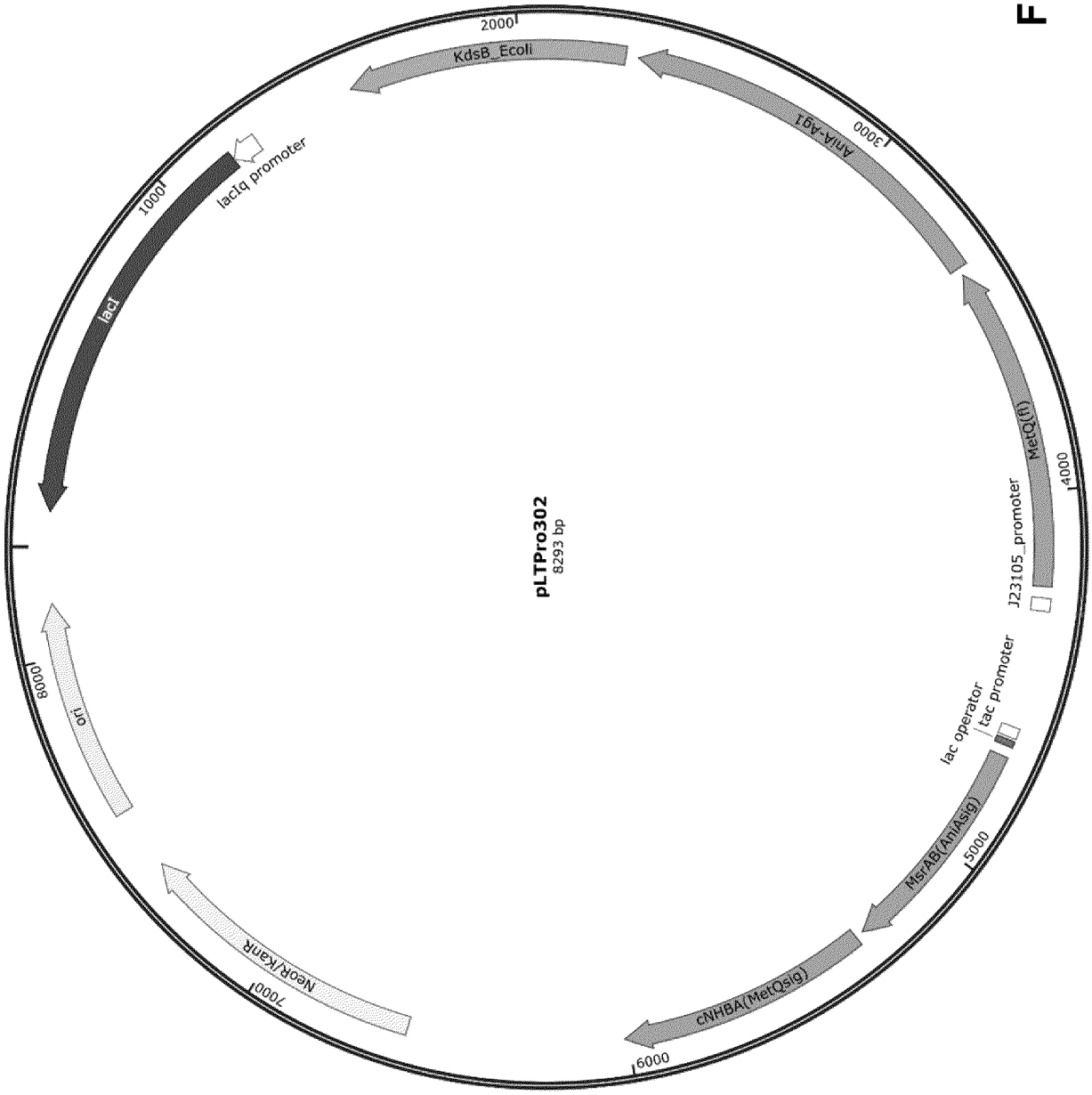

pLTPro231
8158 bp
2000
MetQ
RBS
RBS
3000
AmiA
RBS
NHBA
4000
rrnB T2 terminator
5000
Kanamycin resistance cassette
ori
6000
7000
lacI
lacIq promoter
8000
tac promoter
lac operator
ribosome binding site (RBS)
MetAB
RBS
1000
KdsB

FIG. 1A

FIG. 1B


pLTPro302
8293 bp
2000
KdsB_Ecoli
3000
AnlA-Ag1
4000
MetQ(fl)
J23105_promoter
5000
lac operator
tac promoter
NsrAB(AniAsig)
6000
cNHBA(MetQsig)
7000
NeoR/KanR
8000
ori
1000
lacI
lacIq promoter

pLTPro231 sequence [SEQ ID NO: 66]

ATGCTTCTGGCGTCAGGCAGCCATCGGAAGCTGTGGTATGGCTGTGCAGGTCGTAAATCACTGCATAATTCGTGTCGCTCAAGGCGCACTCCCGTTCTGGATAATGTTTTTT
GCGCCGACATCATAACGGTTCTGGCAAATATTCTGAAATGAGCTG**TTGACAATTAATCATCGGCTCGTATAATG**TGTGGAA***TTGTGAGCGGATAACAA***TTTCA*CACAGG*AAA
CAGATGAAACGCCAAGCATTAGCCGCAATGATTGCTTCCTTATTCGCATTGGCCGCCTGCGGTGGCGAACAAGCTGCTCAAGCCCCTGCCGAAACCCCTGCCGCTTCCGCAG
AAGCCGCAAGTTCCGCCGCACAAGCTACCGCCGAAACGCCTGCACCGCACACTTTATCCACGTTAAAAACCGCGGACAACCGCCCCGCCAGTGTTTATTTGAAAAAAGACAA
ACCGACGCTGATTAAATTTTGGGCGAGCTGGTGTCCTTTATGTTTGTCCGAATTGGGACAGGCCGAGAAATGGGCGCAAGATGCAAAATTCAGCTCCGCCAACCTGATTACC
GTCGCCTCCCCCGGCTTTTTGCACGAGAAAAAAGACGGCGAGTTTCAAAAATGGTATGCCGGTTTGAACTACCCCAAGCTGCCCGTCGTTACCGACAACGGCGGCACGATCG
CCCAAAACCTGAATATCAGCGTTTATCCTTCTTGGGCGTTAATCGGTAAAGACGGCGACGTGCAGCGCATCGTCAAAGGCAGCATCAACGAAGCGCAGGCATTGGCGTTAAT
CCGCAACCCGAATGCCGATTTGGGCAGTTTGAAACATTCGTAAGAGCTGAATTCGAGCTC*AGGAGGA*GGGATATGAGTTTTGTGGTCATTATTCCCGCGCGCTACGCGTCCA
CGCGTCTGCCCGGTAAACCATTGGTTGATATTAACGGCAAACCCATGATTGTTCATGTTCTTGAACGCGCGCGTGAATCAGGTGCCGAGCGCATCATCGTGGCAACCGATCA
TGAGGATGTTGCCCGCGCCGTTGAAGCCGCTGGCGGTGAAGTATGTATGACGCGCGCCGATCATCAGTCAGGAACAGAACGTCTGGCGGAAGTTGTCGAAAAATGCGCATTC
AGCGACGACACGGTGATCGTTAATGTGCAGGGTGATGAACCGATGATCCCTGCGACAATCATTCGTCAGGTTGCTGATAACCTCGCTCAGCGTCAGGTGGGTATGGCGACTC
TGGCGGTGCCAATCCACAATGCGGAAGAAGCGTTTAACCCGAATGCGGTGAAAGTGGTTCTCGACGCTGAAGGGTATGCACTGTACTTCTCTCGCGCCACCATTCCTTGGGA
TCGTGATCGTTTTGCAGAAGGCCTTGAAACCGTTGGCGATAACTTCCTGCGTCATCTTGGTATTTATGGCTACCGTGCAGGCTTTATCCGTCGTTACGTCAACTGGCAGCCA
AGTCCGTTAGAACACATCGAAATGTTAGAGCAGCTTCGTGTTCTGTGGTACGGCGAAAAAATCCATGTTGCTGTTGCTCAGGAAGTTCCTGGCACAGGTGTGGATACCCCTG
AAGATCTTGAGCGCGTTCGCGCTGAAATGCGCTAGGCTAGCAGCTC*AGGAGGA*GATAACAGATGAAAACCTTCTTCAAAACCCTTTCCGCCGCCGCACTCGCGCTCATCCTC
GCAGCCTGCGGCGGTCAAAAAGACAGCGCGCCCGCAGCCTCTGCCGCCGCCCCTTCTGCCGATAACGGCGCGGCGAAAAAAGAAATCGTCTTCGGCACGACCGTCGGCGACT
TCGGCGATATGGTCAAAGAACAAATCCAAGCCGAGCTGGAGAAAAAAGGCTACACCGTCAAATTGGTCGAATTTACCGACTATGTGCGCCCGAATCTGGCATTGGCGGAGGG
CGAGTTGGACATCAACGTCTTCCAACACAAACCCTATCTTGACGATTTCAAAAAAGAACACAACCTGGACATCACCGAAGCCTTCCAAGTGCCGACCGCGCCTTTGGGACTG
TATCCGGGCAAACTGAAATCGCTGGAAGAAGTCAAAGACGGCAGCACCGTATCCGCGCCCAACGACCCGTCCAACTTCGCACGCGCCTTGGTGATGCTGAACGAACTGGGTT
GGATCAAACTCAAAGACGGCATCAATCCGCTGACCGCATCCAAAGCCGATATCGCGGAAAACCTGAAAAACATCAAAATCGTCGAGCTTGAAGCCGCACAACTGCCGCGCAG
CCGCGCCGACGTGGATTTTGCCGTCGTCAACGGCAACTACGCCATAAGCAGCGGCATGAAGCTGACCGAAGCCCTGTTCCAAGAGCCGAGCTTTGCCTATGTCAACTGGTCT
GCCGTCAAAACCGCCGACAAAGACAGCCAATGGCTTAAAGACGTAACCGAGGCCTATAACTCCGACGCGTTCAAAGCCTACGCGCACAAACGCTTCGAGGGCTACAAATACC
CTGCCGCATGGAATGAAGGCGCAGCCAAATAAAAGCTT*AGGAGGA*GATAACAGATGAAACGCCAAGCATTAGCCGCAATGATTGCTTCCTTATTCGCATTGGCCGCCTGCGG
TGGCGAACAAGCTGCTCAAGCCCCTGCCGAAACCCCTGCCGCTTCCGCAGAAGCCGCAAGTTCCGCCGCACAAGCTACCGCCGAAACGCCTGCAGGCGAACTGCCCGTCATC
GATGCGGTGACCACCCACGCTCCCGAAGTACCTCCCGCAATCGACCGCGACTATCCTGCCAAAGTACGCGTAAAAATGGAAACCGTCGAAAAAACCATGAAAATGGACGACG
GGGTGGAATACCGCTACTGGACATTTGACGGCGACGTTCCGGGCCGTATGATCCGCGTACGCGAAGGCGATACGGTTGAAGTCGAATTCTCCAACAATCCTTCTTCTACCGT
TCCGCACAACGTCGACTTCCACGCCGCAACCGGTCAGGGCGGCGGTGCAGCCGCGACCTTTACCGCCCCGGGCCGCACTTCCACATTCAGCTTCAAAGCCCTGCAACCGGGC
CTGTACATCTACCACTGCGCCGTCGCGCCGGTCGGTATGCACATCGCCAACGGTATGTACGGTCTGATTTTGGTCGAGCCTAAAGAAGGCCTGCCGAAAGTGGATAAAGAGT
TCTACATCGTCCAAGGCGACTTCTACACCAAAGGCAAAAAAGGCGCGCAAGGCCTGCAACCGTTCGATATGGACAAAGCCGTTGCCGAACAGCCTGAATACGTCGTATTCAA
CGGCCACGTAGGCGCTATCGCCGGCGATAACGCCCTGAAAGCCAAAGCAGGCGAAACCGTGCGTATGTACGTCGGTAACGGCGGCCCGAACTTGGTGTCTTCCTTCCACGTC
ATCGGCGAAATCTTCGACAAAGTTTATGTTGAAGGCGGCAAACTGATTAACGAAAACGTACAAAGCACCATCGTGCCTGCCGGCGGTTCTGCCATCGTCGAATTCAAAGTCG
ACATCCCGGGCAACTACACTTTGGTCGACCACTCCATCTTCCGCGCATTCAACAAAGGCGCGTTGGGGCAATTGAAAGTAGAGTAA*GGTACC**AGGAGGA*GATAACAG*ATGAA*
AACCTTCTTCAAAACCCTTTCCGCCGCCGCACTCGCGCTCATCCTCGCAGCCTGCGGCGGTCAAAAAGACAGCGCGCCCGCAGCCTCTGCCGCCGCCCCTTCTGCCGATAAC
GGCGCGGCGTCGCTTCCGGCCGAGATTCCGCTGATTCCCGTCAATCAGGCCGATACGCTGATTGTGGATGGGGAAGCGGTCAGCCTGACGGGGCATTCCGGCAATATCTTCG
CGCCCGAAGGGAATTACCGGTATCTGACTTACGGGGCGGAAAAATTGCCCGGCGGATCGTATGCCCTCCGTGTGCAAGGCGAACCGGCAAAAGGCGAAATGCTTGCGGGCAC
GGCCGTGTACAACGGCGAAGTGCTGCATTTCCATATGGAAAACGGCCGTCCGTACCCGTCCGGAGGCAGGTTTGCCGCAAAAGTCGATTTCGGCAGCAAATCTGTGGACGGC
ATTATCGACAGCAGCGATGATTTGCATATGGGTACGCAAAAATTCAAAGCCGCCATCGATGGAAACGGCTTTAAGGGGACTTG

FIG. 2A

GACGGAAAATGGCGGCGGGGATGTTTCGGAAGGTTTTACGGCCCGGCCGAGGAAGTGGCGGGAAAATACAGCTATCGCCCGACAGATGCTGAAAAGGGCGGATTCGG
CGTGTTTGCCGGCAAAAAAGATCGGGATTGAGGATCCTGGCTGTTTTGGCGGATGAGAGAAGAAATTCGTCGCCCGCCATAAACTGCCAGGCATCAAATTAAGCAGAAGGC
CATCCGTCAGGATGGCCTTCTGCTTAATTTGATGCCTGGCAGTTTATGGCGGGCGACGAATCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTT
TTCTAAATATACATTCAAATATGTATCCGCTCATGAGCTTCACGCTGCCGCAAGCACTCAGGGCGCAAGGGCTGCTAAAGGAAGCGGAACACGTAGAAAGCCAGTCCGCAG
AAACGGTGCTGACCCCGGATGAATGTCAGCTACTGGGCTATCTGGACAAGGGAAAACGCAAGCGCAAAGAGAAAGCAGGTAGCTTGCAGTGGGCTTACATGGCGATAGCTA
GACTGGGCGGTTTTATGGACAGCAAGCGAACCGGAATTGCCAGCTGGGGCGCCCTCTGGTAAGGTTGGGAAGCCCTGCAAAGTAAACTGGATGGCTTTCTTGCCGCCAAGG
ATCTGATGGCGCAGGGGATCAAGATCTGATCAAGAGACAGGATGAGGATCGTTTCGCATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGG
CTATTCGGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGT
GCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGGCTG
CTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACGCTTGATCCGGCT
ACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTGTCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCG
CCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTGGAAAATGGCCGCTTT
TCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTC
CTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGAGTTCTTCTGACTGTCAGACCAAGTTTACTCATATATACTTTAGATT
GATTTAAAACTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCC
GTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAG
CTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTTCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCG
CCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGG
TCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGG
AGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCAC
CTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCT
CACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATAACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGCGAGTCAGTG
AGCGAGGAAGCCGAACGCCAGCAAGACGTAGCCCAGCGCGTCGGCCGAATTCGCGCTAACTTACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTC
GTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCCAGGGTGGTTTTTTCTTTTCACCAGTGAGACGGGCAACAGCTGATTGCCCT
TCACCGCCTGGCCCTGAGAGAGTTGCAGCAAGCGGTCCACGCTGGTTTGCCCCAGCAGGCGAAAAATCCTGTTTGATGGTGGTTAACGGCGGGATATAACATGAGCTGTCTT
CGGTATCGTCGTATCCCACTACCGAGATATCCGCACCAACGCGCAGCCCGGACTCTCGGTAATGGCGCGCATTGCGCCCAGCGCCATCTGATCGTTGGCAACCAGCATCGCAG
TGGGAACGATGCCCTCATTCAGCATTTGCATGGTTTGTTGAAAACCGGACATGGCACTCCAGTCGCCTTCCCGTTCCGCTATCGGCTGAATTTGATTGCGAGTGAGATATT
TATGCCAGCCAGACGCGATTAGCGCCGAGACAGAACTTAATGGGCCCGCTAACAGCGCGATTTGCTGGTGACCCAATGCGACCAGATGCTCCACGCCCAGTCGCGTAC
CGTCTTCATGAGCGCAACGCAATTAATGTGAGTTAGCTCACTCATTAGGCACCCCAGGCTTTACACATGCTCCTCGCCCCGTTGCACGTCAATAATGACGTATGTTCCATA
CCAGCGGATAGTTAAATGATCAGCCCACTGACGCGTTGCGCGAGAAGATTGTGCACCGCCGCTTTACAGGCTTCGACGCCGCTTCGTTCTTACCATCGACACCACCACGCTGG
CACCCAGTTGATCGGCGCGAGATTTAATCGCCGCGACAATTTGCGACGGCGCGTGCAGGGCCAGACTGGAGGTGGCAACGCCAATCAGCAACGACTGTTTGCCCGCCAGTT
GTTGTGCCACGCGGTTGGGAATGTAATTCAGCTCCGCCATCGCCGCTTCCACTTTTTCCCGCGTTTTCGCAGAAACGTGGCCTGGCCTGGTTCACCACGCGGGAAACGGTCT
GATAAGAGACACCGGCATACTCTGCGACATCGTATAACGTTACTGGTTTCACATTCACCACCCTGAATTGACTCTCTTCCGGGCGCTATCATGCCATACCGCGAAAGGTTT
TGCACCATTCGATGGTGTCAACGTAAATGCATGCCGCTTCGCCTTCGCGCGCGAATTGGCCGCCATGCCGGCGATAATGGCCTGCTTCTCGCCGAAACGTTTGGTGGCGGG
ACCAGTGACGAAGGCTTGAGCGAGGGCGTGCAAGATTCCGAATACCGCAAGCGACAGGCCGATCATCGTCGCGCTCCAGCGAAAGCGGTCCTCGCCGAAAATGACCCAGAG
CGCTGCCGGCACCTGTCCTACGAGTTGCATGATAAAGAAGACAGTCATAAGTGCGGCGACGATAGTCATGCCCCGCGCCCACCGGAAGGAGCTGACTGGGTTGAAGGCTCT
CAAGGGCATCGGTCGAGATCCCGGGCCTTATCGACTGCACGGTGCACCA

FIG. 2A (continued)

GCGCAGCGAGTCAGTGAGCGAGGAAGCCGAACGCCAGCAAGACGTAGCCCAGCGCGTCGGCCAATTCGCGCTAACTTACATTAATTGCGTTGCGCTCACTGCCCGCTT
TTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCCAGGGTGGTTTTTCTTTTCACCAGTG
AGACGGGCAACAGCTGATTGCCCTTCACCGCCTGGCCCTGAGAGAGTTGCAGCAAGCGGTCCACGCTGGTTTGCCCCAGCAGGCGAAAATCCTGTTTGATGGTGGTT
AACGGCGGGATATAACATGAGCTGTCTTCGGTATCGTCGTATCCCACTACCGAGATATCCGCACCAACGCGCAGCCCGGACTCGGTAATGGCGCGCATTGCGCCCAG
CGCCATCTTGATCGTTGGCAACCAGCATCGCAGTGGGAACGATGCCCTCATTCAGCATTTGCATGGTTTGTTGAAAACCGGACATGGCACTCCAGTCGCCTTCCCGTT
CCGCTATCGGCTGAATTTGATTGCGAGTGAGATATTTATGCCAGCCAGACGCGCAGACGGCCGAGACAGAACTTAATGGGCCCGCTAACAGCGCGATTTGCTGGG
TGACCCAATGCGACCAGATGCTCCACGCCCAGTCGCGTACCGTCTTCATGGGAGAAAATAATACTGTTGATGGGTGTCTGGTCAGAGACATCAAGAAATAACGCCGG
AACATTAGTGCAGGCAGCTTCCACAGCAATGGCATCCTGGTCATCCAGCGGATAGTTAATGATCAGCCCACTGACGCGTTGCGCGAGAAGATTGTGCACCGCCGCTT
TACAGGCTTCGACGCCGCTTCGTTCTACCATCGACACCACCACGCTGGCACCCAGTTGATCGGCGCGAGATTTAATCGCCGCGACAATTTGCGACGGCGCGTGCAGG
GCCAGACTGGAGGTGGCAACGCCAATCAGCAACGACTGTTTGCCCGCCAGTTGTTGTGCCACGCGGTTGGGAATGTAATTCAGCTCCGCCATCGCCGCTTCCACTTT
TTCCCGCGTTTTCGCAGAAACGTGGCCTGGTTCACCACGCGGGAAACGGTCTGATAAGAGACACCGGCATACTCTGCGACATCGTATAACGTTACTGGTTTCA
CATTCACCACCCTGAATTGACTCTCTTCCGGGCGCTATCATGCCATACCGCGAAAGGTTTTGCGCCATTCGATGGTGTCAACGTAAATGCATGCCGCTTCGCCTTCG
CGCGCGAATTGGCCGCCATGCCGGCGATAATGGCCTGCTTCTCGCCGAAACGTTTGGTGGCGGGACCAGTGACGAAGGCTTGAGCGAGGGCGTGCAAGATTCCGAAT
ACCGCAAGCGACAGGCCGATCATCGTCGCGCTCCAGCGAAAGCGGTCCTCGCCGAAAATGACCCAGAGCCTCCGGTCGAGAGGCTTGAGGAGCTT
TTGACTTTCTGCTTACTGAATTTCGGTGGTCGCCGTTACTAGTCTAGCGCATTTCAGCGCGAACGCGCTCAAGATCTTCAGGGGTATCCACACCTGTGCCAGGAACTT
CCTGAGCAACAGCAACATGGATTTTTTCGCCGTACCACAGAACACGAAGCTGCTCTAACATTTCGATGTGTTCTAACGGACTTGGCTGCCAGTTGACGTAACGACGG
ATAAAGCCTGCACGGTAGCCATAAATACCAAGATGACGCAGGAAGTTATCGCCAACGGTTTCAAGGCCTTCTGCAAAACGATCACGATCCCAAGAATGGTGGCGCG
AGAGAAGTACAGTGCATACCCTTCAGCGTCGAGAACCACTTTCACCGCATTGTGGATTGGCACCGCCAGAGTCGCCATACCCA
CCTGACGCTGAGCGAGGTTATCAGCAACCTGACGAATGATTGTCGCAGGGATCATCGGTTCATCACCCTGCACATTAACGATCACCGTGTCGTCGCTGAATGCGCAT
TTTTCGACAACTTCCGCCAGACGTTCTGTTCCTGACTGATGATCGGCGCGCGTCATACATACTTCACCGCCAGCGGCTTCAACGGCGCGGGCAACATCCTCATGATC
GGTTGCCACGATGATGCGCTCGGCACCTGATTCACGCGCGCGTTCAAGAACATCATGGGTTTGCCGTTAATATCAACCAATGGTTTACCGGGCAGACGCG
TGGACGCGTAGCGCGCGGGAATAATGACCACAAAACTCATATCCCTCCTCCTGAGCTCGAATTCAGCTCCTAGTTTACTCTCATTTCAATTGCCCCAACGCGCCTTT
GTTGAATGCGCGGAAGATGGAGTGGTCGACCAAAGTGTAGTTGCCCGGGATGTCGAACTTTGAATTCGAGCAGAACCGCCGGCAGGCACGATGGTGCTTTGTA
CGTTTTCGTTAATCAGTTTGCCGCCTTCAACATAAACTTTGTCGAAGATTTCGCCGATGACGTGGAAGGAAGACACCAAGTTCGGGCCGCCGTTACCGACGTACATA
CGCACGGTTTCGCCTGCTTTGGCTTTCAGGGCGTTATCGCCGGCGATAGCGCCTACGTGGCCGTTGAATACGACGTATTCAGGCTGTTCGTCAACGGCTTTGTCCAT
ATCGAACGGTTGCAGGCCTTGCGCGCCTTTTTTGCCTTTTGGTGTAGAAGTCGCCTTGATAGAACTCTTTATCCACTTTCGGCAGGCCTTCTTTAGGCTCGA
CCAAAATCAGACCGTACATACCGTTGGCGATGTGCATACCGACCGGCGCGACGGCCGGTTGCAGGGCCCGGTTGCAGGGCTTTGAAGCTGAATGTGGAA
GTGCGGCCCGGGGCGGTAAAGGTCGCGGCTGCACCGCCGCCTGACCGGTTGTGCGGAACGGTAGAAGGATTGTTGGAGAAGAATTC
GACTTCAACCGTATCGCCTTCGCGTACTTTGGCAGGATAGTCGCGGTCGATTGCGGGAGGTACTTCGGGAGCGTGGGTGGTCACCGCATCGATGACGGGCAGTTCGCCT
CGACGGTTTCCATTTTTACGCGTACTTTGGCAGGATAGTCGCGGTCGATTGCGGGAGGTACTTCGGGAGCGTGGGTGGTCACCGCATCGATGACGGGCAGTTCGCCT
GCAGGCGTTTCGGCGGTAGCTTGTGCGGCGGAACTTGCGGCTTCTGCGGAAGCGGCAGGGGTTTCGGCAGGGGCTTGAGCAGCTTGTTCGCCACCGCAGGCGGCCAA
TGCGAATAAGGAAGCAATCATTGCGGCTAATGCTTGGCGTTTCATCTCGTTATCTCCTCCTAAGCTTTTATTTGGCTGCGCCTTCATTCCATGCGGCAGGGTATTTGT
AGCCCTCGAAGCGTTTGTGCGCGTAGGCTTTGAACGCGTCGGAGTTATAGGCCTCGGTTACGTCTTTAAGCCATTGGCTGTCTTGTCGGCGGTTTTGACGGCAGAC
CAGTTGACATAGGCAAAGCTCGGCTCTTGGAACAGGGCTTCGGTCAGCTTCATGCCGCTGTTATGGCGTAGTTGCCGTTGACGACGGCAAAATCCACGTCGGCGCG
GCTGCGCGGCAGTTGTGCGGCTTCAAGCTCGACGATTTTGATGTTTTTCAGGTTTTCCGCGATATCGGCTTTGGATGCGGTCAGCGGATTGATGCCGTCTTTGAGTT
TGATCCAACCCAGTTCGTTCAGCATCACCAAGGCGCGTGCGAAGTTGGACGGGTCGTTGGGCGCGGATACGGTGCTGCCGTCTTTGACTTCTTCCAGCGATTTCAGT
TTGCCCGGATACAGTCCCAAAGGCGCGGTCGGCACTTGGAAGGCTTCGGTGATGTCCAGGTTGTGTTCTTTTTTGAAATCGTCAAGATAGGGTTTGTGTTGGAAGAC
GTTGATGTCCAACTCGCCCTCCGCCAATGCCAGGTCGGCGCACATAGTCGGTAAATTCGACCAATTTGACGGTGTAGCCTTTTTTCTCCAGCTCGGCTTGGATTT
GTTCTTTGACCATATCGCCGAAGTCGCCGACGGTCGTGCCGAAGACGATTTCTTTTTTCGCCGCCGTTATCGGCAGAAGGGCGGCGGCAGAGGTCGCGGGCGCG
CTGTCTTTTTGACCGCCAGCTGCAGGATGAGCGCGAGTGCGGCGGCGAAAAGGGTTTTTGAAGAAGGTTTTTCATCTGTTATCTCCTCCTCAATTCCACAGTAGTA
GCTAGCATAGTACCTAGGACTGAGCTAGCCGTAAATGCTGCCGGCACCTGTCCTACGAGTTGCATGA

