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 aspect, there is provided an isolated anti-WTA (wall teichoic acid) monoclonal antibody comprising a light (L) chain and a heavy (H) chain, wherein: 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 another aspect, there is provided an isolated anti-WTA monoclonal antibody comprising a light (L) chain and a heavy (H) chain, wherein: 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 NO:37), and CDR H3 comprising the sequence of SSILVRGALGRYFDL (SEQ ID NO:38).

In another aspect, there is provided an isolated anti-WTA monoclonal antibody comprising an amino acid sequence selected from the group consisting of:

(a) CDR L1 comprising the sequence of RASQTISGWLA (SEQ ID NO:39), CDR L2 comprising the sequence of KASTLES (SEQ ID NO:40), and CDR L3 comprising the sequence of QQYKSYSFN (SEQ ID NO:41); and CDR H1 comprising the sequence of SYDIN (SEQ ID NO:42), CDR H2 comprising the sequence of WMNANSGNTGYAQKFQG (SEQ ID NO:43), and CDR H3 comprising the sequence of SSILVRGALGRYFDL (SEQ ID NO:44);

(b) CDR L1 comprising the sequence of RASQFVSRTSLA (SEQ ID NO:45), CDR L2 comprising the sequence of ETSSRAT (SEQ ID NO:46), and CDR L3 comprising the sequence of HKYGSGPRT (SEQ ID NO:47); and CDR H1 comprising the sequence of NYDFI (SEQ ID NO:48), CDR H2 comprising the sequence of WMNPNSYNTGYGQKFQG (SEQ ID NO:49), and CDR H3 comprising the sequence of AVRGQLLSEY (SEQ ID NO:50);

(c) CDR L1 comprising the sequence of RASQSVSSSYLA (SEQ ID NO:51), CDR L2 comprising the sequence of DASSRAT (SEQ ID NO:52), and CDR L3 comprising the sequence of QKYGSTPRP (SEQ ID NO:53); and CDR H1 comprising the sequence of SYDIN (SEQ ID NO:54), CDR H2 comprising the sequence of WMNPNSGNTNYAQRFQG (SEQ ID NO:55), and CDR H3 comprising the sequence of ERWSKDTGHYYYYGMDV (SEQ ID NO:56);

(d) CDR L1 comprising the sequence of RASLDITNHLA (SEQ ID NO:57), CDR L2 comprising the sequence of EASILQS (SEQ ID NO:58), and CDR L3 comprising the sequence of EKCNSTPRT (SEQ ID NO:59); and CDR H1 comprising the sequence of NYDIN (SEQ ID NO:60), CDR H2 comprising the sequence of WMNPSSGRTGYAPKFRG (SEQ ID NO:61), and CDR H3 comprising the sequence of GGGYYDSSGNYHISGLDV (SEQ ID NO:62);

(e) CDR L1 comprising the sequence of RASQSVGAIYLA (SEQ ID NO:63), CDR L2 comprising the sequence of GVSNRAT (SEQ ID NO:64), and CDR L3 comprising the sequence of QLYTSSRALT (SEQ ID NO:65); and CDR H1 comprising the sequence of AYAMN (SEQ ID NO:66), CDR H2 comprising the sequence of SITKNSDSLYYADSVKG (SEQ ID NO:67), and CDR H3 comprising the sequence of LAARIMATDY (SEQ ID NO:68);

(f) CDR L1 comprising the sequence of RASQGIRNGLG (SEQ ID NO:69), CDR L2 comprising the sequence of PASTLES (SEQ ID NO:70), and CDR L3 comprising the

sequence of LQDHNYPPT (SEQ ID NO:71); and CDR H1 comprising the sequence of YYSMI (SEQ ID NO:72), CDR H2 comprising the sequence of SIDSSSRYLYYADSVKG (SEQ ID NO:73), and CDR H3 comprising the sequence of DGDDILSVYRGSGRPFDY (SEQ ID NO:74);

(g) CDR L1 comprising the sequence of RASQGIRNGLG (SEQ ID NO:75), CDR L2 comprising the sequence of PASTLES (SEQ ID NO:76), and CDR L3 comprising the sequence of LQDHNYPPS (SEQ ID NO:77); and CDR H1 comprising the sequence of YYSMI (SEQ ID NO:78), CDR H2 comprising the sequence of SIDSSSRYRYYTDSVKG (SEQ ID NO:79), and CDR H3 comprising the sequence of DGDDILSVYQGSGRPFDY (SEQ ID NO:80);

(h) CDR L1 comprising the sequence of RASQSVRTNVA (SEQ ID NO:81), CDR L2 comprising the sequence of GASTRAS (SEQ ID NO:82), and CDR L3 comprising the sequence of LQYNTWPRT (SEQ ID NO:83); and CDR H1 comprising the sequence of TNDMS (SEQ ID NO:84), CDR H2 comprising the sequence of TIIGIDDTTHYADSVRG (SEQ ID NO:85), and CDR H3 comprising the sequence of NSGIYSF (SEQ ID NO:86)

(i) CDR L1 comprising the sequence of RASQDIGSSLA (SEQ ID NO:87), CDR L2 comprising the sequence of ATSTLQS (SEQ ID NO:88), and CDR L3 comprising the sequence of QQLNNYVHS (SEQ ID NO:89); and CDR H1 comprising the sequence of DYAMG (SEQ ID NO:90), CDR H2 comprising the sequence of VVTGHSYRTHYADSVKG (SEQ ID NO:91), and CDR H3 comprising the sequence of RIWSYGDDSFDV (SEQ ID NO:92);

(j) CDR L1 comprising the sequence of RASQSIGDRLA (SEQ ID NO:93), CDR L2 comprising the sequence of WASNLEG (SEQ ID NO:94), and CDR L3 comprising the sequence of QQYKSQWS (SEQ ID NO:95); and CDR H1 comprising the sequence of SYAMN (SEQ ID NO:96), CDR H2 comprising the sequence of YISSIETIYYADSVKG (SEQ ID NO:97), and CDR H3 comprising the sequence of DRLVDVPLSSPNS (SEQ ID NO:98);

(k) 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 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).

~~In one aspect~~Disclosed is~~, there is provided~~ an isolated anti-WTA monoclonal antibody comprising 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 selected from SEQ ID NO.26, SEQ ID NO.28, SEQ ID NO.30, and SEQ ID NO.32. 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 aspect, there is provided~~ Disclosed is an isolated anti-WTA monoclonal antibody comprising 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 selected from SEQ ID NO.25, SEQ ID NO.27, SEQ ID NO.29, and SEQ ID NO.31. 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;

(iii) VL of SEQ ID NO. 29 and VH of SEQ ID NO. 30; or

(iv) VL of SEQ ID NO. 31 and VH of SEQ ID NO. 32.

~~In another aspect, there is provided~~Disclosed is an 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 KSSQSVLSRANNNYYVA (SEQ ID NO:1), CDR L2 comprising the sequence of WASTREF (SEQ ID NO:2), and CDR L3 comprising the sequence of QQYYTSRRT (SEQ ID NO:3); and the H chain comprising CDR H1 comprising the sequence of DYYMH (SEQ ID NO:4), CDR H2 comprising the sequence of WINPKSGGTNYAQRFQG (SEQ ID NO:5), and CDR H3 comprising the sequence of DCGSGGLRDF (SEQ ID NO:6);

(b) the L chain comprising CDR L1 comprising the sequence of RSNQNLLSSSNNNYLA (SEQ ID NO:7), CDR L2 comprising the sequence of WASTRES (SEQ ID NO:8), and CDR L3 comprising the sequence of QQYYANPRT (SEQ ID NO:9); and the H chain comprising CDR H1 comprising the sequence of DYYIH (SEQ ID NO:10), CDR H2 comprising the sequence of WINPNTGGTYYAQKFRD (SEQ ID NO:11), and CDR H3 comprising the sequence of DCGRGGLRDI (SEQ ID NO:12);

(c) the L chain comprising CDR L1 comprising the sequence of KSNQNVLASSNDKNYLA (SEQ ID NO:13), CDR L2 comprising the sequence of WASIRES (SEQ ID NO:14), and CDR L3 comprising the sequence of QQYYTNPRT (SEQ ID NO:15); and the H chain comprising CDR H1 comprising the sequence of DYYIH (SEQ ID NO:16), CDR H2 comprising the sequence of WINPNTGGTNYAQKFQG (SEQ ID NO:17), and CDR H3 comprising the sequence of DCGNAGLRDI (SEQ ID NO:18); or

(d) the L chain comprising CDR L1 comprising the sequence of KSSQNVLYSSNNKNYLA (SEQ ID NO:19), CDR L2 comprising the sequence of WASTRES (SEQ ID NO:20), and CDR L3 comprising the sequence of QQYYTSPPYT (SEQ ID NO:21); and the H chain comprising CDR H1 comprising the sequence of SYWIG (SEQ ID NO:22), CDR H2 comprising the sequence of IIHPGDSKTRYSPSFQG (SEQ ID NO:23), and CDR H3 comprising the sequence of LYCSGGSCYSDRAFSSLGAGGYYYYGMGV (SEQ ID NO:24).

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.

In another aspect, there is provided an antibody that binds to the same epitope as any one of the antibodies described herein. 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 is an anti-WTA monoclonal antibody that binds to WTA beta.

~~In another aspect, there is provided~~Disclosed is an 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 another aspect, there is provided~~Disclosed is an isolated anti-WTA monoclonal antibody comprising 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 Xaa at position 1 in SEQ ID NO.112 is Q or E, and Xaa at position 2 in SEQ ID NO.112 is M, I or V. Disclosed is 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 another aspect, there is provided~~Disclosed is an isolated anti-WTA monoclonal antibody comprising 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 another aspect, there is provided~~Disclosed is an isolated anti-WTA monoclonal antibody comprising 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 SEQ ID NO.120 or SEQ ID NO.156. ~~In another aspect, there is provided~~Disclosed is an isolated anti-WTA monoclonal antibody comprising: (a) 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 SEQ ID NO.119; (b) a light chain variable region (VL) and a heavy chain variable region (VH), wherein the VL comprises the sequence of SEQ ID NO.119 and the VH comprises the sequence SEQ ID NO.120. or SEQ ID NO.156; (c) a light chain variable region (VL), wherein the VL comprises a sequence having at least 95% sequence identity over the length of the VL sequence selected from the VL sequence of SEQ ID NO.158, SEQ ID NO.159, SEQ ID NO.160, SEQ ID NO.161, SEQ ID NO.162, SEQ ID NO.163, SEQ ID NO.164, SEQ ID NO.165, SEQ ID NO.166, SEQ ID NO.167, and SEQ ID NO.168; or (d) a heavy chain variable region (VH) comprising an amino acid sequence having at least 95% sequence identity over the length of the VH sequence elected from the VH sequence of SEQ ID NO.127, SEQ ID NO.133, SEQ ID NO.134, SEQ ID NO.169, SEQ ID NO.170, SEQ ID NO.171, SEQ ID NO.172, SEQ ID NO.173, SEQ ID NO.174, SEQ ID NO.175, and SEQ ID NO.176. 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 SEQ ID NO.119. In some embodiments, the isolated anti-WTA monoclonal antibody comprising 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 SEQ ID NO.119. In any of the preceding embodiments, the sequence identity may be 96%, 97%, 98%, 99%, or 100%. In some embodiments, the isolated anti-WTA monoclonal antibody comprising a light chain variable region (VL) and a heavy chain variable region (VH), wherein the VL comprises the sequence of SEQ ID NO.119 and the VH comprises the sequence SEQ ID NO.120 or SEQ ID NO.156.

In some embodiments, the isolated anti-WTA monoclonal antibody comprising a light chain variable region (VL), wherein the VL comprises a sequence having at least 95% sequence identity over the length of the VL sequence selected from the VL sequence of SEQ ID NO.158, SEQ ID NO.159, SEQ ID NO.160, SEQ ID NO.161, SEQ ID NO.162, SEQ ID NO.163, SEQ ID NO.164, SEQ ID NO.165, SEQ ID NO.166, SEQ ID NO.167, and SEQ ID NO.168. In some embodiments, the isolated anti-WTA monoclonal antibody comprising a heavy chain variable region (VH) comprising an amino acid sequence having at least 95% sequence identity over the length of the VH sequence elected from the VH sequence of SEQ ID NO.127, SEQ ID NO.133, SEQ ID NO.134, SEQ ID NO.169, SEQ ID NO.170, SEQ ID NO.171, SEQ ID NO.172, SEQ ID NO.173, SEQ ID NO.174, SEQ ID NO.175, and SEQ ID NO.176. In any of the preceding embodiments, the sequence identity may be 96%, 97%, 98%, 99%, or 100%. ~~In another aspect, there is provided~~Disclosed is an isolated anti-WTA monoclonal antibody comprising a light chain variable region (VL) and a heavy chain variable region (VH), wherein:

(a) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.158, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.169;

of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.134; or

(k) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.168, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.127.

~~In another aspect, there is provided~~Disclosed is an isolated anti-WTA monoclonal antibody comprising a light chain variable region (VL) and a heavy chain variable region (VH), wherein:

(a) the VL of the antibody comprises the VL sequence of SEQ ID NO.158, and the VH of the antibody comprises the VH sequence of SEQ ID NO.169;

(b) the VL of the antibody comprises the VL sequence of SEQ ID NO.159, and the VH of the antibody comprises the VH sequence of SEQ ID NO.170;

(c) the VL of the antibody comprises the VL sequence of SEQ ID NO.160, and the VH of the antibody comprises the VH sequence of SEQ ID NO.171;

(d) the VL of the antibody comprises the VL sequence of SEQ ID NO.161, and the VH of the antibody comprises the VH sequence of SEQ ID NO.172;

(e) the VL of the antibody comprises the VL sequence of SEQ ID NO.162, and the VH of the antibody comprises the VH sequence of SEQ ID NO.173;

(f) the VL of the antibody comprises the VL sequence of SEQ ID NO.163, and the VH of the antibody comprises the VH sequence of SEQ ID NO.174;

(g) the VL of the antibody comprises the VL sequence of SEQ ID NO.164, and the VH of the antibody comprises the VH sequence of SEQ ID NO.175;

(h) the VL of the antibody comprises the VL sequence of SEQ ID NO.165, and the VH of the antibody comprises the VH sequence of SEQ ID NO.176;

(i) the VL of the antibody comprises the VL sequence of SEQ ID NO.166, and the VH of the antibody comprises the VH sequence of SEQ ID NO.133;

(j) the VL of the antibody comprises the VL sequence of SEQ ID NO.167, and the VH comprises the VH sequence of SEQ ID NO.134;

(k) the VL of the antibody comprises the VL sequence of SEQ ID NO.168, and the VH comprises the VH sequence of SEQ ID NO.127;

(l) the VL of the antibody comprises the VL sequence of SEQ ID NO.113, and the VH comprises the VH sequence of SEQ ID NO.114; or

(m) the VL of the antibody comprises the VL sequence of SEQ ID NO.121, and the VH comprises the VH sequence of SEQ ID NO.138.

