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NOTES

Isolation and Sequence Analysis of the *Chlamydia pneumoniae* GroE Operon

LYNNE C. KIKUTA, MIRJA PUOLAKKAINEN, CHO-CHOU KUO, AND LEE ANN CAMPBELL*
Department of Pathobiology, University of Washington, Seattle, Washington 98195

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***Chlamydia pneumoniae* has emerged as an important human respiratory pathogen. From a lambda gt11 gene bank constructed from *C. pneumoniae* isolate AR-39 DNA, an immunoreactive plaque containing a 3.0-kb insert was purified. In immunoblots, a 60-kDa protein was recognized by anti-*C. pneumoniae* rabbit immune serum. The recombinant protein was reactive with a *Chlamydia* genus-specific monoclonal antibody recognizing a 60-kDa protein found in the Sarkosyl-soluble fraction and with rabbit immune serum prepared against the *Chlamydia trachomatis* 60-kDa GroEL homolog associated with the delayed-type hypersensitivity response. DNA sequence analysis confirmed that the *C. pneumoniae* gene product is an analog of the *C. trachomatis* delayed-type hypersensitivity antigen and the *Escherichia coli* GroEL heat shock protein.**

Chlamydia pneumoniae is an important respiratory pathogen in humans, causing pharyngitis, bronchitis, and pneumonia (12, 13). It has also been suggested that this organism plays a role in the etiology of coronary heart disease (25a) and in clinical syndromes associated with immunopathological responses, including sarcoidosis and erythema nodosum (11, 15). In other chlamydial diseases which exhibit chronic sequelae, immunopathology has been associated with a 60-kDa protein which is an analog of the GroEL heat shock protein of *Escherichia coli* (8, 24).

Analysis of the human serological response to *C. pneumoniae* infection has identified reactivities to shared chlamydial antigenic determinants (39.5-, 60-, and 75-kDa proteins) and a 98-kDa protein containing a *C. pneumoniae*-specific determinant (7). Structural and antigenic analysis has shown that the 39.5-kDa protein is analogous to the major outer membrane proteins (MOMPs) characterized for the other *Chlamydia* spp. (5). Unlike *Chlamydia trachomatis* and *Chlamydia psittaci* MOMPs, the *C. pneumoniae* MOMP does not appear to be the immunodominant antigen recognized during human infection (7). It also appears to be less antigenically complex, as no serological specific determinants on the *C. pneumoniae* MOMP have yet been identified (5, 7, 25).

To date, molecular studies focusing on antigens recognized during *C. pneumoniae* infection have resulted in the isolation and characterization of genes encoding the MOMP and a 75-kDa protein. DNA sequence analysis of the 75-kDa protein showed that it was a homolog of the *E. coli dnaK* gene and a member of the hsp70 family of heat shock proteins (20). In this report, we describe the isolation, characterization, and sequence analysis of a *C. pneumoniae* gene encoding an immunoreactive 60-kDa protein.

C. pneumoniae isolate AR-39 was adapted to grow in HeLa 229 cells (21). Elementary bodies were purified through a linear gradient of meglumine diatrizoate and frozen at −70°C until used (16).

A gene bank was constructed with *C. pneumoniae* isolate AR-39 DNA which was digested with *Eco*RI, ligated to lambda gt11, and packaged with the Packagene Lambda DNA Packaging System according to the directions of the manufacturer (Promega Biotec, Madison, Wis.). *E. coli* Y1090 and Y1089 were used for lytic and lysogenic growth of lambda gt11, respectively, by standard protocol (17). The gene bank was screened with anti-*C. pneumoniae* rabbit immune serum by using horseradish peroxidase or alkaline phosphatase-based detection assays as previously described (6, 23). Lambda gt11 recombinant lysogens were prepared as described by Huynh et al. (17). Fusion proteins were analyzed by the sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) method of Laemmli (22). Immunoblots were done as described previously (20).

Monoclonal antibody (MAb) against gel-purified *C. pneumoniae* proteins were prepared as described previously (27). The characterization of MAb RR-60 is reported in this article. Rabbit immune serum prepared against the 60-kDa GroEL protein of *C. trachomatis* L2/434/Bu was graciously provided by Patrick Bavoil (University of Rochester, Rochester, N.Y.).