FIG. 2B

TAAAGAAGACAGTCATAAGTGCGGCGACGATAGTCATGCCCCGCGCCCACCGGAAGGAGCTGACTGGGTTGAAGGCTCTCAAGGGCATCGGTCGAGATCC

GGGCTTATCGACTGCACGGTGCACCAATGCTTCTGGCGTCAGGCAGCCATCGGAAGCTGTGGTATGGCTGTGCAGGTCGTAAATCACTGCATAATTCGTG

TCGCTCAAGGCGCACTCCCGTTCTGGATAATGTTTTTTGCGCCGACATCATAACGGTTCTGGCAAATATTCTGAAATGAGCTG**TTGACAATTAATCATCG**

GCTCGTATAATGTGTGGAA***TTGTGAGCGGATAACAA***TTTCACACAGGAAACAGATGAAACGCCAAGCATTAGCCGCAATGATTGCTTCC

TTATTCGCATTGGCCGCCTGCGGTGGCGAACAAGCTGCTCAAGCCCCTGCCGAAACCCCTGCCGCTTCCGCAGAAGCCGCAAGTTCCGCCGCACAAGCTA

CCGCCGAAACGCCTGCACCGCACACTTTATCCACGTTTAAAAACCGCGGACAACCGCCCCGCCAGTGTTTATTTGAAAAAGACAAACCGACGCTGATTAA

ATTTTGGGCGAGCTGGTGTCCTTTATGTTTGTCCGAATTGGGACAGGCCGAGAAATGGGCGCAAGATGCAAAATTCAGCTCCGCCAACCTGATTACCGTC

GCCTCCCCCGGCTTTTTGCACGAGAAAAAAGACGGCGAGTTTCAAAAATGGTATGCCGGTTTGAACTACCCCAAGCTGCCCGTCGTTACCGACAACGGCG

GCACGATCGCCCAAAACCTGAATATCAGCGTTTATCCTTCTTGGGCGTTAATCGGTAAAGACGGCGACGTGCAGCGCATCGTCAAAGGCAGCATCAACGA

AGCGCAGGCATTGGCGTTAATCCGCAACCCGAATGCCGATTTGGGCAGTTTGAAACATTCGTAAGGTACCAGGAGGAGATAACAGATGAAAACCTTTCTTTC

AAAACCCTTTCCGCCGCCATCTCGCTCATCCTCGCAGCCTGCGGCGGTCAAAAAGACACAGCTGCGCTCTGCCGCCCTTCTTGCCGATA

ACGGCGCGGCGTCGCTTCCGGCCGAGATTCCGCTGATTCCCGTCAATCAGGCCGATACGCTGATTGTGGATGGGAAGCGGTCAGCCTGACGGGGCATTC

CGGCAATATCTTCGCGCCCGAAGGGAATTACCGGTATCTGACTTACGGGGCGGAAAAATTGCCCGGCGGATCGTATGCCCTCCGTGTGCAAGGCGAACCG

GCAAAAGGCGAAATGCTTGCGGGCACGGCCGTGTACAACGGCGAAGTGCTGCATTTCCATATGGAAAACGGCCGTCCGTACCCGTCCGGAGGCAGGTTTG

CCGCAAAAGTCGATTTCGGCAGCAAATCTGTGGACGGCATTATCGACAGCAGCGATGATTTGCATATGGGTACGCAAAAATTCAAAGCCGCCATCGATGG

AAACGGCTTTAAGGGACTTGACGGAAAATGGCGGCGGGGATGTTTCCGGAAGGTTTTACGGCCCGGCCGAGGAAGTGGCGGGAAAATACAGCTAT

CGCCCGACAGATGCTGAAAAGGCGGATTCGGCGTGTTTGCCGGCAAAAAAGATCGGGATTGAAAGCTTGGCTGTTTTGGCGGATGAGAGAAGAAATTCG

TCGCCCGCCATAAACTGCCAGGCATCAAATTAAGCAGAAGGCCATCCGTCAGGATGGCCTTCTGCTTAATTTGATGCCTGGCAGTTTATGGCGGGCGACG

AATCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAAATACATTCAAATATGTATCCGCTCATGAGCTTTCACGCTG

CCGCAAGCACTCAGGGCGCAAGGGCTGCTAAAGGAAGCGGAACACGTAGAAAGCCAGTCCGCAGAAACGGTGCTGACCCCGGATGAATGTCAGCTACTGG

GCTATCTGGACAAGGGAAAACGCGAAGCAGAAAGCAGGTAGCTTGCAGTGGGCTTACATGGCGATAGCTAGACTGGGCGGTTTTATGGACAGCAA

GCGAACCGGAATTGCCAGCTGGGGCGCCTCTGGTAAGGTTGGGAAGCCCTGCAAAGTAAACTGGATGGCTTTCTTGCCGCCAAGGATCTGATGGCGCAG

GGGATCAAGATCTGATCAAGAGACAGGATGAGGATCGTTTCGCATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTA

TTCGGCTATGACTGGGCACAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACC

TGTCCGGTGCCCTGAATGAACTGCAGGACGAGGCAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGA

AGCGGGAAGGGACTGGCTGCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCA

ATGCGGCGGCTGCATACGCTTGATCCGGCTACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTG

TCGATCAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCGTCGT

GACCCATGGCGATGCCTGCTTGCCGAAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCGGACCGCTATCAG

GACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTATCGCCGCTCCCGATTCGCAGC

GCATCGCCTTCTATCGCCTTCTTGACGAGTTCTTCTGACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAAACTTCATTTTTAATTTAA

AAGGATCTAGGTGAAGATCCTTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAA

GGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCTAC

CAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTTCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGT

AGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTA

CCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAGC

TATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGG

AAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAAC

GCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATAACCGTATTA

CCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGA [SEQ ID NO: 67]

FIG. 2B (continued)

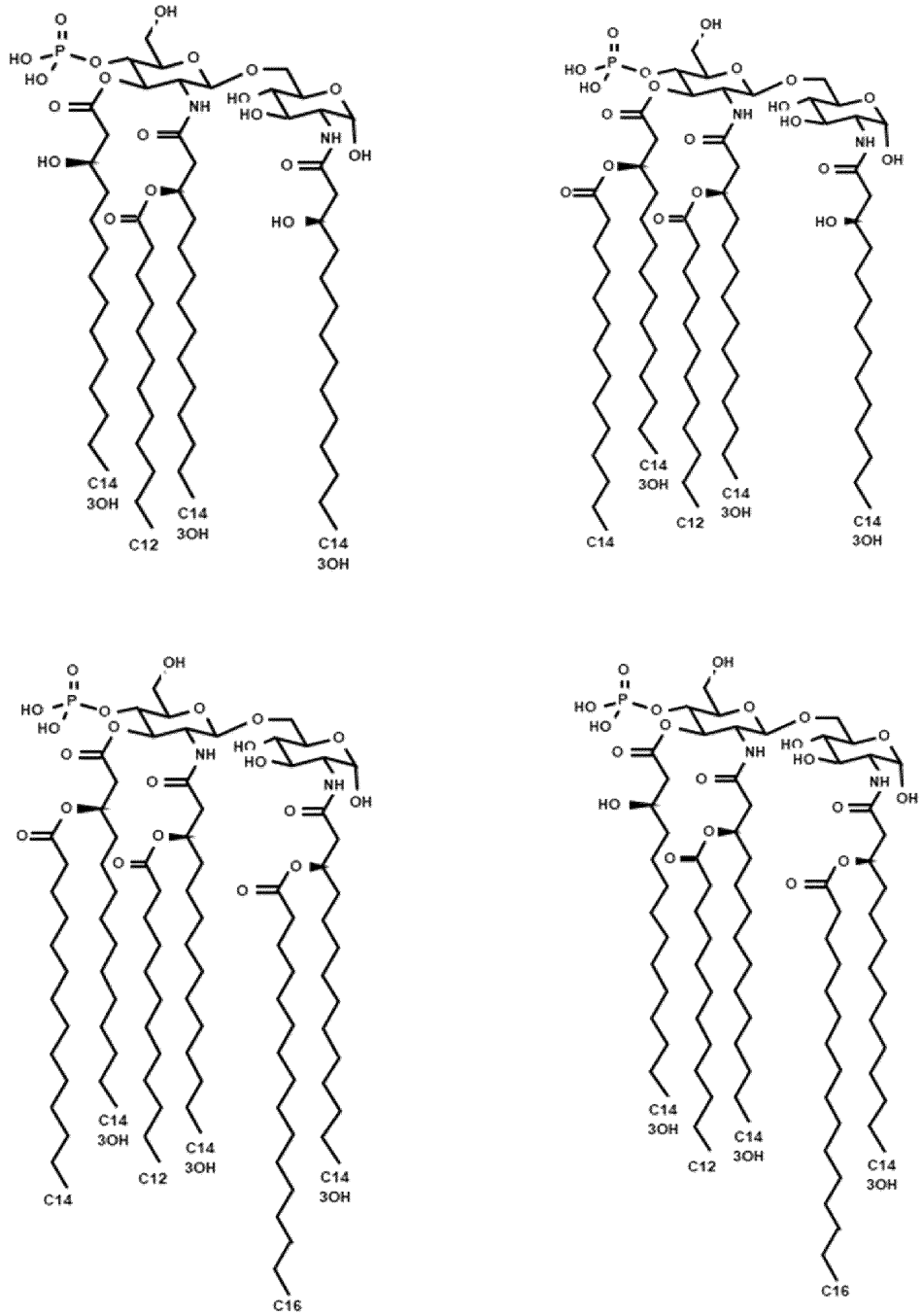

C14 3OH
C12
C14 3OH
C14 3OH
C14
C12
C14 3OH
C14 3OH
C14 3OH
C12
C14 3OH
C14 3OH
C14
C12
C14 3OH
C14 3OH
C16

FIG. 3A

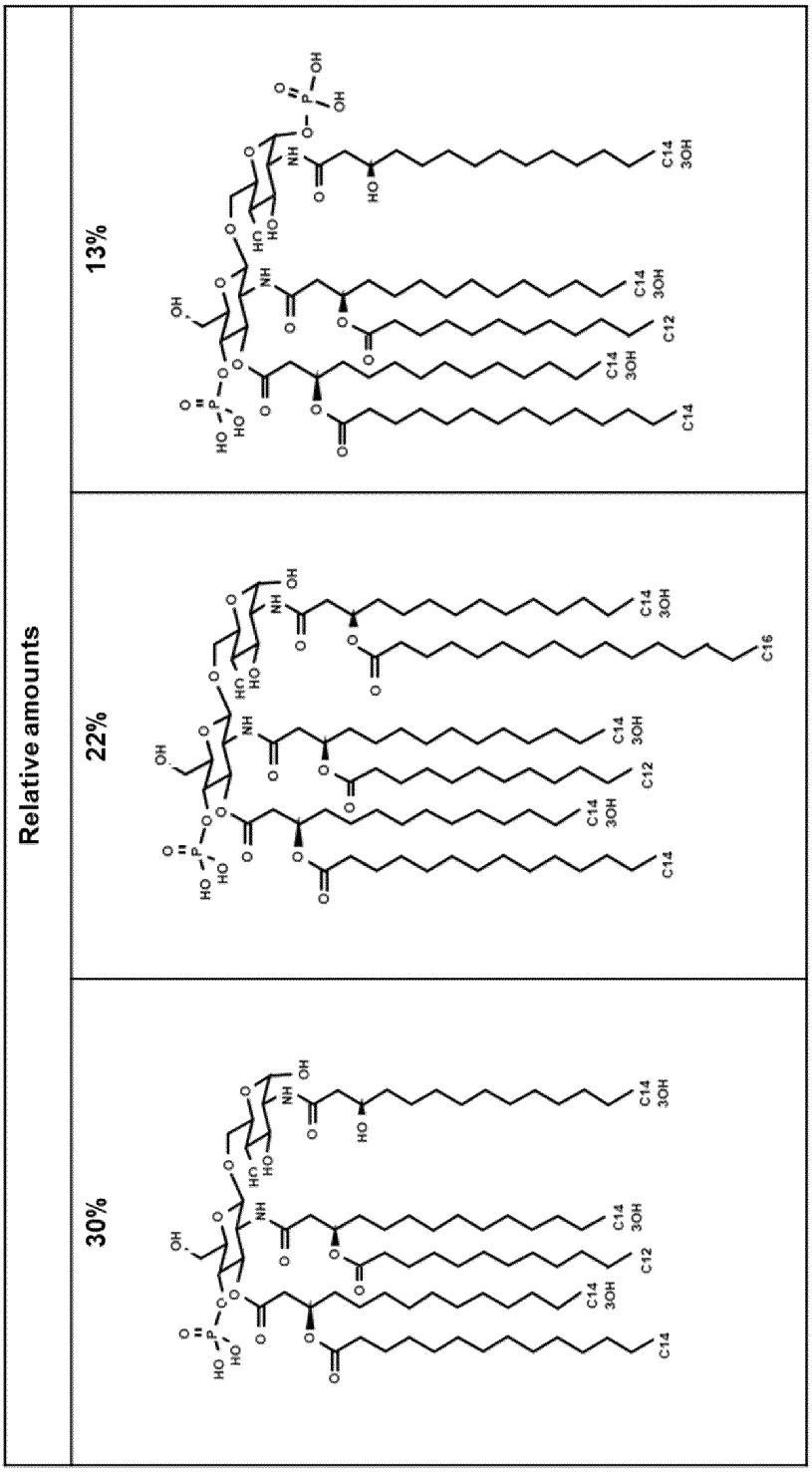


FIG. 3B

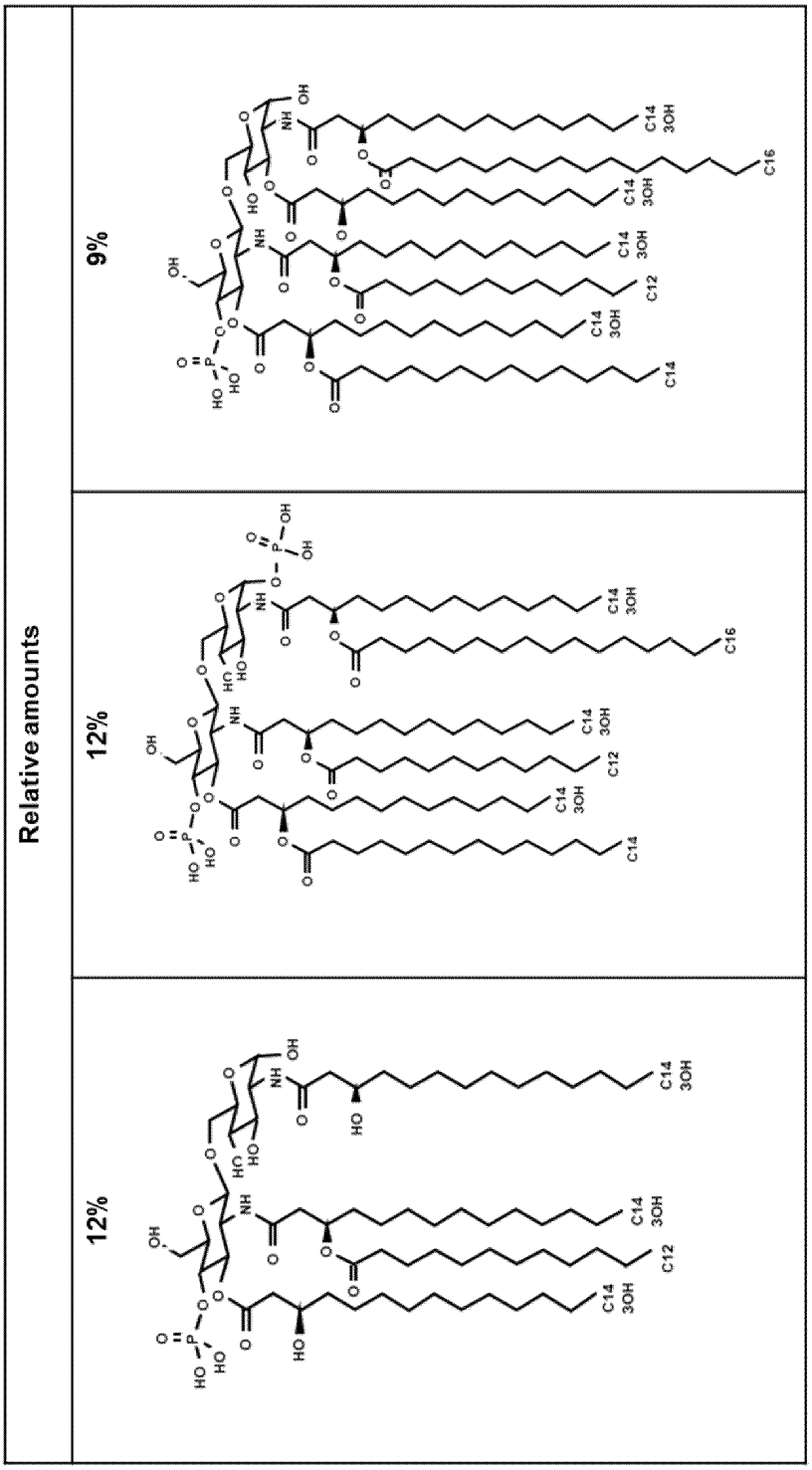


FIG. 3B (Continued)

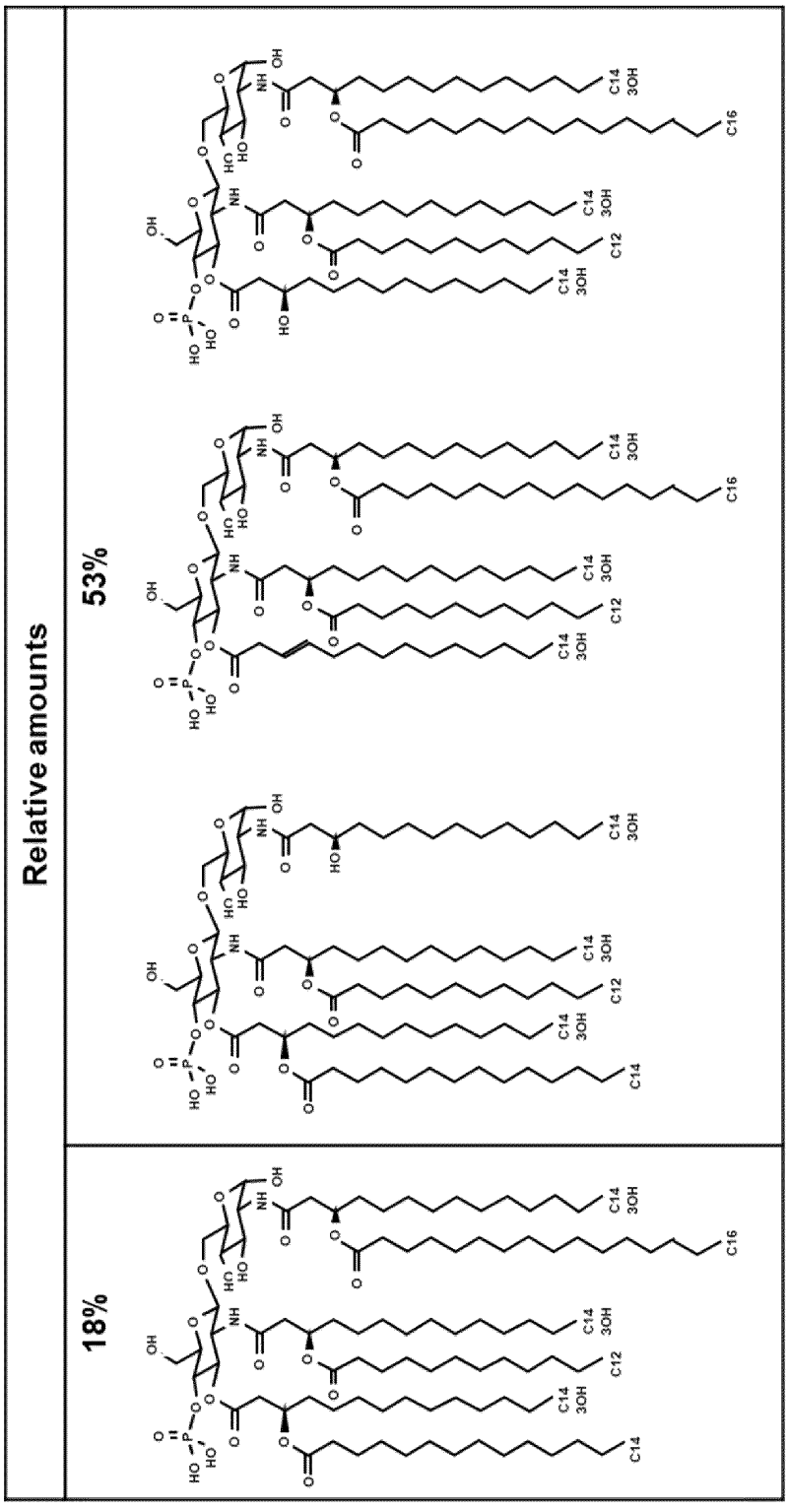


FIG. 3C

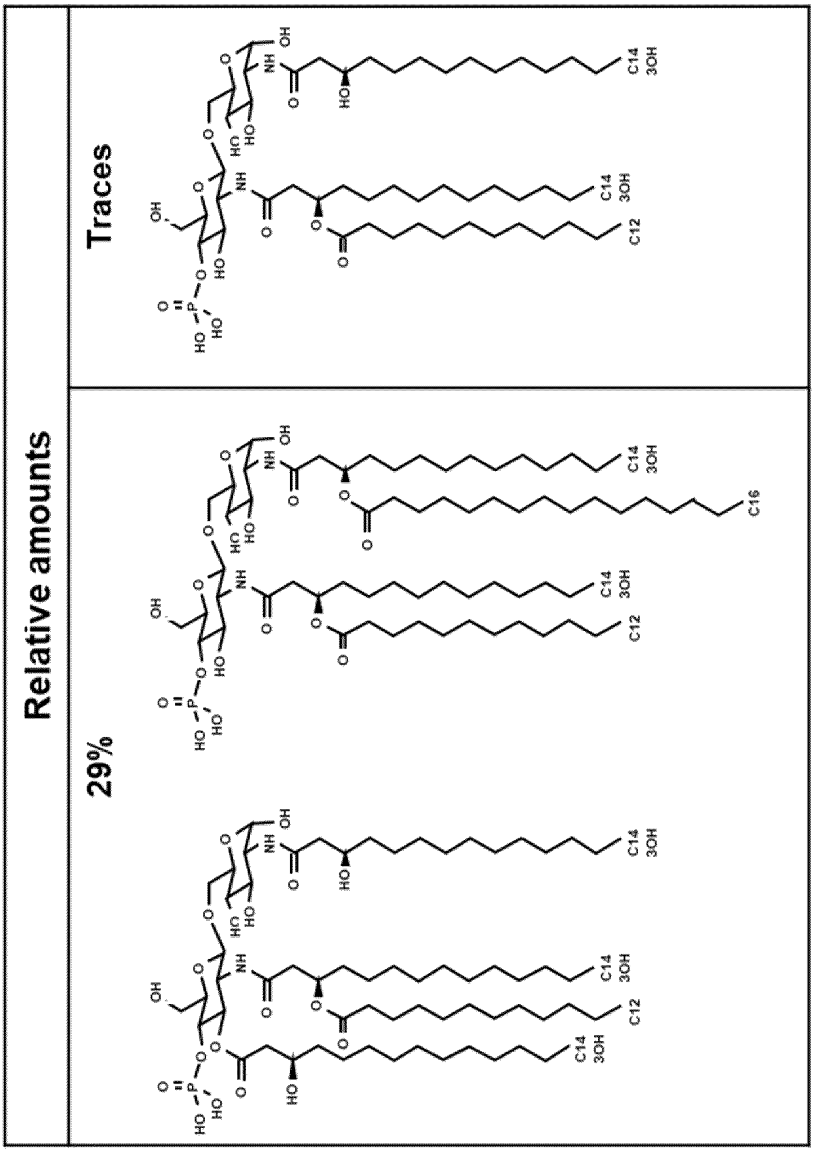


FIG. 3C (Continued)

