conjugate (AAC). US 5545721 and US 6660267 describe synthesis of a non-specific immunoglobulin-antibiotic conjugate that binds to the surface of target bacteria via the antibiotic, and uses thereof for treating sepsis. US 7569677 and related patents suggest prophetically antibiotic-conjugated antibodies that have an antigen-binding portion specific for a bacterial antigen (such as SA capsular polysaccharide), but lack a constant region that reacts with a bacterial Fc-binding protein (e.g., staphylococcal protein A).

SUMMARY

The disclosure provides compositions referred to as "antibody-antibiotic conjugates," or "AAC") comprising an antibody conjugated by a covalent attachment to one or more rifamycin-type antibiotic moieties.

Disclosed is an isolated anti-WTA monoclonal antibody, comprising a light chain and a H chain, the L chain comprising CDR L1, CDR L2, and CDR L3 and the H chain comprising CDR H1, CDR H2 and CDR H3, wherein the CDR L1, CDR L2, and CDR L3 and CDR H1, CDR H2 and CDR H3 comprise the amino acid sequences of the CDRs of each of Abs 4461 (SEQ ID NO. 1-6), 4624 (SEQ ID NO. 7-12), 4399 (SEQ ID NO. 13-18), and 6267 (SEQ ID NO. 19-24) respectively, as shown in Tables 6A and 6B.

In one embodiment, the isolated anti-WTA monoclonal antibody comprises a heavy chain variable region comprising a heavy chain variable region (VH), wherein the VH comprises at least 95% sequence identity over the length of the VH region selected from the VH sequence of SEQ ID NO.26, SEQ ID NO.28, SEQ ID NO.30, SEQ ID NO.32 of antibodies 4461, 4624, 4399, and 6267, respectively. In one embodiment this antibody further comprises a L chain variable region (VL) wherein the VL comprises at least 95% sequence identity over the length of the VL region selected from the VL sequence of SEQ ID NO.25, SEQ ID NO.27, SEQ ID NO.29, SEQ ID NO.31 of antibodies 4461, 4624, 4399, and 6267, respectively. In another embodiment, the isolated anti-WTA monoclonal antibody comprises a L chain variable region (VL) wherein the VL comprises at least 95% sequence identity over the length of the VL region selected from the VL sequence of SEQ ID NO.25, SEQ ID NO.27, SEQ ID NO.29, SEQ ID NO.31 of antibodies 4461, 4624, 4399, and 6267, respectively. In any of the preceding embodiments, the sequence identity may be 96%, 97%, 98%, 99% or 100%.

In more specific embodiments, the antibody comprises:

(i) VL of SEQ ID NO. 25 and VH of SEQ ID NO. 26;

(ii) VL of SEQ ID NO. 27 and VH of SEQ ID NO. 28;

In any one of the preceding embodiments, the antibody may be an antigen-binding fragment lacking a Fc region. In some embodiments, the antibody is a F(ab) or F(ab')$_2$. In some embodiments, the antibody further comprises a heavy chain constant region and/or a light chain constant region, wherein the heavy chain constant region and/or the light chain constant region comprise one or more amino acids that are substituted with cysteine residues. In some embodiments, the heavy chain constant region comprises amino acid substitution A118C and/or S400C, and/or the light chain constant region comprises amino acid substitution V205C, wherein the numbering is according to the EU numbering. In some embodiments, the heavy chain constant region comprises the amino acid sequence of SEQ ID NO:149 and/or the light chain constant region comprises the amino acid sequence of SEQ ID NO:151. In some embodiments, the heavy chain constant region comprises the amino acid sequence of SEQ ID NO:149 and the light chain constant region comprises the amino acid sequence of SEQ ID NO:150. In some embodiments, the heavy chain constant region comprises the amino acid sequence of SEQ ID NO:148 and the light chain constant region comprises the amino acid sequence of SEQ ID NO:151.

In one embodiment, the Ab of any one of the preceding embodiments binds WTA alpha.