In some embodiments of the antibodies described above, the antibody is 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 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 another aspect, there is provided~~Disclosed is an isolated anti-WTA monoclonal antibody comprising (a) a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence of SEQ ID NO.114, SEQ ID NO.116, or SEQ ID NO.117, and the light chain of the antibody comprises the sequence of SEQ ID NO.113; wherein amino acid Xaa at position 2 of SEQ ID NO.116 or SEQ ID NO.117 is M, I, or V; (b) a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence of SEQ ID NO.114, SEQ ID NO.116, or SEQ ID NO.117, and the light chain of the antibody comprises the sequence of SEQ ID NO.115; wherein amino acid Xaa at position 2 of SEQ ID NO.116 or SEQ ID NO.117 is M, I, or V; (c) a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence selected from the group consisting of SEQ ID NO.139, SEQ ID NO.140, SEQ ID NO.141, SEQ ID NO.142, SEQ ID NO.143, and SEQ ID NO.144; and the light chain of the antibody comprises the sequence of SEQ ID NO.113; (d) a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence selected from the group consisting of SEQ ID NO.139, SEQ ID NO.140, SEQ ID NO.141, SEQ ID NO.142, SEQ ID NO.143, and SEQ ID NO.144; and the light chain of the antibody comprises the sequence of SEQ ID NO.115; (e) 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 or SEQ ID NO.123; or (f) 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, the isolated anti-WTA monoclonal antibody comprising a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence of SEQ ID NO.114, SEQ ID NO.116, or SEQ ID NO.117, and the light chain of the antibody comprises the sequence of SEQ ID NO.113; wherein amino acid Xaa at position 2 of SEQ ID NO.116 or SEQ ID NO.117 is M, I or V. In some embodiments, isolated anti-WTA monoclonal antibody comprising a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence of SEQ ID NO.114, SEQ ID NO.116, or SEQ ID NO.117, and the light chain of the antibody comprises the sequence of SEQ ID NO.115; wherein amino acid Xaa at position 2 of SEQ ID NO.116 or SEQ ID NO.117 is M, I or V. In some embodiments, the isolated anti-WTA monoclonal antibody comprising a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence selected from the group consisting of SEQ ID NO.139, SEQ ID NO.140, SEQ ID NO.141, SEQ ID NO.142, SEQ ID NO.143, and SEQ ID NO.144; and the light chain of the antibody comprises the sequence of SEQ ID NO.113. In some embodiments, the isolated anti-WTA monoclonal antibody comprising a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence selected from the group consisting of SEQ ID NO.139, SEQ ID NO.140, SEQ ID NO.141, SEQ ID NO.142, SEQ ID NO.143, and SEQ ID NO.144; and the light chain of the antibody comprises the sequence of SEQ ID NO.115.

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.

~~In another aspect, there is provided~~Disclosed is a composition comprising any of the antibodies described herein and a pharmaceutically acceptable carrier. Disclosed is a pharmaceutical composition comprising any of the antibodies disclosed herein, and a pharmaceutically acceptable carrier.

In yet another aspect, there is provided an isolated nucleic acid encoding any of the antibodies disclosed herein. In another aspect, there is provided a vector comprising the nucleic acid described herein. Disclosed is a vector comprising a nucleic acid encoding any of the antibodies disclosed herein. In a further embodiment, the vector is an expression vector.

In another aspect, there is provided an isolated host cell comprising a nucleic acid encoding any of the antibodies described herein. The disclosure 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, there is provided a method of producing an antibody comprising culturing a host cell described herein under conditions suitable for expression of the nucleic acid; and recovering the antibody produced by the cell. The disclosure 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.

In another aspect, there is provided a pharmaceutical composition comprising any of the antibody-antibiotic conjugate compounds described herein, and a pharmaceutically acceptable carrier, glidant, diluent, or excipient. Disclosed is a pharmaceutical composition comprising an antibody-antibiotic conjugate compound of the disclosure.

~~In another aspect, there is provided~~Disclosed is use of an antibody-antibiotic conjugate compound comprising an anti-wall teichoic acid (WTA) antibody covalently attached by a peptide linker to a rifamycin-type antibiotic, in the manufacture of a medicament for treating a bacterial infection in a patient. ~~In another aspect, there is provided~~Disclosed is use of any one of antibody-antibiotic conjugates described herein in the manufacture of a medicament for treating a bacterial infection in a patient. Disclosed 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.

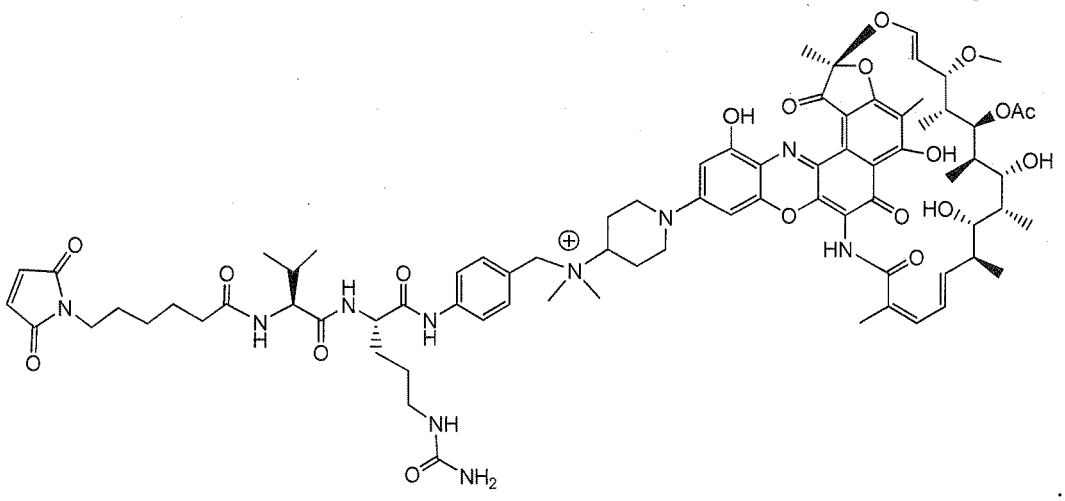
In another embodiment, the method of treatment further comprises administering a second therapeutic agent. In a further embodiment, the second therapeutic agent is an antibiotic including an antibiotic against Staph aureus in general or MRSA in particular.

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.

In another aspect, there is provided a process for making any one of the antibody-antibiotic conjugates described herein comprising conjugating a rifamycin-type antibiotic to an anti-wall teichoic acid (WTA) antibody. Disclosed 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.



In another aspect, there is provided use of any one of the anti-WTA-antibiotic conjugates described herein in the manufacture of a medicament for killing intracellular *Staphylococcus aureus* ~~Staph aureus~~ in the host cells of a *Staphylococcus aureus*-~~staph aureus~~infected patient without killing the host cells. 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 disclosures 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 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 KSSQSVLSRANNNYYVA (SEQ ID NO:1), CDR L2 comprising the sequence of WASTREF (SEQ ID NO:2), and CDR L3 comprising the sequence of QQYYTSRRT (SEQ ID NO:3); and the H chain comprising CDR H1 comprising the sequence of DYYMH (SEQ ID NO:4), CDR H2 comprising the sequence of WINPKSGGTNYAQRFQG (SEQ ID NO:5), and CDR H3 comprising the sequence of DCGSGGLRDF (SEQ ID NO:6);

(b) the L chain comprising CDR L1 comprising the sequence of RSNQNLLSSSNNNYLA (SEQ ID NO:7), CDR L2 comprising the sequence of WASTRES (SEQ ID NO:8), and CDR L3 comprising the sequence of QQYYANPRT (SEQ ID NO:9); and the H chain comprising CDR H1 comprising the sequence of DYYIH (SEQ ID NO:10), CDR H2 comprising the sequence of WINPNTGGTYYAQKFRD (SEQ ID NO:11), and CDR H3 comprising the sequence of DCGRGGLRDI (SEQ ID NO:12);

(c) the L chain comprising CDR L1 comprising the sequence of KSNQNVLASSNDKNYLA (SEQ ID NO:13), CDR L2 comprising the sequence of WASIRES (SEQ ID NO:14), and CDR L3 comprising the sequence of QQYYTNPRT (SEQ ID NO:15); and the H chain comprising CDR H1 comprising the sequence of DYYIH (SEQ ID NO:16), CDR H2 comprising the sequence of WINPNTGGTNYAQKFQG (SEQ ID NO:17), and CDR H3 comprising the sequence of DCGNAGLRDI (SEQ ID NO:18); or

(d) the L chain comprising CDR L1 comprising the sequence of KSSQNVLYSSNNKNYLA (SEQ ID NO:19), CDR L2 comprising the sequence of WASTRES (SEQ ID NO:20), and CDR L3 comprising the sequence of QQYYTSPPYT (SEQ ID NO:21); and the H chain comprising CDR H1 comprising the sequence of SYWIG (SEQ ID NO:22), CDR H2 comprising the sequence of IIHPGDSKTRYSPSFQG (SEQ ID NO:23), and CDR H3 comprising the sequence of LYCSGGSCYSDRAFSSLGAGGYYYYGMGV (SEQ ID NO:24).

2. An isolated anti-WTA monoclonal antibody comprising 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 selected from SEQ ID NO.26, SEQ ID NO.28, SEQ ID NO.30, and SEQ ID NO.32.

3. The antibody of claim 2, further comprising a L 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 selected from SEQ ID NO.25, SEQ ID NO.27, SEQ ID NO.29, and SEQ ID NO.31.

4. An isolated anti-WTA monoclonal antibody comprising 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 selected from SEQ ID NO.25, SEQ ID NO.27, SEQ ID NO.29, and SEQ ID NO.31.

5. The antibody of claim 3, wherein the antibody comprises:

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

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

   (iii) the VL comprising the sequence of SEQ ID NO. 29 and the VH comprising the sequence of SEQ ID NO. 30; or

   (iv) the VL comprising the sequence of SEQ ID NO. 31 and the VH comprising the sequence of SEQ ID NO. 32.

6. The antibody of any one of claims 1-5, wherein the antibody is an antigen-binding fragment lacking a Fc region; wherein optionally the antibody is a F(ab) or $F(ab')_2$.

7. The antibody of any one of claims 1-6, wherein 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; wherein optionally 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.

8. The antibody of any one of claims 1-5, wherein:

(a) the antibody further comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO:149 and/or a light chain constant region comprising the amino acid sequence of SEQ ID NO:151;

(b) the antibody further comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO:149 and a light chain constant region comprising the amino acid sequence of SEQ ID NO:150; or

(c) the antibody further comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO:148 and a light chain constant region comprising the amino acid sequence of SEQ ID NO:151.

9. The antibody of any one of claims 1-8, wherein the antibody binds WTA alpha.

10. An 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 NO:37), and CDR H3 comprising the sequence of SSILVRGALGRYFDL (SEQ ID NO:38);

(b) the L chain comprising CDR L1 comprising the sequence of RASQTISGWLA (SEQ ID NO:39), CDR L2 comprising the sequence of KASTLES (SEQ ID NO:40), and CDR L3 comprising the sequence of QQYKSYSFN (SEQ ID NO:41); and the H chain comprising CDR H1 comprising the sequence of SYDIN (SEQ ID NO:42), CDR H2 comprising the sequence of WMNANSGNTGYAQKFQG (SEQ ID

NO:43), and CDR H3 comprising the sequence of SSILVRGALGRYFDL (SEQ ID NO:44);

(c) the L chain comprising CDR L1 comprising the sequence of RASQFVSRTSLA (SEQ ID NO:45), CDR L2 comprising the sequence of ETSSRAT (SEQ ID NO:46), and CDR L3 comprising the sequence of HKYGSGPRT (SEQ ID NO:47); and the H chain comprising CDR H1 comprising the sequence of NYDFI (SEQ ID NO:48), CDR H2 comprising the sequence of WMNPNSYNTGYGQKFQG (SEQ ID NO:49), and CDR H3 comprising the sequence of AVRGQLLSEY (SEQ ID NO:50);

(d) the L chain comprising CDR L1 comprising the sequence of RASQSVSSSYLA (SEQ ID NO:51), CDR L2 comprising the sequence of DASSRAT (SEQ ID NO:52), and CDR L3 comprising the sequence of QKYGSTPRP (SEQ ID NO:53); and the H chain comprising CDR H1 comprising the sequence of SYDIN (SEQ ID NO:54), CDR H2 comprising the sequence of WMNPNSGNTNYAQRFQG (SEQ ID NO:55), and CDR H3 comprising the sequence of ERWSKDTGHYYYYGMDV (SEQ ID NO:56);

(e) the L chain comprising CDR L1 comprising the sequence of RASLDITNHLA (SEQ ID NO:57), CDR L2 comprising the sequence of EASILQS (SEQ ID NO:58), and CDR L3 comprising the sequence of EKCNSTPRT (SEQ ID NO:59); and the H chain comprising CDR H1 comprising the sequence of NYDIN (SEQ ID NO:60), CDR H2 comprising the sequence of WMNPSSGRTGYAPKFRG (SEQ ID NO:61), and CDR H3 comprising the sequence of GGGYYDSSGNYHISGLDV (SEQ ID NO:62);