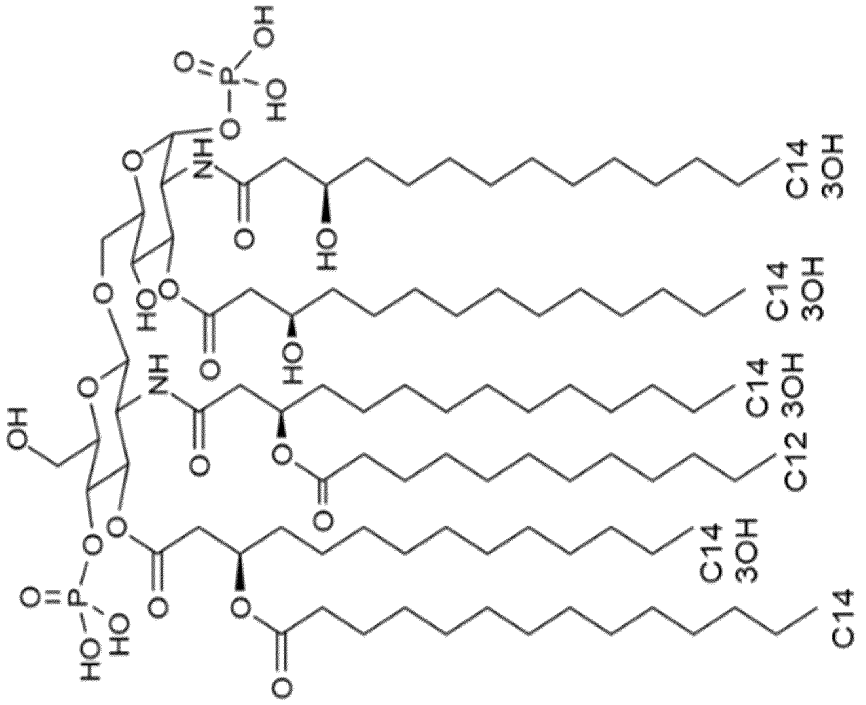


FIG. 3D

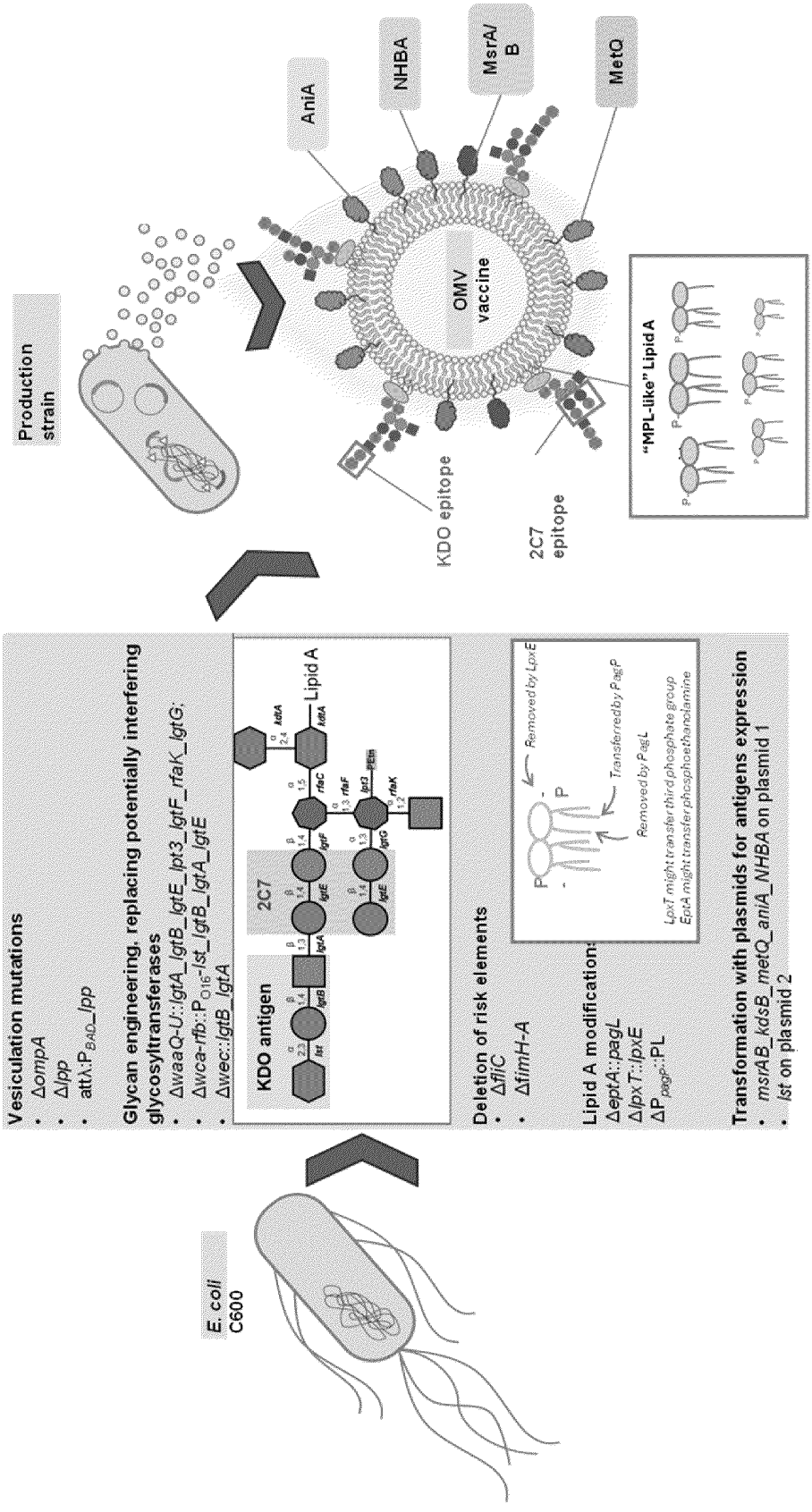

E. coli C600
Vesiculation mutations
ΔompA
Δlpp
attλ:P_BAD_lpp
Glycan engineering, replacing potentially interfering glycosyltransferases
ΔwaaQ-U::lgtA_lgtB_lgtE_lpt3_lgtF_rfaK_lgtG;
Δwca-rfb::P_O16_-lst_lgtB_lgtA_lgtE
Δwec::lgtB_lgtA
KDO antigen
2C7
Lipid A
Deletion of risk elements
ΔfliC
ΔfimH-A
Lipid A modification:
ΔeptA::pagL
ΔlpxT::lpxE
ΔP_pagP_::PL
Removed by LpxE
Transferred by PagP
Removed by PagL
LpxT might transfer third phosphate group
EptA might transfer phosphoethanolamine
Transformation with plasmids for antigens expression
msrAB_kdsB_metQ_aniA_NHBA on plasmid 1
lst on plasmid 2
Production strain
AniA
NHBA
MsrA/B
MetQ
OMV vaccine
KDO epitope
2C7 epitope
"MPL-like" Lipid A

FIG. 4

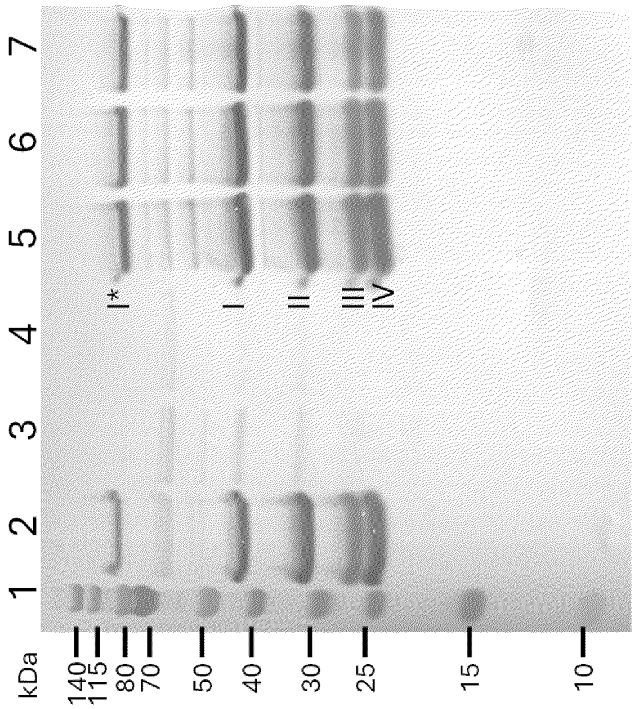


FIG. 5B

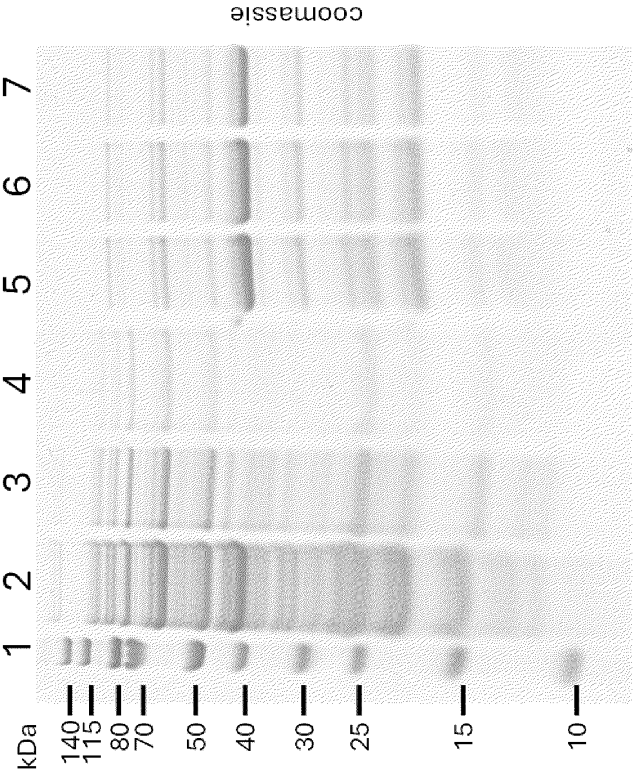


FIG. 5A

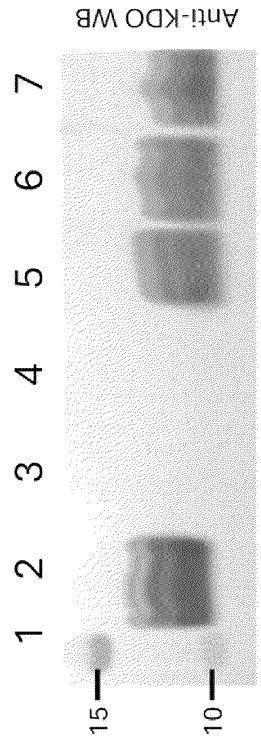


FIG. 5D

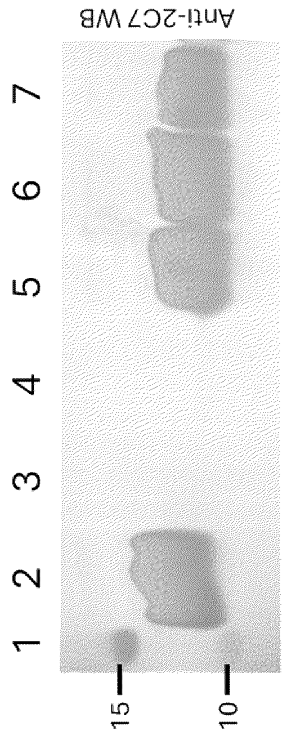


FIG. 5C

Samples:	
1	Molecular weight marker
2	Crude supernatant fermentation
3	TFF permeate
4	TFF wash step
5	TFF retentate
6	TFF retentate filtered 0.45 µM filter
7	TFF retentate filtered 0.2 µM filter

annotations:	
I	AniA 37 kDa
I*	AniA dimer
II	MetQ 31 kDa
III	cNHBA 23 kDa
IV	MsrA/B 21 kDa

FIG. 5E

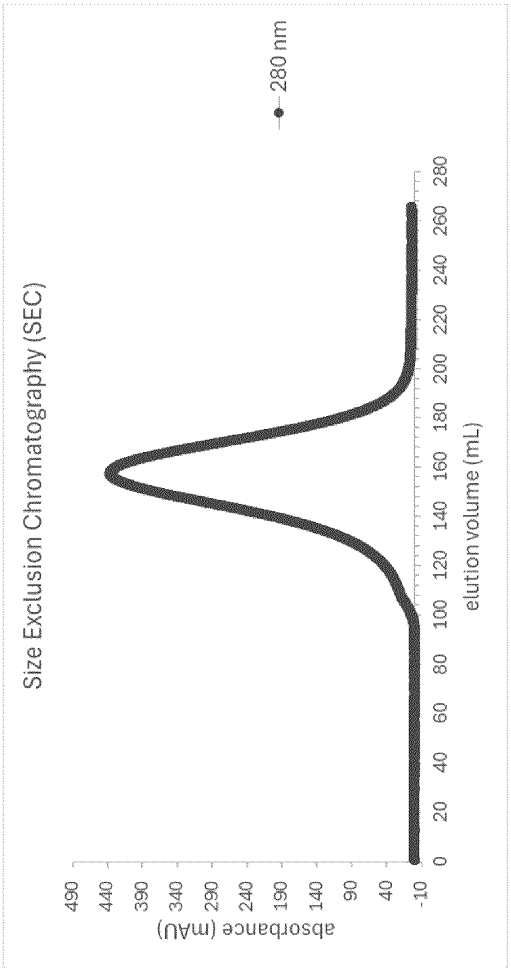

Size Exclusion Chromatography (SEC)
280 nm
absorbance (mAU)
490
440
390
340
290
240
190
140
90
40
-10
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
elution volume (mL)

FIG. 6A

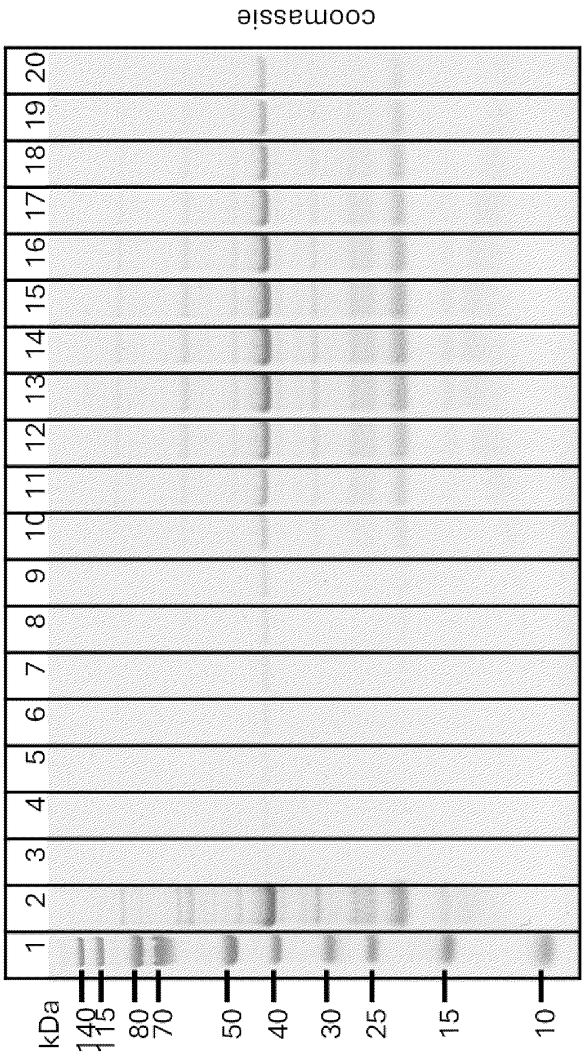

coomassie
kDa
140
115
80
70
50
40
30
25
15
10
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20

FIG. 6B

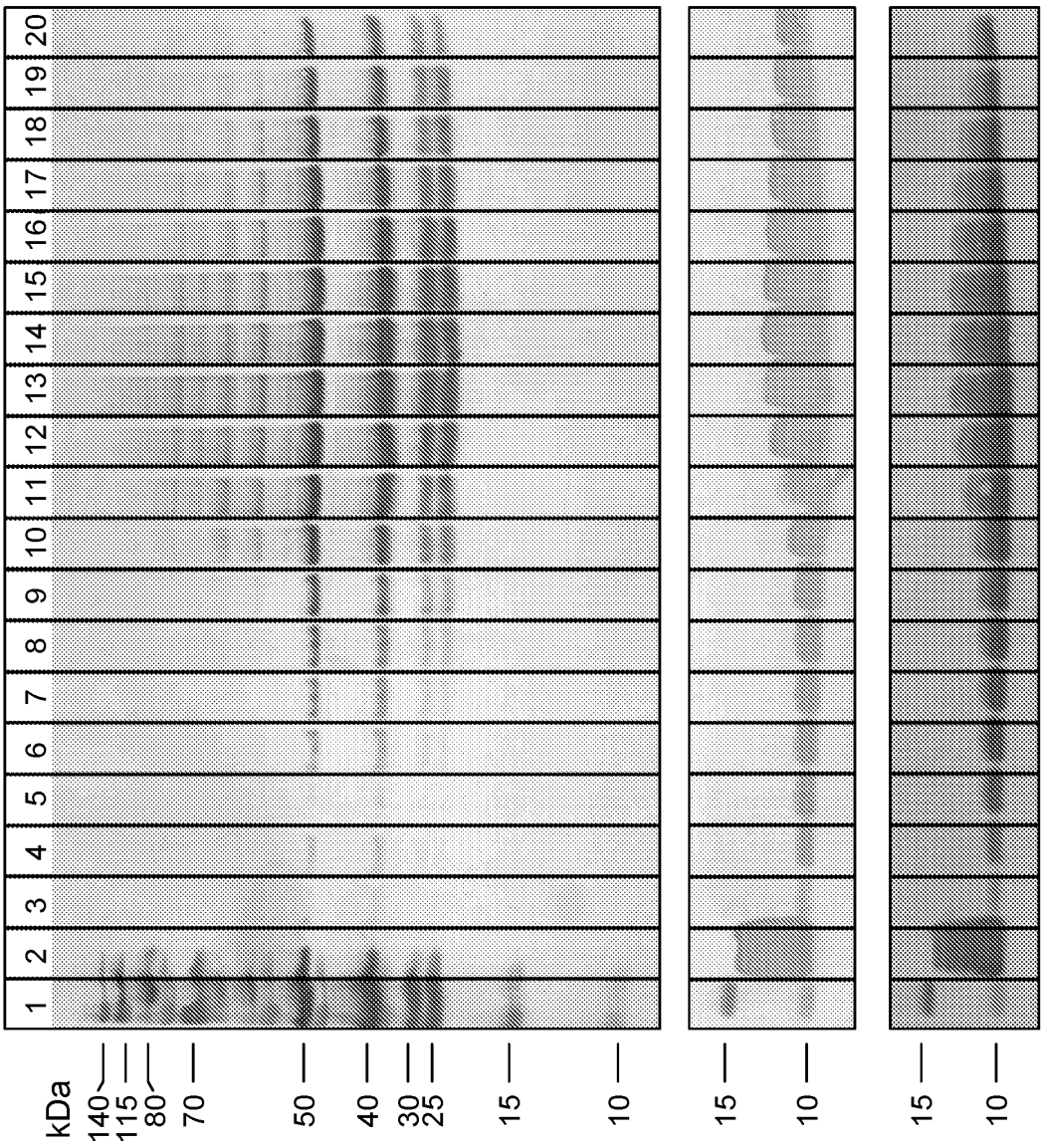


FIG. 6C

FIG. 6D

FIG. 6E

1	Molecular weight marker
2	Before SEC
Fraction with elution volume of	
3	97 ml
4	100 mL
5	104 mL
6	108 mL
7	112 mL

Fraction with elution volume of	
8	116 ml
9	120 ml
10	128 ml
11	136 ml
12	144 ml
13	152 ml
14	160 ml

Fraction with elution volume of	
15	164 ml
16	170 ml
17	174 ml
18	178 ml
19	182 ml
20	186 ml

FIG. 6F

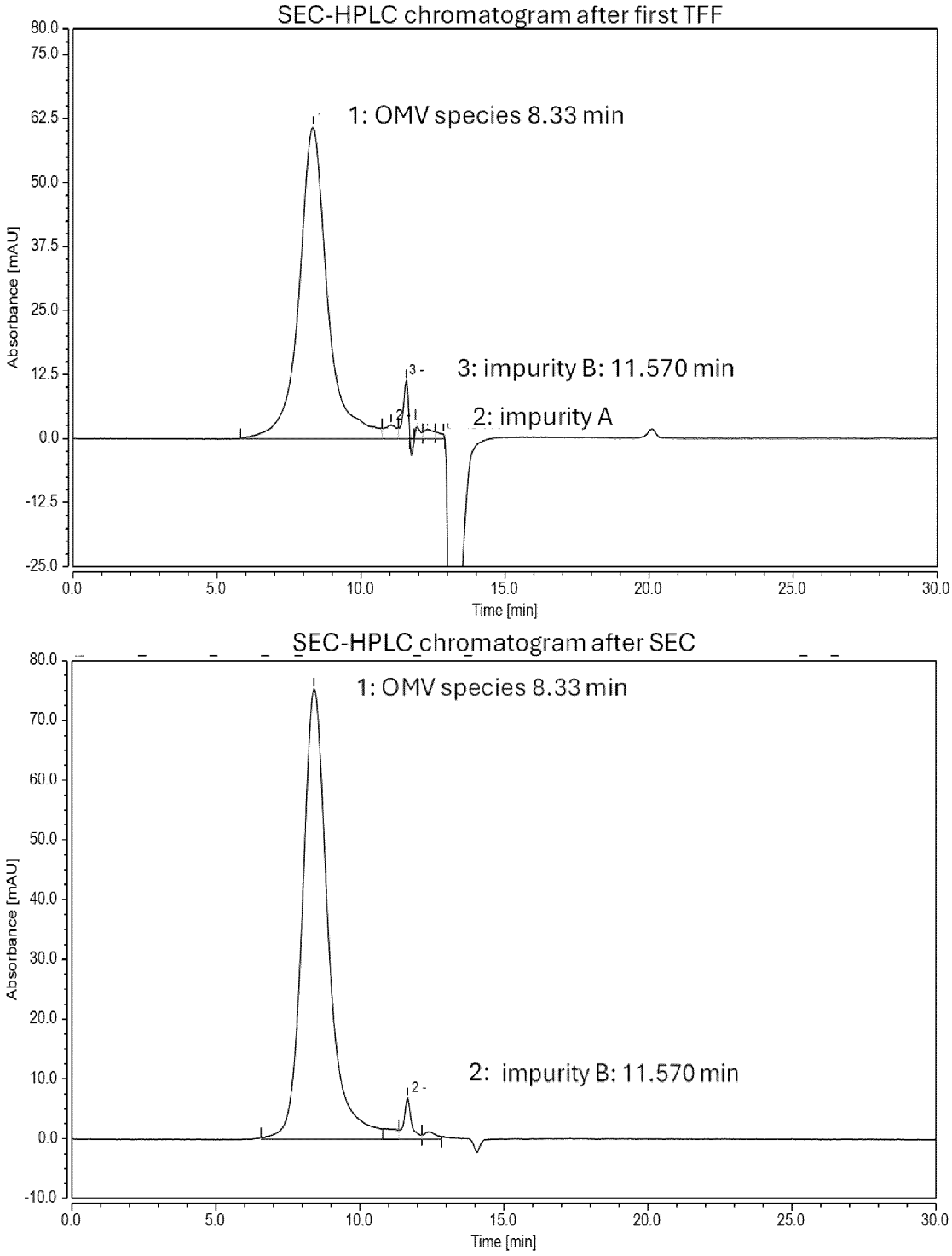

SEC-HPLC chromatogram after first TFF
1: OMV species 8.33 min
3: impurity B: 11.570 min
2: impurity A
Absorbance [mAU]
Time [min]
SEC-HPLC chromatogram after SEC
1: OMV species 8.33 min
2: impurity B: 11.570 min
Absorbance [mAU]
Time [min]

FIG. 7A

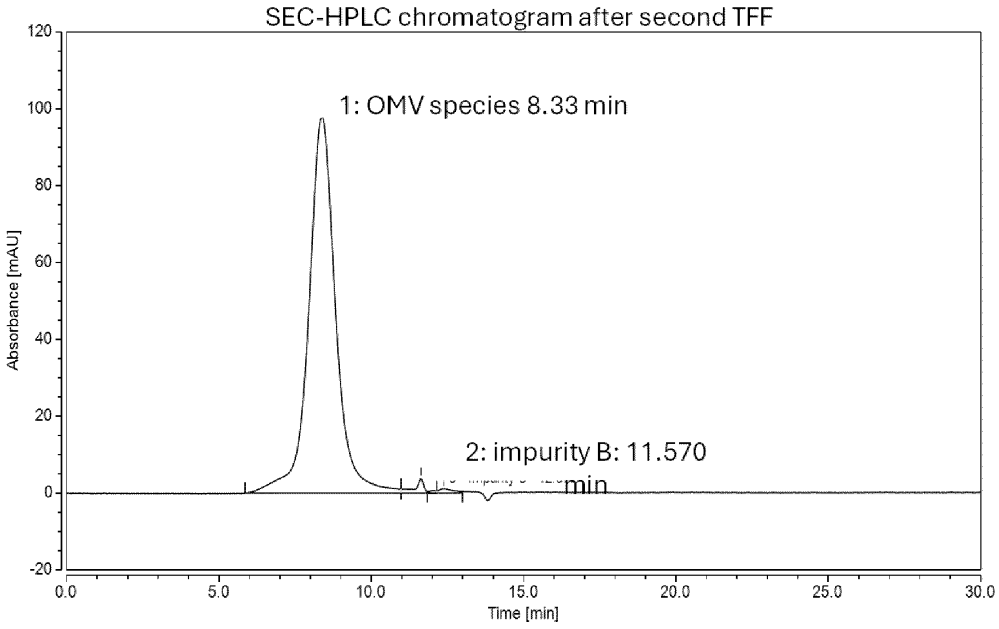


FIG. 7A (continued)