Disclosed herein is an isolated anti-WTA monoclonal antibody comprising a light chain and a H chain, the L chain comprising CDR L1, CDR L2, and CDR L3 and/or the H chain comprising CDR H1, CDR H2 and CDR H3, wherein the CDR L1, CDR L2, and CDR L3 and CDR H1, CDR H2 and CDR H3 comprise the amino acid sequences of the corresponding CDRs of each of Abs shown in Figure 14 (SEQ ID NO. 33-110). Disclosed herein is an isolated anti-WTA monoclonal antibody comprising a light chain and a H chain, the L chain comprising CDR L1, CDR L2, and CDR L3 and/or the H chain comprising CDR H1, CDR H2 and CDR H3, wherein the CDR L1, CDR L2, and CDR L3 and CDR H1, CDR H2 and CDR H3 comprise the amino acid sequences of the corresponding CDRs of each of Abs shown in Figure 15A, 15B, 16A and 16B (antibodies 6078, 6078.v2HC-Cys, 6078.v2LC-Cys, 6078.v3HC-Cys, 6078.v3LC-Cys, 6078.v4HC-Cys, 6078.v4LC-Cys, 6078.v4HCLC-Cys, 4497, 4497.v8HC-Cys, 4497.v8LC-Cys, and 4497.v8HCLC-Cys). In a specific embodiment these Abs bind WTA beta.

Disclosed herein is an isolated anti-WTA monoclonal antibody, specifically anti-WTA beta monoclonal antibody which comprises a L chain variable region (VL) wherein the VL comprises at least 95% sequence identity over the length of the VL region selected from the VL sequence corresponding to each of the antibodies 6078, 6263,

4450, 6297, 6239, 6232, 6259, 6292, 4462, 6265, 6253, 4497, and 4487 respectively, as shown in Figures 17A-1 to17A-2 at Kabat positions 1-107. In further embodiments, the antibody further comprises a heavy chain variable region comprising a heavy chain variable region (VH), wherein the VH comprises at least 95% sequence identity over the length of the VH region selected from the VH sequences corresponding to each of the antibodies 6078, 6263, 4450, 6297, 6239, 6232, 6259, 6292, 4462, 6265, 6253, 4497, and 4487 respectively, as shown in Figures 17B-1 to 17B-2 at Kabat positions 1-113. In any of the preceding embodiments, the sequence identity may be 96%, 97%, 98%, 99% or 100%. In a more specific embodiment of the antibody, the VH comprises the sequence of SEQ ID NO. 112 and the VL comprises the SEQ ID NO. 111.

Disclosed herein is an isolated anti-WTA monoclonal antibody, specifically anti-WTA beta monoclonal antibody which comprises a L chain variable region (VL) wherein the VL comprises at least 95% sequence identity over the length of the VL region selected from the VL sequence corresponding to each of the antibodies as shown in Figures 15A or 16A (antibodies 6078, 6078.v2HC-Cys, 6078.v2LC-Cys, 6078.v3HC-Cys, 6078.v3LC-Cys, 6078.v4HC-Cys, 6078.v4LC-Cys, 6078.v4HCLC-Cys, 4497, 4497.v8HC-Cys, 4497.v8LC-Cys, and 4497.v8HCLC-Cys) at Kabat positions 1-107. In further embodiments, the antibody further comprises a heavy chain variable region comprising a heavy chain variable region (VH), wherein the VH comprises at least 95% sequence identity over the length of the VH region selected from the VH sequences corresponding to each of the antibodies as shown in Figures 15B and 16B (antibodies 6078, 6078.v2HC-Cys, 6078.v2LC-Cys, 6078.v3HC-Cys, 6078.v3LC-Cys, 6078.v4HC-Cys, 6078.v4LC-Cys, 6078.v4HCLC-Cys, 4497, 4497.v8HC-Cys, 4497.v8LC-Cys, and 4497.v8HCLC-Cys) at Kabat positions 1-113. In any of the preceding embodiments, the sequence identity may be 96%, 97%, 98%, 99% or 100%.

In a certain embodiment, the isolated anti-WTA beta antibody is one wherein the light chain comprises the sequence of SEQ ID NO. 115 and the H chain having an engineered cysteine comprises the sequence of SEQ ID NO. 116. In another embodiment, the antibody is one wherein the light chain comprises the sequence of SEQ ID NO. 115 and the H chain having an engineered cysteine comprises the sequence of SEQ ID NO. 117, wherein X is M, I or V. In a different embodiment the L chain comprising the sequence of SEQ ID NO.113) is paired with a Cys-engineered H chain variant of SEQ ID NO. 117; the variant is one wherein X is M, I or V.

