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The type I macrophage scavenger receptor binds to Gram-positive bacteria and recognizes lipoteichoic acid

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ABSTRACT **Macrophage scavenger receptors exhibit unusually broad binding specificity for polyanionic ligands and have been implicated in atherosclerosis and various host defense functions. Using a radiolabeled, secreted form of the type I bovine macrophage scavenger receptor in an *in vitro* binding assay, we have found that this receptor binds to intact Gram-positive bacteria, including *Streptococcus pyogenes, Streptococcus agalactiae, Staphylococcus aureus, Enterococcus hirae*, and *Listeria monocytogenes*. Competition binding studies using purified lipoteichoic acid, an anionic polymer expressed on the surface of most Gram-positive bacteria, show that lipoteichoic acids are scavenger receptor ligands and probably mediate binding of the receptor to Gram-positive bacteria. Lipoteichoic acids, for which no host cell receptors have previously been identified, are implicated in the pathogenesis of septic shock due to Gram-positive bacteria. Scavenger receptors may participate in host defense by clearing lipoteichoic acid and/or intact bacteria from tissues and the circulation during Gram-positive sepsis. Since scavenger receptors have been previously shown to bind to and facilitate bloodstream clearance of Gram-negative bacterial endotoxin (lipopolysaccharide), these receptors may provide a general mechanism for macrophage recognition and internalization of pathogens and their cell surface components.**

Macrophage scavenger receptors exhibit unusual broad ligand binding specificities (reviewed in refs. 1 and 2). Their diverse, high-affinity, polyanionic ligands include (*i*) chemically modified proteins, such as acetylated and oxidized low density lipoprotein and maleylated bovine serum albumin (M-BSA), but not their unmodified counterparts, (*ii*) certain polysaccharides, such as dextran sulfate, but not chondroitin sulfate, (*iii*) four-stranded, but not one- or two-stranded, polynucleotides, including poly(G) and poly(I), and (*iv*) others, such as anionic phospholipids and crocidolite asbestos. The broad ligand binding specificity of scavenger receptors is mediated by a short positively charged collagenous domain in the extracellular region of the receptor (3, 4). The two isoforms of the macrophage scavenger receptor exhibit similar binding properties, despite the presence of a cysteine-rich C-terminal domain of unknown function on the type I isoform that is not present on the type II molecule (5, 6).

The physiologic and pathophysiologic functions of macrophage scavenger receptors have not yet been established with certainty. Scavenger receptor-mediated uptake of modified lipoproteins into macrophages has been suggested to play a key role in the deposition of lipoprotein cholesterol in artery walls during the formation of atherosclerotic plaques (reviewed in refs. 7–9). Because of their broad binding specificity, macrophage scavenger receptors may also participate in host defense activities by recognizing and mediating the endocytosis of a wide variety of pathogenic substances (2, 9). The recent demonstration that scavenger receptors can bind a precursor of Gram-negative bacterial lipid A provided the first support for this proposal (10). These findings suggest that scavenger receptors help define a set of proteins that all contain short collagenous domains and participate in host defense by binding various pathogens (4, 11). Other members of this family include complement component C1q, mannose binding protein, pulmonary surfactant protein D, and conglutinin.

To further investigate the potential role of scavenger receptors in recognizing pathogens, we developed a method for measuring the binding of scavenger receptors to intact bacteria. We report here that a soluble form of the type I bovine scavenger receptor (s-bSR-I) binds to a wide array of Gram-positive bacteria. We also show that lipoteichoic acid (LTA), a virtually ubiquitous Gram-positive bacterial cell surface component, is a scavenger receptor ligand and probably mediates receptor binding to intact bacteria. Thus, scavenger receptors may participate in host defense by clearing LTA and/or Gram-positive bacteria from tissues and the bloodstream.

MATERIALS AND METHODS

Buffers and Reagents. Buffers used in the experiments were as follows: buffer A (20 mM Tris base, pH 8.0/150 mM NaCl/1 mM $CaCl_2$); buffer A plus BSA (buffer A containing 2 mg of BSA per ml and 0.05% NaN_3); buffer B (20 mM Tris base, pH 8.0/150 mM NaCl); buffer C (0.1 M sodium acetate, pH 4.7). Phenylmethylsulfonyl fluoride, leupeptin, pepstatin, L-methionine, poly(G), salicylic acid, and geneticin disulfate were purchased from Sigma. Ham's F-12 medium, L-glutamine, and penicillin/streptomycin were purchased from GIBCO/BRL. [^{35}S]Methionine (Trans^{35}S-label with 70% methionine) was from ICN. M-BSA coupled to CNBr-activated Sepharose (Pharmacia) (≈3 mg of M-BSA per ml of hydrated resin) was prepared as described (12).