For immunoaffinity column preparation, MAb RR-60 was purified as described by Connelly et al. (9) and coupled to CNBr-activated Sepharose 4B following the manufacturer's directions (Pharmacia LKB Biotechnology, Piscataway, N.J.). The column was equilibrated against 5 column volumes with 0.01 M phosphate-buffered saline (PBS) (pH 7.6) containing 1% Triton X-100. Supernatants from induced preparations of *E. coli* JM107 containing either pLCK-1, which was constructed by subcloning the 3.0-kb *Eco*RI fragment into the vector pGEX-2T, or the vector alone were obtained according to the directions of the manufacturer (Pharmacia) and adsorbed onto the column for 30 min at room temperature. The column was washed with buffer (6 column volumes) until the optical density at 280 nm became 0. The absorbed antigen was eluted with 2.5 M sodium thiocyanate. The eluates from four consecutive runs were pooled, dialyzed, and concentrated by the Micro-ProDiCon (Bio-Molecular Dynamics, Beaverton, Oreg.).

The dideoxy-chain termination method of DNA sequenc-

* Corresponding author.

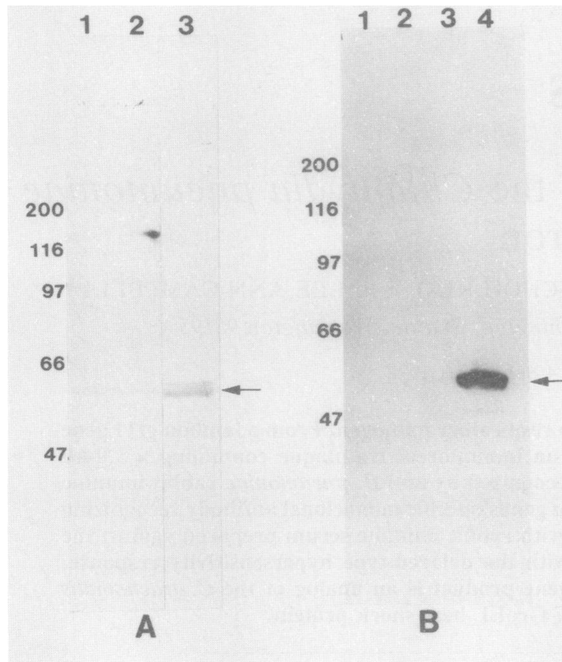

FIG. 1. Immunoblots reacted with anti-*C. pneumoniae* rabbit immune serum (A) and MAb RR-60 (B). (A) Lanes: 1, *E. coli* Y1089; 2, induced *E. coli* Y1089 containing lambda gt11; 3, induced lysogen containing the *C. pneumoniae* 3.0-kb *Eco*RI fragment in lambda gt11. (B) Lanes: 1, *E. coli* Y1089; 2, induced *E. coli* Y1089 containing lambda gt11; 3, induced lysogen from an immunoreactive *C. pneumoniae* recombinant containing a 2.0-kb *Eco*RI fragment in lambda gt11 expressing a portion of the *C. pneumoniae* hsp70 protein (20); 4, induced lysogen containing the *C. pneumoniae* 3.0-kb *Eco*RI fragment in lambda gt11. Arrows indicate the 60-kDa immunoreactive protein (panel A, lane 3; panel B, lane 4).