Another isolated anti-WTA beta antibody provided by the disclosure comprises a heavy chain and a light, wherein the heavy chain comprises a VH having at least 95% sequence identity to SEQ ID NO. 120. In an additional embodiment, this antibody further comprises a VL having at least 95% sequence identity to SEQ ID NO. 119. In a specific embodiment, the anti-WTA beta antibody comprises a light chain and a heavy chain, wherein the L chain comprises a VL sequence of SEQ ID NO. 119 and the H chain comprises a VH sequence of SEQ ID NO. 120. In a yet more specific embodiment, the isolated antibody that binds WTA beta comprises a L chain of SEQ ID NO. 121 and a H chain of SEQ ID NO. 122.

The anti-WTA beta Cys-engineered H and L chain variants can be paired in any of the following combinations to form full Abs for conjugating to linker-Abx intermediates to generate anti-WTA AACs of the disclosure. In one embodiment, the L chain comprises the sequence of SEQ ID NO.121 and the H chain comprises the sequence of SEQ ID NO. 124. In another embodiment, the isolated antibody comprises a L chain of SEQ ID NO. 123 and a H chain comprising a sequence of SEQ ID NO.124 or SEQ ID NO.157. In a particular embodiment, the anti- WTA beta antibody as well as the anti-WTA beta AAC of the disclosure comprises a L chain of SEQ ID NO. 123.

Yet another embodiment is an antibody that binds to the same epitope as each of the anti-WTA alpha Abs of Figure 13A and Figure 13B. Also provided is an antibody that binds to the same epitope as each of the anti-WTA beta Abs of Figure 14, Figures 15A and 15B, Figures 16A and 16B, and Figures 17A and 17B.

In a further embodiment, the anti-WTA beta and anti-WTA alpha antibodies of the present disclosure are antigen-binding fragments lacking the Fc region, preferably $F(ab')_2$ or F(ab). Thus, the present disclosure provides antibody-antibiotic conjugates wherein the WTA antibody is a $F(ab')_2$ or F(ab).

Disclosed herein is an anti-WTA monoclonal antibody that binds to WTA beta.

In some embodiments, the isolated anti-WTA (wall teichoic acid) monoclonal antibody comprising a light (L) chain and a heavy (H) chain, wherein:

(a) the L chain comprising CDR L1 comprising the sequence of RASQTISGWLA (SEQ ID NO:33), CDR L2 comprising the sequence of KASTLES (SEQ ID NO:34), and CDR L3 comprising the sequence of QQYKSYSFN (SEQ ID NO:35); and the H chain comprising CDR H1 comprising the sequence of SYDIN (SEQ ID NO:36), CDR H2 comprising the sequence of WMNANSGNTGYAQKFQG (SEQ ID

(l) the L chain comprising CDR L1 comprising the sequence of KSSQSIFRTSRNKNLLN (SEQ ID NO:99), CDR L2 comprising the sequence of WASTRKS (SEQ ID NO:100), and CDR L3 comprising the sequence of QQYFSPPYT (SEQ ID NO:101); and the H chain comprising CDR H1 comprising the sequence of SFWMH (SEQ ID NO:102), CDR H2 comprising the sequence of FTNNEGTTTAYADSVRG (SEQ ID NO:103), and CDR H3 comprising the sequence of GDGGLDD (SEQ ID NO:104);

(m) the L chain comprising CDR L1 comprising the sequence of _RASQFTNHYLN (SEQ ID NO:105), CDR L2 comprising the sequence of VASNLQS (SEQ ID NO:106), and CDR L3 comprising the sequence of QQSYRTPYT (SEQ ID NO:107); and the H chain comprising CDR H1 comprising the sequence of SGYYN (SEQ ID NO:108), CDR H2 comprising the sequence of YILSGAHTDIKASLGS (SEQ ID NO:109), and CDR H3 comprising the sequence of SGVYSKYSLDV (SEQ ID NO:110); or

(n) the L chain comprising CDR L1 comprising the sequence of KSSQSIFRTSRNKNLLN (SEQ ID NO:99), CDR L2 comprising the sequence of WASTRKS (SEQ ID NO:100), and CDR L3 comprising the sequence of QQYFSPPYT (SEQ ID NO:101); and the H chain comprising CDR H1 comprising the sequence of SFWMH (SEQ ID NO:102), CDR H2 comprising the sequence of FTNNEGTTTAYADSVRG (SEQ ID NO:103), and CDR H3 comprising the sequence of GEGGLDD (SEQ ID NO:118).