Purified LTA from *Streptococcus pyogenes*, isolated as described (13), was generously provided by James Dale and Harry Courtney, Veterans Affairs Hospital, Memphis, TN. Purified LTA was suspended in LTA buffer (0.25% deoxycholate/0.2 M NaCl/1 mM EDTA/0.02% NaN_3/10 mM Tris·HCl, pH 8.0) prior to use.

Bacterial Strains. *S. pyogenes* strains T1/195/2, S43/192/4, J17E/165/3, T2/44/RB4/119, and T22/76/2 in addition to a spontaneous M protein-negative mutant (T28/51/4-4) with a large deletion in the *mry/emm* operon (14) and its parent wild type (T28/150A/5) were from Vincent Fischetti (Rockefeller University, New York). A Tn*916* mutant (JRS75) of *S. pyogenes* that lacks M protein and carboxypeptidase (15) and its type 6 parent strain (JRS4) were donated by June Scott (Emory University, Atlanta). *S. pyogenes*

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Abbreviations: LTA, lipoteichoic acid; M-BSA, maleylated bovine serum albumin; CHO, Chinese hamster ovary; s-bSR-I, soluble type I bovine scavenger receptor; FITC, fluorescein isothiocyanate.

wild-type strain 87-282 and its acapsular Tn*916* mutant, TX-4, were kindly provided by Mike Wessels (Channing Laboratory, Boston) (16). *Streptococcus agalactiae* strains A909 (type Ia) and COH 31-15 (unencapsulated Tn*918* mutant of type II strain COH 15) were also from M. Wessels (17). *S. agalactiae* strains 110 and 181 were from Steve Mattingly (Univ. of Texas Health Science Center, San Antonio, TX). *Staphylococcus aureus* capsular type 5 strain Reynolds and its transconjugate mutants, strains JL 236 (Tn*918*-induced capsule deficient mutant) and JL 240 (ethyl methanesulfonate-derived capsule negative mutant), in addition to type 8 strain Becker and its mutant, JL 252 (Tn*551*-induced capsule negative mutant), were generously donated by Jean Lee (Channing Laboratory) (18). *Streptococcus mutans* (ATCC 25175), *Enterococcus hirae* (ATCC 9790), *Listeria monocytogenes* (ATCC 43251), and *Bacillus subtilis* (ATCC 6633) were obtained from the American Type Tissue Collection (Rockville, MD). Strains of *Streptococcus pneumoniae* (rough, type 6, type 8) were from our laboratory.

Growth of Bacteria. Gram-positive bacteria were grown overnight on either LB agar plates (*L. monocytogenes, B. subtilis*) or 5% sheep blood agar plates (for all remaining organisms). Fresh colonies were inoculated into Todd Hewitt broth (Difco) and were grown to stationary phase (16–18 hr; 1×10^9 colony-forming units/ml) at 37°C without shaking. Initial experiments indicated greater binding of scavenger receptor to organisms grown to stationary phase compared to organisms used at logarithmic phase. Thus stationary-phase organisms were used in all experiments presented here, although results were similar for logarithmic-phase organisms. Bacterial strains were harvested by centrifugation at $3500 \times g$ for 10 min and washed twice in cold buffer B before resuspending to a final density of $\approx 1 \times 10^9$ bacteria per ml ($OD_{600} = 2.0$).

Fluorescein Isothiocyanate (FITC)-Labeled *S. pyogenes*. Stationary-phase organisms were suspended in phosphate-buffered saline (PBS) to $OD_{600} = 1.0$. To 5 ml of organisms, 5 μl of FITC (100 mg/ml in dimethyl sulfoxide) was added, and the mixture was incubated at 37°C for 60 min with periodic mixing in a Vortex. Organisms were washed twice in PBS and then suspended in Ham's F-12 medium containing 10% fetal calf serum.