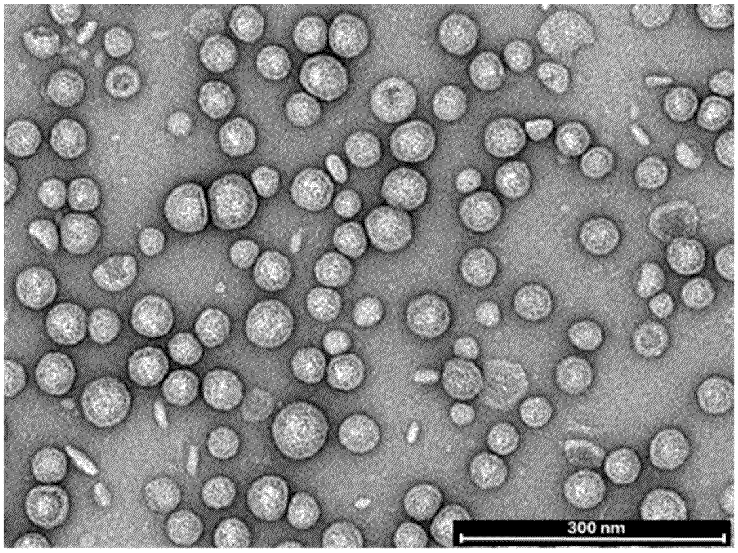


FIG. 7B

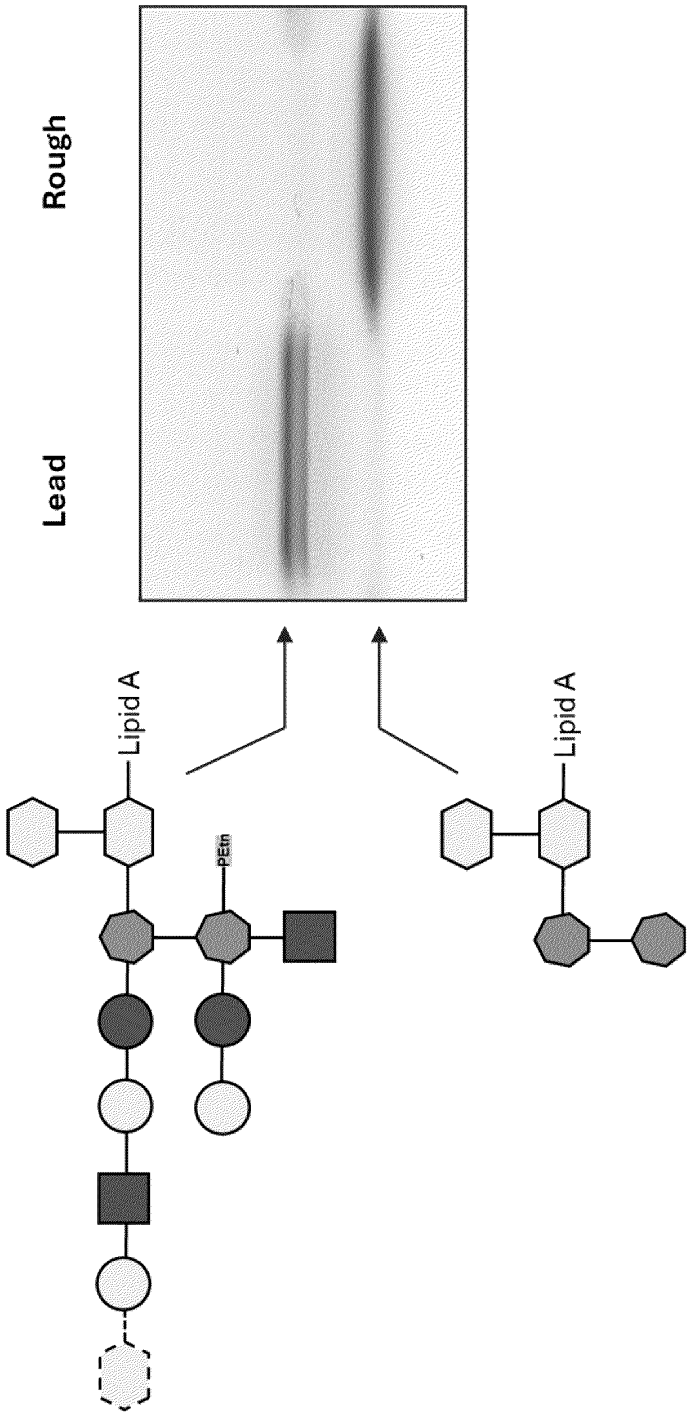


FIG. 8A

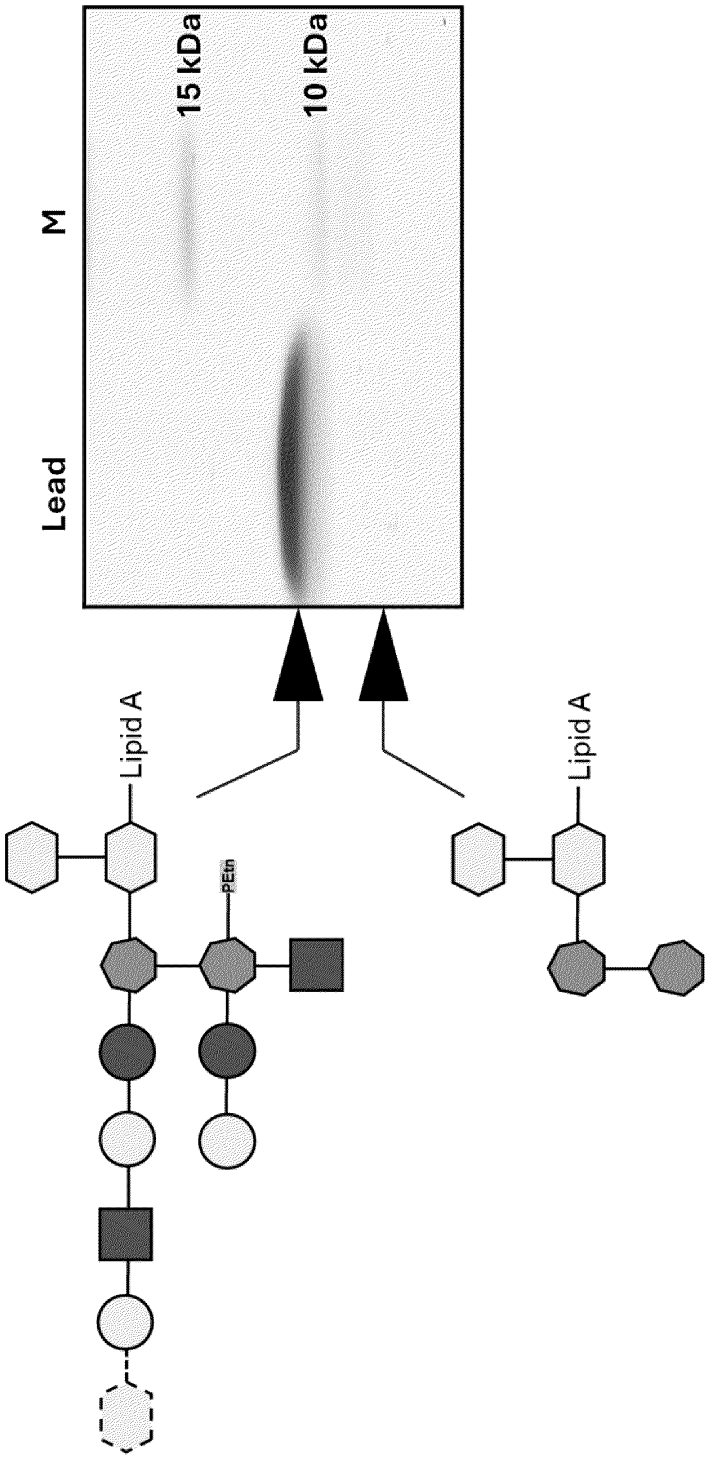
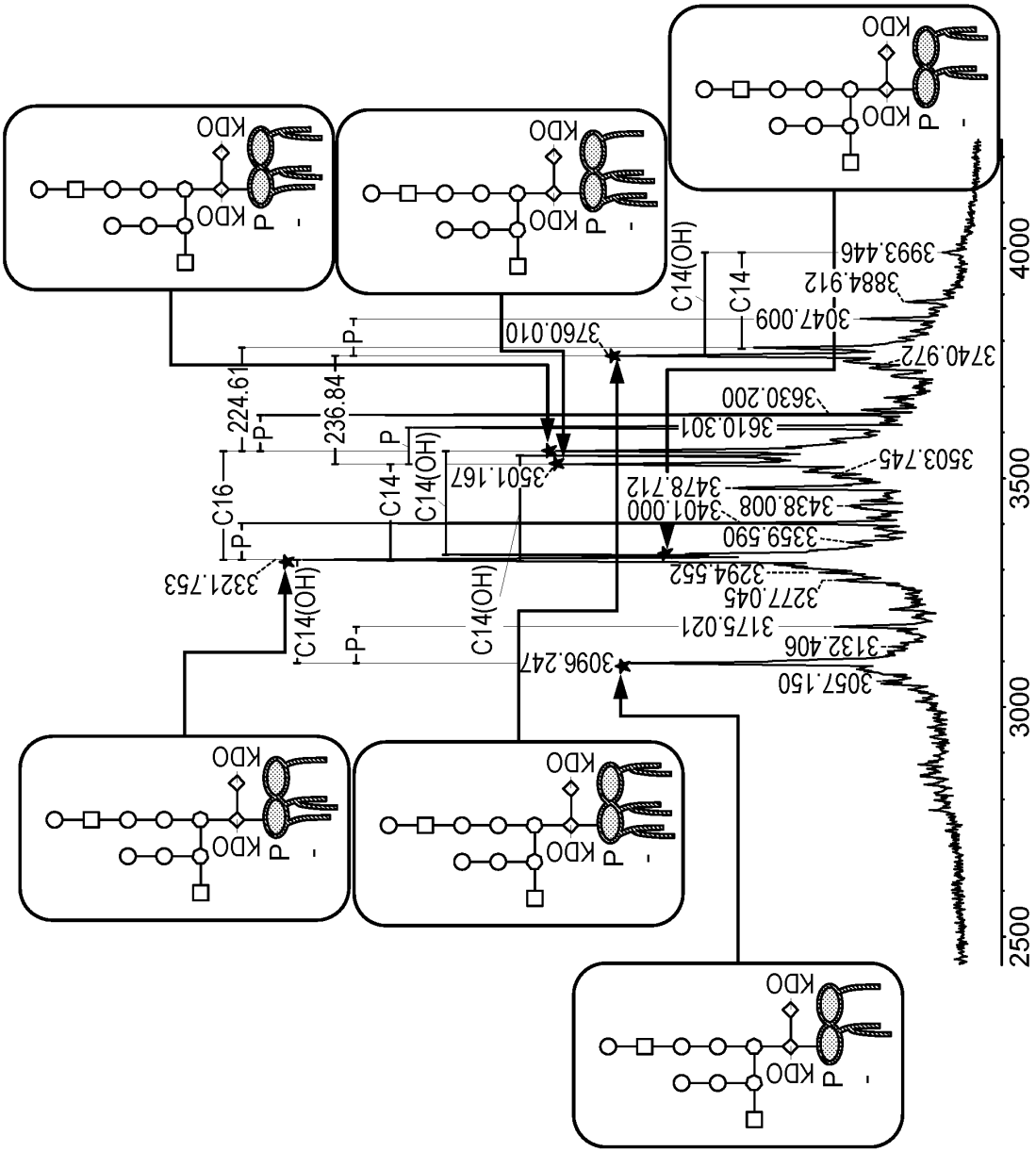


FIG. 8B

FIG. 9A


KDO
P
-
C14(OH)
C14
3993.446
3884.912
3047.009
3760.010
3740.972
3630.200
3610.301
3503.745
3501.167
3478.712
3438.008
3401.000
3359.590
3321.753
3294.552
3277.045
3175.021
3132.406
3096.247
3057.150
224.61
236.84
C16
2500
3000
3500
4000

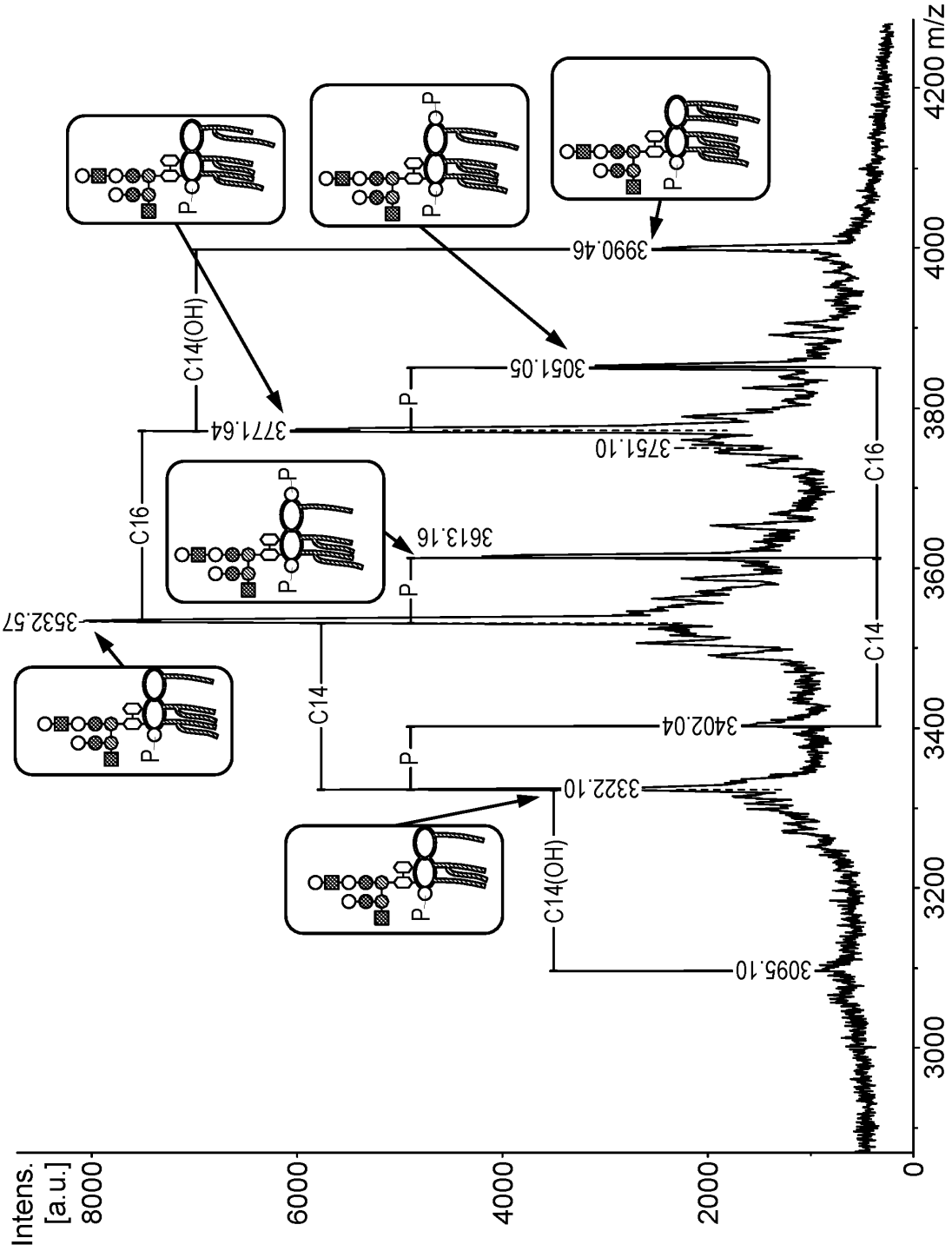

Intens. [a.u.]
8000
6000
4000
2000
0
3000
3200
3400
3600
3800
4000
4200 m/z
3990.46
3051.05
3771.64
3751.10
3613.16
3532.57
3402.04
3322.10
3095.10
C14(OH)
C16
C14
C16
C14
C14(OH)
P

FIG. 9B

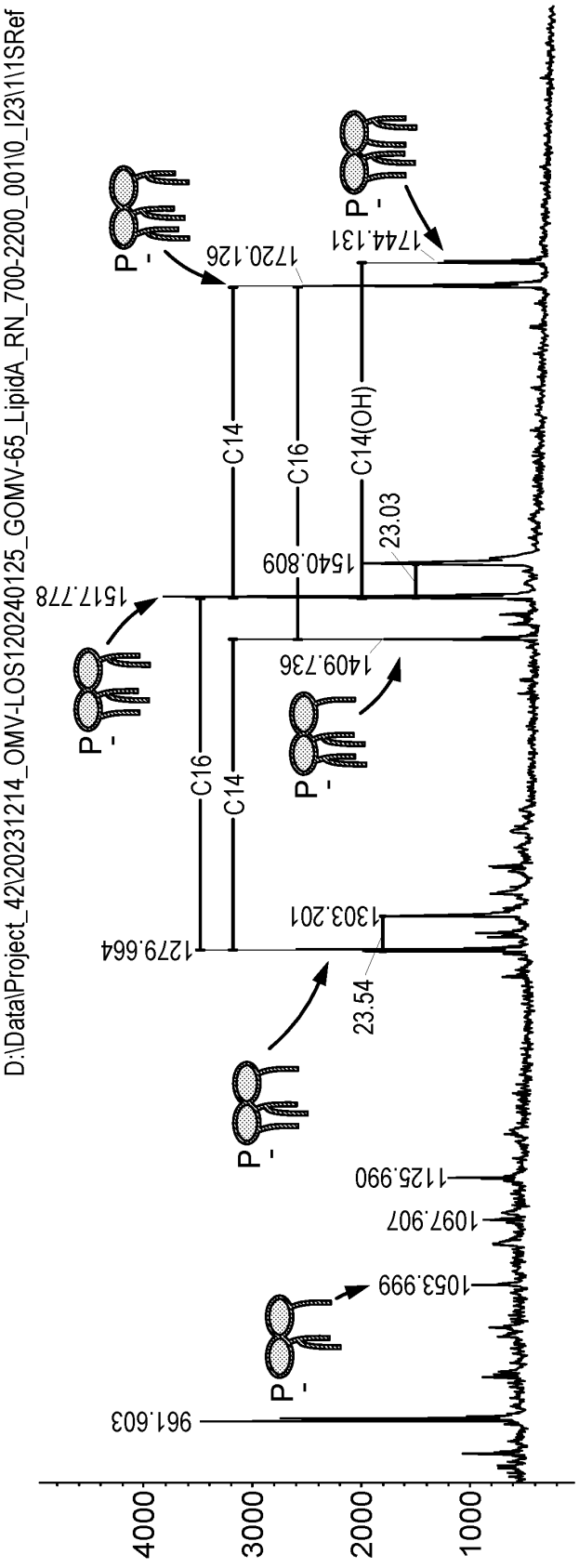

D:\Data\Project_42\20231214_OMV-LOS120240125_GOMV-65_LipidA_RN_700-2200_001\0_I23\1\1SRef
961.603
1053.999
1097.907
1125.990
1279.664
1303.201
23.54
1409.736
1517.778
1540.809
23.03
1720.126
1744.131
C14
C16
C14(OH)
C16
C14
P -
4000
3000
2000
1000

FIG. 10A

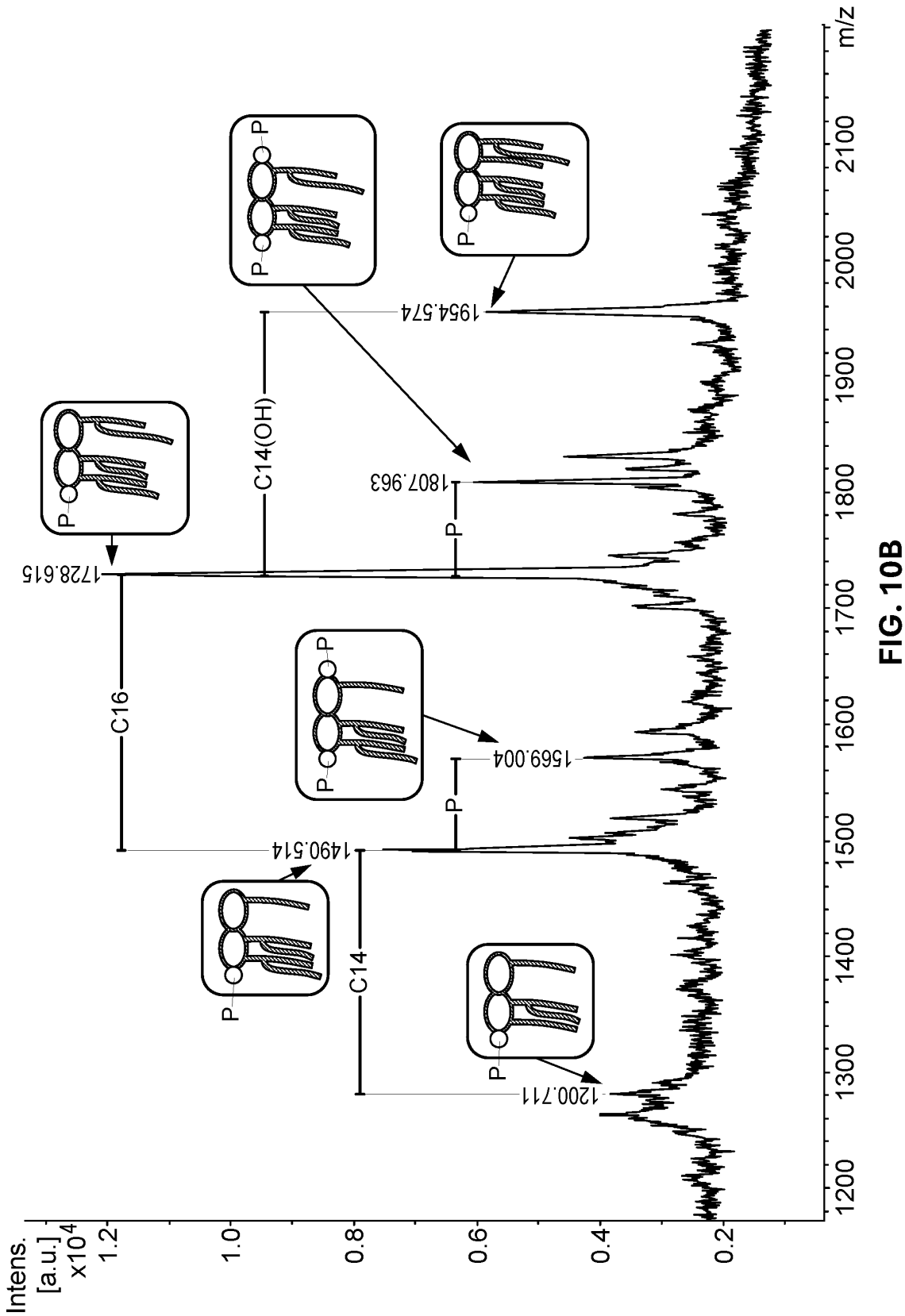
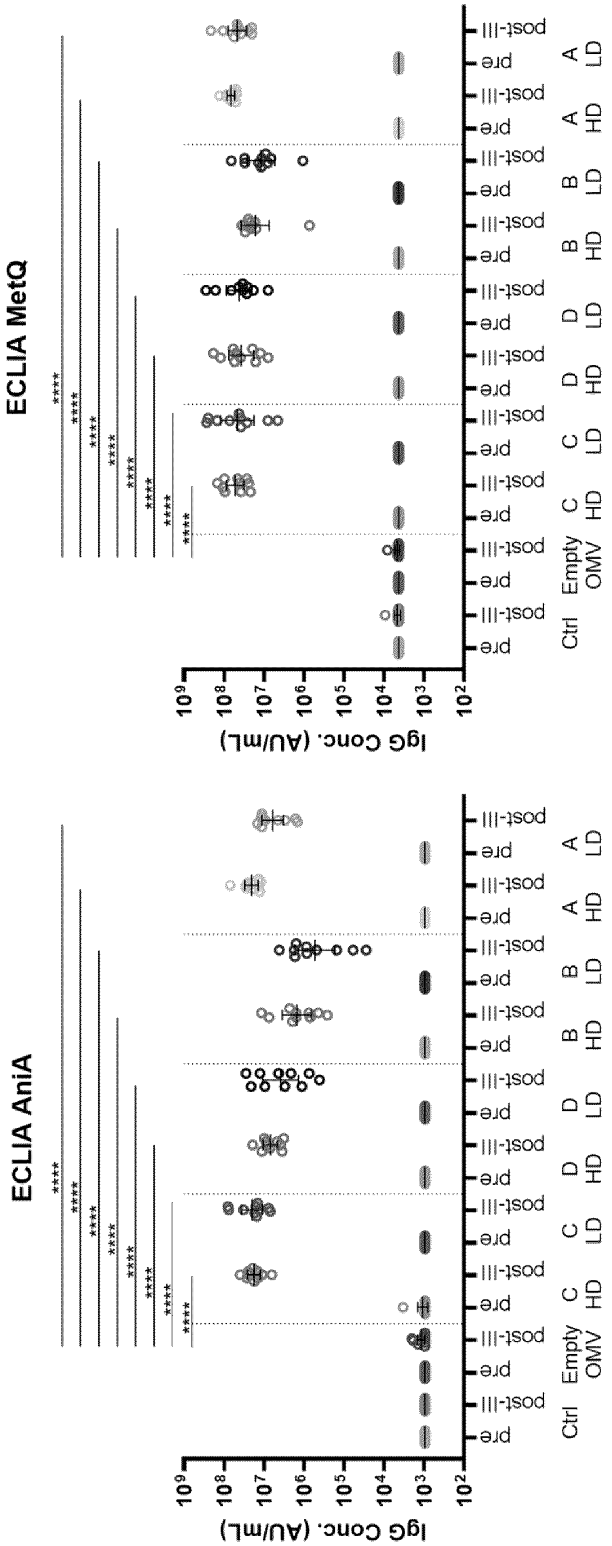

Intens.
[a.u.]
x10^4
1.2
1.0
0.8
0.6
0.4
0.2
1200
1300
1400
1500
1600
1700
1800
1900
2000
2100
m/z
1728.615
1807.963
1954.574
1569.004
1490.514
1200.711
C16
C14(OH)
C14
P