In one aspect, there is provided an anti-wall teichoic acid (WTA) monoclonal antibody, wherein the anti-wall teichoic acid monoclonal antibody binds to Staphylococcus aureus, and the VL of the anti-WTA monoclonal antibody comprises CDR L1 comprising the sequence of KSSQSIFRTSRNKNLLN (SEQ ID NO:99), CDR L2 comprising the sequence of WASTRKS (SEQ ID NO:100), and CDR L3 comprising the sequence of QQYFSPPYT (SEQ ID NO:101); and the VH of the anti-WTA monoclonal antibody comprises CDR H1 comprising the sequence of SFWMH (SEQ ID NO:102), CDR H2 comprising the sequence of FTNNEGTTTAYADSVRG (SEQ ID NO:103), and CDR H3 comprising the sequence of GEGGLDD (SEQ ID NO:118) or GDGGLDD (SEQ ID NO:104).

In some embodiments, the isolated anti-WTA monoclonal antibody comprises a heavy chain variable region (VH), wherein the VH comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.112, wherein amino acid Xaa at position 1 of SEQ ID NO.112 is Q or E, and amino acid Xaa at position 2 of SEQ ID NO.112 is M, I or V. In some embodiments, the antibody further comprises a light chain variable region (VL), wherein the VL comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.111. In some embodiments, the isolated anti-WTA monoclonal antibody comprises a light chain variable region (VL), wherein the VL comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.111. In any of the preceding embodiments, the sequence identity may be 96%, 97%, 98%, 99%, or 100%. In some embodiments, the VH of the antibody comprises the sequence of SEQ ID NO. 112 and the VL of the antibody comprises the sequence of SEQ ID NO.111.

In some embodiments, the isolated anti-WTA monoclonal antibody comprising a heavy chain and a light chain, wherein the heavy chain comprises the sequence of SEQ ID NO:146, SEQ ID NO.147, SEQ ID NO.157 or SEQ ID NO.124, and the light chain comprises the sequence of SEQ ID NO.121. In some embodiments, the isolated anti-WTA monoclonal antibody comprising a heavy chain and a light chain, wherein the heavy chain comprises the sequence of SEQ ID NO:146, SEQ ID NO.147, SEQ ID NO.157 or SEQ ID NO.124, and the light chain comprises the sequence of SEQ ID NO.123. In some embodiments, the isolated anti-WTA monoclonal antibody comprising a heavy chain and a light chain, wherein the heavy chain comprises the sequence of SEQ ID NO:146, SEQ ID NO.147, SEQ ID NO.157 or SEQ ID NO.124, and the light chain comprises the sequence of SEQ ID NO.145.

In some embodiments of any of the antibodies described above, the antibody is not an IgM isotype. In some embodiments of any of the antibodies described above, the antibody is an IgG (e.g., IgG1, IgG2, IgG3, IgG4), IgE, IgD, or IgA (e.g., IgA1 or IgA2) isotype. In some embodiments of any of the antibodies described above, the antibody is produced by a host cell in cell culture. In some embodiments, the host cell is a non-human cell. In some embodiments, the host cell is prokaryotic or eukaryotic. In some embodiments, the host cell is a mammalian cell (e.g., a human or non-human mammalian cell). In some embodiments, the host cell is a CHO cell.

Disclosed herein is a pharmaceutical composition comprising any of the antibodies disclosed herein, and a pharmaceutically acceptable carrier.

In yet another aspect, the invention also provides an isolated nucleic acid encoding any of the antibodies disclosed herein. In still another aspect, the invention provides a vector comprising a nucleic acid encoding any of the antibodies disclosed herein. In a further embodiment, the vector is an expression vector.

In one aspect, the invention also provides a host cell comprising a nucleic acid encoding any of the antibodies disclosed herein. In a further embodiment, the host cell is prokaryotic or eukaryotic. In some embodiments, the host cell is a mammalian cell (e.g., a human or non-human mammalian cell). In some embodiments, the host cell is a CHO cell.

In another aspect, the invention further provides a method of producing an antibody comprising culturing a host cell comprising a nucleic acid encoding any of the antibodies disclosed herein under conditions suitable for expression of the nucleic acid; and recovering the antibody produced by the cell. In some embodiments, the method further comprises purifying the antibody.

Disclosed herein is an antibody-antibiotic conjugate (AAC) compound comprising an anti-wall teichoic acid (WTA) antibody of the disclosure, covalently attached by a peptide linker to a rifamycin-type antibiotic. In some embodiments of the antibody –antibiotic conjugates disclosed herein, the anti-wall teichoic acid (WTA) antibody binds to *Staphylococcus aureus*. In some embodiments, the anti-wall teichoic acid antibody binds to methicillin-resistant *Staphylococcus aureus* (MRSA).