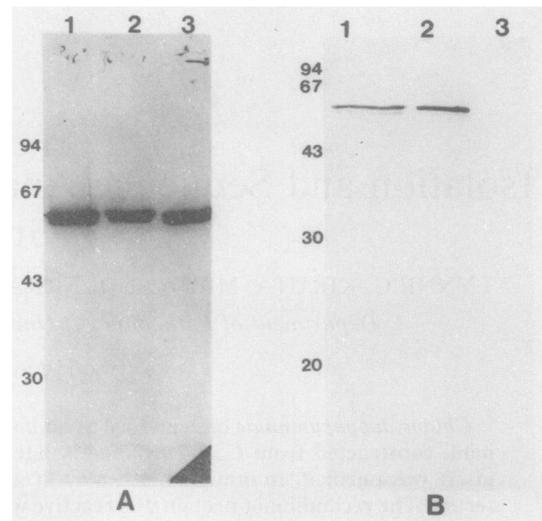

FIG. 2. Immunoblot demonstrating RR-60 recognition of a *Chlamydia* genus-specific epitope (A) found in the Sarkosyl-soluble fraction of *C. pneumoniae* (B). (A) Lanes: 1, *C. pneumoniae* TW-183; 2, *C. trachomatis* L2/434/Bu; and 3, *C. psittaci* 6BC. (B) Lanes: 1, *C. pneumoniae* AR-39 whole-cell lysate; 2, *C. pneumoniae* AR-39 Sarkosyl-soluble fraction; and 3, *C. pneumoniae* AR-39 Sarkosyl-insoluble fraction.

ing of Sanger et al. (26) was carried out on single-stranded fragments cloned into M13mp18 (29) with the Sequenase kit (United States Biochemical Corp., Cleveland, Ohio). Nested deletions of the 3.0-kb *Eco*RI fragment cloned in both orientations in M13mp18 were generated with the Erase-a-Base kit (Promega). Sequence analyses were performed by the Pustell sequence analysis program (IBI) and the University of Wisconsin Genetics Computer Group programs.

From a lambda gt11 gene bank screened by immunoassay with anti-*C. pneumoniae* rabbit immune serum, an immunoreactive recombinant which contained a 3.0-kb insert was identified. The lysates obtained from induced lysogens were analyzed by SDS-PAGE. Protein profiles demonstrated induction of a ca. 145-kDa fusion protein observed in the recombinant in comparison with the β-galactosidase portion, a 116-kDa polypeptide, observed in the lambda gt11 lysogen (data not shown). The 145-kDa fusion protein was not recognized by anti-*C. pneumoniae* rabbit immune serum. However, a ca. 60-kDa protein which reacted weakly with anti-*C. pneumoniae* rabbit immune serum was found in lysates prepared from the recombinant but not in lysates prepared from the lambda gt11 lysogen (Fig. 1A). These results suggested that this protein was expressed from the *C. pneumoniae* 3.0-kb *Eco*RI fragment. The recombinant 60-kDa protein was recognized by MAb RR-60, which had been prepared by immunizing mice with gel-purified *C. pneumoniae* 60-kDa protein (Fig. 1B). There was no reactivity with the induced lysogen without insert or with the host strain (Fig. 1B). To determine whether RR-60 was specific for *C. pneumoniae*, it was tested with whole-cell lysates of *C. pneumoniae*, *C. trachomatis* and *C. psittaci*. As shown in Fig. 2A, RR-60 recognizes a genus-reactive determinant on a 60-kDa *Chlamydia* protein.

At least two 60-kDa proteins have been identified for *C. trachomatis* and *C. psittaci*. One is a cysteine-rich, Sarkosyl-insoluble protein which is an essential structural component of the outer membrane (Omp2) (1). The second 60-kDa protein is a Sarkosyl-soluble protein that is antigenically similar to the GroEL heat shock protein (8, 24). The GroEL homolog has been shown to be identical to the chlamydial delayed-type hypersensitivity antigen described by Morrison et al. (2, 24). In order to determine which, if either, of these proteins was recognized by RR-60, Sarkosyl-soluble and -insoluble fractions were prepared as described by Caldwell et al. (4). As shown in Fig. 2B, this MAb reacted with a 60-kDa protein in whole-cell lysates of *C. pneumoniae* and with the Sarkosyl-extracted fraction. No reactivity was observed with the Sarkosyl-insoluble fraction prepared from *C. pneumoniae*. The same pattern of recognition was observed with samples prepared from *C. trachomatis* L2/434/Bu (data not shown). Reactivity with the Sarkosyl-soluble fractions suggested that the recombinant *C. pneumoniae* protein recognized by RR-60 was similar to the chlamydial delayed-type hypersensitivity antigen.