Preparation of Metabolically Labeled s-bSR-I. Untransfected Chinese hamster ovary (CHO) cells and transfected CHO cells (CHO[s-bSR-I]-A2) expressing a truncated, secreted form of the s-bSR-I have been described (12). The trimeric s-bSR-I comprises all four extracellular domains of the intact receptor and exhibits the same broad binding specificity as the full-length integral membrane form of the receptor. CHO cells were grown in medium A (Ham's F-12 medium supplemented with 100 units of penicillin per ml, 100 μg of streptomycin per ml, and 2 mM glutamine) containing 5% (vol/vol) fetal calf serum (medium B). Transfected cells were grown in medium B containing 0.5 mg of G418 per ml. [^{35}S]Methionine-labeled conditioned medium was prepared from transfected CHO[s-bSR-I]-A2 cells and untransfected CHO cells as described (12) and designated [^{35}S]s-bSR-I medium and [^{35}S]control medium, respectively. Protease inhibitors added to conditioned medium were 1 mM phenylmethylsulfonyl fluoride, 1 μM leupeptin, and 1 μM pepstatin.

Microbial Binding Assay. Thirty minutes prior to binding assays, unlabeled L-methionine (10 mM final concentration) was added to suspensions of microorganisms grown as described above to minimize incorporation of free [^{35}S]methionine into microbial proteins during the assays. One-milliliter assay mixtures comprising 200 μl of bacterial suspension ($\approx 2 \times 10^8$ bacteria), 50 μl of buffer A, and 750 μl of either [^{35}S]s-bSR-I or [^{35}S]control medium were prepared in microcentrifuge tubes and incubated overnight on a rotator at 4°C. Suspensions of M-BSA-coupled Sepharose beads (M-BSA beads) (25 μl) were used in place of microorganism suspensions as positive controls. In the experiment shown in Fig. 3, the total assay volume was 0.25 ml instead of 1.0 ml and each assay contained 50 μl of LTA buffer with the indicated amounts of LTA and 10 μl of M-BSA beads. The amounts of scavenger receptor binding shown in Fig. 3 were measured with a Molecular Dynamics PhosphorImager.

After the overnight incubation, the bacteria were pelleted by centrifugation in a microcentrifuge at $12,500 \times g$ for 5 min at 4°C and washed twice with cold buffer A. In experiments examining the ability of LTA to inhibit the binding of the s-bSR-I to M-BSA beads, the beads were allowed to settle by gravity before each washing step, to prevent pelleting of LTA micelles. The washed pellets were then resuspended in SDS/PAGE sample buffer containing 2% 2-mercaptoethanol and boiled for 5 min, and insoluble material was removed by centrifugation at $12,500 \times g$ for 2 min. The reduced samples were fractionated by electrophoresis through 10% polyacrylamide gels (12) and the labeled proteins were visualized by autoradiography with Kodak XAR film. Prior to autoradiography, the gels were impregnated with either 0.125 M sodium salicylate in 30% (vol/vol) methanol or Autofluor (National Diagnostics).

Cell Binding Assay. P388D1 cells were maintained in dishes in Ham's F-12 medium with 10% fetal calf serum, 100 units of penicillin per ml, and 100 μg of streptomycin per ml. For experiments, ≈12,500 cells were plated on 1-cm glass coverslips in medium lacking antibiotics. Cells were allowed to adhere for at least 24–36 hr and then washed in Ham's F-12 medium containing 10% fetal calf serum. *S. pyogenes*, either unlabeled or FITC-labeled, was added (final dilution of 1:250 from a stock solution of $OD_{600} = 1.0$) in the presence or absence of various concentrations of poly(G). Mixtures were incubated for 30 min at 37°C in 5% CO_2, washed three times in PBS, and fixed with 100% cold methanol. Samples containing non-FITC-labeled organisms were Gram-stained, and then coverslips were mounted with Moviol and 1,4-diazabicyclo[2.2.2]octane. Slides were viewed in blinded fashion by two observers using fluorescence and phase-contrast microscopy and a Nikon Microphot FXA epifluorescence microscope. The results presented below (bacteria bound per 100 P388D1 cells) represent the means ± standard deviations determined from three experiments in which at least 100 P388D1 cells were counted for each condition.