FIG. 10B



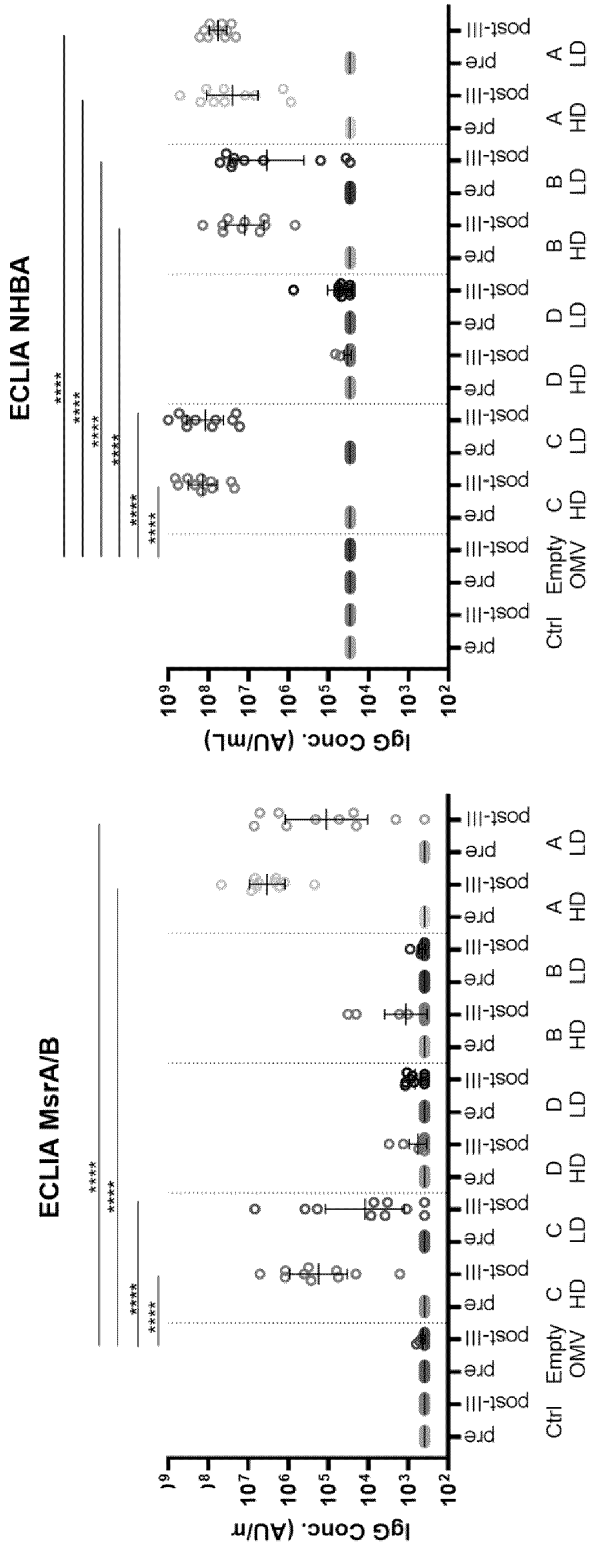
FIG. 11A



A: vaccine candidate A (=lead candidate)
B: vaccine candidate B
C: vaccine candidate C
D: vaccine candidate D
Ctrl: buffer and alum-only control
Empty OMV: control with OMVs containing none of the 6 neisserial antigens

HD: high dose (25 µg)
LD: low dose (5 µg)

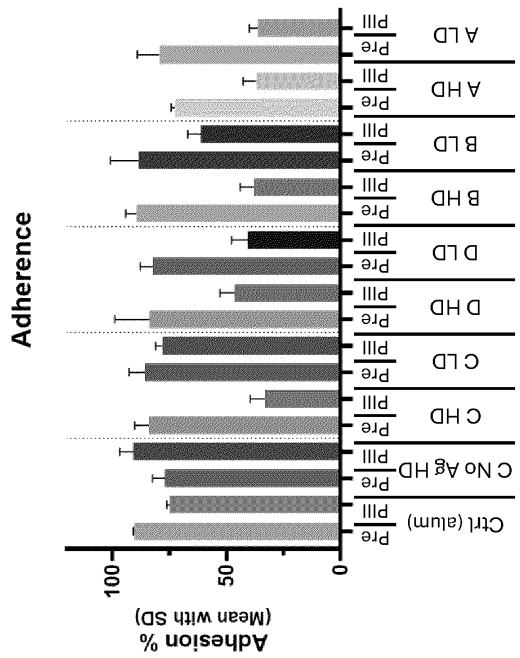
FIG. 11B



A: vaccine candidate A (=lead candidate)
B: vaccine candidate B
C: vaccine candidate C
D: vaccine candidate D
Ctrl: buffer and alum-only control
Empty OMV: control with OMVs containing none of the 6 neisserial antigens

HD: high dose (25 µg)
LD: low dose (5 µg)

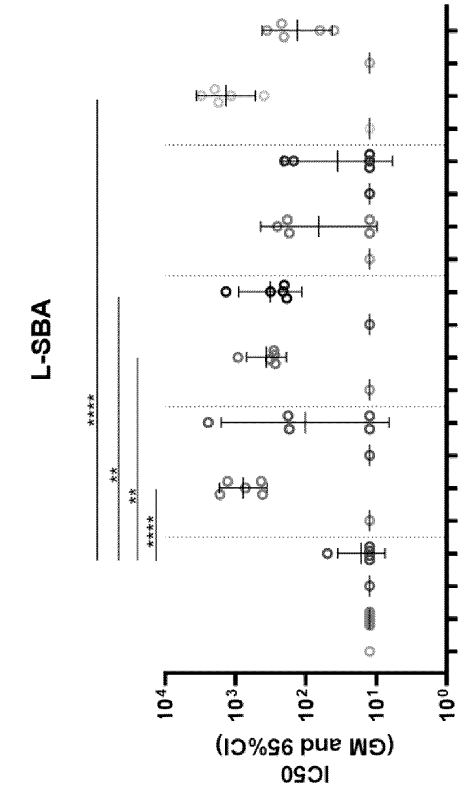
FIG. 11B (continued)



A: vaccine candidate A (=lead candidate)
B: vaccine candidate B
C: vaccine candidate C
D: vaccine candidate D
Ctrl: buffer and alum-only control
Empty OMV: control with OMVs containing none of the 6 neisserial antigens

HD: high dose (25 µg)
LD: low dose (5 µg)

FIG. 12B



	Ctrl (alum)	noAg_HD	C_HD	C_LD	D_HD	D_LD	B_HD	B_LD	A_HD	A_HD
Fold increase	1	2	73	46	34	37	10	6	134	14

FIG. 12A

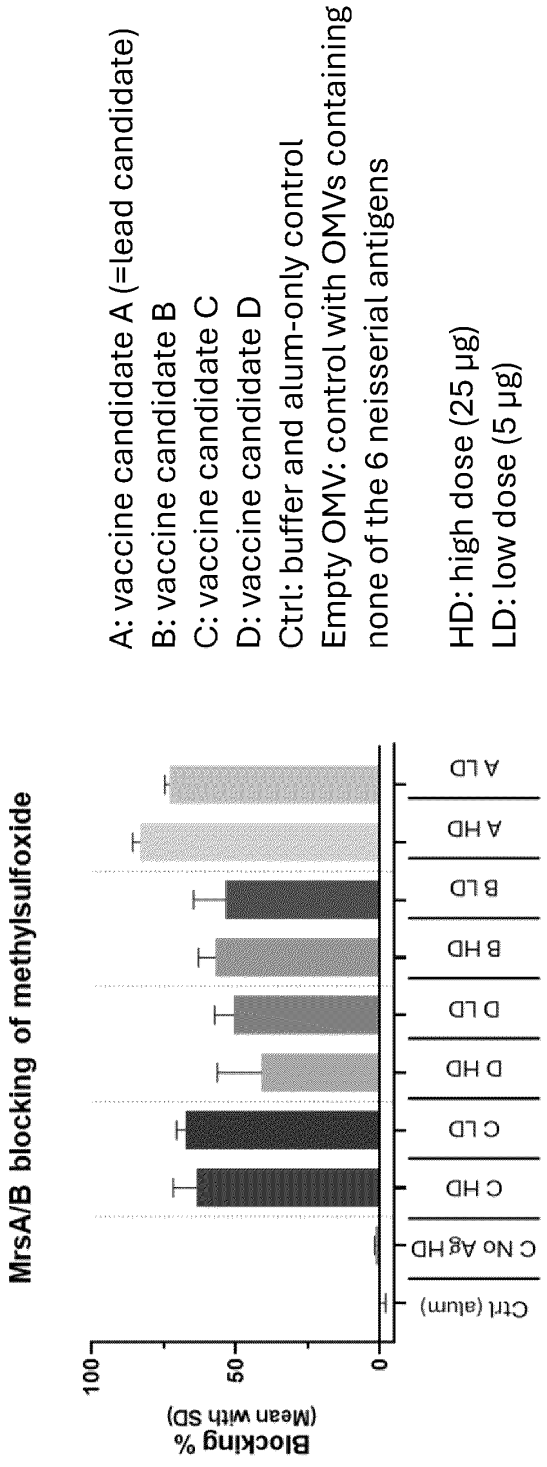

MrsA/B blocking of methylsulfoxide
Blocking %
(Mean with SD)
100
50
0
Ctrl (alum)
C No Ag HD
C HD
C LD
D HD
D LD
B HD
B LD
A HD
A LD
A: vaccine candidate A (=lead candidate)
B: vaccine candidate B
C: vaccine candidate C
D: vaccine candidate D
Ctrl: buffer and alum-only control
Empty OMV: control with OMVs containing none of the 6 neisserial antigens
HD: high dose (25 µg)
LD: low dose (5 µg)

FIG. 13

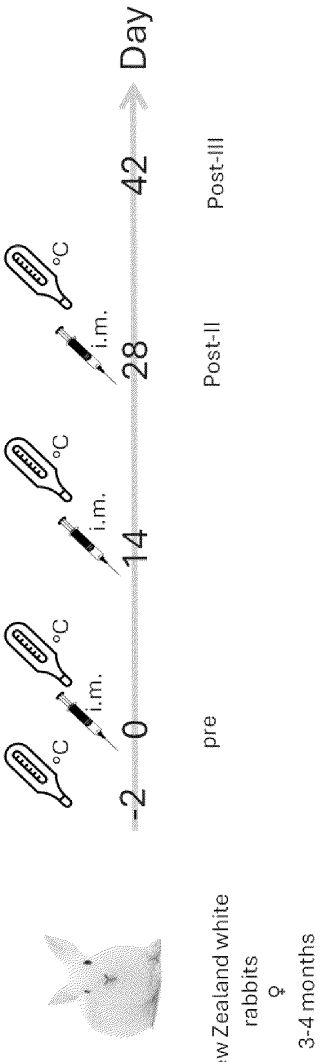


FIG. 14A

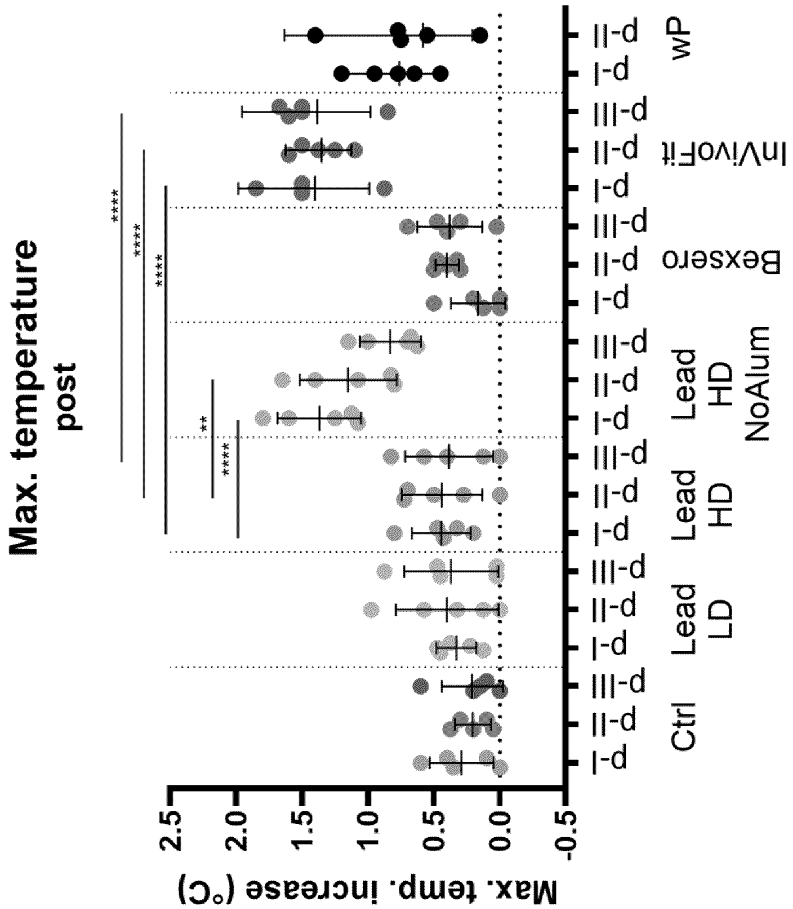


FIG. 14B

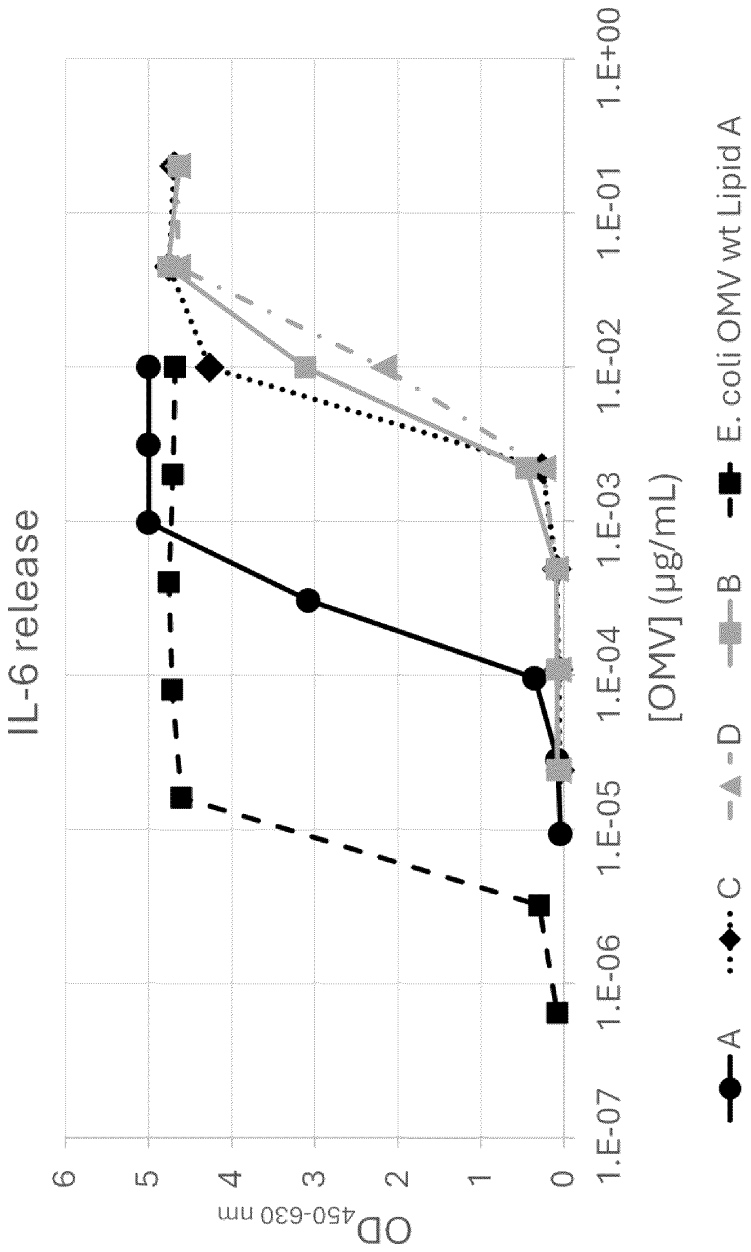

IL-6 release
OD450-630 nm
0
1
2
3
4
5
6
1.E-07
1.E-06
1.E-05
1.E-04
1.E-03
1.E-02
1.E-01
1.E+00
[OMV] (µg/mL)
A
C
D
B
E. coli OMV wt Lipid A
A: vaccine candidate A (=lead candidate)
B: vaccine candidate B
C: vaccine candidate C
D: vaccine candidate D

FIG. 15

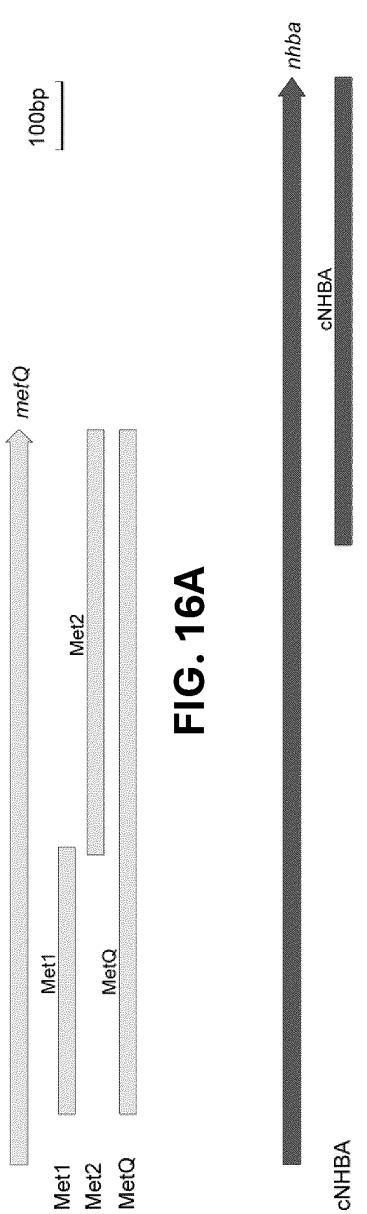


FIG. 16A

FIG. 16B

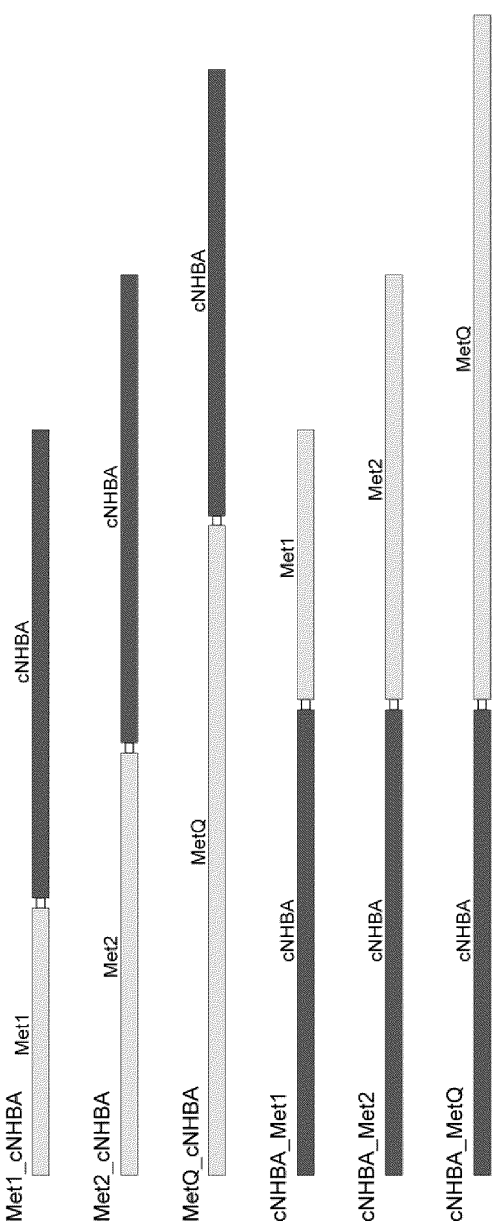


FIG. 16C

FIG. 17A

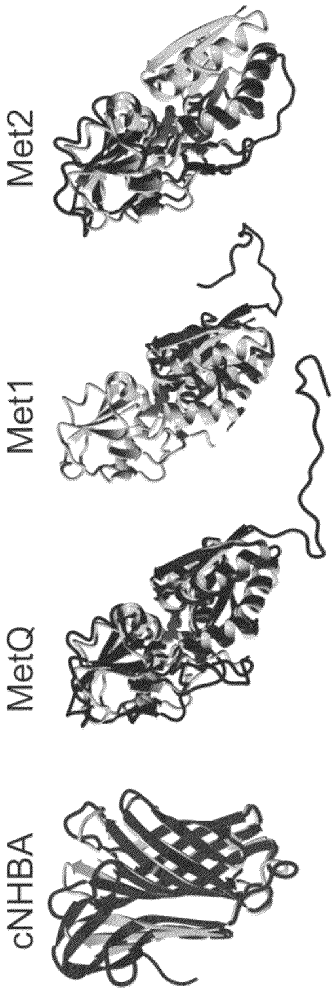
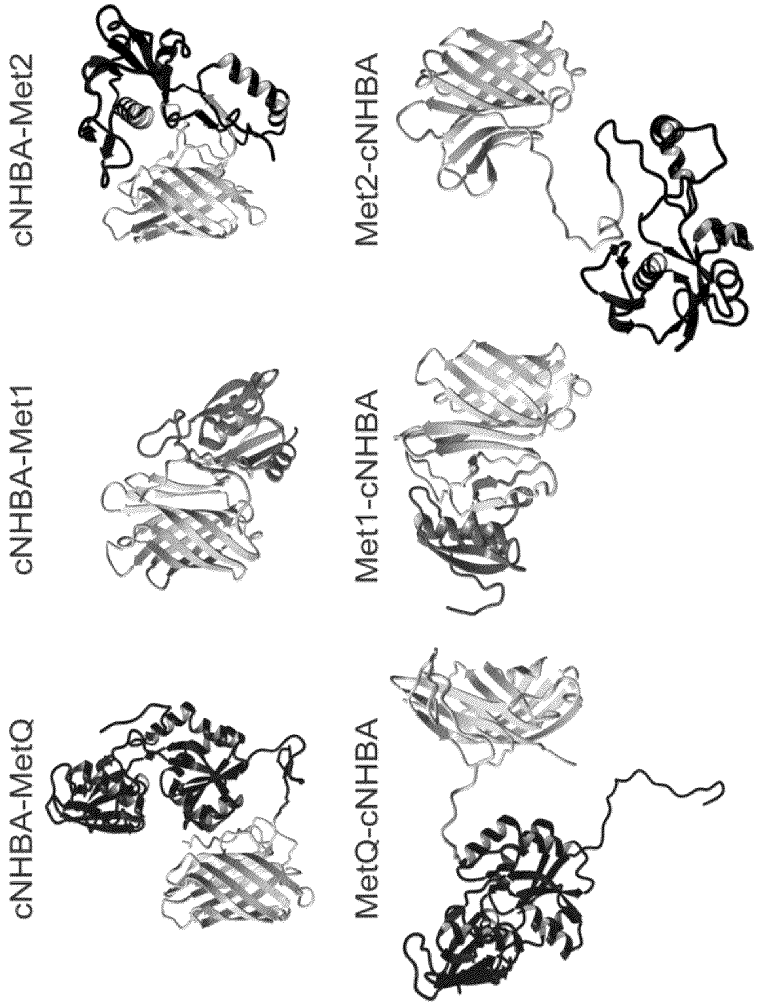


FIG. 17B



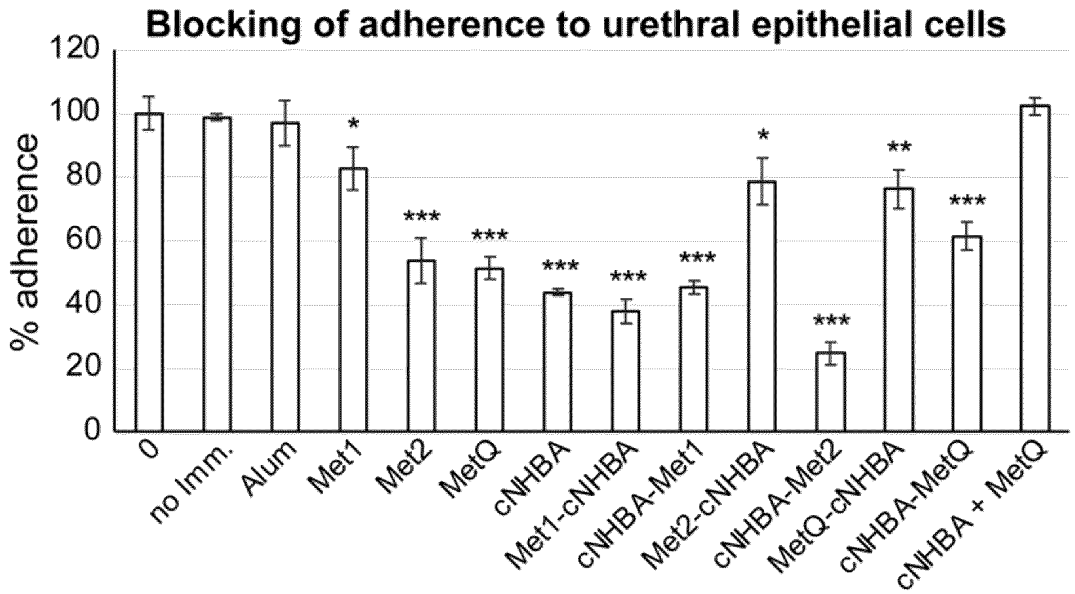


FIG. 18A

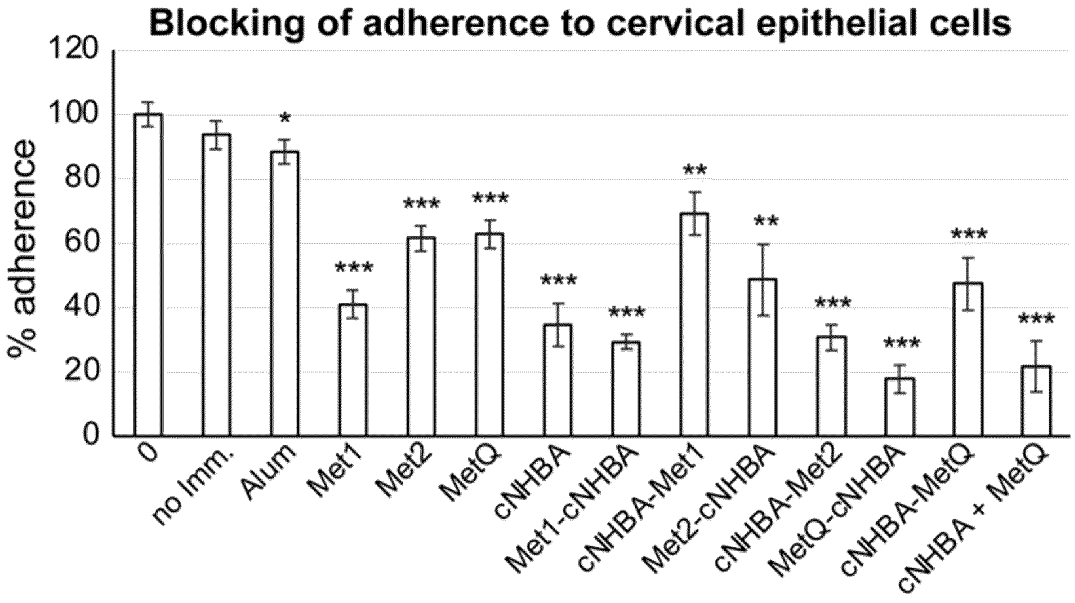


FIG. 18B

Vaccine candidate	IgG		IgG1		IgG2a		IgG2b		IgG3		IgA		IgM	
	Ng 1291[1]	Ng WHO X[1]	MetQ	NHBA	MetQ	NHBA	MetQ	NHBA	MetQ	NHBA	MetQ	NHBA	MetQ	NHBA
unimmunised	800	800	<1,000	<1,000	<100	<100	<100	<100	<100	<100	<25	<25	100	100
Alum only	800	400	<1,000	<1,000	<100	<100	<100	<100	<100	100	25	<25	200	<100
Met1	12,800	6,400	65,536,000	-	<100	-	400	-	<100	-	25	-	3,200	-
Met2	102,400	102,400	131,072,000	-	<100	-	3,200	-	100	-	25	-	3,200	-
MetQ	3,276,800	1,638,400	32,768,000	-	100	-	100	-	100	-	25	-	1,600	-
cNHBA	3,200	25,600	-	8,192,000	-	200	-	1,600	-	200	-	50	-	2,000
Met1-cNHBA	12,800	6,400	65,536,000	16,384,000	<100	<100	400	200	<100	100	25	50	3,200	2,000
cNHBA-Met1	6,400	3,200	65,536,000	16,384,000	<100	<100	<100	200	<100	100	25	100	3,200	2,000
Met2-cNHBA	204,800	25,600	131,072,000	8,192,000	<100	<100	200	200	<100	<100	25	100	6,400	2,000
cNHBA-Met2	51,200	25,600	65,536,000	32,768,000	<100	<100	100	1,600	<100	200	25	100	1,600	4,000
MetQ-cNHBA	1,638,400	819,200	65,536,000	16,384,000	800	<100	200	800	<100	400	25	100	3,200	2,000
cNHBA-MetQ	204,800	102,400	32,768,000	16,384,000	100	<100	400	400	100	100	25	100	6,400	2,000
cNHBA + MetQ	12,800	25,600	32,768,000	1,024,000	<100	<100	100	100	<100	<100	25	50	1,600	2,000

[1] Whole cell *N. gonorrhoeae* (Ng) 1291 and WHO X strains. Values above the unnimunised or alum only immunised controls are shaded gray.