To confirm that the 60-kDa protein was antigenically related to the *C. trachomatis* GroEL homolog, polyclonal monospecific rabbit serum produced against the *C. trachomatis* protein (provided by P. Bavoil) was tested for reactivity with the *C. pneumoniae* recombinant. Because this antiserum also cross-reacts with the GroEL protein of the *E. coli* host strain, an affinity column was used to purify the recombinant *C. pneumoniae* 60-kDa protein from the *E. coli* hsp60 protein. This affinity column was prepared with the *Chlamydia*-specific MAb RR-60, which does not react with

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-476                 AATTTCACACAGGAAACAGCTATGACCATGATTACGAATCTACGGAGGTGTTGTAACCTCGGATTCCCTATCTGCATTAGAATGGGCTAGAATCCCTC

-378 ACTTCTACTATAATTTCTATGTTTATCAATATGCGACAGGTATCATAGCTGCCCTCTCCTTTGCTGAAAAAATTCTTACACAAGAACCAGGGCTCTCGAACTTTATTTAAAATTTTTTG

-259 AAAAGCGGAAGGTCTGACTTCCCACTCAATATATTAAAGAAATCGGGATTGGATATGACCACCTCTGCCTCCATTAGATAAAGCCTTTGCATTCATTACGAAAAAGATAGACCTACTCT

-140 CTTCCTTGCTTTCAGAAGATTGAGTTTTTAGCACTTAAAATTATTGAGTGCTAAAATTATTGCACAAAAAAAAACGCTTTGTTATCGTGATTGCAGAAATAGCAAAGTCTCTTAGAACG

-21  TAAAACA|TAAGGAGC|ATATAA ATG TCT GAT CAA GCA ACG ACC CTC CGA ATT AAA CCT TTG GGC GAT AGA ATC TTG GTA AAA AGG GAA GAA GAA
1                            M   S   D   Q   A   T   T   L   R   I   K   P   L   G   D   R   I   L   V   K   R   E   E   E

73   GAA GCC ACT GCT CGT GGA GGA ATC ATC TTA CCC GAT ACA GCA AAA AAG AAA CAA GAT CGT GCT GAG GTC CTT GTT TTA GGC ACA GGC AAA
25    E   A   T   A   R   G   G   I   I   L   P   D   T   A   K   K   K   Q   D   R   A   E   V   L   V   L   G   T   G   K

163  CGA ACT GAT GAC GGT ACT CTA CTT CCT TTC GAA GTT CAA GTT GGC GAT ATC ATT TTA ATG GAT AAG TAT GCA GGT CAA GAA ATC ACA ATC
55    R   T   D   D   G   T   L   L   P   F   E   V   Q   V   G   D   I   I   L   M   D   K   Y   A   G   Q   E   I   T   I

271  GAT GAC GAA GAG TAT GTC ATT CTA CAG TCC AGT GAA ATC ATG GCC GTC CTA AAA TAA AATACTAGTTTGCAGATTATAGAAAGT|TAAGGAGAA|CAACG
91    D   D   E   E   Y   V   I   L   Q   S   S   E   I   M   A   V   L   K  STOP

351  ATG GCA GCG AAA AAT ATT AAA TAT AAT GAA GAA GCC AGA AAA AAA ATA CAT AAA GGG GTA AAA ACT CTT GCA GAA GCA GTA AAA GTT ACT
1     M   A   A   K   N   I   K   Y   N   E   E   A   R   K   K   I   H   K   G   V   K   T   L   A   E   A   V   K   V   T

441  CTA GGT CCT AAA GGA CGT CAC GTA GTT ATA GAT AAG AGC TTT GGC TCT CCC CAA GTG ACT AAA GAT GGT GTT ACT GTA GCT AAA GAA ATC
31    L   G   P   K   G   R   H   V   V   I   D   K   S   F   G   S   P   Q   V   T   K   D   G   V   T   V   A   K   E   I

531  GAG CTC GAA GAC AAA CAT GAA AAC ATG GGC GCT CAG ATG GTA AAA GAA GTC GCC AGC AAA ACT GCT GAC AAA GCA GGC GAC GGA ACT ACA
61    E   L   E   D   K   H   E   N   M   G   A   Q   M   V   K   E   V   A   S   K   T   A   D   K   A   G   D   G   T   T

621  ACA GCA ACT GTT CTT GCA GAA GCA ATC TAT AGC GAA GGT CTA AGA AAT GTC ACT GCC GGT GCC AAT CCT ATG GAC CTA AAA AGA GGT ATC
91    T   A   T   V   L   A   E   A   I   Y   S   E   G   L   R   N   V   T   A   G   A   N   P   M   D   L   K   R   G   I