RESULTS

s-bSR-I Binds to *S. pyogenes*. To determine if a secreted form of the s-bSR-I could directly bind to the surface of whole bacteria, we incubated bacteria at 4°C overnight with [^{35}S]methionine-labeled conditioned medium either from transfected CHO cells expressing the secreted receptor ([^{35}S]s-bSR-I medium) or from control untransfected CHO cells ([^{35}S]control medium). The bacteria and any bound protein were then solubilized with detergents and the bound metabolically labeled proteins were visualized after gel electrophoresis by autoradiography. Fig. 1*A* shows that when *S. pyogenes* strain T1/195/2 was incubated with [^{35}S]s-bSR-I medium, the most prominent of the labeled proteins bound to the bacteria was ≈78 kDa (lane 1), the mass of s-bSR-I (12). This protein was absent from *S. pyogenes* incubated with [^{35}S]control medium (see Fig. 1*B*), and these binding data were similar to data for the binding of [^{35}S]s-bSR-I to Sepharose beads covalently derivatized with the scavenger receptor ligand M-BSA (M-BSA beads, not shown). Therefore, we conclude that the 78-kDa binding protein was [^{35}S]s-bSR-I. Because the labeled scavenger receptor in [^{35}S]s-bSR-I medium represented only a small fraction of the total labeled protein (not shown), yet it was the major component of the bound proteins (lane 1), [^{35}S]s-bSR-I binding to *S. pyogenes*

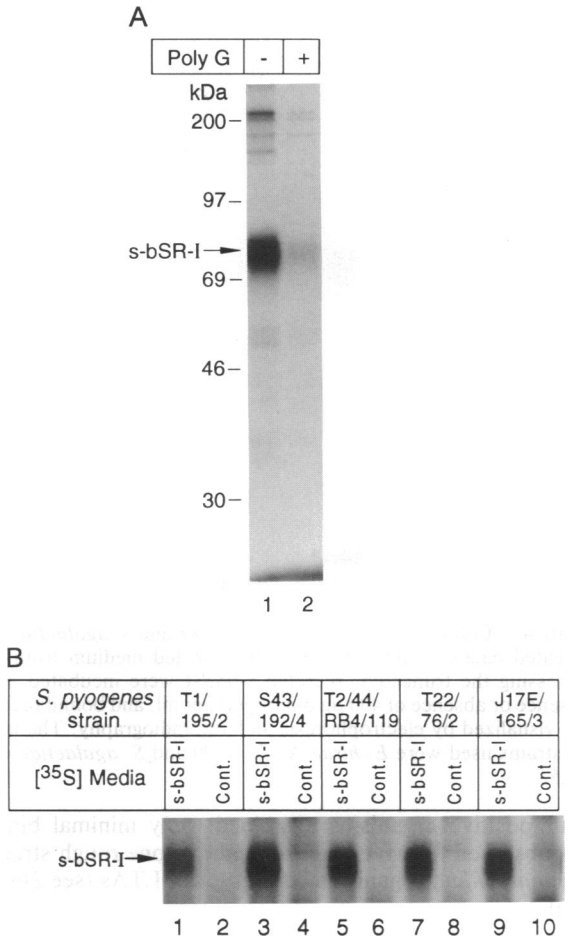

FIG. 1. Binding of s-bSR-I to *S. pyogenes*. [^{35}S]Methionine-labeled medium from transfected CHO cells expressing the truncated, secreted s-bSR-I or from untransfected controls (Cont.) was prepared and incubated overnight at 4°C with *S. pyogenes* T1/195/2 (*A*) or the indicated *S. pyogenes* strains (*B*). In lane 2 of *A*, the mixture was supplemented with 400 μg of the scavenger receptor ligand poly(G) per ml. After the incubation, the bacteria were washed and dissolved by boiling in reducing sample buffer, and bound ^{35}S-labeled components were resolved by 10% polyacrylamide gel electrophoresis and visualized by autoradiography.

appears to have been specific. In preliminary studies we also observed the binding of a soluble form of the type II bovine scavenger receptor as well as soluble forms of human type I and II scavenger receptor to Gram-positive bacteria (not shown).