(f) the L chain comprising CDR L1 comprising the sequence of RASQSVGAIYLA (SEQ ID NO:63), CDR L2 comprising the sequence of GVSNRAT (SEQ ID NO:64), and CDR L3 comprising the sequence of QLYTSSRALT (SEQ ID NO:65); and the H chain comprising CDR H1 comprising the sequence of AYAMN (SEQ ID NO:66), CDR H2 comprising the sequence of SITKNSDSLYYADSVKG (SEQ ID NO:67), and CDR H3 comprising the sequence of LAARIMATDY (SEQ ID NO:68);

(g) the L chain comprising CDR L1 comprising the sequence of RASQGIRNGLG (SEQ ID NO:69), CDR L2 comprising the sequence of PASTLES (SEQ ID NO:70), and CDR L3 comprising the sequence of LQDHNYPPT (SEQ ID NO:71); and the H

chain comprising CDR H1 comprising the sequence of YYSMI (SEQ ID NO:72), CDR H2 comprising the sequence of SIDSSSRYLYYADSVKG (SEQ ID NO:73), and CDR H3 comprising the sequence of DGDDILSVYRGSGRPFDY (SEQ ID NO:74);

(h) the L chain comprising CDR L1 comprising the sequence of _RASQGIRNGLG (SEQ ID NO:75), CDR L2 comprising the sequence of PASTLES (SEQ ID NO:76), and CDR L3 comprising the sequence of LQDHNYPPS (SEQ ID NO:77); and the H chain comprising CDR H1 comprising the sequence of YYSMI (SEQ ID NO:78), CDR H2 comprising the sequence of SIDSSSRYRYYTDSVKG (SEQ ID NO:79), and CDR H3 comprising the sequence of DGDDILSVYQGSGRPFDY (SEQ ID NO:80);

(i) the L chain comprising CDR L1 comprising the sequence of _RASQSVRTNVA (SEQ ID NO:81), CDR L2 comprising the sequence of GASTRAS (SEQ ID NO:82), and CDR L3 comprising the sequence of LQYNTWPRT (SEQ ID NO:83); and the H chain comprising CDR H1 comprising the sequence of TNDMS (SEQ ID NO:84), CDR H2 comprising the sequence of TIIGIDDTTHYADSVRG (SEQ ID NO:85), and CDR H3 comprising the sequence of NSGIYSF (SEQ ID NO:86)

(j) the L chain comprising CDR L1 comprising the sequence of RASQDIGSSLA (SEQ ID NO:87), CDR L2 comprising the sequence of ATSTLQS (SEQ ID NO:88), and CDR L3 comprising the sequence of QQLNNYVHS (SEQ ID NO:89); and the H chain comprising CDR H1 comprising the sequence of DYAMG (SEQ ID NO:90), CDR H2 comprising the sequence of VVTGHSYRTHYADSVKG (SEQ ID NO:91), and CDR H3 comprising the sequence of RIWSYGDDSFDV (SEQ ID NO:92);

(k) the L chain comprising CDR L1 comprising the sequence of RASQSIGDRLA (SEQ ID NO:93), CDR L2 comprising the sequence of WASNLEG (SEQ ID NO:94), and CDR L3 comprising the sequence of QQYKSQWS (SEQ ID NO:95); and the H chain comprising CDR H1 comprising the sequence of SYAMN (SEQ ID NO:96), CDR H2 comprising the sequence of YISSIETIYYADSVKG (SEQ ID NO:97), and CDR H3 comprising the sequence of DRLVDVPLSSPNS (SEQ ID NO:98);

(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).

11. An isolated anti-WTA monoclonal antibody comprising 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 Xaa at position 1 in SEQ ID NO.112 is Q or E, and Xaa at position 2 in SEQ ID NO.112 is M, I or V.

12. The antibody of claim 11, further comprising 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.

13. An isolated anti-WTA monoclonal antibody comprising 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.

14. The antibody of claim 13, wherein the VH comprises the sequence of SEQ ID NO. 112 and the VL comprises the sequence of SEQ ID NO.111, wherein Xaa at position 1 in SEQ ID NO.112 is Q or E, and Xaa at position 2 in SEQ ID NO.112 is M, I or V.

15. An isolated anti-WTA monoclonal antibody comprising 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 SEQ ID NO.120 or SEQ ID NO.156.

16. The antibody of claim 15, further comprising 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 SEQ ID NO.119.

17. An isolated anti-WTA monoclonal antibody comprising:

(a) 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 SEQ ID NO.119;

(b) a light chain variable region (VL) and a heavy chain variable region (VH), wherein the VL comprises the sequence of SEQ ID NO.119 and the VH comprises the sequence SEQ ID NO.120. or SEQ ID NO.156;

(c) a light chain variable region (VL), wherein the VL comprises a sequence having at least 95% sequence identity over the length of the VL sequence selected from the VL sequence of SEQ ID NO.158, SEQ ID NO.159, SEQ ID NO.160, SEQ ID NO.161, SEQ ID NO.162, SEQ ID NO.163, SEQ ID NO.164, SEQ ID NO.165, SEQ ID NO.166, SEQ ID NO.167, and SEQ ID NO.168; or

(d) a heavy chain variable region (VH) comprising an amino acid sequence having at least 95% sequence identity over the length of the VH sequence elected from the VH sequence of SEQ ID NO.127, SEQ ID NO.133, SEQ ID NO.134, SEQ ID NO.169, SEQ ID NO.170, SEQ ID NO.171, SEQ ID NO.172, SEQ ID NO.173, SEQ ID NO.174, SEQ ID NO.175, and SEQ ID NO.176.

18. An isolated anti-WTA monoclonal antibody comprising a light chain variable region (VL) and a heavy chain variable region (VH), wherein:

(a) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.158, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.169;

(b) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.159, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.170;

(c) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.160, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.171;

(d) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.161, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.172;

(e) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.162, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.173;

(f) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.163, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.174;

(g) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.164, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.175;

(h) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.165, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.176;

(i) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.166, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.133;

(j) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.167, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.134; or

(k) the VL of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VL sequence of SEQ ID NO.168, and the VH of the antibody comprises an amino acid sequence having at least 95% sequence identity over the length of the VH sequence of SEQ ID NO.127.

19. An isolated anti-WTA monoclonal antibody comprising a light chain variable region (VL) and a heavy chain variable region (VH), wherein:

(a) the VL of the antibody comprises the VL sequence of SEQ ID NO.158, and the VH of the antibody comprises the VH sequence of SEQ ID NO.169;

(b) the VL of the antibody comprises the VL sequence of SEQ ID NO.159, and the VH of the antibody comprises the VH sequence of SEQ ID NO.170;

(c) the VL of the antibody comprises the VL sequence of SEQ ID NO.160, and the VH of the antibody comprises the VH sequence of SEQ ID NO.171;

(d) the VL of the antibody comprises the VL sequence of SEQ ID NO.161, and the VH of the antibody comprises the VH sequence of SEQ ID NO.172;

(e) the VL of the antibody comprises the VL sequence of SEQ ID NO.162, and the VH of the antibody comprises the VH sequence of SEQ ID NO.173;

(f) the VL of the antibody comprises the VL sequence of SEQ ID NO.163, and the VH of the antibody comprises the VH sequence of SEQ ID NO.174;

(g) the VL of the antibody comprises the VL sequence of SEQ ID NO.164, and the VH of the antibody comprises the VH sequence of SEQ ID NO.175;

(h) the VL of the antibody comprises the VL sequence of SEQ ID NO.165, and the VH of the antibody comprises the VH sequence of SEQ ID NO.176;

(i) the VL of the antibody comprises the VL sequence of SEQ ID NO.166, and the VH of the antibody comprises the VH sequence of SEQ ID NO.133;

(j) the VL of the antibody comprises the VL sequence of SEQ ID NO.167, and the VH comprises the VH sequence of SEQ ID NO.134;

(k) the VL of the antibody comprises the VL sequence of SEQ ID NO.168, and the VH comprises the VH sequence of SEQ ID NO.127;

(l) the VL of the antibody comprises the VL sequence of SEQ ID NO.113, and the VH comprises the VH sequence of SEQ ID NO.114; or

(m) the VL of the antibody comprises the VL sequence of SEQ ID NO.121, and the VH comprises the VH sequence of SEQ ID NO.138.

20. The antibody of any one of claims 10-19, wherein the antibody is an antigen-binding fragment lacking a Fc region; wherein optionally the antibody is a F(ab) or $F(ab')_2$.

21. The antibody of any one of claims 10-20, wherein 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; wherein optionally 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.

22. The antibody of any one of claims 10-19, wherein:

(a) the antibody further comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO:149 and/or a light chain constant region comprising the amino acid sequence of SEQ ID NO:151;

(b) the antibody further comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO:149 and a light chain constant region comprising the amino acid sequence of SEQ ID NO:150; or

(c) the antibody further comprises a heavy chain constant region comprising the amino acid sequence of SEQ ID NO:148 and a light chain constant region comprising the amino acid sequence of SEQ ID NO:151.

23. An isolated anti-WTA monoclonal antibody comprising

(a) a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence of SEQ ID NO.114, SEQ ID NO.116, or SEQ ID NO.117, and the light chain of the antibody comprises the sequence of SEQ ID NO.113; wherein amino acid Xaa at position 2 of SEQ ID NO.116 or SEQ ID NO.117 is M, I, or V;

(b) a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence of SEQ ID NO.114, SEQ ID NO.116, or SEQ ID NO.117, and the light chain of the antibody comprises the sequence of SEQ ID NO.115; wherein amino acid Xaa at position 2 of SEQ ID NO.116 or SEQ ID NO.117 is M, I, or V;

(c) a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence selected from the group consisting of SEQ ID NO.139, SEQ ID NO.140, SEQ ID NO.141, SEQ ID NO.142, SEQ ID NO.143, and SEQ ID NO.144; and the light chain of the antibody comprises the sequence of SEQ ID NO.113;

(d) a light chain and a heavy chain, wherein the heavy chain of the antibody comprises the sequence selected from the group consisting of SEQ ID NO.139, SEQ ID NO.140, SEQ ID NO.141, SEQ ID NO.142, SEQ ID NO.143, and SEQ ID NO.144; and the light chain of the antibody comprises the sequence of SEQ ID NO.115;

(e) 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 or SEQ ID NO.123; or

(f) 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.

24. The antibody of any one of claims 10-23, wherein the antibody binds WTA beta.

25. An antibody that binds to the same epitope as the antibody of any one of claims 1-24.

26. The antibody of any one of claims 1-25, wherein the antibody is produced in a host cell in cell culture; wherein optionally the host cell is a Chinese hamster ovary (CHO) cell.

27. A composition comprising an antibody of any one of claims 1-26 and a pharmaceutically acceptable carrier.

28. An isolated nucleic acid encoding an antibody of any one of claims 1-25.

29. A vector comprising the nucleic acid of claim 28.

30. An isolated host cell comprising a nucleic acid encoding an antibody of any one of claims 1-25.

31. A method of producing an antibody comprising culturing a host cell of claim 30 under conditions suitable for expression of the nucleic acid; and recovering the antibody produced by the cell.

32. An antibody-antibiotic conjugate compound comprising an anti-wall teichoic acid (WTA) antibody of any one of claims 1 to 26, covalently attached by a peptide linker to a rifamycin-type antibiotic.

33. The antibody-antibiotic conjugate compound of claim 32 wherein 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.

34. The antibody-antibiotic conjugate compound of claim 32 or 33, wherein the anti-wall teichoic acid (WTA) antibody binds to *Staphylococcus aureus*; wherein optionally the anti-wall teichoic acid (WTA) antibody binds to methicillin-resistant *Staphylococcus aureus* (MRSA).

35. The antibody-antibiotic conjugate of any one of claims 32-34, wherein the rifamycin-type antibiotic is a rifalazil-type antibiotic.

36. The antibody-antibiotic conjugate of any one of claims 32-35, wherein the rifamycin-type antibiotic comprises a quaternary amine attached to the peptide linker.

37. The antibody-antibiotic conjugate of any one of claims 32-36, wherein the peptide linker is attached to a cysteine or an engineered cysteine of the anti-wall teichoic acid (WTA) antibody.

38. The antibody-antibiotic conjugate of any one of claims 32-37, wherein the peptide linker is a *S. aureus* endopeptidase or cysteine protease cleavable linker; wherein optionally the peptide linker is

(a) a staphopain B or a staphopain A cleavable linker, or

(b) a human protease cathepsin B cleavable linker,

wherein optionally the peptide linker is a val-cit dipeptide linker.

39. The antibody-antibiotic conjugate of claim 32 having the formula:

$$Ab–(L–abx)_p$$

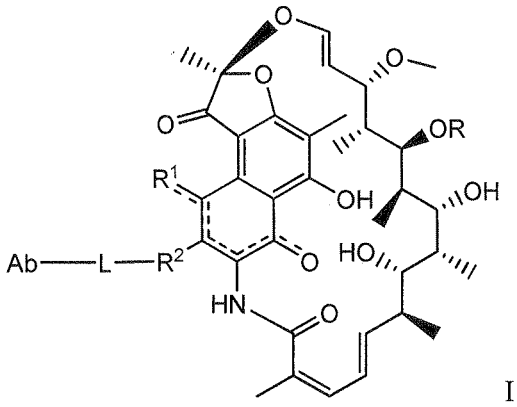
wherein:
Ab is the anti-wall teichoic acid antibody;
L is the peptide linker having the formula:

$$–Str–Pep–Y–$$

where Str is a stretcher unit; Pep is a peptide of two to twelve amino acid residues, and Y is a spacer unit;
abx is the rifamycin-type antibiotic; and
p is an integer from 1 to 8.

