL; P < .05; n = 6; figure 3A). Similarly, LPS of E. coli also stimulated the secretion of IL-10 and IL-6 by U937 cells. The IL-10 secretion increased as a function of C. pneumoniae infection level in U937 cell cultures (figure 3B). Finally, the infection of human adherent mononuclear cells with a low MOI (0.02) induced a strong IL-10 production (figure 3B). In addition, heat-inactivated C. pneumoniae stimulated the IL-10 secretion by U937 cells (data not shown).

To know whether IL-10 could be responsible, at least in part, for the down-regulation of MHC class I expression on C. pneumoniae–inoculated U937 cells, the presence of IL-10R at the surface of U937 cells was first determined, and practically all infected U937 cells (100%) were found to be positive by cytofluorometric analysis (data not shown). Then we added rhIL-10 (0.05–5 ng/mL) to culture supernatants of C.pn. for monocytes (C, uninfected monocytes). Culture supernatants were analyzed by ELISA to determine IL-6 or IL-10 concentrations. Results are the mean of 2 for IL-6 or 6 (for IL-10) independent experiments. *P < .05 by Student’s t test, as compared with control (C).

![Figure 2](image2.png)

**Figure 2.** Effects of Chlamydia pneumoniae viability and Escherichia coli lipopolysaccharide (LPS) on major histocompatibility complex (MHC) class I antigen expression in U937 cells. U937 cells (5 × 10⁵/mL) were infected with C. pneumoniae (C.pn.) or E. coli (LPS; 1 µg/mL) for 24 h. After 24 h of incubation, the culture supernatants (C.pn.) were analyzed by ELISA for the IL-6 or IL-10 concentration. Results are the mean of 2 independent experiments (for IL-6) or 6 (for IL-10) independent experiments. *P < .05 by Student’s t test, as compared with control (C).

![Figure 3](image3.png)

**Figure 3.** Effect of Chlamydia pneumoniae infection on interleukin (IL)–10 production by the U937 cell line and monocytes. A. U937 cells (5 × 10⁵/mL) were inoculated with C. pneumoniae (C.pn. [TW183 strain]; MOI, 0.02) or were treated with Escherichia coli lipopolysaccharide (LPS; 1 µg/mL). After 24 h of incubation, the culture supernatants were analyzed by ELISA to determine IL-6 or IL-10 concentrations. Results are the mean of 2 (for IL-6) or 6 (for IL-10) independent experiments. *P < .05 by Student’s t test, as compared with control (C). B. U937 cells (5 × 10⁵/mL) or adherent cells (monocytes) isolated from peripheral blood mononuclear cells were infected with C. pneumoniae (strain VR1360), using increasing concentrations (MOIs of 0.01, 0.1, and 1) of C.pn. for U937 cells and an MOI of 0.02 of C.pn. for monocytes (C, uninfected monocytes). Culture supernatants were analyzed by ELISA for the IL-10 concentration 24 h after the infection. Results are the mean of 2 independent experiments for U937 and are the mean ± SD of 3 independent experiments, using 3 different healthy donors, for monocytes.
mL of the antibody allowed us to keep the MHC class I expression at the level of uninfected cells 6–48 h after the infection (figure 4C).

Effects of C. pneumoniae on cultured human peripheral blood monocytes. Although U937 cells have some monocytic phenotype features, they do not express MHC class II antigens. To extend our observations, experiments were performed with peripheral blood monocytes cultured for 2, 3, or 4 days. As shown in a representative experiment (figure 5A), the C. pneumoniae infection induced an inhibition of MHC class I antigen expression, whereas the MHC class II antigen expression was not decreased. For MHC class I expression, the arithmetic mean of 7 independent experiments, each using a different donor, was as follows: MFI of 1695 ± 304 arbitrary units (AU) on infected cells (MOI, 0.1) versus MFI of 2416 ± 155 AU on control cells (P < .02). In contrast, for MHC class II antigens, the MFI was 711 ± 131 AU on cells from infected cultures (MOI, 0.1) versus 627 ± 146 AU on control cells (mean of 6 independent experiments; no significant difference).

The concentrations of IL-10 and TGF-β1 (known to be an immunosuppressive cytokine) were determined in supernatants of monocyte cultures infected with C. pneumoniae, and an increase in IL-10 concentration was observed as a function of MOI increase (figure 5A). The means of 4 independent experiments were as follows: 147 ± 43 pg/mL (P < .05) with an MOI of 0.1 and 1700 ± 1127 pg/mL with an MOI of 3 versus 44 ± 39 pg/mL in control cell supernatants. In contrast, the TGF-β1 secretion seemed unaltered (911 ± 375 and 954 ± 398 pg/mL, with MOIs of 0.1 and 3, respectively, vs. 918 ± 365 pg/mL in controls; n = 6). In addition, the evaluation of TGF-β1 concentration in infected U937 cells (MOI, 0.1) confirmed the observation made in cultured monocytes: 895 ± 189 pg/mL in control cells versus 843 ± 170 pg/mL in infected cell cultures (n = 3). Finally, to study the effect of IL-10 on MHC class I antigen inhibition, experiments were performed in the presence of anti–IL-10 polyclonal antibodies. As observed with U937 cells by use of the anti–IL-10R monoclonal antibody, the addition of anti–IL-10 reversed the MHC class I antigen inhibition in cultured monocytes (figure 5B).