In some embodiments of the antibody-antibiotic conjugates disclosed herein, the antibody comprises: i) L chain and H chain CDRs of SEQ ID NOs 99-104 or the L chain and H chain CDRs of SEQ ID NOs. 33-38; or ii) the VL of SEQ ID NO.119 or SEQ ID NO. 123 paired with the VH of SEQ ID NO.120 or SEQ ID NO. 156; or iii) the VL of SEQ ID NO.111 paired with the VH of SEQ ID NO.112.

In some embodiments, the rifamycin-type antibiotic is a rifalazil-type antibiotic. In some embodiments, the rifamycin-type antibiotic comprises a quaternary amine attached to the peptide linker. In some embodiments, the antibiotic is attached to the antibody via a peptide linker which is attached to an engineered cysteine of the anti-WTA antibody. The engineered cysteine may be in the L or H chain of the modified antibody. In some embodiments, the cysteine residue is in the L chain. In some embodiments, the cysteine residue is in the H chain.

The antibody-antibiotic conjugate compounds of the disclosure can comprise a peptide linker which is a *S. aureus* cysteine protease cleavable linker; such linkers include a staphopain B or a staphopain A cleavable linker. In one embodiment, the *S. aureus* protease is an endopeptidase. In another embodiment the linker is a host protease cleavable linker preferably a human protease cathepsin B cleavable linker (e.g., a val-cit dipeptide linker).

An exemplary embodiment of an antibody-antibiotic conjugate compound has the formula:

$$Ab–(L–abx)_p$$

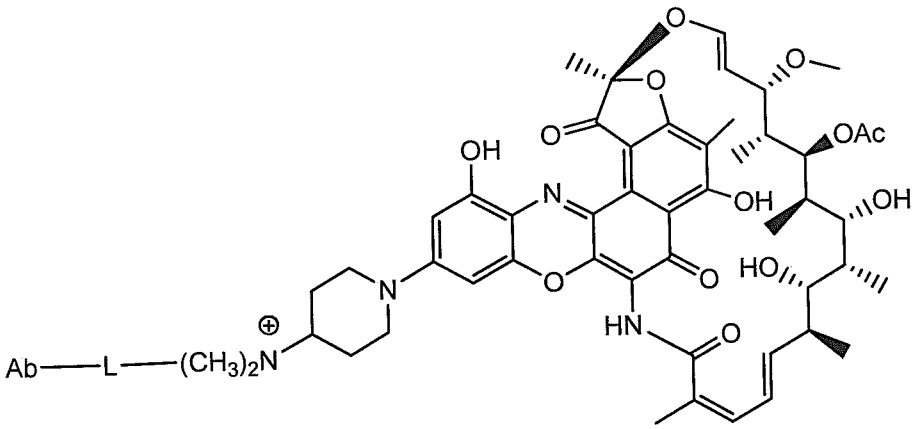
wherein:

Ab is the anti-wall teichoic acid antibody;

L is the peptide linker having the formula:

$$–Str–Pep–Y–$$

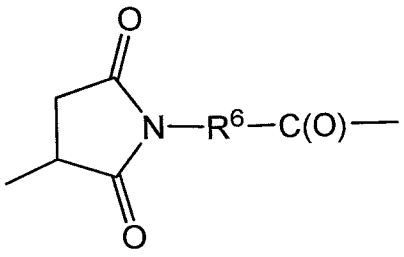
where Str is a stretcher unit; Pep is a peptide of two to twelve amino acid residues, and Y is a spacer unit;



In some embodiments, provided is an antibody-antibiotic conjugate (AAC) compound comprising an anti-wall teichoic acid (WTA) antibody of the disclosure, covalently attached by a peptide linker to a rifamycin-type antibiotic, where the peptide linker has the formula:

$$-Str-Pep-Y-$$

where Str is a stretcher unit covalently attached to the anti-wall teichoic acid (WTA) antibody; Pep is a peptide of two to twelve amino acid residues, and Y is a spacer unit covalently attached to the rifamycin-type antibiotic. In some of these embodiments, Str has the formula:



wherein R^6 is selected from the group consisting of C_1-C_{10} alkylene-, -C_3-C_8 carbocyclo, -O-(C_1-C_8 alkyl)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -$(CH_2CH_2O)_r$-, and -$(CH_2CH_2O)_r$-CH_2-; and r is an integer ranging from 1 to 10. In one variation, R^6 is -$(CH_2)_5$- . In some of these embodiments, Pep comprises two to twelve amino acid residues independently selected from glycine, alanine, phenylalanine, lysine, arginine, valine, and citrulline. In one variation, Pep is selected from valine-citrulline (val-cit, vc); phenylalanine-lysine (fk); GGAFAGGG (SEQ ID NO: 126); tpm-cit; GPImeLFF (SEQ ID NO: 129); valine-citrulline-phenylalanine (val-cit-phe); GGAFA (SEQ ID NO: 131); and LAFG (SEQ

Disclosed herein is a pharmaceutical composition comprising an antibody-antibiotic conjugate compound of the disclosure.