711  GAC AAA GCC GTA AAA GTT GTT GTT GAT GAA CTC AAA AAA ATT AGT AAA CCT GTA CAA CAT CAC AAA GAA ATC GCT CAA GTA GCT ACT ATC
121   D   K   A   V   K   V   V   V   D   E   L   K   K   I   S   K   P   V   Q   H   H   K   E   I   A   Q   V   A   T   I

801  TCA GCA AAT AAT GAT TCC GAA ATC GGA AAT CTT ATT GCA GAA GCT ATG GAA AAA GTT GGT AAA AAC GGA TCC ATT ACT GTT GAA GAA GCT
151   S   A   N   N   D   S   E   I   G   N   L   I   A   E   A   M   E   K   V   G   K   N   G   S   I   T   V   E   E   A

891  AAA GGC TTC GAA ACT GTT CTC GAC GTT GTA GAA GGA ATG AAC TTC AAC CGT GGA TAC CTC TCC AGC TAC TTC TCC ACA AAT CCA GAA ACT
181   K   G   F   E   T   V   L   D   V   V   E   G   M   N   F   N   R   G   Y   L   S   S   Y   F   S   T   N   P   E   T

981  CAA GAA TGC GTT TTA GAA GAC GCT CTG ATT CTA ATC TAC GAT AAA AAA ATC TCT GGA ATT AAA GAC TTC CTT CCA GTT TTA CAA CAA GTA
211   Q   E   C   V   L   E   D   A   L   I   L   I   Y   D   K   K   I   S   G   I   K   D   F   L   P   V   L   Q   Q   V

1071 GCA GAA TCT GGA CGC CCT CTT TTA ATC ATT GCA GAA GAA ATT GAA GGA GAA GCT TTA GCA ACT CTA GTA GTC AAT AGA CTC CGT GCA GGA
241   A   E   S   G   R   P   L   L   I   I   A   E   E   I   E   G   E   A   L   A   T   L   V   V   N   R   L   R   A   G

1161 TTC AGA GTC TGT GCA GTG AAA GCT CCT GGT TTC GGT GAC AGA AGA AAA GCT ATG TTA GAA GAC ATC GCT ATC CTT ACT GGT GGC CAA CTA
271   F   R   V   C   A   V   K   A   P   G   F   G   D   R   R   K   A   M   L   E   D   I   A   I   L   T   G   G   Q   L

1251 GTT AGC GAA GAA CTT GGC ATG AAA CTA GAG AAT ACA ACT CTA GCA ATG TTA GGA AAA GCT AAG AAA GTT ATC GTA ACT AAA GAA GAT ACC
301   V   S   E   E   L   G   M   K   L   E   N   T   T   L   A   M   L   G   K   A   K   K   V   I   V   T   K   E   D   T

1341 ACA ATC GTC GAA GGC TTA GGA AAC AAA CCT GAT ATC CAA GCT CGA TGC GAC AAT ATT AAA AAA CAA ATC GAA GAT AGC ACT TCA GAT TAC
331   T   I   V   E   G   L   G   N   K   P   D   I   Q   A   R   C   D   N   I   K   K   Q   I   E   D   S   T   S   D   Y

1431 GAC AAA GAA AAA CTC CAA GAG CGT TTA GCT AAA CTC TCC GGT GGT GTC GCC GTA ATC CGC GTA GGA GCT GCT ACC GAA ATA GAG ATG AAA
361   D   K   E   K   L   Q   E   R   L   A   K   L   S   G   G   V   A   V   I   R   V   G   A   A   T   E   I   E   M   K

1521 GAG AAA AAA GAC AGA GTA GAT GAT GCA CAA CAC GCA ACC ATT GCA GCT GTC GAA GAA GGA ATC CTC CCT GGT GGT GGA ACT GCC TTA GTT
391   E   K   K   D   R   V   D   D   A   Q   H   A   T   I   A   A   V   E   E   G   I   L   P   G   G   G   T   A   L   V

1611 CGC TGT ATC CCT ACA CTA GAA GCT TTC CTT CCT ATG CTA GCA AAC GAA GAC GAA GCT ATT GGT ACT CGT ATT ATT CTA AAA GCA TTA ACA
421   R   C   I   P   T   L   E   A   F   L   P   M   L   A   N   E   D   E   A   I   G   T   R   I   I   L   K   A   L   T