FIG. 19

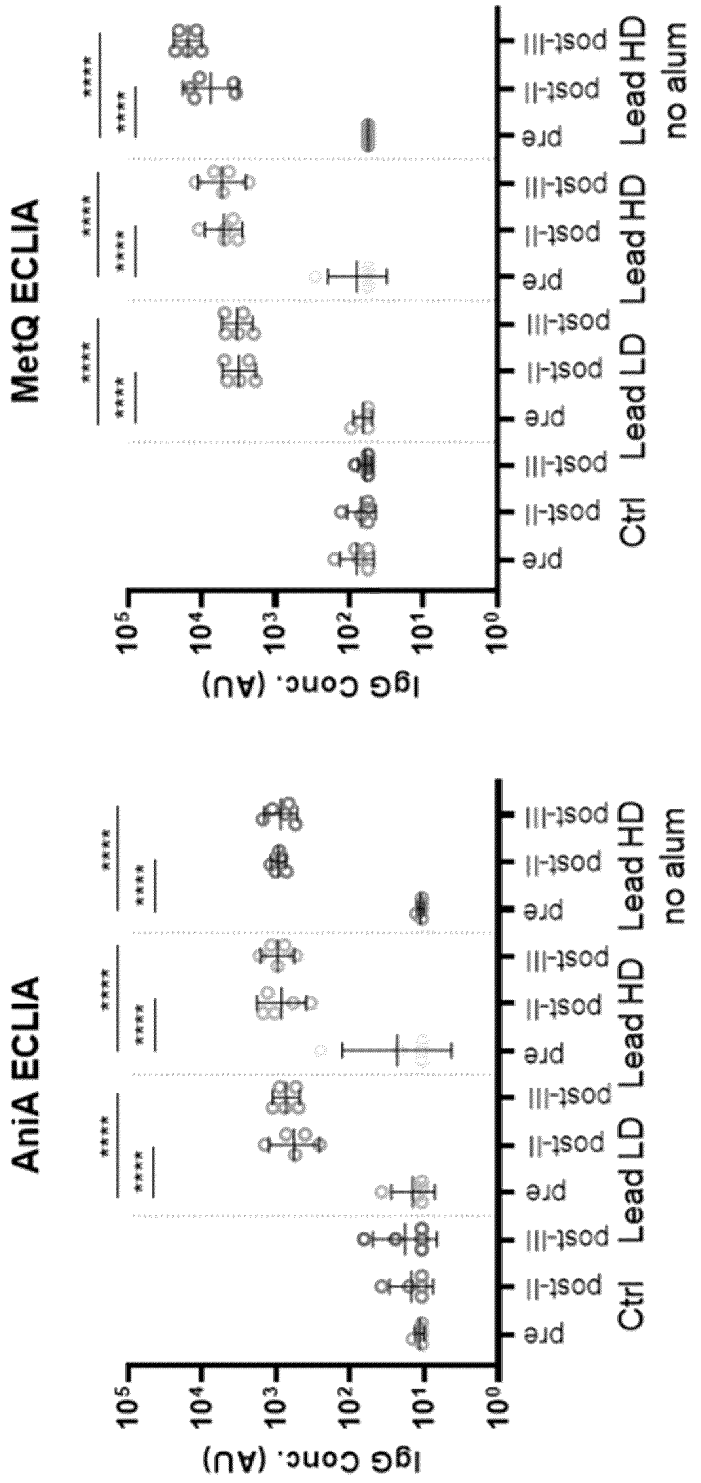

MetQ ECLIA
AniA ECLIA
IgG Conc. (AU)
10^5
10^4
10^3
10^2
10^1
10^0
****
pre
post-I
post-II
Ctrl
Lead LD
Lead HD
no alum

FIG. 20

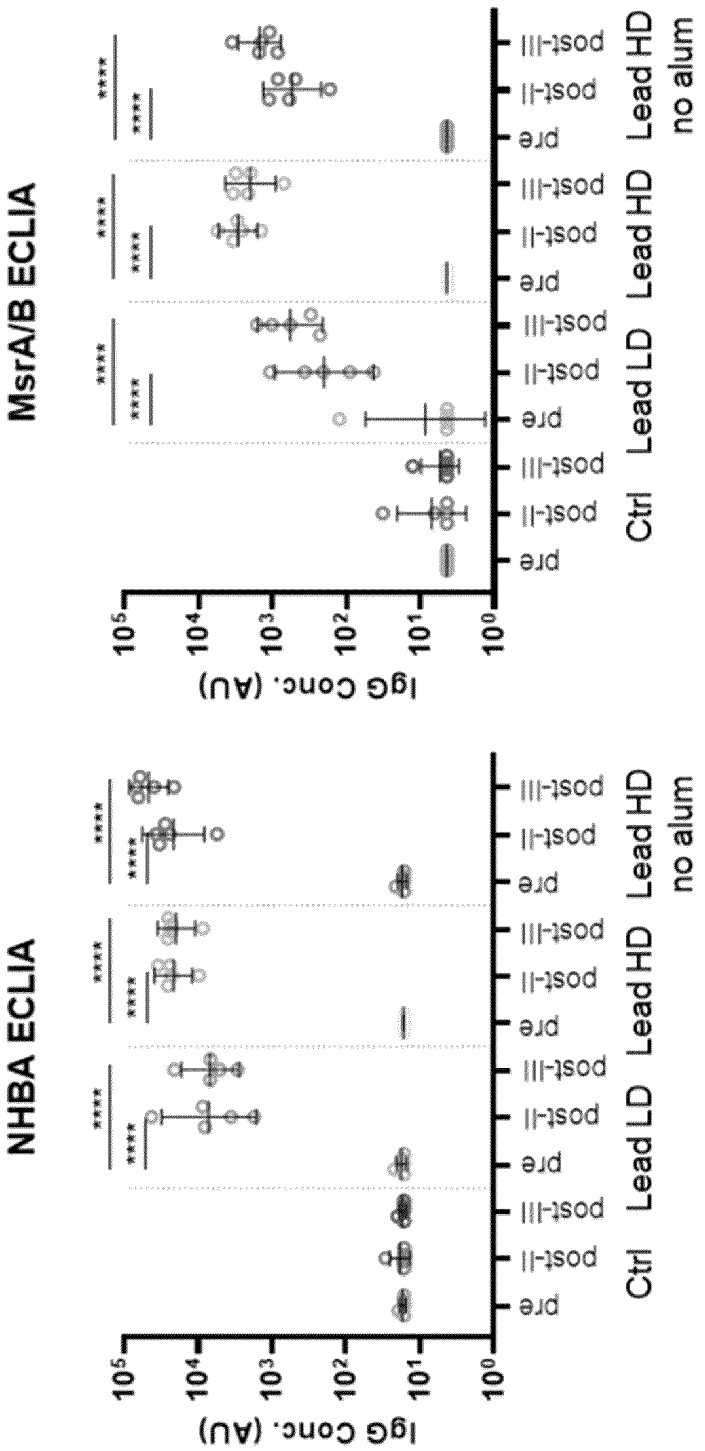


FIG. 20 (continued)

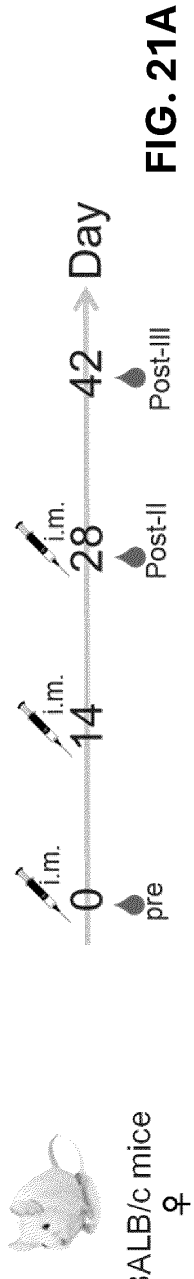


FIG. 21A

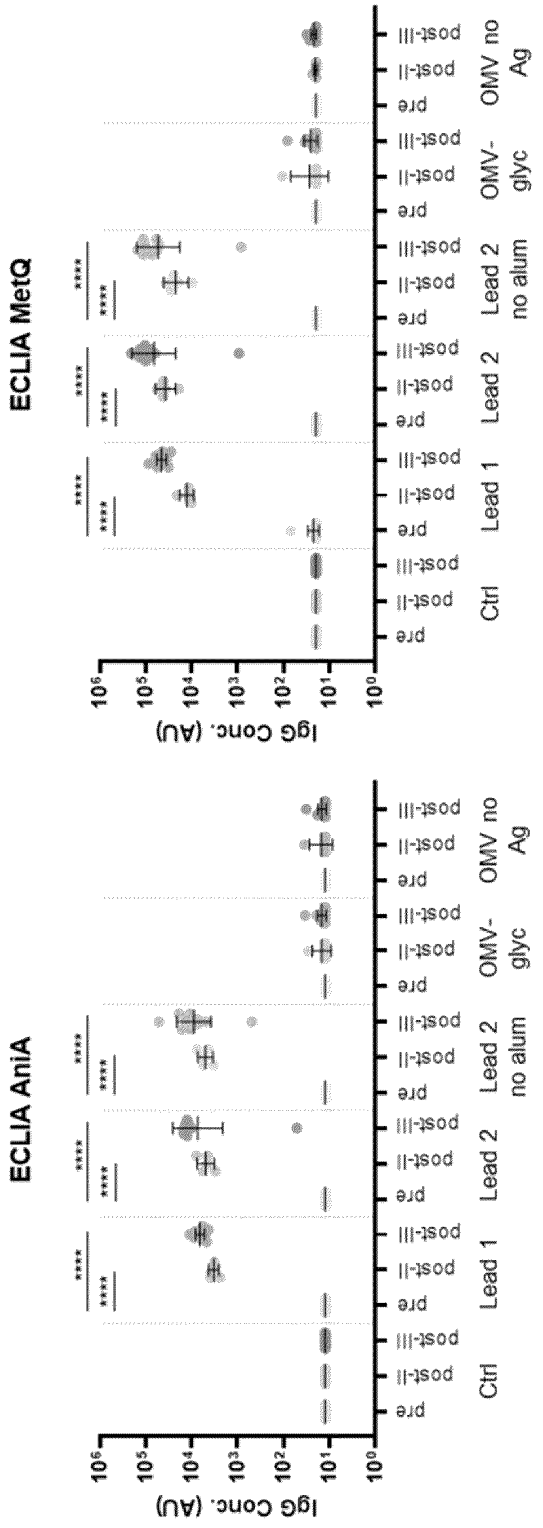


FIG. 21B

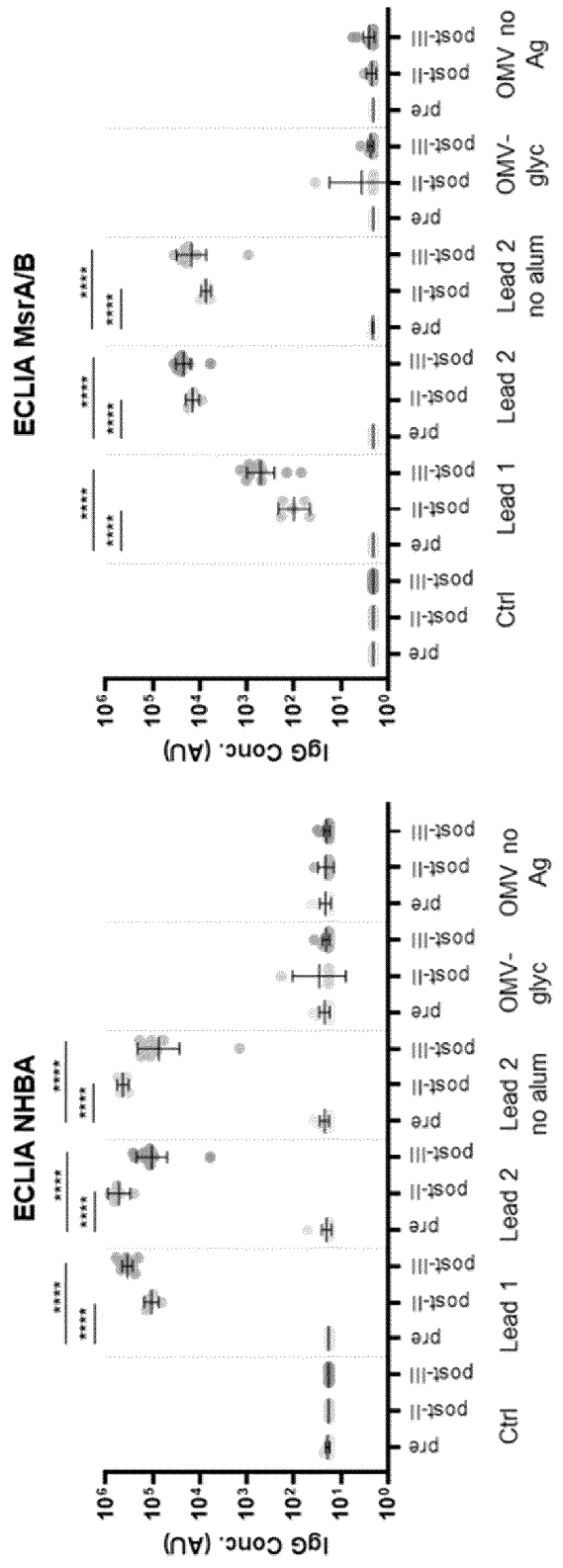


FIG. 21B (continued)

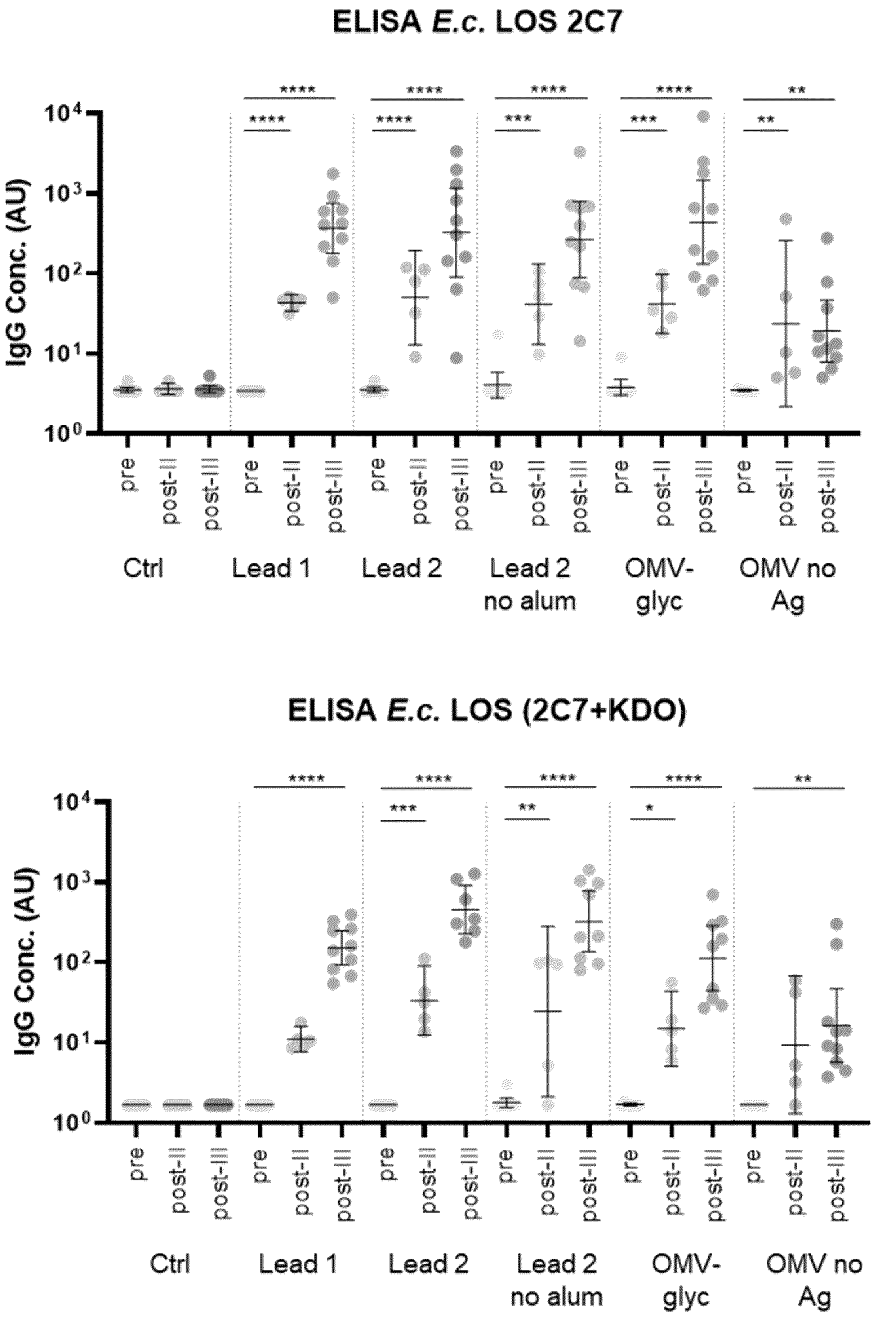

ELISA E.c. LOS 2C7
IgG Conc. (AU)
pre
post-II
post-III
Ctrl
Lead 1
Lead 2
Lead 2 no alum
OMV-glyc
OMV no Ag
ELISA E.c. LOS (2C7+KDO)
IgG Conc. (AU)
pre
post-II
post-III
Ctrl
Lead 1
Lead 2
Lead 2 no alum
OMV-glyc
OMV no Ag

FIG. 22

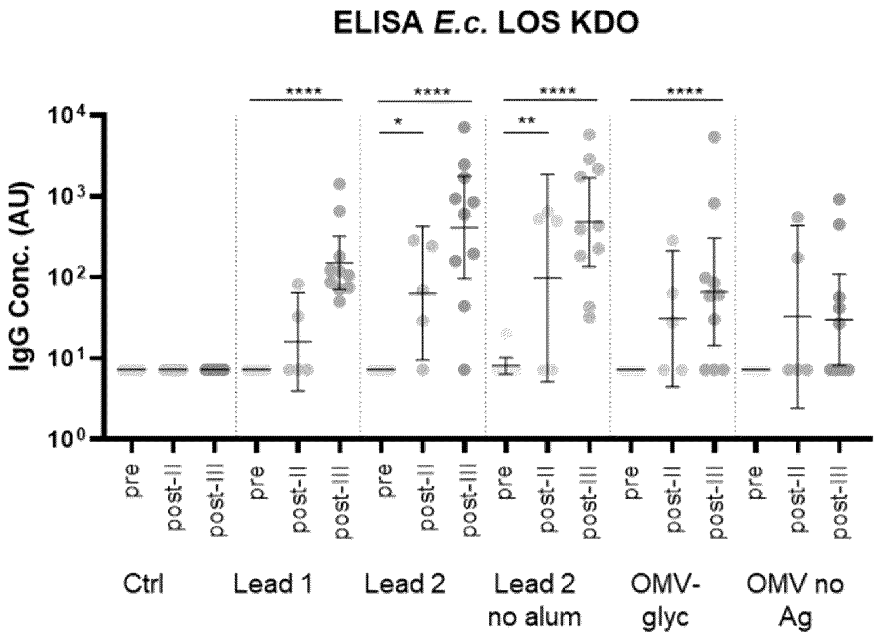


FIG. 22 (continued)

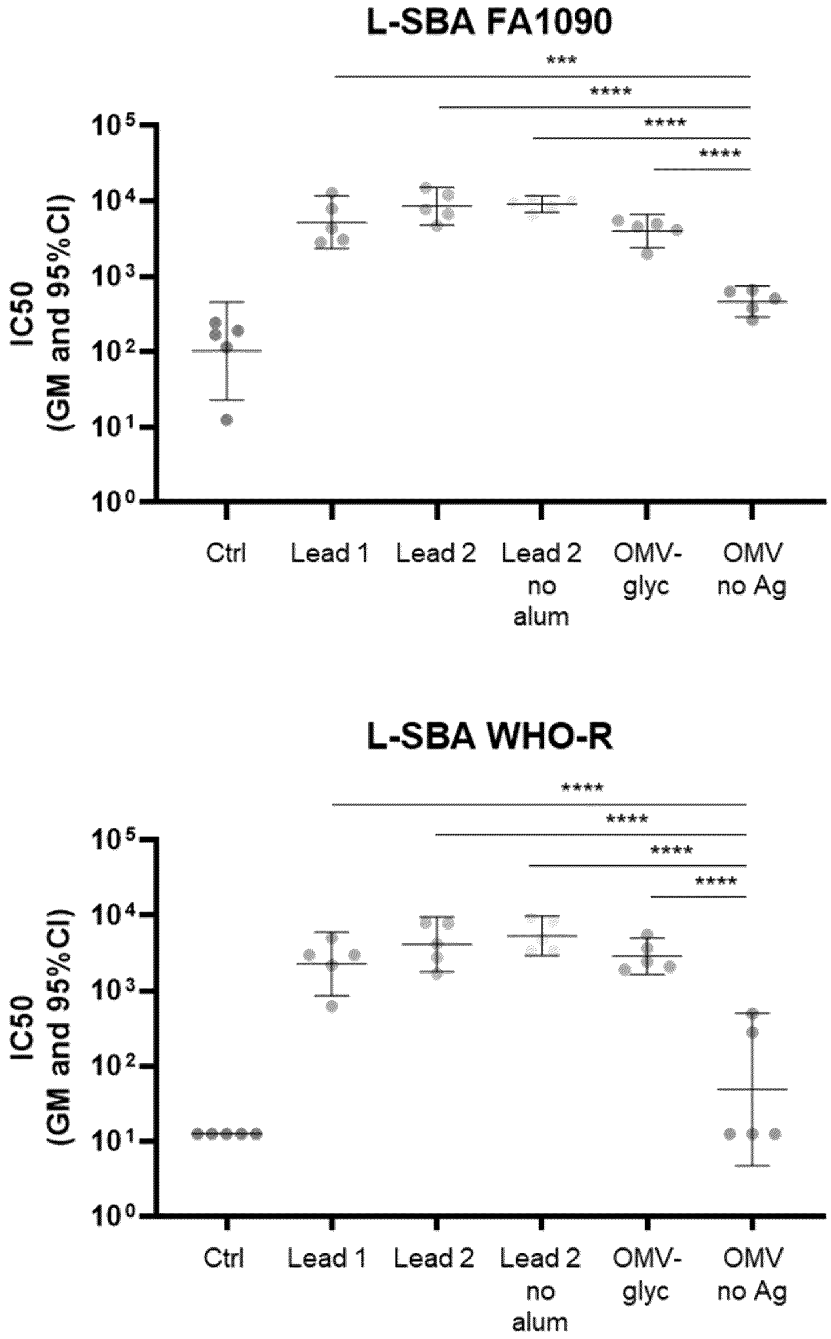

L-SBA FA1090
***
****
****
****
IC50 (GM and 95%CI)
10^5
10^4
10^3
10^2
10^1
10^0
Ctrl
Lead 1
Lead 2
Lead 2 no alum
OMV-glyc
OMV no Ag
L-SBA WHO-R
****
****
****
****
IC50 (GM and 95%CI)
10^5
10^4
10^3
10^2
10^1
10^0
Ctrl
Lead 1
Lead 2
Lead 2 no alum
OMV-glyc
OMV no Ag