Discussion

We observed that infection of U937 cells by C. pneumoniae induced an increase in CD54 expression, without any effect on CD18 adhesion molecules. Several reports have shown that C. pneumoniae is able to stimulate the expression of adhesion molecules on endothelial cells [11–13], resulting in vitro in increased monocyte adhesion and transendothelial migration [13]. However, almost nothing is known about the effect of C. pneumoniae on adhesion molecule expression by monocytes or macrophages. Analysis of our present data suggests that C. pneumoniae might potentiate some adhesion molecule expression on monocytes.

Of particular interest is the inhibition of MHC class I antigen expression observed in U937 cells and in cultured monocytes. In U937 cells, this effect was observed as soon as 6 h after infection. In contrast, C. pneumoniae infection seemed not to modulate the expression of MHC class II molecules at the surface of monocytes or macrophages 24 h after the infection, but we cannot exclude an effect after this time. Finally, our results
nuclear cells and were cultured for 3 days before infection. Adherent cells (monocytes) were isolated from peripheral blood mononuclear cells and were then cultured for 24 h in the presence or absence of C. pneumoniae (strain VR1360), using bacterial concentrations of 0.1 and 3 MOI, and were then cultured for 24 h. Left. Monocytic cells were analyzed by cytofluorimetry for their major histocompatibility complex (MHC) class I and class II expression, measured as arbitrary units (AU) of mean fluorescence intensity (MFI). Right. Culture supernatants were analyzed by ELISA for their interleukin (IL)-10 and transforming growth factor (TGF)-β levels. Results are means of triplicates (SD, <10%). B. Cells were inoculated (+) or not inoculated (−) with C. pneumoniae (C.pn. [VR1360]; MOI, 0.1) and were cultured for 24 h in the absence (−) or presence (+) of anti-IL-10 polyclonal antibodies (5 μg/mL). MHC class I expression was determined by cytofluorimetry. Results are means of 2 independent experiments. Similar results were observed with 1 μg/mL of anti-IL-10 polyclonal antibodies.

Figure 5. Effect of Chlamydia pneumoniae infection on cultured monocytes. To obtain primary monocyte-derived macrophages, adherent cells (monocytes) were isolated from peripheral blood mononuclear cells and were cultured for 3 days before infection. A. In a representative experiment, cells were infected with C. pneumoniae (strain VR1360), using bacterial concentrations of 0.1 and 3 MOI, and were then cultured for 24 h. Left. Monocytic cells were analyzed by cytofluorimetry for their major histocompatibility complex (MHC) class I and class II expression, measured as arbitrary units (AU) of mean fluorescence intensity (MFI). Right. Culture supernatants were analyzed by ELISA for their interleukin (IL)-10 and transforming growth factor (TGF)-β levels. Results are means of triplicates (SD, <10%). B. Cells were inoculated (+) or not inoculated (−) with C. pneumoniae (C.pn. [VR1360]; MOI, 0.1) and were cultured for 24 h in the absence (−) or presence (+) of anti-IL-10 polyclonal antibodies (5 μg/mL). MHC class I expression was determined by cytofluorimetry. Results are means of 2 independent experiments. Similar results were observed with 1 μg/mL of anti-IL-10 polyclonal antibodies.

Our results indicate that C. pneumoniae infection of monocytic cells can trigger the production of IL-10. The IL-10 concentration in cell cultures was MOI dependent, which suggests that the potentialization of cytokine production increased with the number of cells endocytosing the EBs. However, the decrease in MHC class I molecules leveled off when the MOI was ~0.01–0.1, probably because IL-10 saturates the available receptors. In addition, heat-inactivated C. pneumoniae triggered MHC class I molecule inhibition and increased IL-10 production in U937 cells, suggesting that the effect of the bacterium is due to a heat-stable component from the EB (such as chlamydial LPS). In agreement with studies using endothelial cells [12, 13, 35], preliminary results in our laboratory indicate that C. pneumoniae might activate NF-kB in U937 cells in the same way as the LPS of E. coli. However, further experiments with purified chlamydial LPS will be necessary to demonstrate its implication in the down-regulation of MHC class I expression.

IL-10 is a cytokine that shows various effects on molecules critical for the immune response, such as down-regulation of MHC and CD1 molecules and of antigen presentation by these molecules [32–34, 36]. Several findings have demonstrated that IL-10 may enable intracellular pathogens, such as Schistosoma mansoni [37], Plasmodium falciparum [38], hepatitis C virus [22], and Listeria monocytogenes [39], to escape the immune system—for instance, by down-regulating the Th1 response or by weakening the antibacterial activity of monocytes or macrophages [22, 37–39]. Consequently, it is possible that IL-10 production induced by C. pneumoniae in monocytic cells contributes to bacterial escape from the immune system.

Analysis of the present data suggests that the bacterium may contribute to a local immunosuppression by stimulating or inducing IL-10 secretion, with an inhibitory effect on MHC class I-mediated presentation of infectious antigen as a putative consequence. This would decrease the ability of CD8+ T cells to eliminate infected cells. Finally, because IL-10 is known to be involved in the switch from Th1 to Th2 [40] and because recent data show that severe hypercholesterolemia and lesions in apolipoprotein E-deficient mice are associated with this phenom-
enon [41], it is possible that *C. pneumoniae* might favor this switch of T cells in atherosclerotic lesions.

**Acknowledgments**

We thank Georges Cassar, M.Sc., University of Toulouse, Toulouse, France, for assistance with cytofluorometry and Sylvie Hébrard and Nicole Therville for their technical assistance.

**References**

37. Sher A, Fiorentino D, Caspar P, Pearce E, Mosmann T. Production of IL-