Disclosed herein is a method of treating a bacterial infection by administering to a patient a therapeutically-effective amount of an antibody-antibiotic conjugate compound of any of the above embodiments. In one embodiment, the patient is a human. In one embodiment the bacterial infection is a *Staphylococcus aureus* infection. In some embodiments, the patient has been diagnosed with a Staph aureus infection. In some embodiments, treating the bacterial infection comprises reducing bacterial load.

The disclosure further provides a method of killing intracellular Staph aureus in the host cells of a staph aureus infected patient without killing the host cells by administering an anti-WTA-antibiotic conjugate compound of any of the above embodiments. Another method is provided for killing persister bacterial cells (e.g, staph A) in vivo by contacting the persister bacteria with an AAC of any of the preceding embodiments.

In another embodiment, the method of treatment further comprises administering a second therapeutic agent. In a further embodiment, the second therapeutic agent is an antibiotic including an antibiotic against Staph aureus in general or MRSA in particular.

In one embodiment, the second antibiotic administered in combination with the antibody-antibiotic conjugate compound of the disclosure is selected from the structural classes: (i) aminoglycosides; (ii) beta-lactams; (iii) macrolides/cyclic peptides; (iv) tetracyclines; (v) fluoroquinolines/fluoroquinolones; (vi) and oxazolidinones.

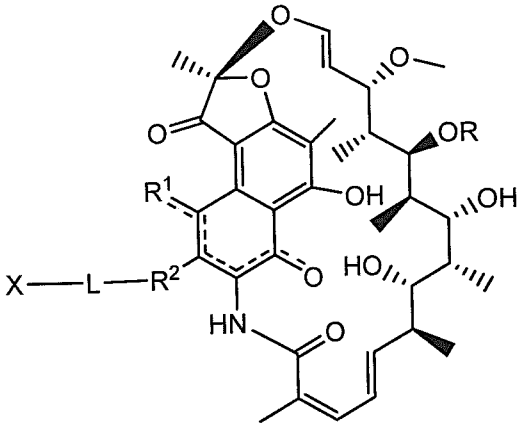
In one embodiment, the second antibiotic administered in combination with the antibody-antibiotic conjugate compound of the disclosure is selected from clindamycin, novobiocin, retapamulin, daptomycin, GSK-2140944, CG-400549, sitafloxacin, teicoplanin, triclosan, napthyridone, radezolid, doxorubicin, ampicillin, vancomycin, imipenem, doripenem, gemcitabine, dalbavancin, and azithromycin.

In some embodiments herein, the bacterial load in the subject has been reduced to an undetectable level after the treatment. In one embodiment, the patient's blood culture is negative after treatment as compared to a positive blood culture before treatment. In some embodiments herein, the bacterial resistance in the subject is undetectable or low. In some embodiments herein, the subject is not responsive to treatment with methicillin or vancomycin.

Disclosed herein is a process for making an antibody or an antibody-antibiotic conjugate compound of the disclosure comprising conjugating a rifamycin-type antibiotic to an anti-wall teichoic acid (WTA) antibody.

Disclosed herein is a kit for treating a bacterial infection comprising a pharmaceutical composition of the disclosure and instructions for use.