FIG. 23

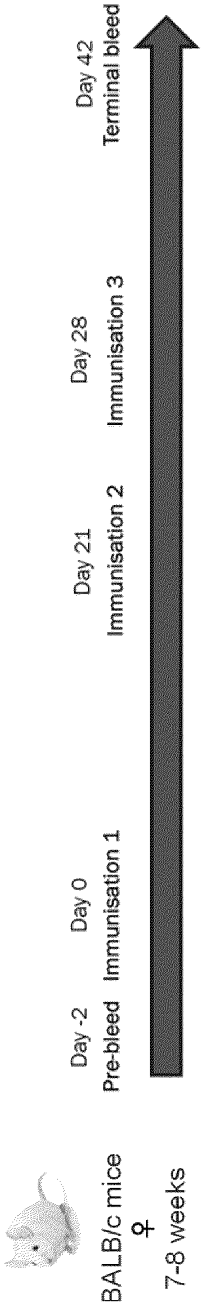

BALB/c mice
♀
7-8 weeks
Day -2
Pre-bleed
Day 0
Immunisation 1
Day 21
Immunisation 2
Day 28
Immunisation 3
Day 42
Terminal bleed

FIG. 24

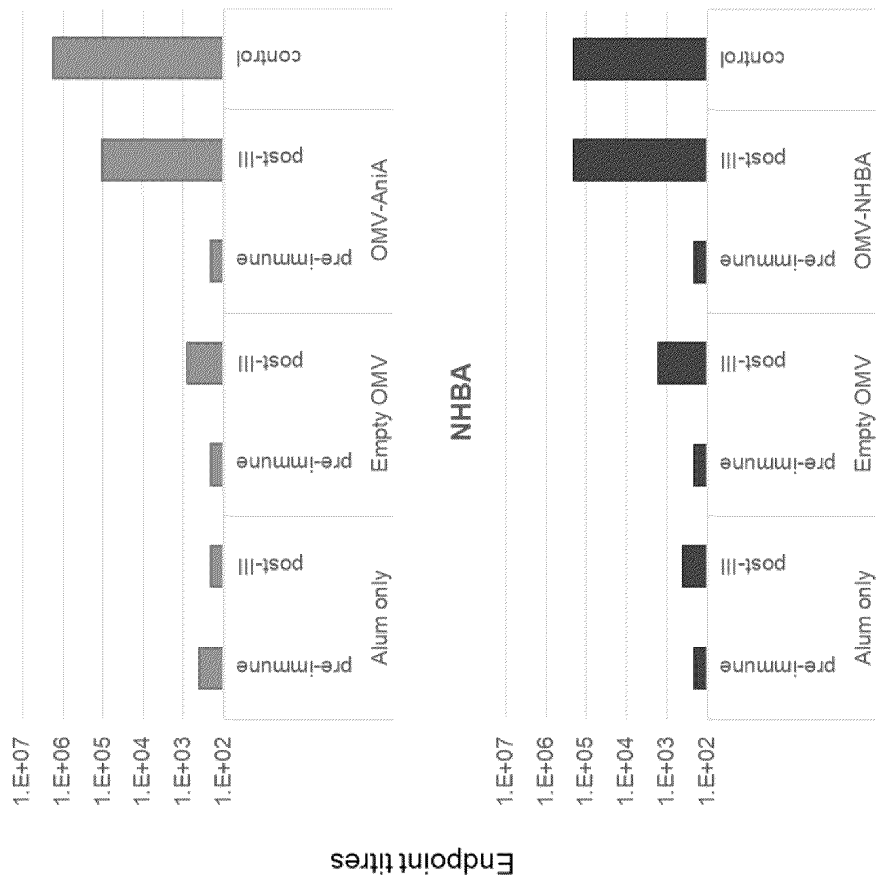

AniA
NHBA
Endpoint titres
1.E+07
1.E+06
1.E+05
1.E+04
1.E+03
1.E+02
pre-immune
post-III
Alum only
pre-immune
post-III
Empty OMV
pre-immune
post-III
OMV-AniA
control
pre-immune
post-III
Alum only
pre-immune
post-III
Empty OMV
pre-immune
post-III
OMV-NHBA
control

FIG. 25

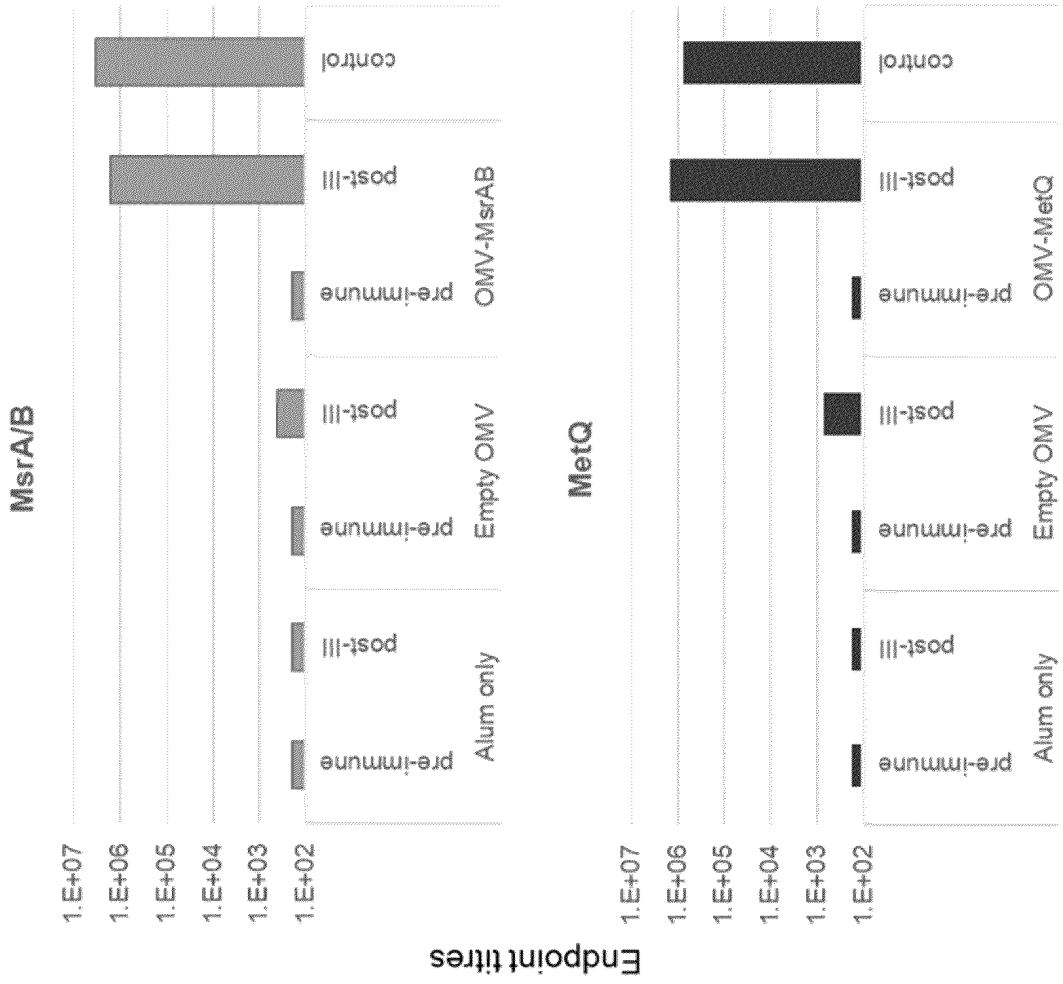


FIG. 25 (continued)

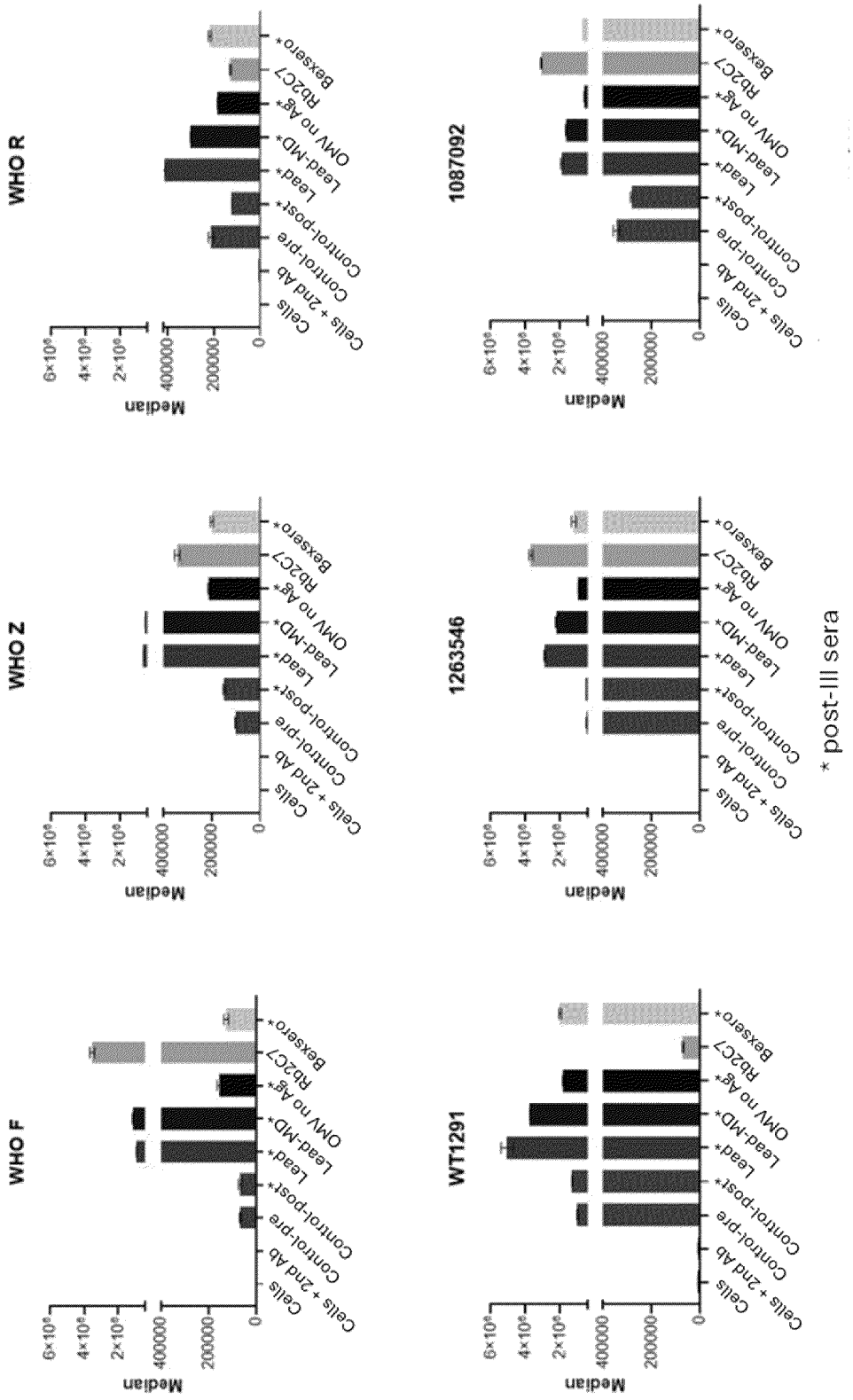

WHO R
WHO Z
WHO F
1087092
1263546
WT1291
Median
6×10⁶
4×10⁶
2×10⁶
400000
200000
0
Cells
Cells + 2nd Ab
Control-pre
Control-post*
Lead*
Lead-MD*
OMV no Ag*
Rb2C7
Bexsero*
* post-III sera

FIG. 26

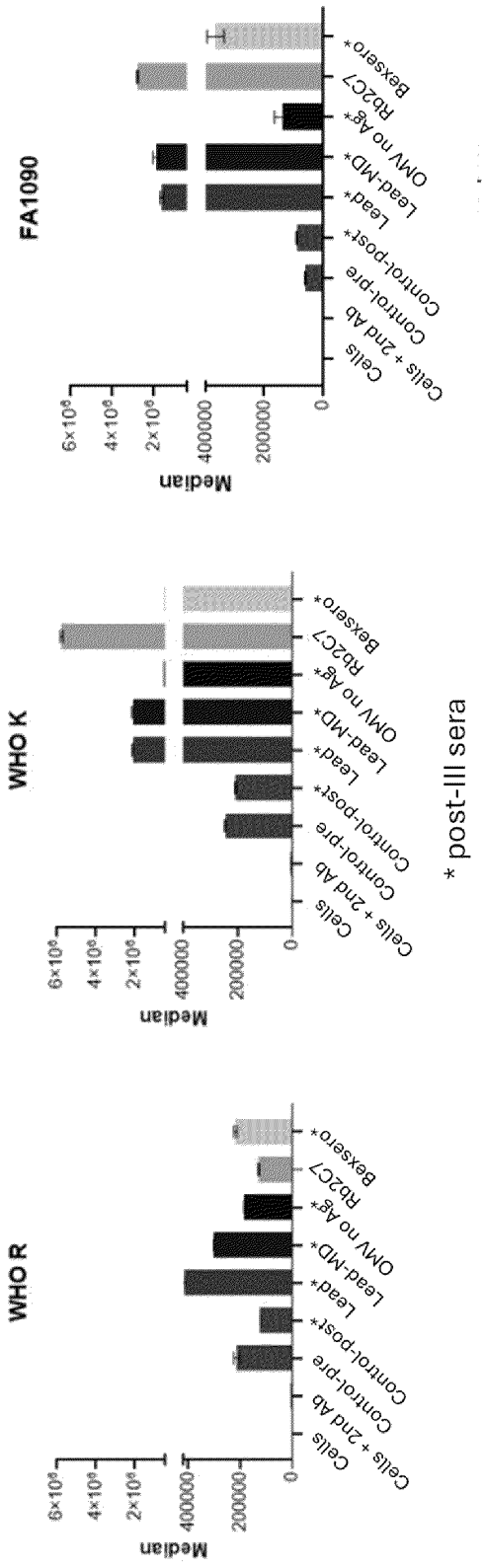
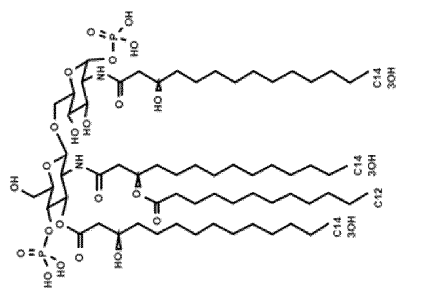


FIG. 26 (continued)

Main species



Minor species

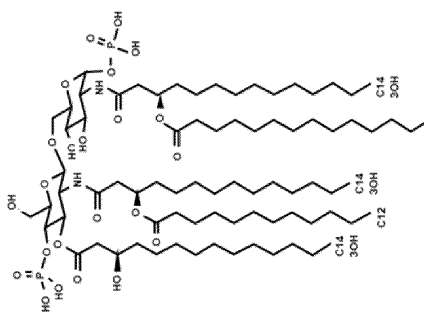
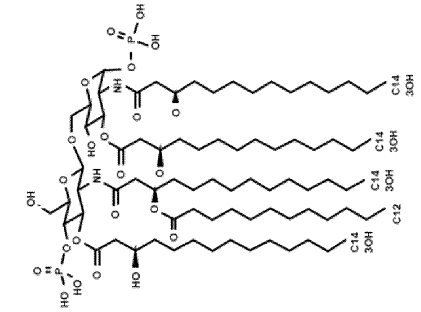


FIG. 27A

Main species



Minor species

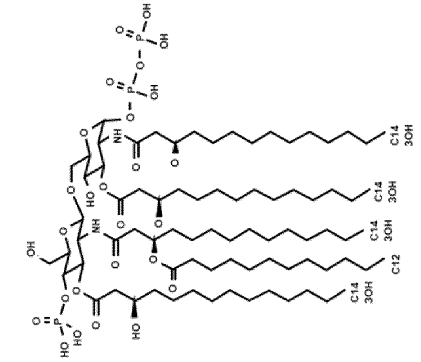
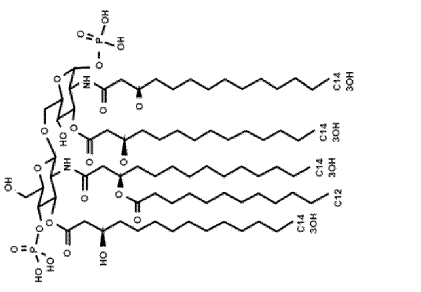


FIG. 27C

Main species



Minor species

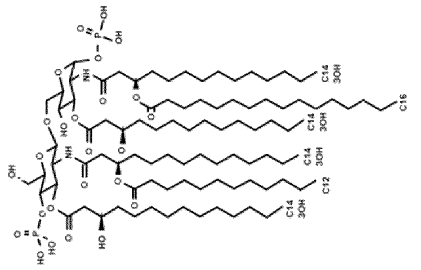


FIG. 27B

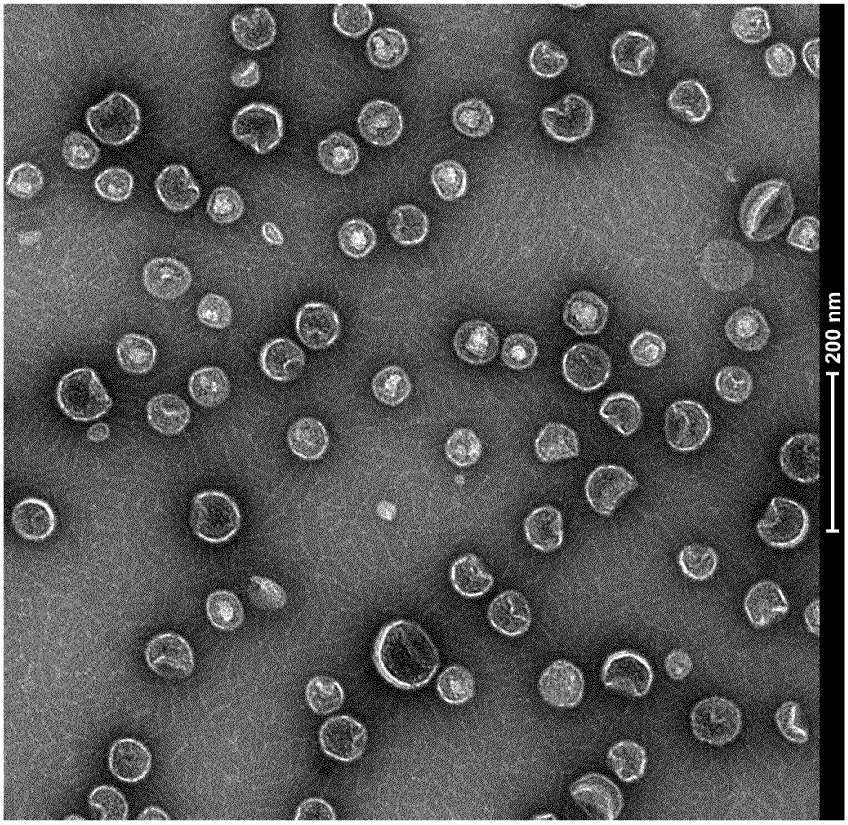


FIG. 28

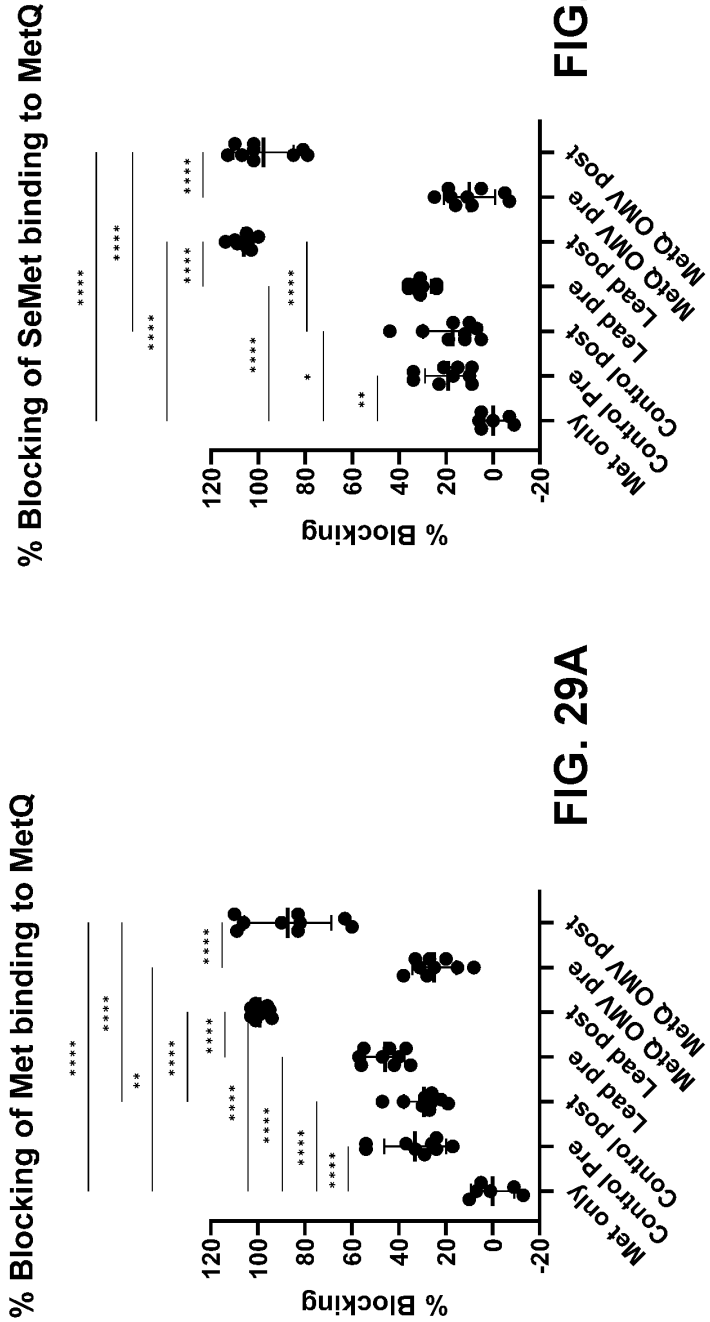
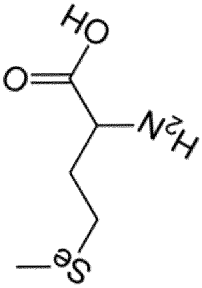
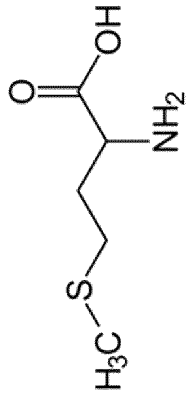


FIG. 29A

FIG. 29B



SeMet=Selenomethionine



Met=Methionine

FIG. 29C

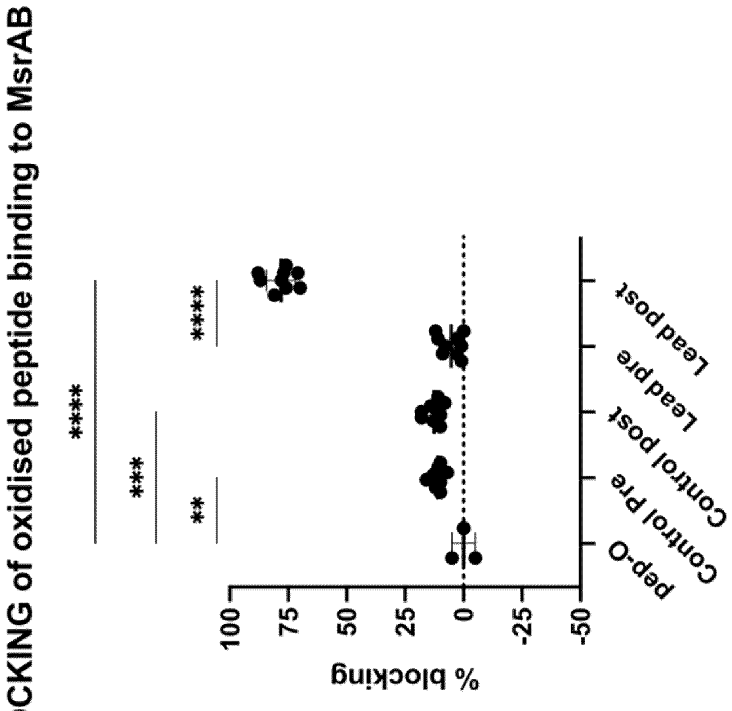


FIG. 30B

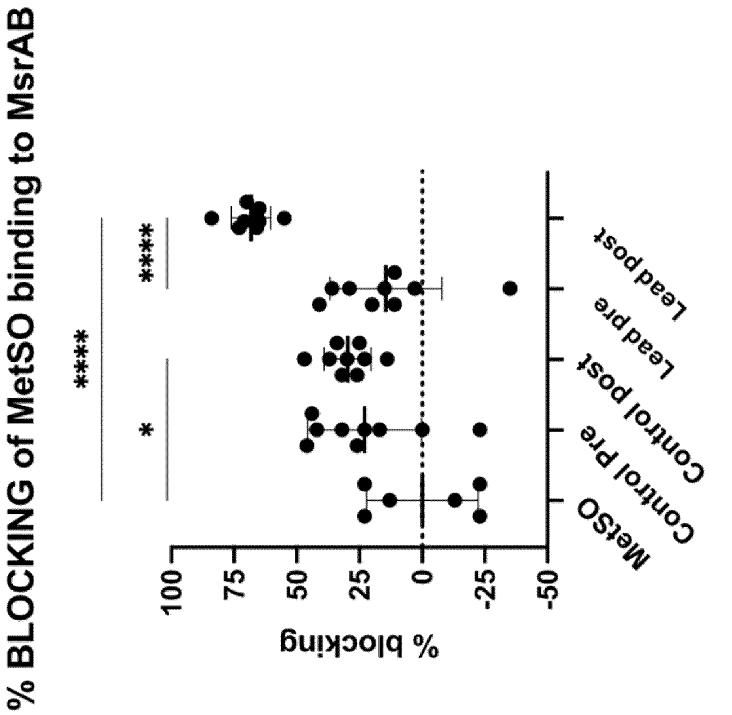


FIG. 30A

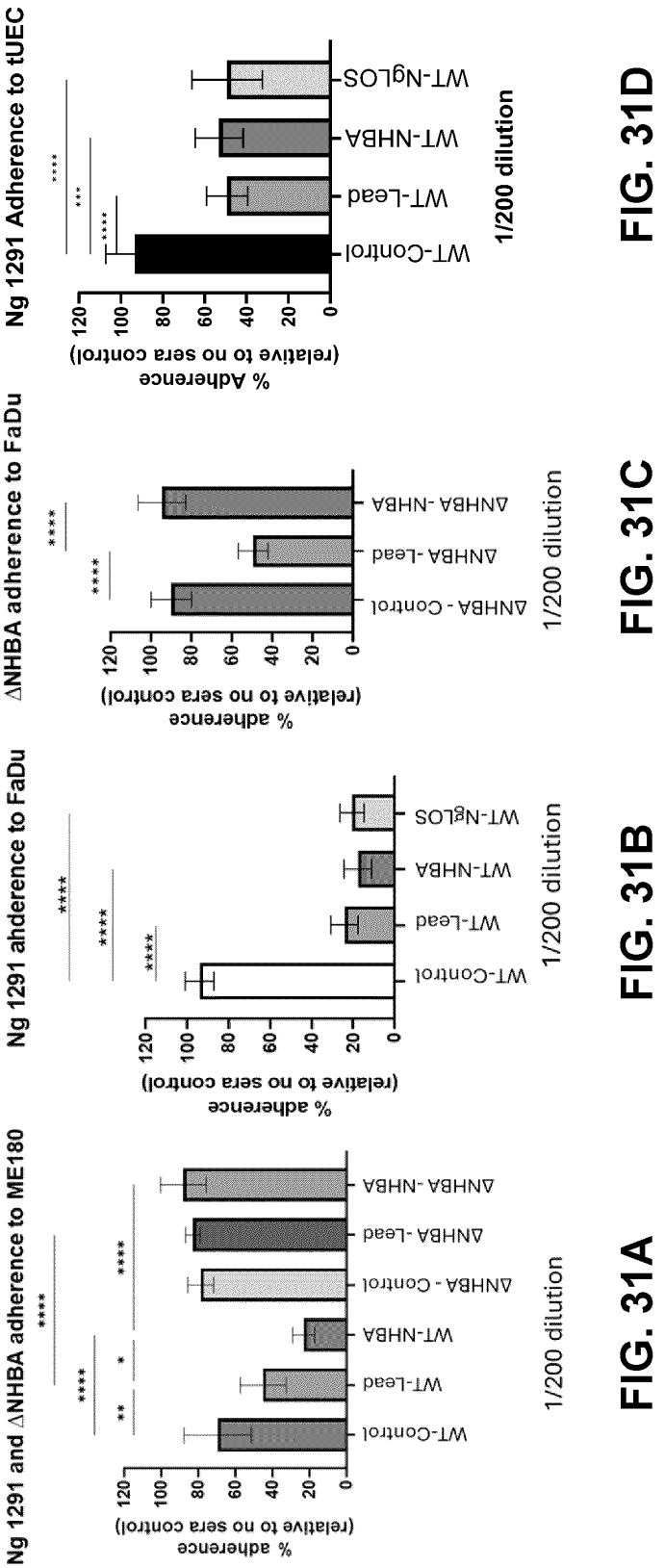


FIG. 31A FIG. 31B FIG. 31C FIG. 31D

WT-Control: wild type Ng1291 + Control rabbit sera
WT-Lead: wild type Ng1291 + Lead rabbit sera post-III
WT-NHBA: wild type Ng1291 + OMV containing only NHBA antigen rabbit sera
WT-NgLOS: wild type Ng1291 + OMV containing only NgLOS antigen rabbit sera
ΔNHBA -Control: NHBA knock out strain + Control rabbit sera
ΔNHBA -Lead: NHBA knock out strain + Lead rabbit sera post-III
ΔNHBA -NHBA: NHBA knock out strain + OMV containing only NHBA antigen rabbit sera