40. The antibody-antibiotic conjugate of claim 39, wherein p is 2 to 4.

41. The antibody-antibiotic conjugate compound of claim 32 having Formula I:



I

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;

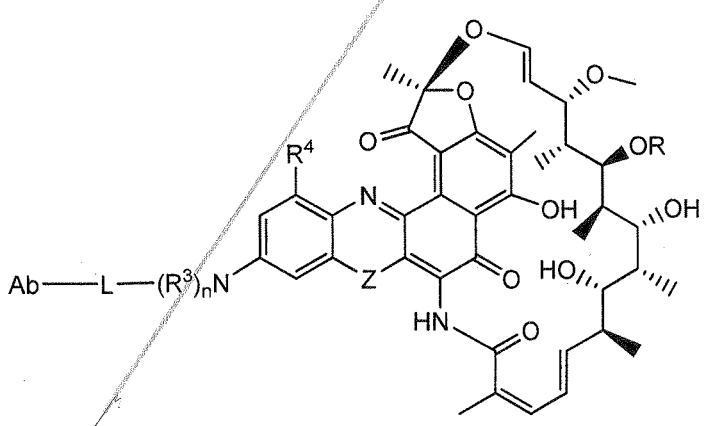
R^2 is CH=N–(heterocyclyl), wherein the heterocyclyl is optionally substituted with one or more groups independently selected from $C(O)CH_3$, C_1–C_{12} alkyl, C_1–C_{12} heteroaryl, C_2–C_{20} heterocyclyl, C_6–C_{20} aryl, and C_3–C_{12} carbocyclyl;

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 the peptide linker attached to R^2 or the fused heteroaryl or heterocyclyl formed by R^1 and R^2; and

Ab is the anti-wall teichoic acid (WTA) antibody.

42. The antibody-antibiotic conjugate compound of claim 41 having the formula: (a)



wherein

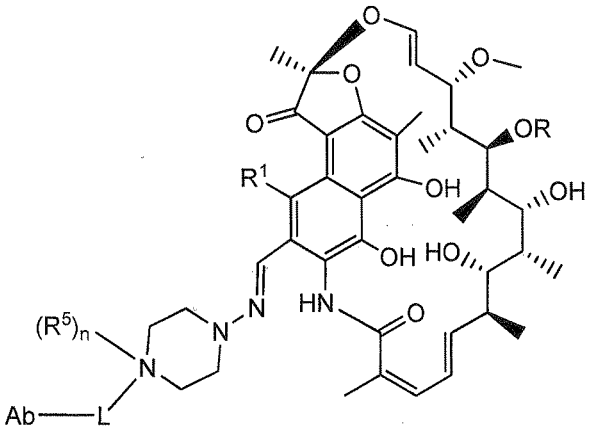
R^3 is independently selected from H and C_1–C_{12} alkyl;

n is 1 or 2;

R^4 is selected from H, F, Cl, Br, I, C_1–C_{12} alkyl, and OH; and

Z is selected from NH, N(C_1–C_{12} alkyl), O and S;

(b)

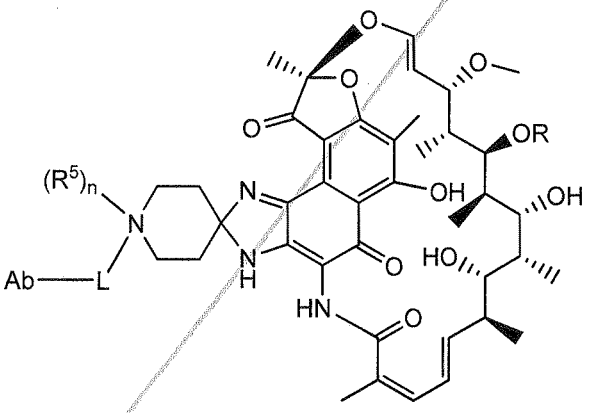


wherein

R^5 is selected from H and C_1–C_{12} alkyl; and

n is 0 or 1;

(c)

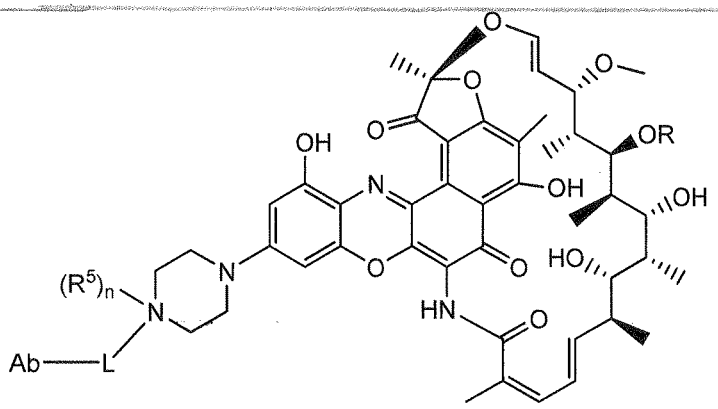


wherein

R^5 is selected from H and C_1–C_{12} alkyl; and

n is 0 or 1;

(d)

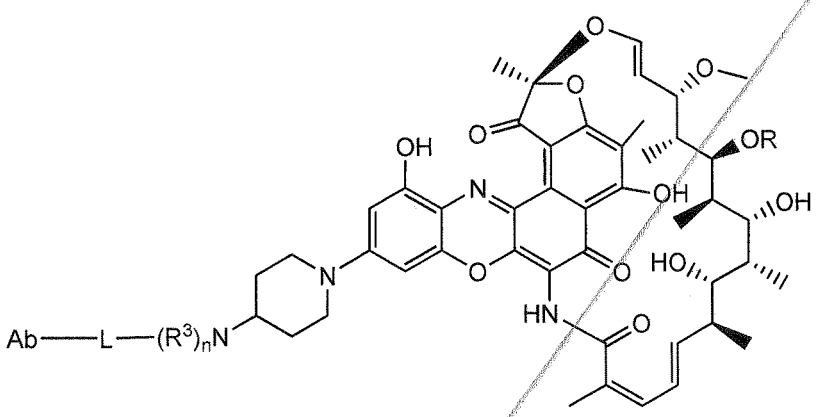


wherein

R^5 is independently selected from H and C_1–C_{12} alkyl; and

n is 0 or 1;

(e)

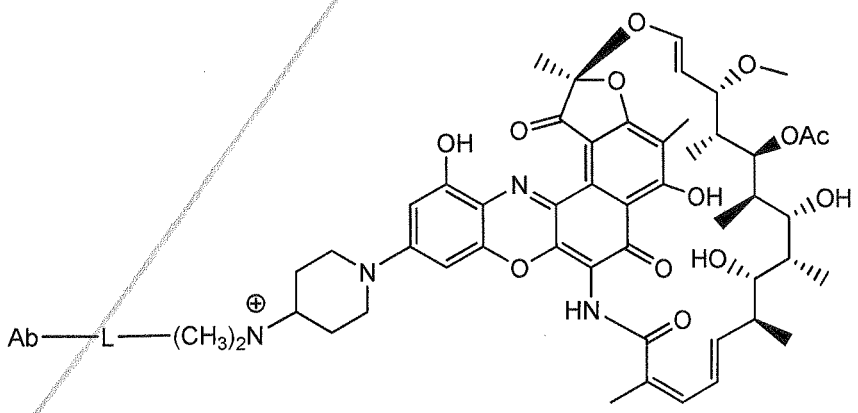


wherein

R^3 is independently selected from H and C_1–C_{12} alkyl; and

n is 1 or 2; or

(f)



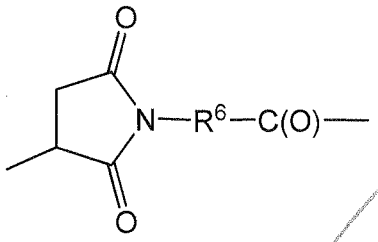
43. The antibody-antibiotic conjugate compound of claim 32, wherein the peptide linker has the formula:

–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.

44. The antibody-antibiotic conjugate of claim 43, wherein:

(a) Str has the formula:



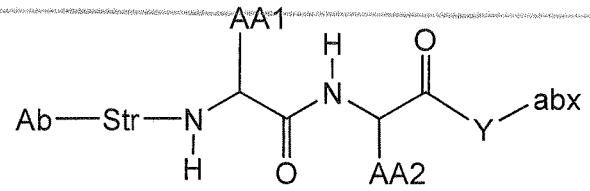
wherein R^6 is selected from the group consisting of C_1-C_{10} alkylene-, -C_3-C_8 carbocyclo, -O-(C_1-C_8 alkyl)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -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;

wherein optionally R^6 is -$(CH_2)_5$-;

(b) Pep comprises two to twelve amino acid residues independently selected from glycine, alanine, phenylalanine, lysine, arginine, valine, and citrulline; wherein optionally 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 ID NO: 128); or

(c) Y comprises para-aminobenzyl or para-aminobenzyloxycarbonyl.

45. The antibody-antibiotic conjugate of claim 32 having the formula:

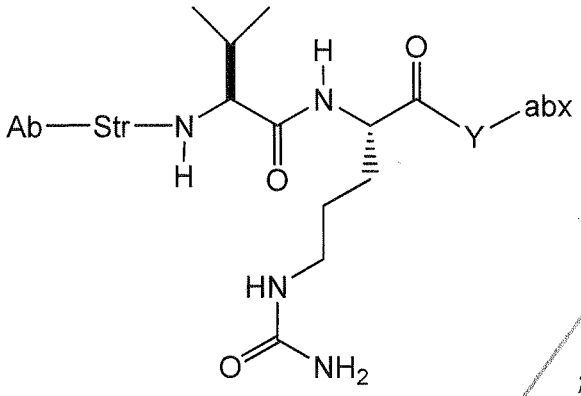


where AA1 and AA2 are independently selected from an amino acid side chain.

46. The antibody-antibiotic conjugate of claim 45, wherein the amino acid side chain is independently selected from H, $-CH_3$, $-CH_2(C_6H_5)$, $-CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $-CHCH(CH_3)CH_3$, and $-CH_2CH_2CH_2NHC(O)NH_2$.

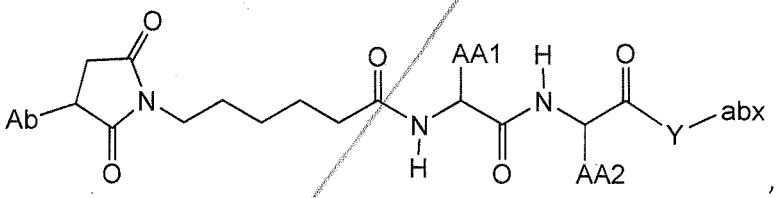
47. The antibody-antibiotic conjugate of claim 45 having the formula:

(a)



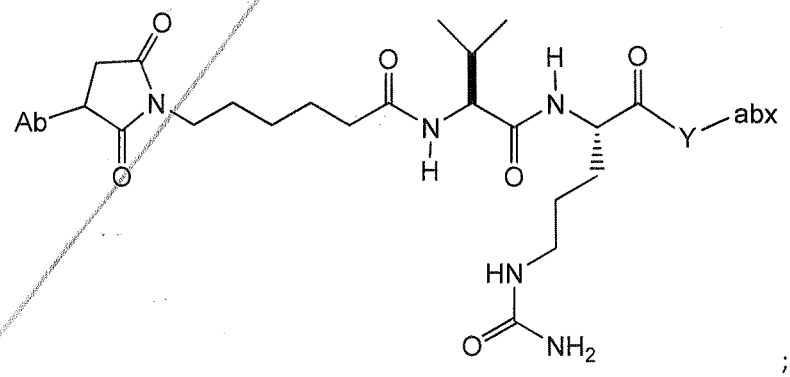
;

(b)



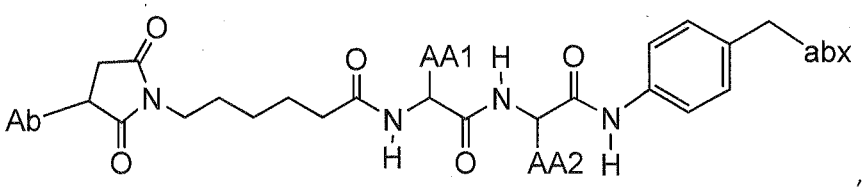
,

optionally having the formula:

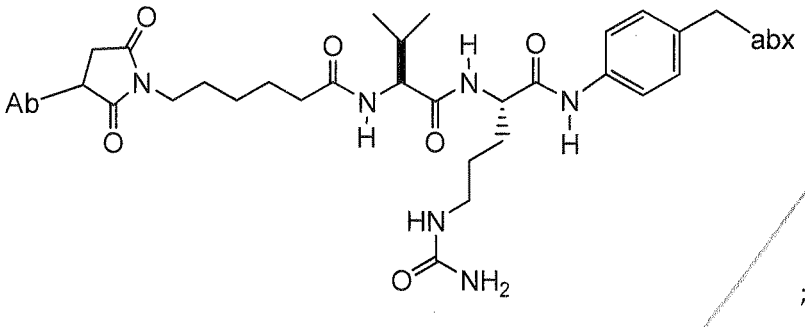


;

(c)

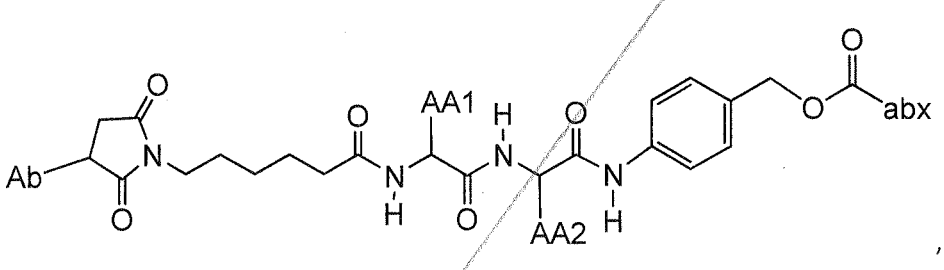


optionally having the formula:

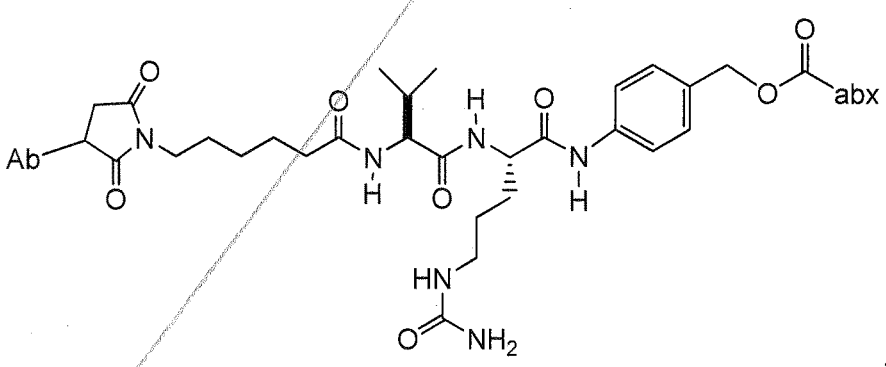


;

(d)

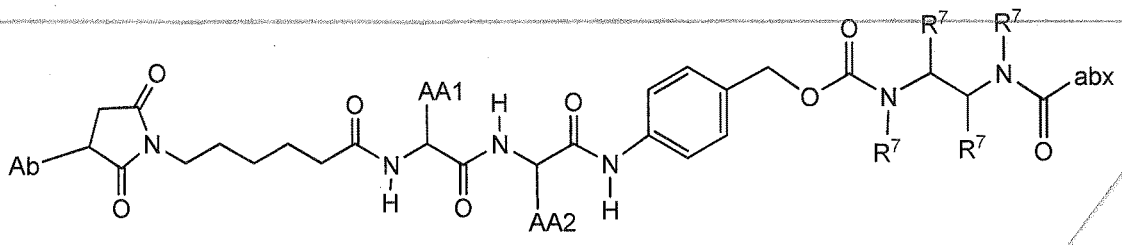


optionally having the formula:



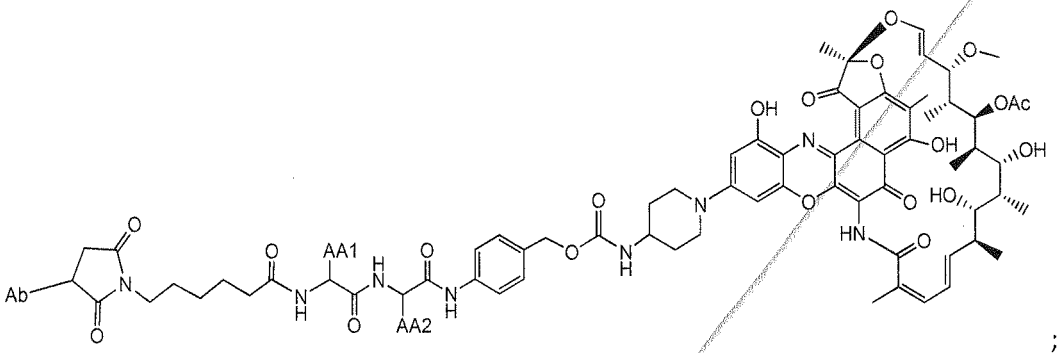
;

(e)



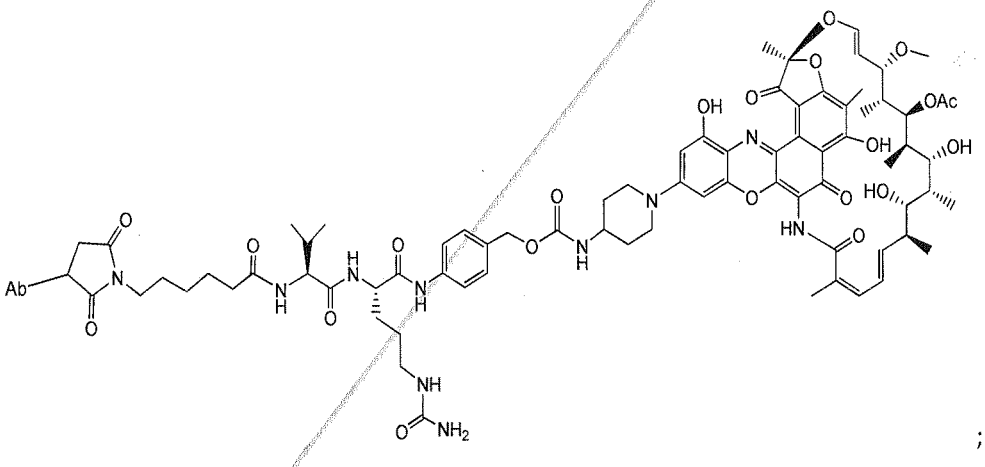
where R^7 is independently selected from H and C_1–C_{12} alkyl;

(f)



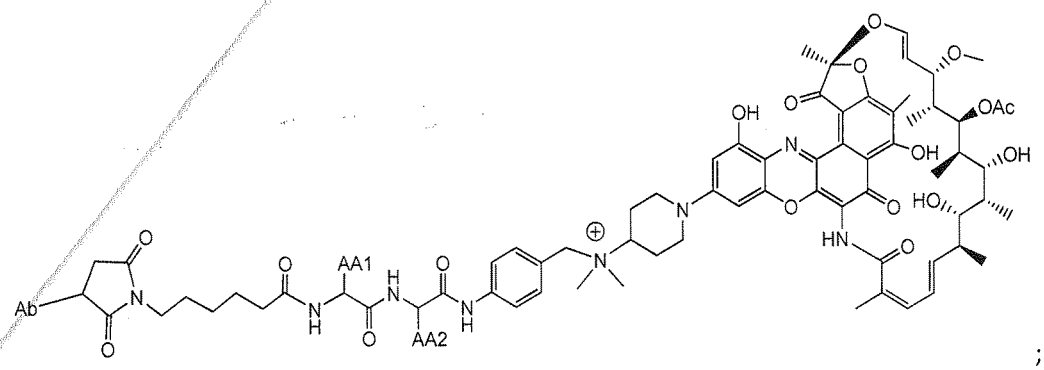
;

optionally having the formula:



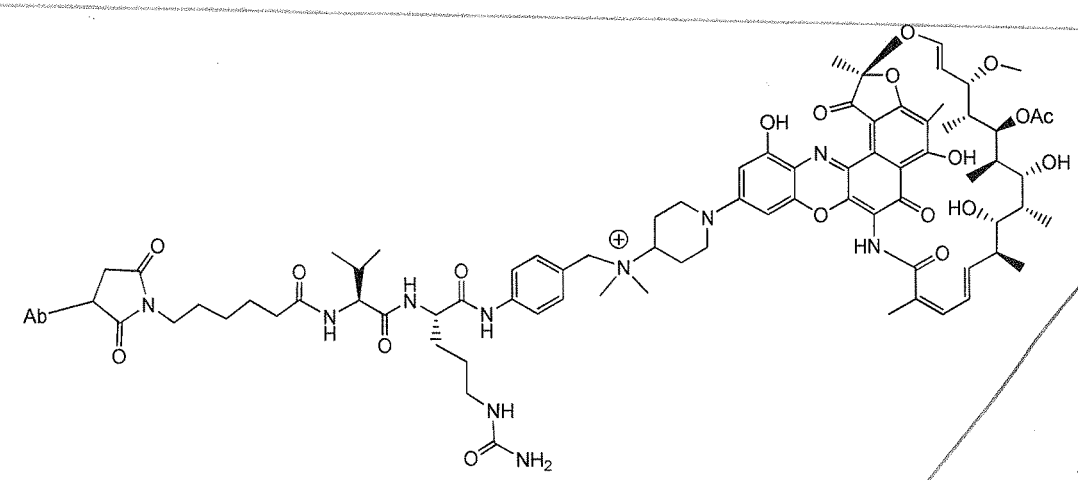
; or

(g)



;

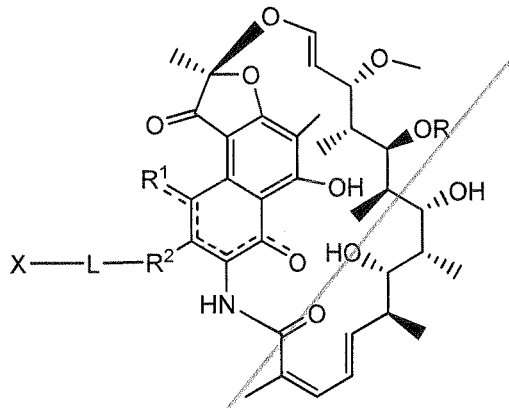
optionally having the formula:



48. A pharmaceutical composition comprising the antibody-antibiotic conjugate compound of any one of claims 32-47, and a pharmaceutically acceptable carrier, glidant, diluent, or excipient.

49. A process for making the antibody-antibiotic conjugate compound of any one of claims 32-47 comprising conjugating a rifamycin-type antibiotic to an anti-wall teichoic acid (WTA) antibody.

50. An antibiotic-linker 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;

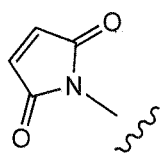
L is a peptide linker attached to R^2 or the fused heteroaryl or heterocyclyl formed by R^1 and R^2; and having the formula:

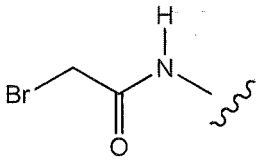
$$-Str-Pep-Y-$$

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

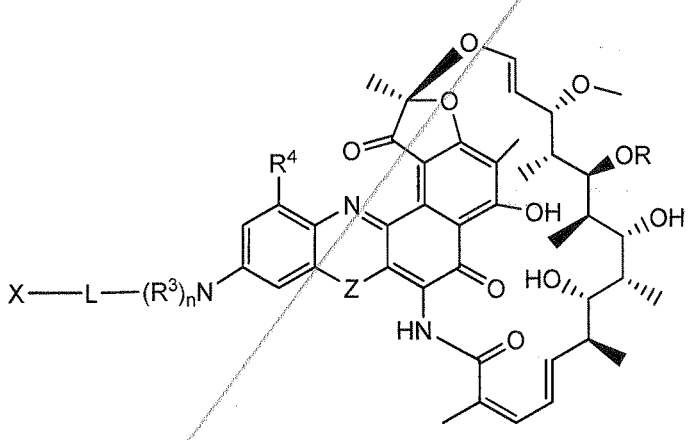
X is a reactive functional group selected from maleimide, thiol, amino, bromide, bromoacetamido, iodoacetamido, p-toluenesulfonate, iodide, hydroxyl, carboxyl, pyridyl disulfide, and N-hydroxysuccinimide.

51. The antibiotic-linker intermediate of claim 50,wherein X is



or


52. The antibiotic-linker intermediate of claim 50 having the formula:



wherein

R^3 is independently selected from H and C_1–C_{12} alkyl;

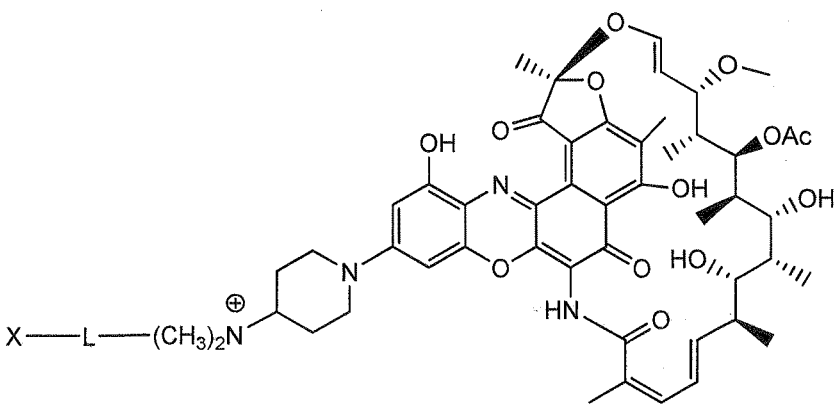
n is 1 or 2;

R^4 is selected from H, F, Cl, Br, I, C_1–C_{12} alkyl, and OH; and

Z is selected from NH, N(C_1–C_{12} alkyl), O and S.

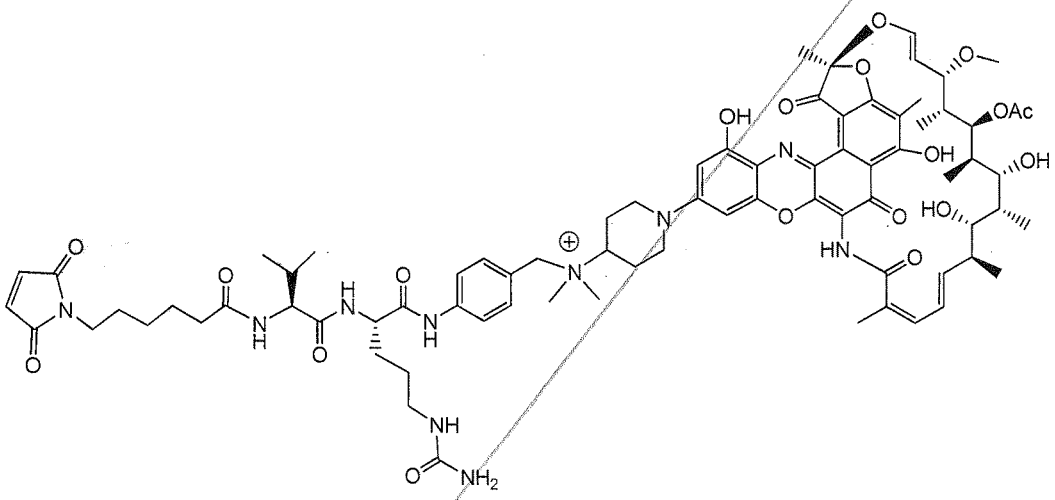
53. The antibiotic-linker intermediate of claim 52 having the formula:

(a)



; or

(b)



54. Use of an antibody-antibiotic conjugate compound comprising an anti-wall teichoic acid (WTA) antibody covalently attached by a peptide linker to a rifamycin-type antibiotic, in the manufacture of a medicament for treating a bacterial infection in a patient.