The polynucleotide ligand poly(G) is an efficient competitive inhibitor of the binding of other polyanionic ligands (1, 12) to the cationic collagenous binding domain on the type I and type II scavenger receptors. Fig. 1*A*, lane 2, shows that the binding of *S. pyogenes* to s-bSR-I resembled binding of other ligands in that poly(G) was an effective competitor (compare to lane 1). This binding was not restricted to the T1/195/2 strain of *S. pyogenes*. Figs. 1 and 2 and Table 1 show that a total of 11 *S. pyogenes* strains representing seven different M protein types bound [^{35}S]s-bSR-I. Thus, [^{35}S]s-bSR-I binding is a general characteristic of *S. pyogenes* that is not strain specific.

The ability of poly(G) to inhibit *S. pyogenes* binding was used in experiments to examine the interaction of FITC-labeled *S. pyogenes* (strain T1/195/2) with a cultured murine macrophage-like cell line, P388D1, shown previously to express macrophage scavenger receptors (19). After a 30-min incubation at 37°C, we observed binding of 72 ± 8 bacteria per 100 P388D1 cells. When poly(G) at concentrations of 2,

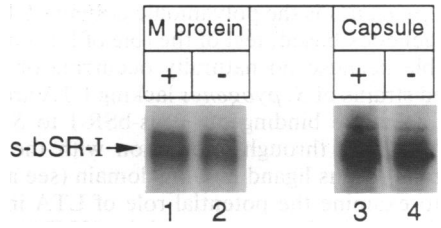

FIG. 2. Role of the M protein and the hyaluronic acid capsule in [^{35}S]s-bSR-I binding to *S. pyogenes*. The indicated bacteria and [^{35}S]methionine-labeled medium from cells expressing the truncated, secreted s-bSR-I were incubated together and bound receptor was visualized by electrophoresis and autoradiography. The bacteria used were *S. pyogenes* M protein-positive (T28/150A/5) and -negative (T28/51/4-4) strains (lanes 1 and 2), and the hyaluronic acid capsule-positive (wild-type 87-282) and -negative (TX-4) strains (lanes 3 and 4).

20, or 200 μg/ml was included in the incubation medium, the number of cell-associated bacteria per 100 P388D1 cells was reduced to 43 ± 4, 28 ± 9, and 22 ± 5, respectively. Similar results were obtained when binding of unlabeled bacteria was assessed by Gram staining (see *Materials and Methods*). These results raise the possibility that association of *S. pyogenes* with intact cultured murine macrophages may be mediated in part by their full-length, cell surface scavenger receptors. Additional studies will be necessary to determine the role of scavenger receptors in the internalization and processing of bacteria by macrophages in culture and *in vivo*.

s-bSR-I Binds to *S. pyogenes* Strains Lacking M Protein or Hyaluronic Acid Capsules. To determine which cell surface component(s) on *S. pyogenes* might be responsible for scavenger receptor binding, we used mutant strains of *S. pyogenes* to assess the role in receptor binding of two well-characterized virulence determinants, M protein and the hyaluronic acid capsule (16, 20–25). Fig. 2, lanes 1 and 2, shows that a type 28 *S. pyogenes* strain and its spontaneous M protein-negative mutant bound s-bSR-I equivalently. Similar results were obtained when assays were performed using a type 6 M protein-negative transposon mutant of *S. pyogenes* and its wild-type parent strain (Table 1, strains JRS75 and JRS4). Thus, the M protein is not necessary for binding. Fig. 2, lanes 3 and 4, also shows that the wild-type *S. pyogenes* strain 87-282 and its acapsular, hyaluronic acid-negative, transposon mutant, TX4, bound [^{35}S]s-bSR-I equally well. Therefore, it is unlikely that the hyaluronic acid capsule played a significant role in binding to s-bSR-I.

***S. pyogenes* LTA is a Ligand for s-bSR-I.** These results show that some other surface component must mediate binding of [^{35}S]s-bSR-I to *S. pyogenes*. Another major surface compo-