Disclosed herein is a linker-antibiotic intermediate having Formula II:



II

wherein:

the dashed lines indicate an optional bond;

R is H, C_1–C_{12} alkyl, or $C(O)CH_3$;

R^1 is OH;

R^2 is CH=N–(heterocyclyl), wherein the heterocyclyl is optionally substituted with one or more groups independently selected from $C(O)CH_3$, C_1–C_{12} alkyl, C_1–C_{12} heteroaryl, C_2–C_{20} heterocyclyl, C_6–C_{20} aryl, and C_3–C_{12} carbocyclyl;

or R^1 and R^2 form a five- or six-membered fused heteroaryl or heterocyclyl, and optionally forming a spiro or fused six-membered heteroaryl, heterocyclyl, aryl, or carbocyclyl ring, wherein the spiro or fused six-membered heteroaryl, heterocyclyl, aryl, or carbocyclyl ring is optionally substituted H, F, Cl, Br, I, C_1–C_{12} alkyl, or OH;

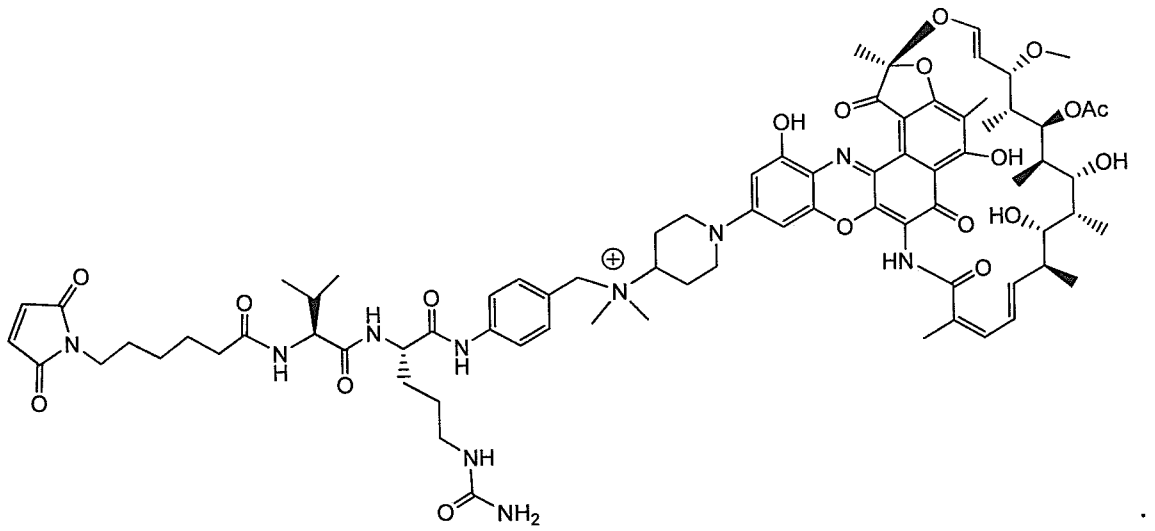
L is a peptide linker attached to R^2 or the fused heteroaryl or heterocyclyl formed by R^1 and R^2; and having the formula:

$$-Str-Pep-Y-$$

where Str is a stretcher unit; Pep is a peptide of two to twelve amino acid residues, and Y is a spacer unit; and

X is a reactive functional group selected from maleimide, thiol, amino, bromide, bromoacetamido, iodoacetamido, p-toluenesulfonate, iodide, hydroxyl, carboxyl, pyridyl disulfide, and N-hydroxysuccinimide.

In some embodiments of the linker-antibiotic intermediate of Formula II, X is



Also provided is a method of killing intracellular *Staph aureus* in the host cells of a *Staph aureus* infected patient without killing the host cells comprising administering an anti-WTA-antibiotic conjugate detailed herein.

It is to be understood that one, some, or all of the properties of the various embodiments described herein may be combined to form other embodiments of the present disclosure. These and other aspects of the disclosure will become apparent to one of skill in the art.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows that exposure to vancomycin or rifampicin kills MRSA gradually. Vancomycin was tested at 2 μg/mL (open square) and 20 μg/mL (closed square). Rifampicin was tested at 0.02 μg/mL (open triangle) and 0.2 μg/mL (closed triangle).

Figure 2 shows infected peritoneal cells were able to transfer infection to osteoblasts in the presence of vancomycin.

Figure 3 shows the cell wall of Gram-positive bacteria, such as S. aureus with a cartoon representation of wall teichoic acids (WTA), Lipo teichoic acid (LTA) and the Peptidoglycan (PGN) sheaths that stabilize the cell membrane and provide attachment sites.

Figure 4 shows the chemical structure and glycosyl modifications of Wall Teichoic Acid (WTA), described in detail under Definitions.

Figure 5 shows a possible mechanism of drug activation for antibody-antibiotic conjugates (AAC). Active antibiotic (Abx) is released after internalization of the AAC inside mammalian cells.