55. Use of an antibody-antibiotic conjugate of any one of claims 32-47 in the manufacture of a medicament for treating a bacterial infection in a patient.

56. The use of claim 54 or 55, wherein the patient has been diagnosed with a Staph aureau infection; wherein optionally bacterial load in the patient is reduced by the treatment.

57. Use of an anti-WTA-antibiotic conjugate of any one of claims 32-47 in the manufacture of a medicament for killing intracellular Staph aureus in the host cells of a staph aureus infected patient without killing the host cells.

58. The use of claim 57, wherein the persister bacterial cells are killed.

59. The use of any one of claims 54-57, wherein the patient is a human.

60. The use of any one of claims 54-57, wherein the medicament is to be administered with a second therapeutic agent; wherein optionally the second therapeutic agent is an antibiotic; wherein optionally the antibiotic is selected from:

(a) the structural class consisting of (i) aminoglycosides; (ii) beta-lactams; (iii) macrolides/cyclic peptides; (iv) tetracyclines; (v) fluoroquinolines/fluoroquinolones; and (vi) oxazolidinones, or

(b) the group consisting of clindamycin, novobiocin, retapamulin, daptomycin, GSK-2140944, CG-400549, sitafloxacin, teicoplanin, triclosan, napthyridone, radezolid, doxorubicin, ampicillin, vancomycin, imipenem, doripenem, gemcitabine, dalbavancin, and azithromycin.

61. A kit for treating a bacterial infection, comprising:

a) the pharmaceutical composition of claim 48; and

b) instructions for use.

We Claim:

1. An isolated anti-WTA (wall teichoic acid) monoclonal antibody comprising a light (L) chain and a heavy (H) chain, wherein:

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).

2. The isolated anti-WTA monoclonal antibody of claim 1 comprising 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 SEQ ID NO.156.

3. The antibody of claim 2, further comprising 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 SEQ ID NO.119.

4. The isolated anti-WTA monoclonal antibody of claim 1 comprising 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 SEQ ID NO.119.

5. The isolated anti-WTA monoclonal antibody of claim 1 comprising a light chain variable region (VL) and a heavy chain variable region (VH), wherein the VL comprises the sequence of SEQ ID NO.119 and the VH comprises the sequence SEQ ID NO.156.

6. An isolated anti-WTA monoclonal antibody comprising a light (L) chain and a heavy (H) chain, wherein:

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 NO:37), and CDR H3 comprising the sequence of SSILVRGALGRYFDL (SEQ ID NO:38).

7. The isolated anti-WTA monoclonal antibody of claim 6 comprising 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 SEQ ID NO.112.

8. The antibody of claim 7, further comprising 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 SEQ ID NO.111.

9. The isolated anti-WTA monoclonal antibody of claim 6 comprising 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 SEQ ID NO.111.

10. The isolated anti-WTA monoclonal antibody of claim 6 comprising a light chain variable region (VL) and a heavy chain variable region (VH), wherein the VL comprises the sequence of SEQ ID NO.111 and the VH comprises the sequence SEQ ID NO.112.

11. An isolated anti-WTA monoclonal antibody comprising an amino acid sequence selected from the group consisting of:

(a) CDR L1 comprising the sequence of RASQTISGWLA (SEQ ID NO:39), CDR L2 comprising the sequence of KASTLES (SEQ ID NO:40), and CDR L3 comprising the sequence of QQYKSYSFN (SEQ ID NO:41); and CDR H1 comprising the sequence of SYDIN (SEQ ID NO:42), CDR H2 comprising the sequence of WMNANSGNTGYAQKFQG (SEQ ID NO:43), and CDR H3 comprising the sequence of SSILVRGALGRYFDL (SEQ ID NO:44);

(b) CDR L1 comprising the sequence of RASQFVSRTSLA (SEQ ID NO:45), CDR L2 comprising the sequence of ETSSRAT (SEQ ID NO:46), and CDR L3 comprising the sequence of HKYGSGPRT (SEQ ID NO:47); and CDR H1 comprising the sequence of NYDFI (SEQ ID NO:48), CDR H2 comprising the sequence of WMNPNSYNTGYGQKFQG (SEQ ID NO:49), and CDR H3 comprising the sequence of AVRGQLLSEY (SEQ ID NO:50);

(c) CDR L1 comprising the sequence of _RASQSVSSSYLA (SEQ ID NO:51), CDR L2 comprising the sequence of DASSRAT (SEQ ID NO:52), and CDR L3 comprising the sequence of QKYGSTPRP (SEQ ID NO:53); and CDR H1 comprising the sequence of SYDIN (SEQ ID NO:54), CDR H2 comprising the sequence of WMNPNSGNTNYAQRFQG (SEQ ID NO:55), and CDR H3 comprising the sequence of ERWSKDTGHYYYYGMDV (SEQ ID NO:56);

(d) CDR L1 comprising the sequence of RASLDITNHLA (SEQ ID NO:57), CDR L2 comprising the sequence of EASILQS (SEQ ID NO:58), and CDR L3 comprising the sequence of EKCNSTPRT (SEQ ID NO:59); and CDR H1 comprising the sequence of

NYDIN (SEQ ID NO:60), CDR H2 comprising the sequence of WMNPSSGRTGYAPKFRG (SEQ ID NO:61), and CDR H3 comprising the sequence of GGGYYDSSGNYHISGLDV (SEQ ID NO:62);

(e) CDR L1 comprising the sequence of RASQSVGAIYLA (SEQ ID NO:63), CDR L2 comprising the sequence of GVSNRAT (SEQ ID NO:64), and CDR L3 comprising the sequence of QLYTSSRALT (SEQ ID NO:65); and CDR H1 comprising the sequence of AYAMN (SEQ ID NO:66), CDR H2 comprising the sequence of SITKNSDSLYYADSVKG (SEQ ID NO:67), and CDR H3 comprising the sequence of LAARIMATDY (SEQ ID NO:68);

(f) CDR L1 comprising the sequence of RASQGIRNGLG (SEQ ID NO:69), CDR L2 comprising the sequence of PASTLES (SEQ ID NO:70), and CDR L3 comprising the sequence of LQDHNYPPT (SEQ ID NO:71); and CDR H1 comprising the sequence of YYSMI (SEQ ID NO:72), CDR H2 comprising the sequence of SIDSSSRYLYYADSVKG (SEQ ID NO:73), and CDR H3 comprising the sequence of DGDDILSVYRGSGRPFDY (SEQ ID NO:74);

(g) CDR L1 comprising the sequence of _RASQGIRNGLG (SEQ ID NO:75), CDR L2 comprising the sequence of PASTLES (SEQ ID NO:76), and CDR L3 comprising the sequence of LQDHNYPPS (SEQ ID NO:77); and CDR H1 comprising the sequence of YYSMI (SEQ ID NO:78), CDR H2 comprising the sequence of SIDSSSRYRYYTDSVKG (SEQ ID NO:79), and CDR H3 comprising the sequence of DGDDILSVYQGSGRPFDY (SEQ ID NO:80);

(h) CDR L1 comprising the sequence of _RASQSVRTNVA (SEQ ID NO:81), CDR L2 comprising the sequence of GASTRAS (SEQ ID NO:82), and CDR L3 comprising the sequence of LQYNTWPRT (SEQ ID NO:83); and CDR H1 comprising the sequence of TNDMS (SEQ ID NO:84), CDR H2 comprising the sequence of TIIGIDDTTHYADSVRG (SEQ ID NO:85), and CDR H3 comprising the sequence of NSGIYSF (SEQ ID NO:86)

(i) CDR L1 comprising the sequence of RASQDIGSSLA (SEQ ID NO:87), CDR L2 comprising the sequence of ATSTLQS (SEQ ID NO:88), and CDR L3 comprising the sequence of QQLNNYVHS (SEQ ID NO:89); and CDR H1 comprising the sequence of DYAMG (SEQ ID NO:90), CDR H2 comprising the sequence of

VVTGHSYRTHYADSVKG (SEQ ID NO:91), and CDR H3 comprising the sequence of RIWSYGDDSFDV (SEQ ID NO:92);

(j) CDR L1 comprising the sequence of RASQSIGDRLA (SEQ ID NO:93), CDR L2 comprising the sequence of WASNLEG (SEQ ID NO:94), and CDR L3 comprising the sequence of QQYKSQWS (SEQ ID NO:95); and CDR H1 comprising the sequence of SYAMN (SEQ ID NO:96), CDR H2 comprising the sequence of YISSIETIYYADSVKG (SEQ ID NO:97), and CDR H3 comprising the sequence of DRLVDVPLSSPNS (SEQ ID NO:98);

(k) 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 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).

12. The isolated anti-WTA monoclonal antibody of any one of claims 1-5 or 6-11, wherein the antibody is an antigen-binding fragment lacking a Fc region.

13. The isolated anti-WTA monoclonal antibody of claim 12, wherein the antibody is a F(ab) or $F(ab')_2$.

14. The isolated anti-WTA monoclonal antibody of any one of claims 1-5 or 6-11, wherein 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.

15. The isolated anti-WTA monoclonal antibody of claim 13, 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.

16. The isolated anti-WTA monoclonal antibody of any one of claims 1-5 or 6-11, wherein the antibody binds WTA beta.

17. The isolated anti-WTA monoclonal antibody of any one of claims 1-5 or 6-11, wherein the antibody is produced in a host cell in cell culture.

18. The isolated anti-WTA monoclonal antibody of claim 17, wherein the host cell is a Chinese hamster ovary (CHO) cell.

19. An antibody that binds to the same epitope as the antibody of any one of claims 1-18.

20. An isolated nucleic acid encoding an antibody of any one of claims 1-18.

21. A vector comprising the nucleic acid of claim 20.

22. An isolated host cell comprising a nucleic acid encoding an antibody of any one of claims 1-18.

23. A method of producing an antibody comprising culturing a host cell of claim 22 under conditions suitable for expression of the nucleic acid; and recovering the antibody produced by the cell.

24. An antibody-antibiotic conjugate compound comprising an anti-WTA antibody of any one of claims 1-18, covalently attached by a peptide linker to a rifamycin-type antibiotic.

25. The antibody-antibiotic conjugate compound of claim 24, wherein the anti-WTA antibody binds to *Staphylococcus aureus*.

26. The antibody-antibiotic conjugate compound of claim 25, wherein the anti-WTA antibody binds to methicillin-resistant *Staphylococcus aureus* (MRSA).

27. The antibody-antibiotic conjugate of any one of claim 24-26, wherein the rifamycin-type antibiotic is a rifalazil-type antibiotic.

28. The antibody-antibiotic conjugate compound of any one of claim 24-27, wherein the rifamycin-type antibiotic comprises a quaternary amine attached to the peptide linker.

29. The antibody-antibiotic conjugate compound of any one of claim 24-28, wherein the peptide linker is attached to a cysteine or an engineered cysteine of the anti-WTA antibody.

30. The antibody-antibiotic conjugate compound of any one of claim 24-29, wherein the peptide linker is a *S. aureus* endopeptidase or cysteine protease cleavable linker.

31. The antibody-antibiotic conjugate compound of claim 30, wherein the peptide linker is a staphopain B or a staphopain A cleavable linker.

32. The antibody-antibiotic conjugate compound of claim 30, wherein the peptide linker is a human protease cathepsin B cleavable linker.

33. The antibody-antibiotic conjugate compound of claim 32, wherein the peptide linker is a val-cit dipeptide linker.

34. The antibody-antibiotic conjugate compound of claim 24 having 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–

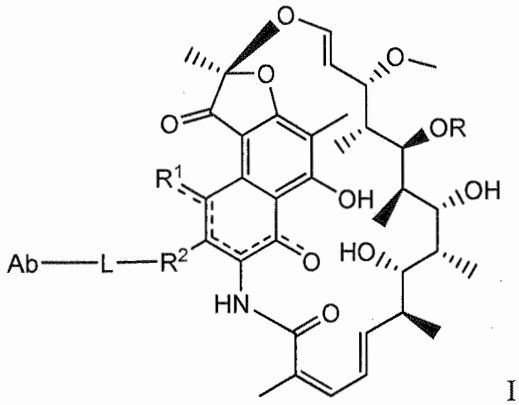
where Str is a stretcher unit; Pep is a peptide of two to twelve amino acid residues, and Y is a spacer unit;

abx is the rifamycin-type antibiotic; and

p is an integer from 1 to 8.

35. The antibody-antibiotic conjugate compound of claim 34, wherein p is 2 to 4.

36. The antibody-antibiotic conjugate compound of claim 24 having Formula I:



I

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;

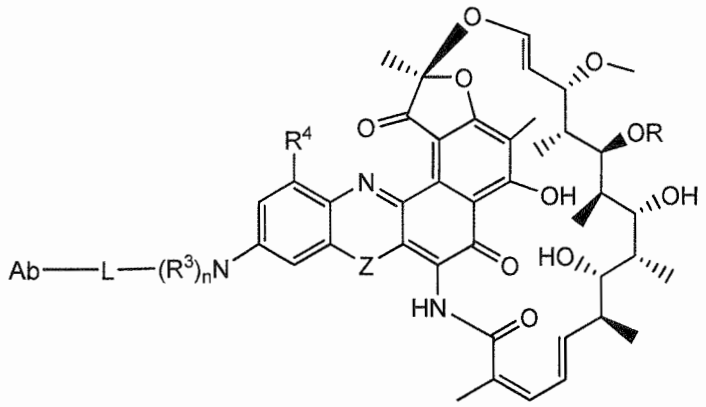
or R^1 and R^2 form a five- or six-membered fused heteroaryl or heterocyclyl, and optionally forming a spiro or fused six-membered heteroaryl, heterocyclyl, aryl, or carbocyclyl ring, wherein the spiro or fused six-membered heteroaryl, heterocyclyl, aryl, or carbocyclyl ring is optionally substituted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

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

Ab is the anti-wall teichoic acid (WTA) antibody.