Table 1. Strains of Gram-positive bacteria that bound secreted [^{35}S]s-bSR-I

S. pyogenes	*S. aureus*
T1/195/2	Reynolds
S43/192/4	JL236
J17E/165/3	JL240
T2/44/RB4/119	Becker
T22/76/2	JL252
T28/51/4-4	*S. agalactiae*
T28/150A/5	A909
JRS75	COH 31-15
JRS4	110
87-282	181
TX-4	
S. mutans ATCC 25175	
E. hirae ATCC 9790	
L. monocytogenes ATCC 43251	
B. subtilis ATCC 6633	

nent of *S. pyogenes* is the polyanionic polymer LTA (26, 27). A direct, genetics-based, test of the role of LTA in binding is not possible because no naturally occurring or genetically engineered strains of *S. pyogenes* lacking LTA are available. However, because binding of [^{35}S]s-bSR-I to *S. pyogenes* apparently occurs through interaction with the receptor's cationic collagenous ligand binding domain (see above), it is possible to examine the potential role of LTA in mediating binding. This can be done by determining if LTA can function as a competitive inhibitor of [^{35}S]s-bSR-I binding to other ligands—e.g., M-BSA beads (12). Fig. 3 shows the results of an experiment in which increasing amounts of *S. pyogenes* LTA were added to mixtures of [^{35}S]s-bSR-I medium and M-BSA beads and the amount of [^{35}S]s-bSR-I binding was quantitated as described in *Materials and Methods*. *S. pyogenes* LTA was an effective inhibitor of binding (IC_{50} = ≈4 μg/ml). LTA also inhibited binding of [^{35}S]s-bSR-I to poly(G) beads, with a similar IC_{50} (not shown). These data suggest that LTA may be the major scavenger receptor binding determinant on *S. pyogenes*.

s-bSR-I Binds to an Array of Gram-Positive Bacteria. The finding that LTA probably mediates binding of scavenger receptors to *S. pyogenes* raised the possibility that many, if not all, Gram-positive bacteria might bind to scavenger receptors because LTA or analogous molecules are ubiquitous cell surface components on these microorganisms (reviewed in refs. 28 and 29). Fig. 4 shows that [^{35}S]s-bSR-I bound to *E. hirae* and *S. agalactiae*. Binding was competitively inhibited by poly(G). In binding studies using a wide variety of Gram-positive bacteria, we observed that most species and strains of bacteria tested bound [^{35}S]s-bSR-I (Table 1). Binding was competitively inhibited with poly(G), although the extent of competition varied slightly between organisms. In addition to the species shown in Fig. 4, [^{35}S]s-bSR-I bound to *S. aureus, S. mutans, L. monocytogenes*, and *B. subtilis*. Isogenic capsule-minus transposon mutants of *S. agalactiae* and *S. aureus* also bound [^{35}S]s-bSR-I equivalently or better than the parent strains, again suggesting that the capsule plays little, if any, role in [^{35}S]s-bSR-I binding. In contrast to the results with all other Gram-positive organisms examined, only minimal binding was observed to two encapusulated and one rough strain of *S. pneumoniae*, organisms with atypical LTAs (see *Discussion*).

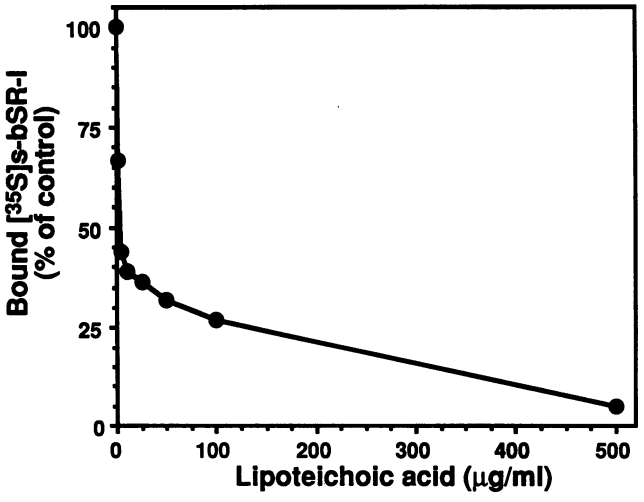

FIG. 3. Inhibition of [^{35}S]s-bSR-I binding to M-BSA beads by LTA from *S. pyogenes*. Binding of [^{35}S]s-bSR-I to M-BSA beads in the presence of the indicated amounts of LTA was performed. After an overnight incubation at 4°C, the adherent proteins were eluted from the beads by boiling in reducing sample buffer, bound [^{35}S]s-bSR-I was resolved by 10% polyacrylamide gel electrophoresis, and the relative amounts of bound [^{35}S]s-bSR-I were determined using a Molecular Dynamics PhosphorImager. All of the values shown were corrected for "nonspecific" background binding by subtracting the value determined in the presence of 400 μg of poly(G) per ml.