1701 GCT CCA TTA AAG CAA ATT GCA AGT AAC GCA GGT AAA GAA GGC GCT ATC ATT TGT CAG CAA GTT CTA GCA AGA TCT GCA AAT GAA GGC TAT
451   A   P   L   K   Q   I   A   S   N   A   G   K   E   G   A   I   I   C   Q   Q   V   L   A   R   S   A   N   E   G   Y

1791 GAT GCT TTA CGT GAC GCT TAT ACA GAT ATG ATT GAC GCA GGA ATT TTA GAT CCA ACT AAA GTG ACT CGC TCA GCT CTA GAA AGC GCA CGT
481   D   A   L   R   D   A   Y   T   D   M   I   D   A   G   I   L   D   P   T   K   V   T   R   S   A   L   E   S   A   R

1881 TCT ATC GCA GGA TTA CTC CTC ACA ACA GAA GCC TTA ATC GCT GAT ATC CCA GAA GAG AAA TCT TCT TCA GCT CCA GCG ATG CCA AGC GCA
511   S   I   A   G   L   L   L   T   T   E   A   L   I   A   D   I   P   E   E   K   S   S   S   A   P   A   M   P   S   A

1971 GGA ATG GAC TAC TAG  TCTCTTAAGCTAGTATTAACAATTTTCCATGAGGTCTCTTTTCTAACTAAAGAAAAGAGACCTTTTTCTTTGGGAATATTCATTTCTTAATCTATCT
541   G   M   D   Y  STOP

2083 TAATTATTAAGATATAAAACTCCTCTGCCTATATGTTTAAACTGCTAAAAAATCTATTTCTTATAGGGTGCTGCATCGTTGGATATTTCTGGATGCGCAAAGAAAGTATCGTTGAGCA

2201 ATGGCTATCTAACCGCCT
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FIG. 3. Nucleotide sequence and deduced amino acid sequence of the *C. pneumoniae* GroE operon. Putative ribosomal binding sites are boxed. The proposed transcription termination site, a 13-bp dyad, is shown with arrows.

the corresponding *E. coli* protein. Supernatants prepared from JM107 containing pLCK-1 or the vector alone were loaded onto the column and eluted as described above. In immunoblot analysis, the eluate from pLCK-1 was reactive with monospecific polyclonal antiserum recognizing the *C. trachomatis* GroEL homolog (data not shown). In contrast, the eluate from the *E. coli* host containing vector alone was not recognized by the antiserum. Reactivity with this *Chlamydia* GroEL serum further proved the antigenic relatedness of the *C. pneumoniae* 60-kDa protein with the *C. trachomatis* GroEL homolog.

To confirm the identity of the *C. pneumoniae* gene, the clone insert was sequenced. This analysis showed that the insert consisted of two open reading frames of 306 and 1,632 bp (Fig. 3). Initiation codons were preceded by Shine-Dalgarno ribosomal binding sites. The larger open reading frame was followed by a 13-bp loop with a predicted free energy of −17.1 kcal (ca. −71,600 J). This hairpin structure