37. The antibody-antibiotic conjugate compound of claim 36, wherein the formula is selected from the group consisting of:

a)



wherein

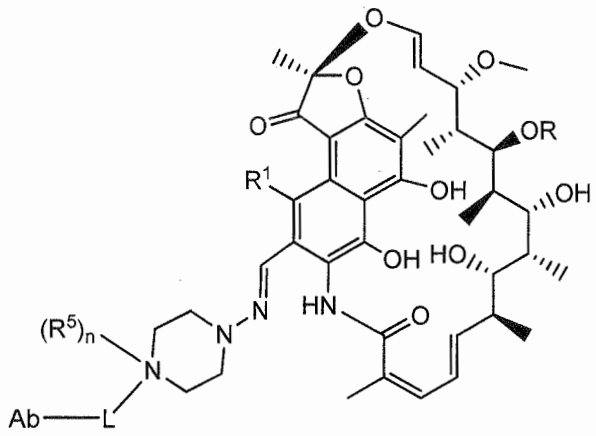
R^3 is independently selected from H and C_1–C_{12} alkyl;

n is 1 or 2;

R^4 is selected from H, F, Cl, Br, I, C_1–C_{12} alkyl, and OH; and

Z is selected from NH, N(C_1–C_{12} alkyl), O and S;

b)

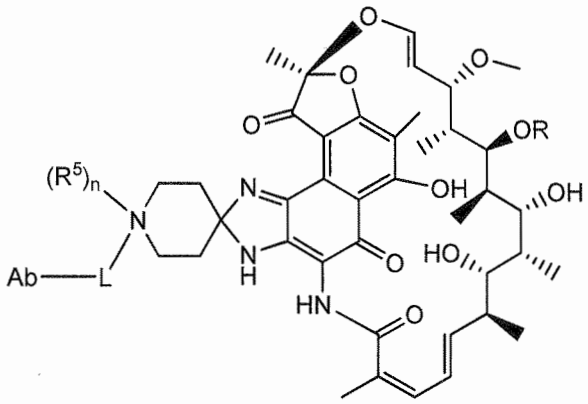


wherein

R^5 is selected from H and C_1–C_{12} alkyl; and

n is 0 or 1;

c)

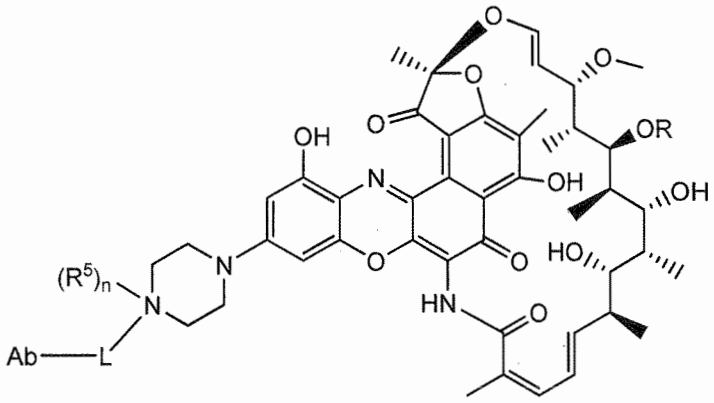


wherein

R^5 is selected from H and C_1–C_{12} alkyl; and

n is 0 or 1;

d)

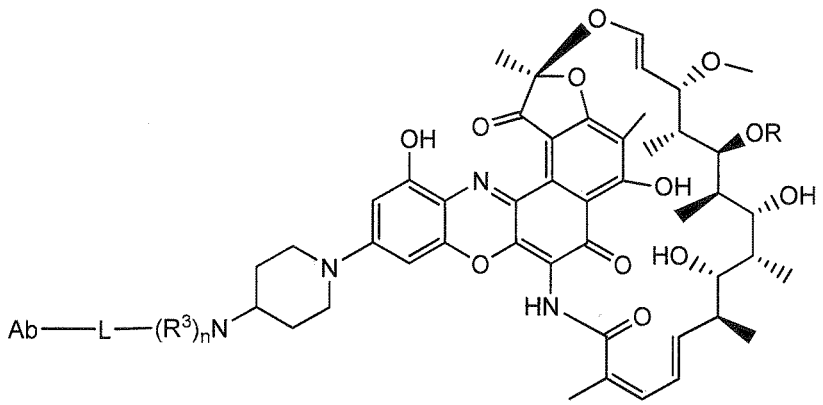


wherein

R^5 is independently selected from H and C_1–C_{12} alkyl; and

n is 0 or 1;

e)

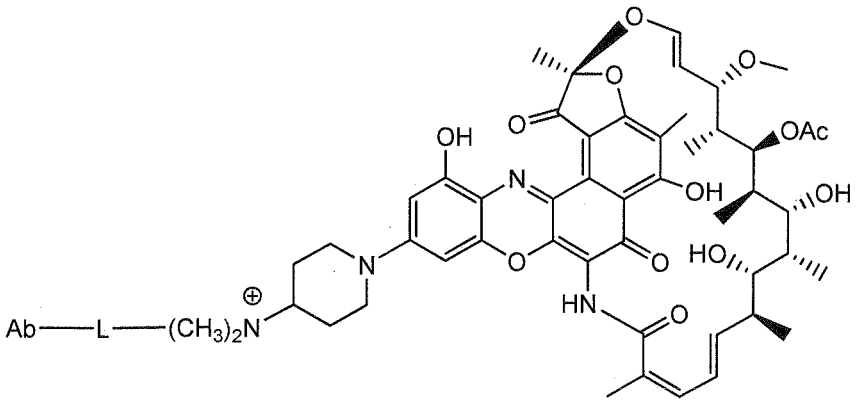


wherein

R^3 is independently selected from H and C_1–C_{12} alkyl; and

n is 1 or 2; and

f)

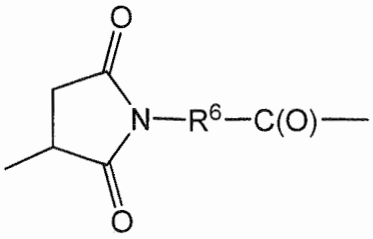


38. The antibody-antibiotic conjugate compound of claim 24, wherein the peptide linker has the formula:

–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.

39. The antibody-antibiotic conjugate compound of claim 38, wherein 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.

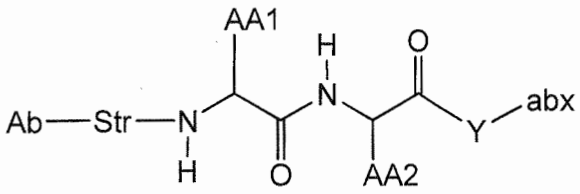
40. The antibody-antibiotic conjugate compound of claim 39, wherein R^6 is -$(CH_2)_5$- .

41. The antibody-antibiotic conjugate compound of claim 38, wherein Pep comprises two to twelve amino acid residues independently selected from glycine, alanine, phenylalanine, lysine, arginine, valine, and citrulline.

42. The antibody-antibiotic conjugate compound of claim 41, wherein 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 ID NO: 128).

43. The antibody-antibiotic conjugate compound of claim 38, wherein Y comprises para-aminobenzyl or para-aminobenzyloxycarbonyl.

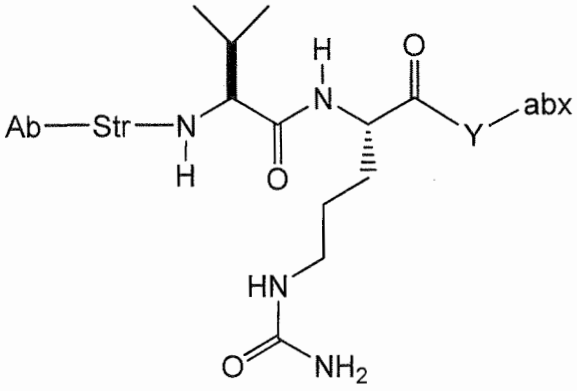
44. The antibody-antibiotic conjugate compound of claim 24 having the formula:



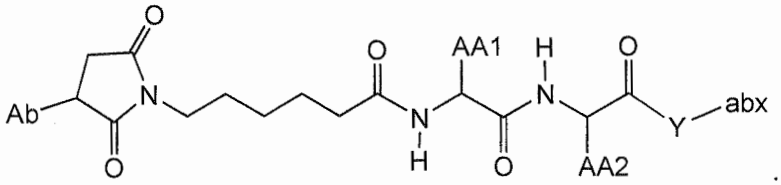
where AA1 and AA2 are independently selected from an amino acid side chain.

45. The antibody-antibiotic conjugate compound of claim 44, wherein the amino acid side chain is independently selected from H, $-CH_3$, $-CH_2(C_6H_5)$, $-CH_2CH_2CH_2CH_2NH_2$, $-CH_2CH_2CH_2NHC(NH)NH_2$, $-CHCH(CH_3)CH_3$, and $-CH_2CH_2CH_2NHC(O)NH_2$.

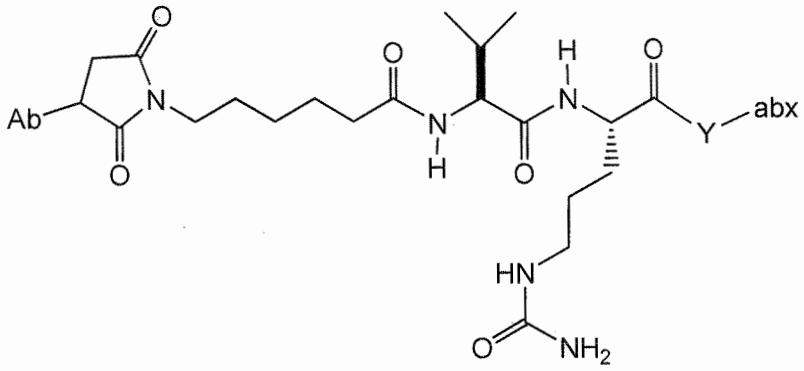
46. The antibody-antibiotic conjugate compound of claim 44 having the formula:



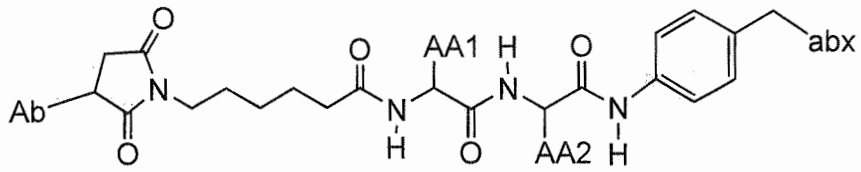
47. The antibody-antibiotic conjugate compound of claim 44 having the formula:



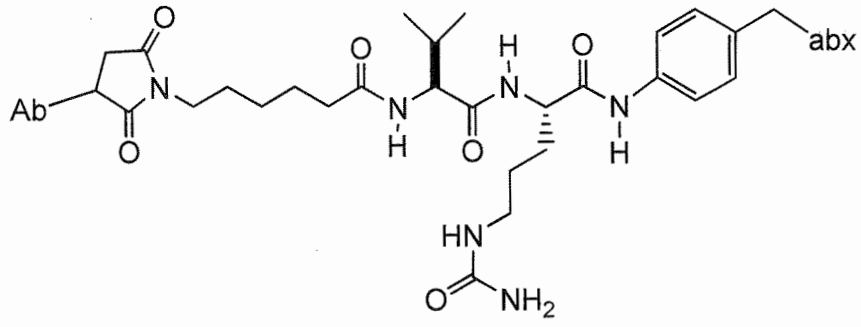
48. The antibody-antibiotic conjugate compound of claim 44 having the formula:



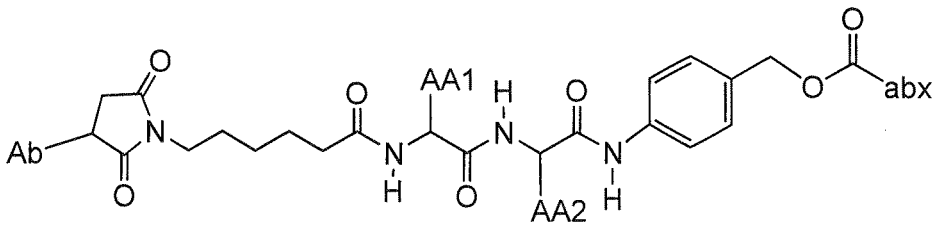
49. The antibody-antibiotic conjugate compound of claim 44 having the formula:



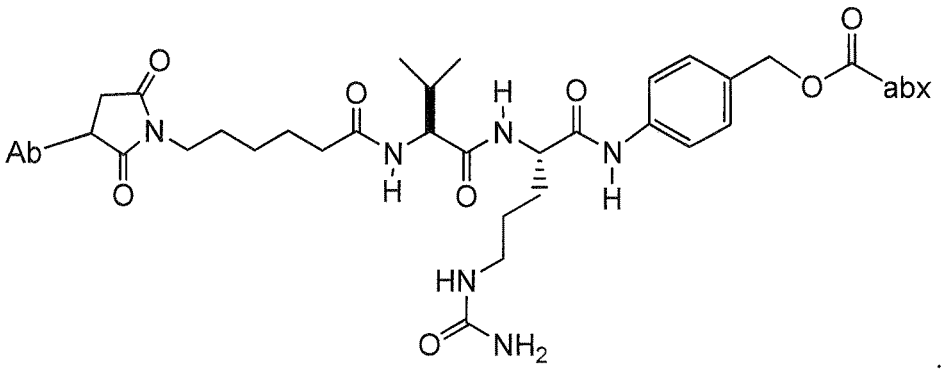
50. The antibody-antibiotic conjugate compound of claim 49 having the formula:



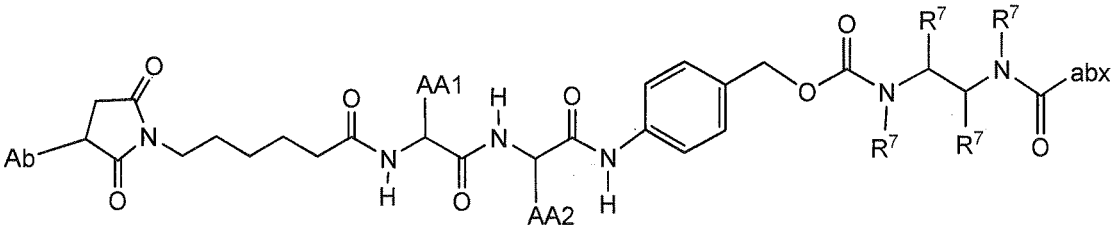
51. The antibody-antibiotic conjugate compound of claim 44 having the formula:



52. The antibody-antibiotic conjugate compound of claim 51 having the formula:

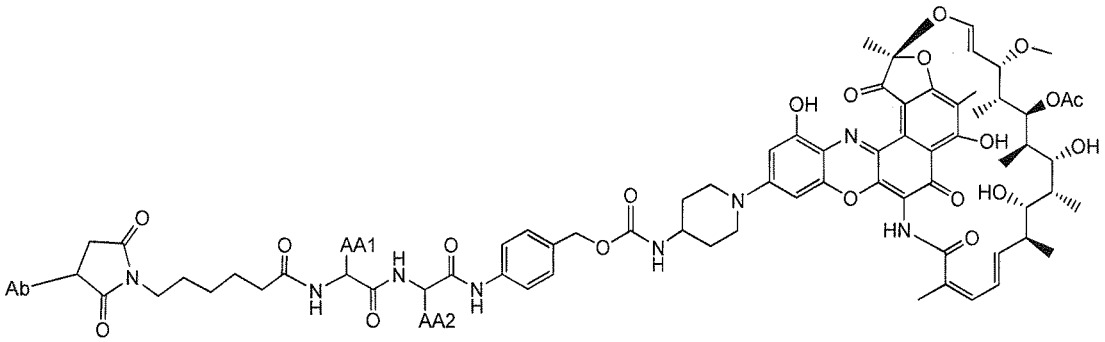


53. The antibody-antibiotic conjugate compound of claim 44 having the formula:

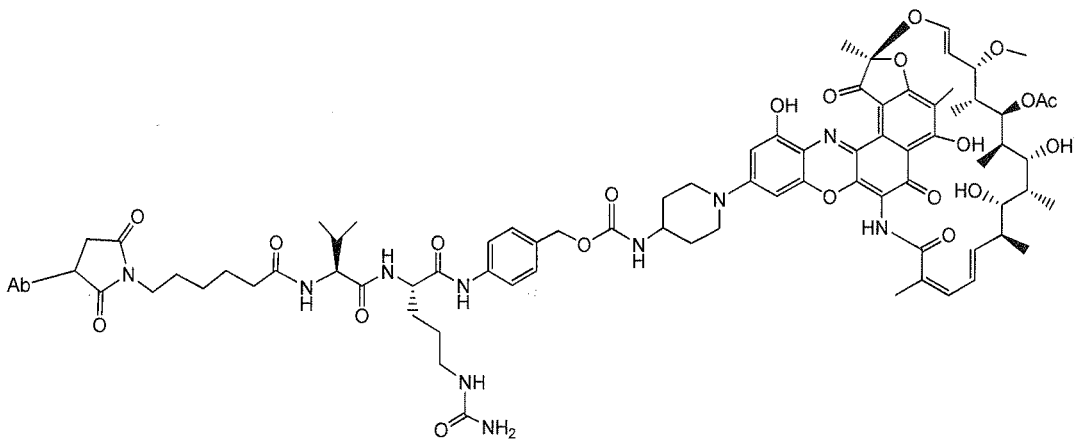


where R^7 is independently selected from H and C_1–C_{12} alkyl.

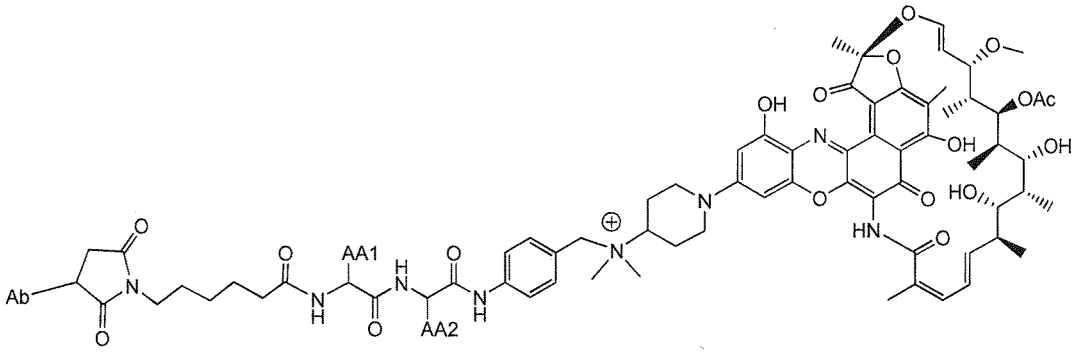
54. The antibody-antibiotic conjugate compound of claim 44 having the formula:



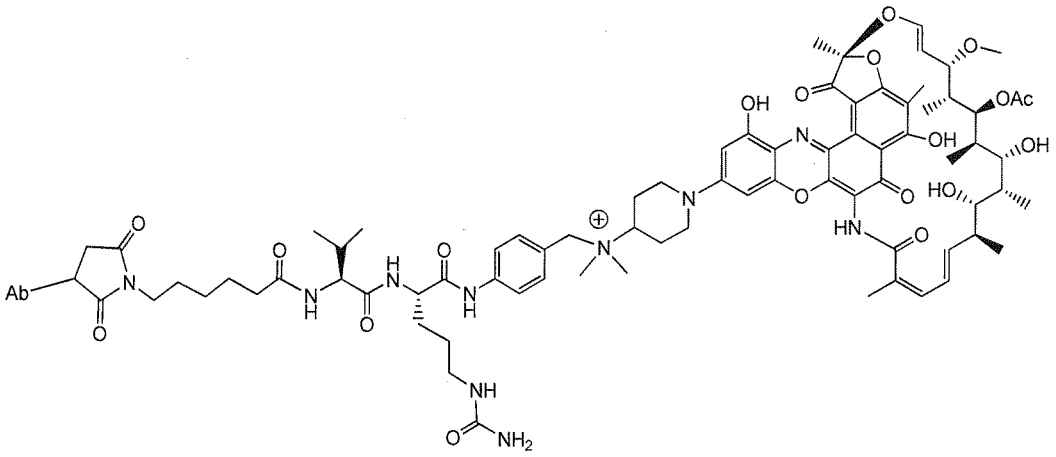
55. The antibody-antibiotic conjugate compound of claim 54 having the formula:



56. The antibody-antibiotic conjugate compound of claim 44 having the formula:



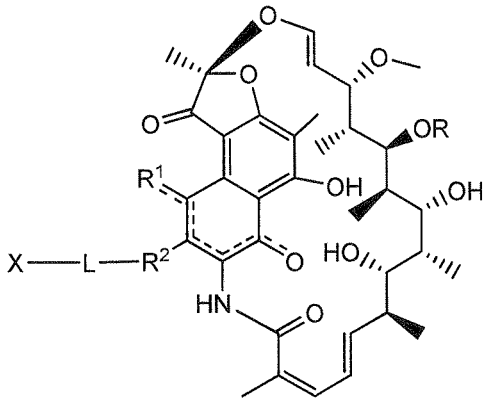
57. The antibody-antibiotic conjugate compound of claim 56 having the formula:



58. A pharmaceutical composition comprising the antibody-antibiotic conjugate compound of any one of claims 24-57, and a pharmaceutically acceptable carrier, glidant, diluent, or excipient.

59. A process for making the antibody-antibiotic conjugate compound of any one of claims 24-57 comprising conjugating a rifamycin-type antibiotic to an anti-WTA antibody.

60. An antibiotic-linker 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;

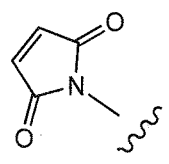
L is a peptide linker attached to R^2 or the fused heteroaryl or heterocyclyl formed by R^1 and R^2; and having the formula:

–Str–Pep–Y–

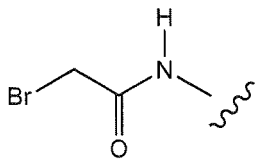
where Str is a stretcher unit; Pep is a peptide of two to twelve amino acid residues, and Y is a spacer unit; and

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

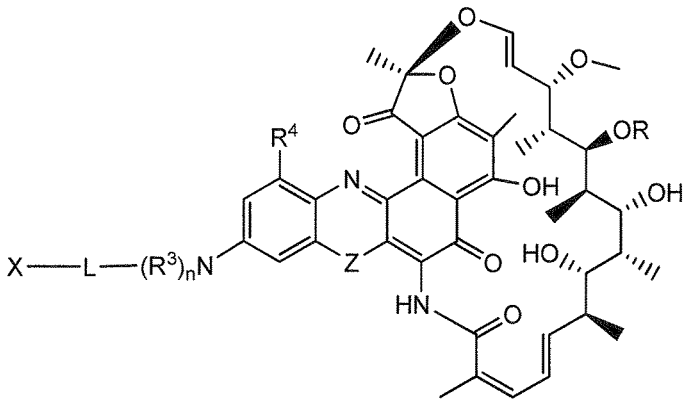
61. The antibiotic-linker intermediate of claim 60,wherein X is



or



62. The antibiotic-linker intermediate of claim 60 having the formula:



wherein

R^3 is independently selected from H and C_1–C_{12} alkyl;

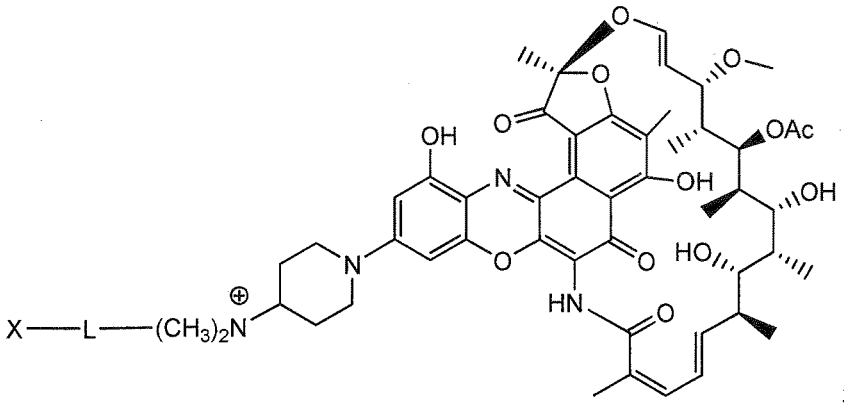
n is 1 or 2;

R^4 is selected from H, F, Cl, Br, I, C_1–C_{12} alkyl, and OH; and

Z is selected from NH, N(C_1–C_{12} alkyl), O and S.

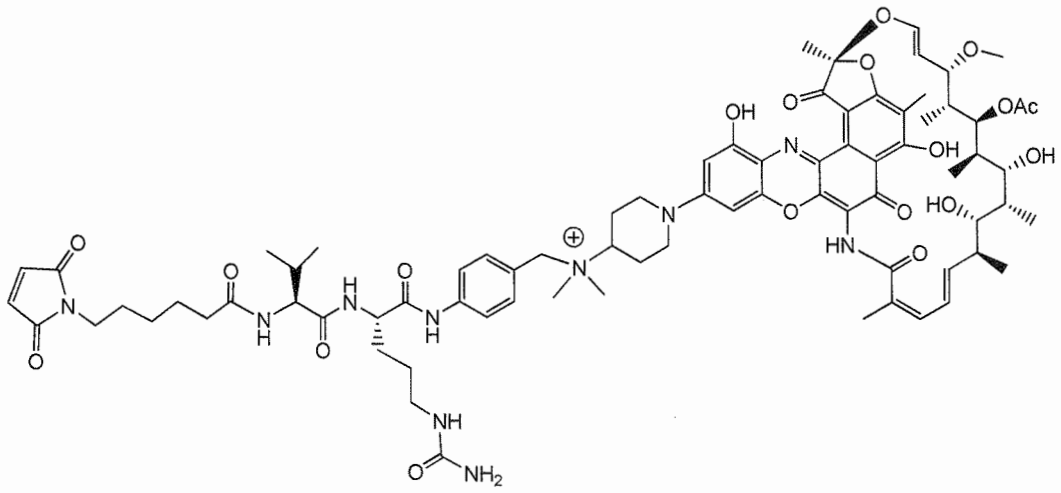
63. The antibiotic-linker intermediate of claim 62 having a formula selected from the group consisting of:

a)



; and

b)



64. Use of an anti-WTA-antibiotic conjugate compound of claim 24-57 in the manufacture of a medicament for killing intracellular *Staphylococcus aureus* in the host cells of a *Staphylococcus aureus*-infected patient without killing the host cells.

65. The use of claim 64, wherein persister bacterial cells are killed.

66. The use of claim 64 or 65, further comprising administration of a second therapeutic agent.

67. The use of claim 66, wherein the second therapeutic agent is an antibiotic.

68. The use of claim 67, wherein the antibiotic is selected from the structural class consisting of (i) aminoglycosides; (ii) beta-lactams; (iii) macrolides/cyclic peptides; (iv) tetracyclines; (v) fluoroquinolines/fluoroquinolones; and (vi) oxazolidinones.

69. The use of claim 67, wherein the antibiotic is selected from the group consisting of clindamycin, novobiocin, retapamulin, daptomycin, GSK-2140944, CG-400549, sitafloxacin, teicoplanin, triclosan, napthyridone, radezolid, doxorubicin, ampicillin, vancomycin, imipenem, doripenem, gemcitabine, dalbavancin, and azithromycin.

70. A kit for treating a bacterial infection, comprising:

a) the pharmaceutical composition of claim 58; and

b) instructions for use.