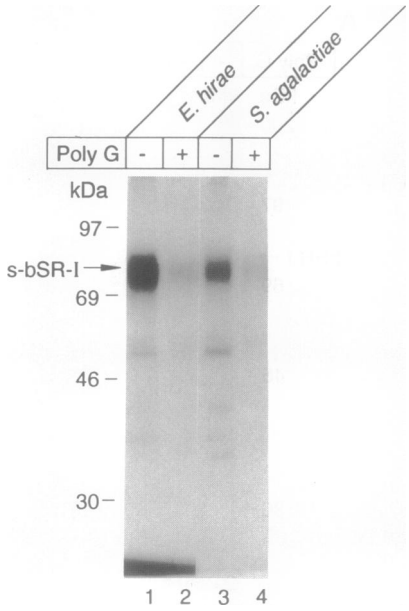

FIG. 4. Binding of [^{35}S]s-bSR-I to *E. hirae* and *S. agalactiae*. The indicated bacteria and [^{35}S]methionine-labeled medium from cells expressing the truncated, secreted s-bSR-I were incubated in the presence or absence of 400 μg of poly(G) per ml, and bound receptor was visualized by electrophoresis and autoradiography. The bacterial strains used were *E. hirae* ATCC 9790 and *S. agalactiae* COH 31-15.

DISCUSSION

In a series of *in vitro* binding studies using a truncated, secreted form of the s-bSR-I, we have shown that the scavenger receptor can bind to the surface of *S. pyogenes* and to a wide variety of other Gram-positive bacteria. The binding to *S. pyogenes* was inhibited by poly(G), a classic scavenger receptor ligand (1). Thus, the binding was probably mediated by interactions of negatively charged sites on the bacterial surface with the positively charged collagenous ligand binding domain of the receptor. Experiments using *S. pyogenes* mutants showed that the binding was independent of the hyaluronic acid capsule and the M protein, two major surface virulence determinants specific for *S. pyogenes* (16, 20–25). LTA, a polyanionic surface component found on most Gram-positive bacteria, was shown by competition assays to be a scavenger receptor ligand. It seems likely that LTA is at least one of the major determinants of scavenger receptor binding to *S. pyogenes*.

LTAs are amphipathic molecules typically consisting of a 1,3-phosphodiester-linked polymer of glycerophosphate linked covalently to either a glycolipid or a phosphatidyl glycolipid (reviewed in refs. 28–30). The resulting structures possess a backbone of repeating negative charges, a common feature of other scavenger receptor ligands, such as poly(G) and lipopolysaccharide micelles. Although there is immunological evidence that LTAs are absent from some Gram-positive bacteria, the presence of alternative polymers (atypical LTAs) in most of these organisms indicates that this class of molecules is a nearly invariant component in the Gram-positive cell wall (reviewed in refs. 29 and 31). The inability to isolate LTA-negative strains of Gram-positive bacteria further suggests that this surface component is critical for these organisms. It is likely that some atypical LTAs might

not tightly bind to scavenger receptors, as suggested by the weak interaction with *S. pneumoniae*, which expresses an unusual LTA containing choline and ribitolphosphate (32, 33).

Bacteremia with Gram-positive organisms can result in septic shock, which is often indistinguishable from that caused by Gram-negative bacteria (reviewed in ref. 35). It is generally accepted that lipopolysaccharide (endotoxin)-mediated release of cytokines, including interleukin 1 and tumor necrosis factor, is responsible for the syndrome of septic shock with Gram-negative organisms. It is likely that LTA serves a similar role in Gram-positive sepsis (reviewed in ref. 35). We have shown previously that the rapid scavenger receptor-mediated hepatic uptake of endotoxin *in vivo* can play a quantitatively significant role in endotoxin clearance and probably does not play a role in endotoxin-induced activation of macrophages (10). These results suggested that scavenger receptors presumably help in protection from endotoxic shock during Gram-negative bacterial sepsis. The current study raises the possibility that scavenger receptors might play a similar role during Gram-positive sepsis in recognizing and removing from tissues and the bloodstream intact Gram-positive organisms and LTA released from their surfaces.

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