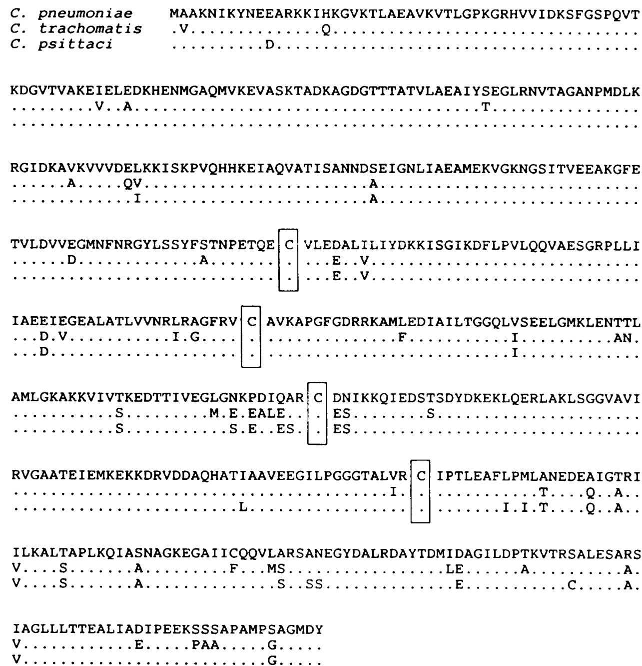

FIG. 4. Comparison of deduced amino acid sequences of GroEL from *C. pneumoniae*, *C. trachomatis* (8), and *C. psittaci* (24). A dot indicates the same amino acid as in the *C. pneumoniae* sequence. Cysteine residues conserved in the three chlamydial species are boxed.

is characteristic of a rho-independent terminator of translation and was followed by four thymidine residues. Sequence comparison showed that the smaller open reading frame had 74% DNA sequence similarity to both the *C. trachomatis* and *C. psittaci groES* genes. The larger open reading frame had 80 and 85% DNA sequence similarity to the *C. trachomatis* and *C. psittaci groEL* genes (8, 24). Thus, the *C. pneumoniae groES*-like and *groEL*-like genes exhibited the same structural organization as the *C. trachomatis* and *C. psittaci* GroE operons, with these regions found in tandem arrangement in a single operon (8).

The smaller open reading frame encoded a protein consisting of 102 amino acids with a molecular mass of 11,315, and the larger open reading frame encoded a protein of 544 amino acids with a molecular mass of 58,284. The translated amino acid sequences of both open reading frames closely resembled the GroES and GroEL amino acid sequences of *C. trachomatis* (89 and 95% similarities, respectively) and *C. psittaci* (93 and 97% similarities, respectively) (8, 24). In *C. trachomatis* and *C. psittaci*, four cysteine residues are conserved within the GroEL protein in regions that are not highly conserved in GroEL homologs from other species. These four cysteine residues were also conserved in *C. pneumoniae* (Fig. 4). Two different forms of the hsp60 have been suggested for the *C. trachomatis* elementary body (2). One is reduced and peripherally associated with the outer membrane, while the other is bound by disulfide linkages to the outer membrane (2). The additional finding of precise conservation of cysteine residues, which also extends to *C. pneumoniae*, has lead to the speculation that the *Chlamydia* GroES-GroEL complex is involved in the rearrangement process of the outer membrane during the transition from the elementary body to the reticulate body (8).

The 60-kDa Sarkosyl-soluble protein has also been implicated in immunopathological findings associated with *C. trachomatis* infection, including infertility and chronic trachoma (3, 24). Antibodies to the Sarkosyl-soluble 60-kDa protein have been found in patients with pelvic inflammatory disease, tubal infertility, and ectopic pregnancy (3, 28). Wagar et al. have suggested that women with pelvic inflammatory disease who develop chronic sequelae are those with antibody to the GroEL homolog (28). An association between antibody response to a chlamydial 60-kDa protein and reactive arthritis has been described; however, whether the antibody response was against chlamydial Omp2 or GroEL protein was not determined (18, 19). In the rat adjuvant arthritis model, arthritis is induced by injection of *Mycobacterium tuberculosis* and transferred to nondiseased rats by introduction of T-cell clones from arthritic rats (30). The *M. tuberculosis* hsp60 protein was identified as the antigen recognized by the arthritogenic T cells. Other studies have also suggested an association of the hsp60 stress proteins with autoimmune pathogenesis in several forms of arthritis, including rheumatoid arthritis, juvenile chronic arthritis, and reactive arthritis, on the basis of the stimulation and subsequent proliferation of T-cell clones with the corresponding hsp60 protein (10, 30).

The role of the 60-kDa protein in *C. pneumoniae* infection is unknown. For *C. trachomatis*, persistent infection or reinfection has been shown to increase adverse inflammatory responses, leading to the immunopathology of the disease (14). Likewise, reinfection with *C. pneumoniae* is common (13) and has been hypothesized to be associated with an increased severity in clinical symptoms and establishment of chronic disease. Morrison et al. have proposed that repeated exposure to the *Chlamydia* delayed-type hypersensitivity antigen contributes to the deleterious effects of *C. trachomatis* and *C. psittaci* infection (24). Possibly, this antigen plays a similar role in *C. pneumoniae* infection.

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