We Claim:

1. An anti-wall teichoic acid (WTA) monoclonal antibody, wherein the anti-wall teichoic acid monoclonal antibody binds to *Staphylococcus aureus*, and the VL of the anti-WTA monoclonal antibody comprises-CDR L1 comprising the sequence of KSSQSIFRTSRNKNLLN (SEQ ID NO:99), CDR L2 comprising the sequence of WASTRKS (SEQ ID NO:100), and CDR L3 comprising the sequence of QQYFSPPYT (SEQ ID NO:101); and the VH of the anti-WTA monoclonal antibody comprises CDR H1 comprising the sequence of SFWMH (SEQ ID NO:102), CDR H2 comprising the sequence of FTNNEGTTTAYADSVRG (SEQ ID NO:103), and CDR H3 comprising the sequence of GEGGLDD (SEQ ID NO:118) or GDGGLDD (SEQ ID NO:104).

2. The anti-wall teichoic acid (WTA) monoclonal antibody of claim 1, wherein the antibody comprises a VL comprising the amino acid sequence SEQ ID NO:119.

3. The anti-wall teichoic acid (WTA) monoclonal antibody of claim 1 or claim 2, wherein the antibody comprises a VH comprising the amino acid sequence of SEQ ID NO:156.

4. The anti-wall teichoic acid (WTA) monoclonal antibody of any one of claims 1 to 3, wherein the antibody comprises a VL and a VH, wherein the VL comprises the sequence of SEQ ID NO:119 and the VH comprises the sequence SEQ ID NO:156.

5. The anti-wall teichoic acid (WTA) monoclonal antibody of any one of claims 1 to 4, wherein the antibody comprises a light chain (LC) wherein the LC comprises the amino acid sequence of SEQ ID NO: 121, and a heavy chain (HC) wherein the HC comprises the amino acid sequence of SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:157 or SEQ ID NO:124.

6. The anti-wall teichoic acid (WTA) monoclonal antibody of any one of claims 1 to 5, wherein the antibody comprises a light chain (LC) wherein the LC comprises the amino acid sequence of SEQ ID NO:123, and a heavy chain (HC) wherein the HC comprises the amino acid sequence of SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:157 or SEQ ID NO:124.

7. The anti-wall teichoic acid (WTA) monoclonal antibody of any one of claims 1 to 5, wherein the antibody comprises a light chain (LC) wherein the LC comprises the amino acid sequence of SEQ ID NO:145, and a heavy chain (HC) wherein the HC comprises the amino acid sequence of SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:157 or SEQ ID NO:124.

8. The anti-wall teichoic acid (WTA) monoclonal antibody of any one of claims 1 to 5, wherein the antibody comprises a VH comprising the amino acid sequence of SEQ ID NO:120.

9. The anti-wall teichoic acid (WTA) monoclonal antibody of claim 1 or claim 2, wherein the antibody comprises a VL and a VH, wherein the VL comprises the sequence of SEQ ID NO:119 and the VH comprises the sequence SEQ ID NO:120.

10. The anti-wall teichoic acid (WTA) monoclonal antibody of any one of claims 1 to 5, wherein the antibody comprises a light chain (LC) wherein the LC comprises the amino acid sequence of SEQ ID NO:121, and a heavy chain (HC) wherein the HC comprises the amino acid sequence of SEQ ID NO:146.

11. The anti-wall teichoic acid (WTA) monoclonal antibody of any one of claims 1 to 5, wherein the antibody comprises a light chain (LC) wherein the LC comprises the amino acid sequence of SEQ ID NO:145, and a heavy chain (HC) wherein the HC comprises the amino acid sequence of SEQ ID NO:157.

12. The anti-wall teichoic acid (WTA) monoclonal antibody of any one of claims 1 to 5, wherein the antibody comprises a light chain (LC) wherein the LC comprises the amino acid sequence of SEQ ID NO:145, and a heavy chain (HC) wherein the HC comprises the amino acid sequence of SEQ ID NO:147.

13. The anti-wall teichoic acid (WTA) monoclonal antibody of claim 1, wherein the heavy chain constant region comprises amino acid substitution A118C, and/or the light chain constant region comprises amino acid substitution V205C, wherein the numbering is according to the EU numbering.

14. An isolated nucleic acid encoding an antibody of any one of claims 1 to 13.

15. A vector comprising the nucleic acid of claim 14.

16. A host cell comprising a nucleic acid encoding an antibody of any one of claims 1 to 13.

17. A method of producing an antibody comprising culturing a host cell of claim 17 under conditions suitable for expression of the nucleic acid; and recovering the antibody produced by the cell.