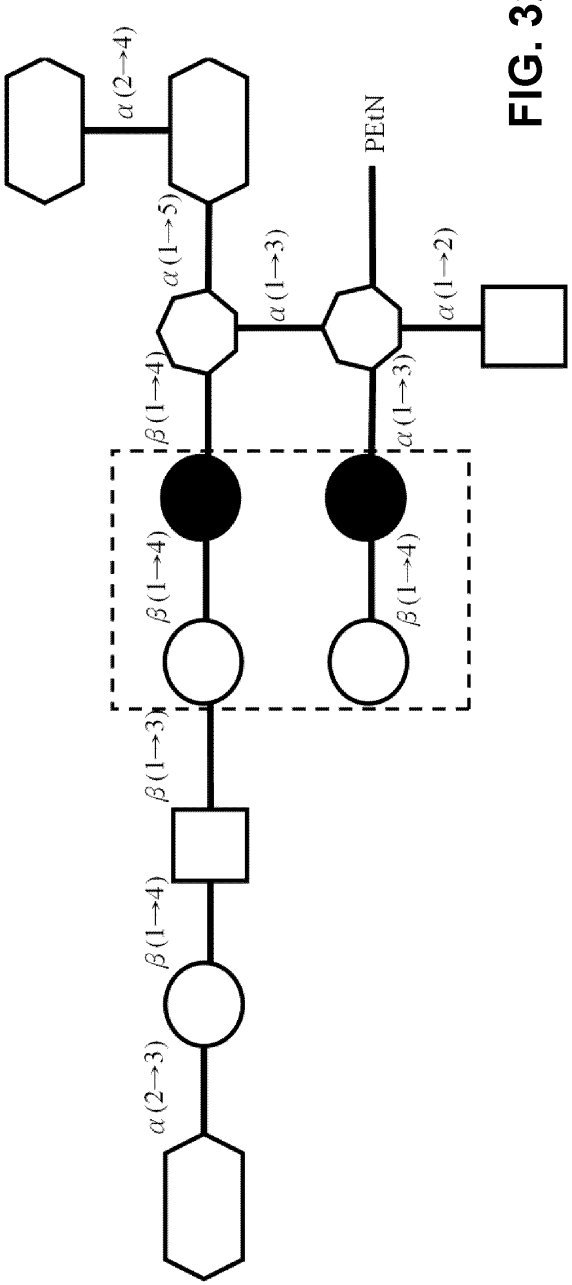


FIG. 32A

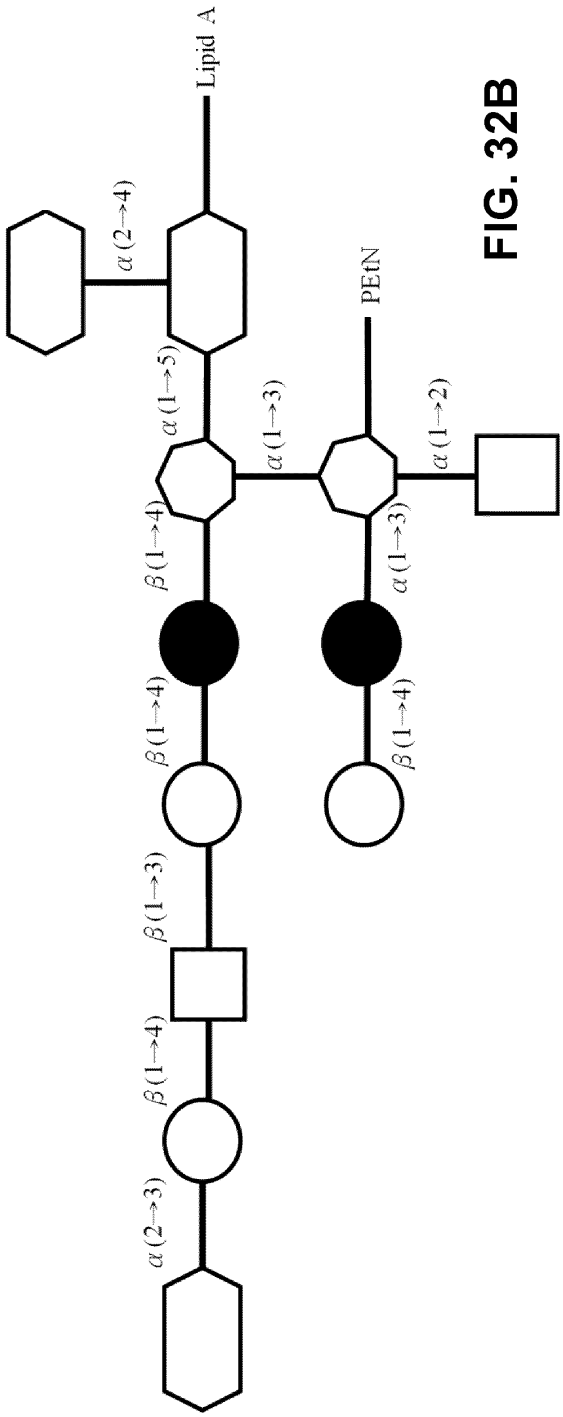


FIG. 32B

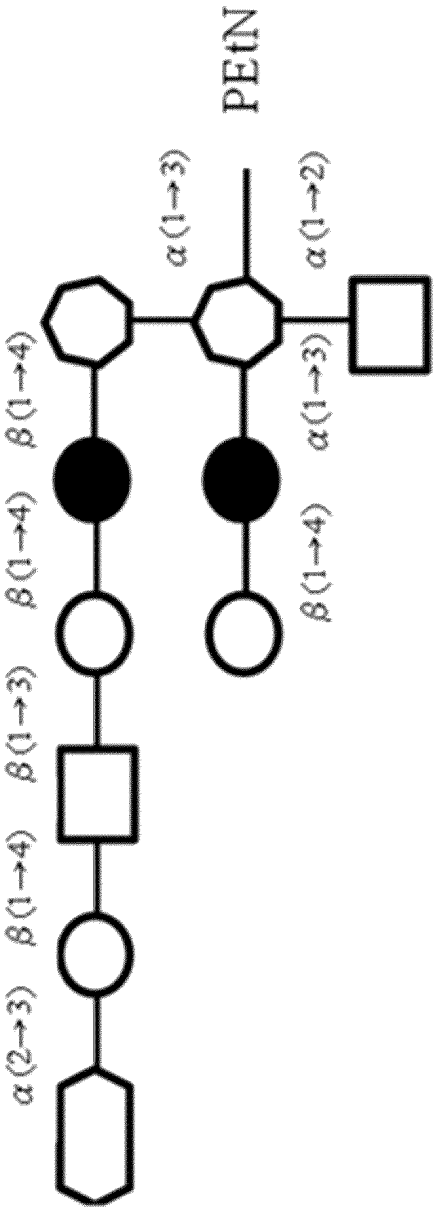


FIG. 32C

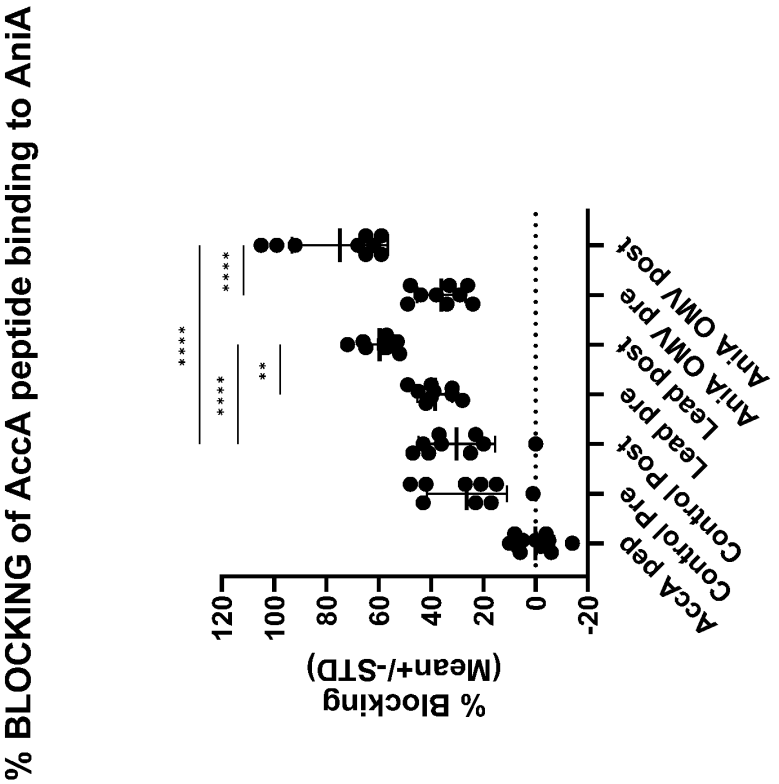
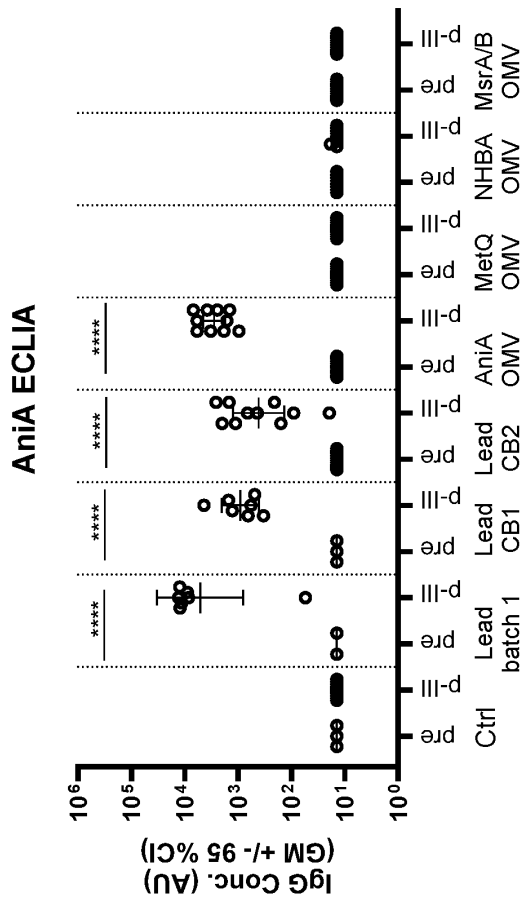

% BLOCKING of AccA peptide binding to AniA
% Blocking
(Mean+/-STD)
120
100
80
60
40
20
0
-20
AccA pep
Control Pre
Control Post
Lead Pre
Lead Post
AniA OMV Pre
AniA OMV post
****
****
****
**

FIG. 33


AniA ECLIA
IgG Conc. (AU)
(GM +/- 95 %CI)
Ctrl
Lead batch 1
Lead CB1
Lead CB2
AniA OMV
MetQ OMV
NHBA OMV
MsrA/B OMV
pre
p-III
****

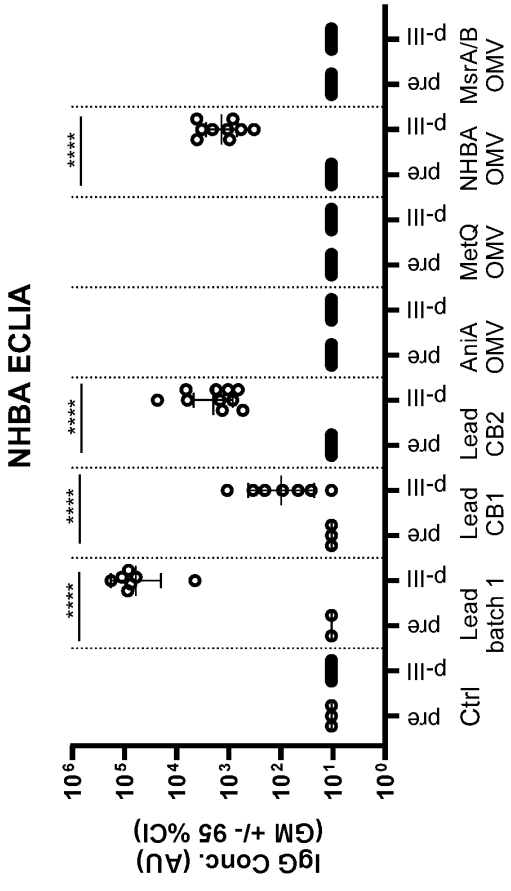
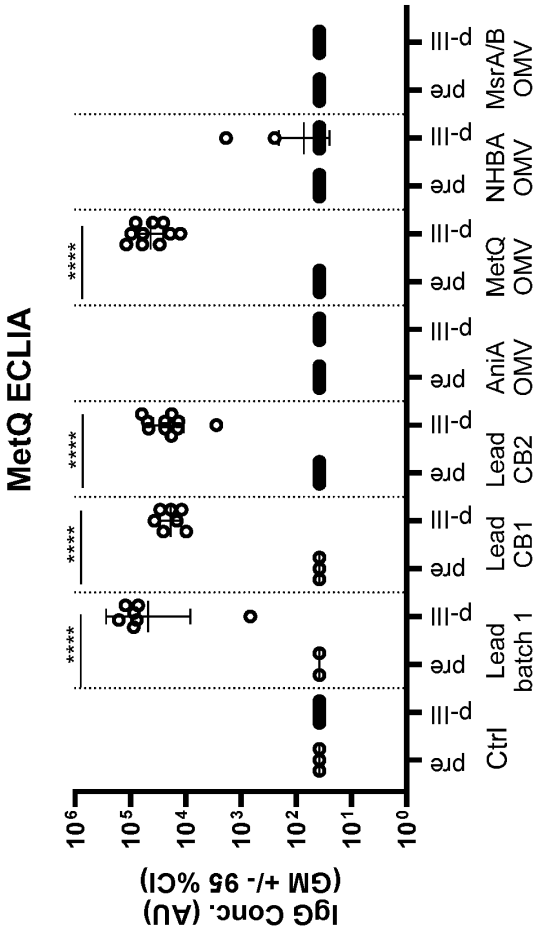

NHBA ECLIA
IgG Conc. (AU)
(GM +/- 95 %CI)
Ctrl
Lead batch 1
Lead CB1
Lead CB2
AniA OMV
MetQ OMV
NHBA OMV
MsrA/B OMV
pre
p-III
****

FIG. 34A



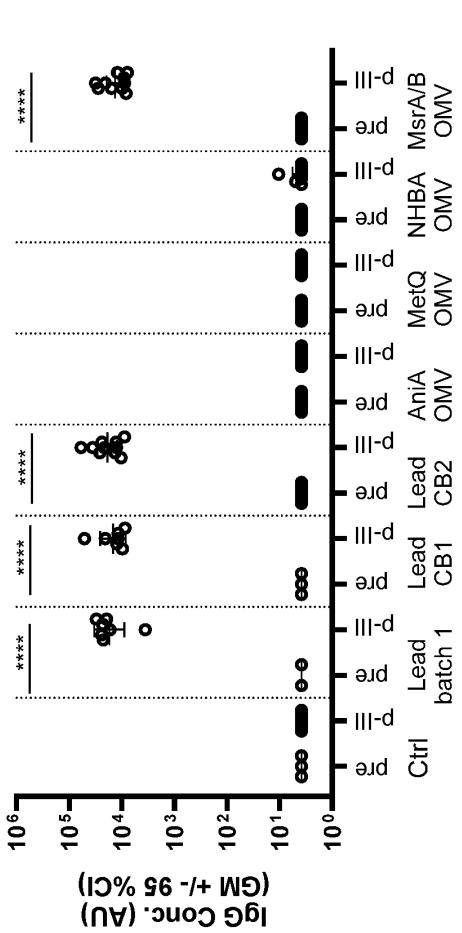


FIG. 34A (continued)

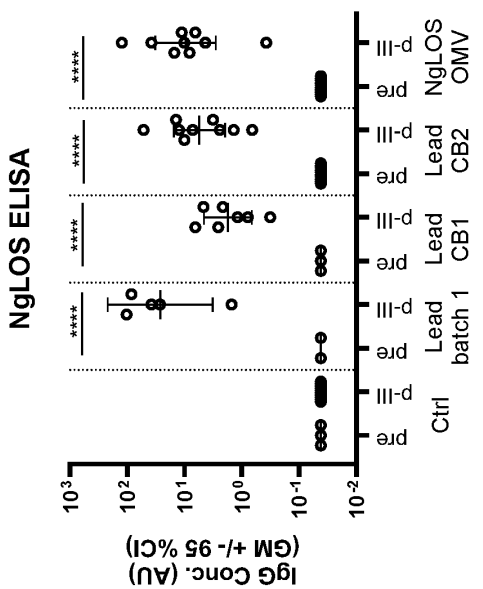
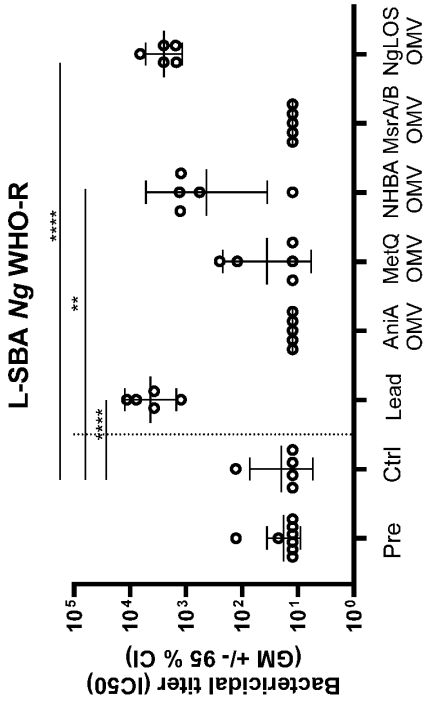


FIG. 34B



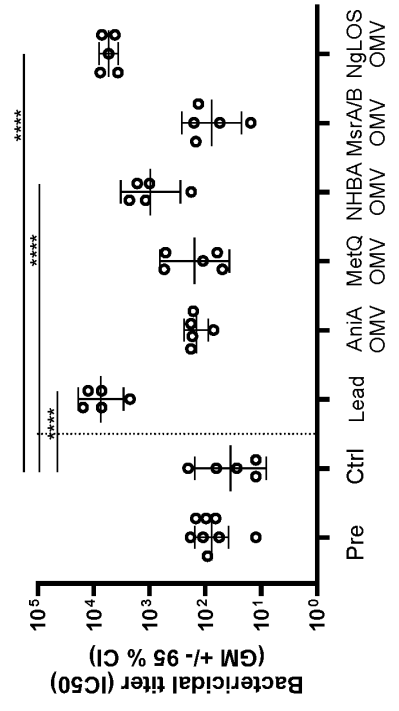


FIG. 34C

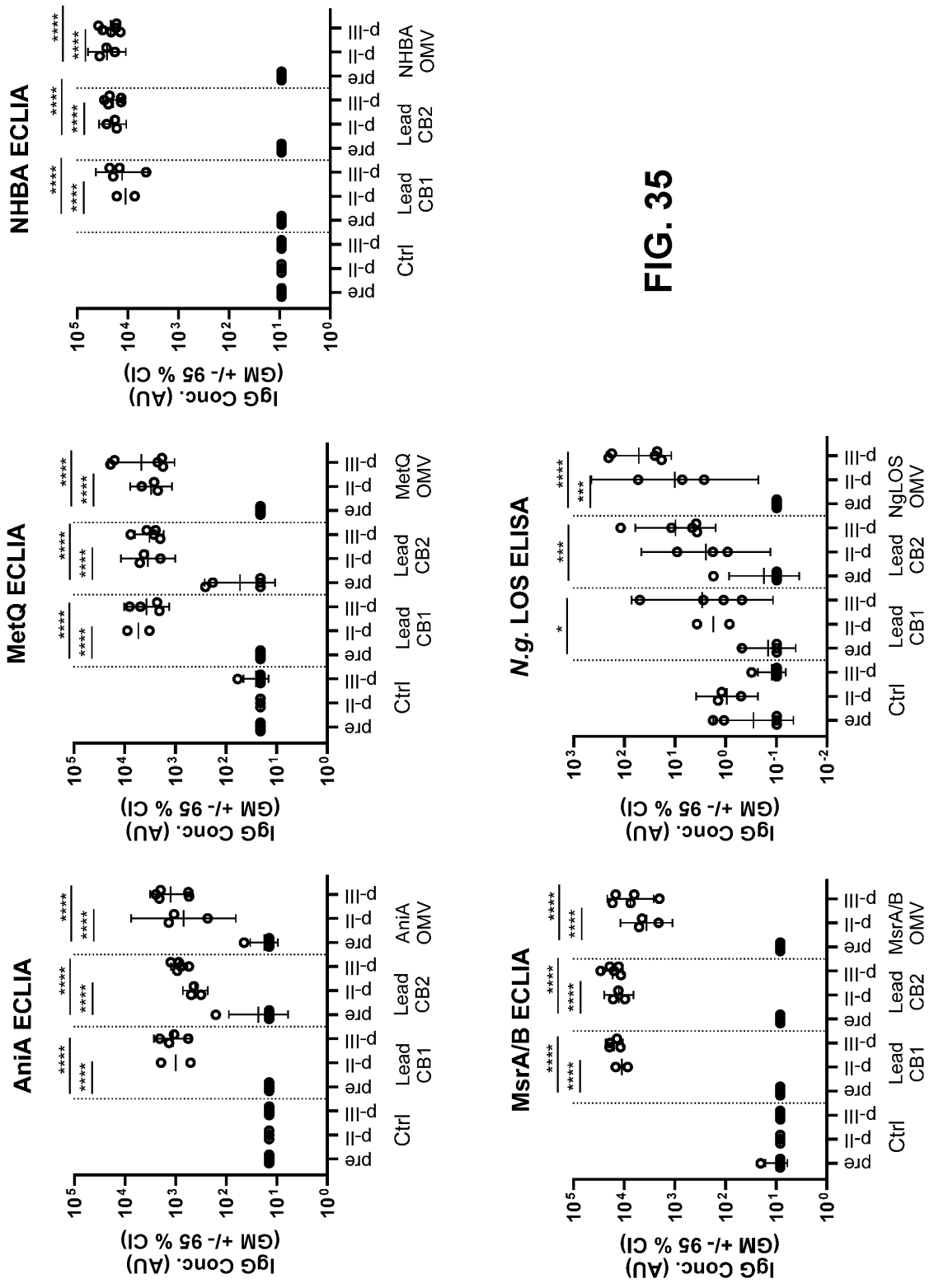

NHBA ECLIA
MetQ ECLIA
AniA ECLIA
N.g. LOS ELISA
MsrA/B ECLIA
IgG Conc. (AU)
(GM +/- 95 % CI)
pre
p-II
p-III
Ctrl
Lead CB1
Lead CB2
NHBA OMV
MetQ OMV
AniA OMV
NgLOS OMV
MsrA/B OMV

FIG. 35

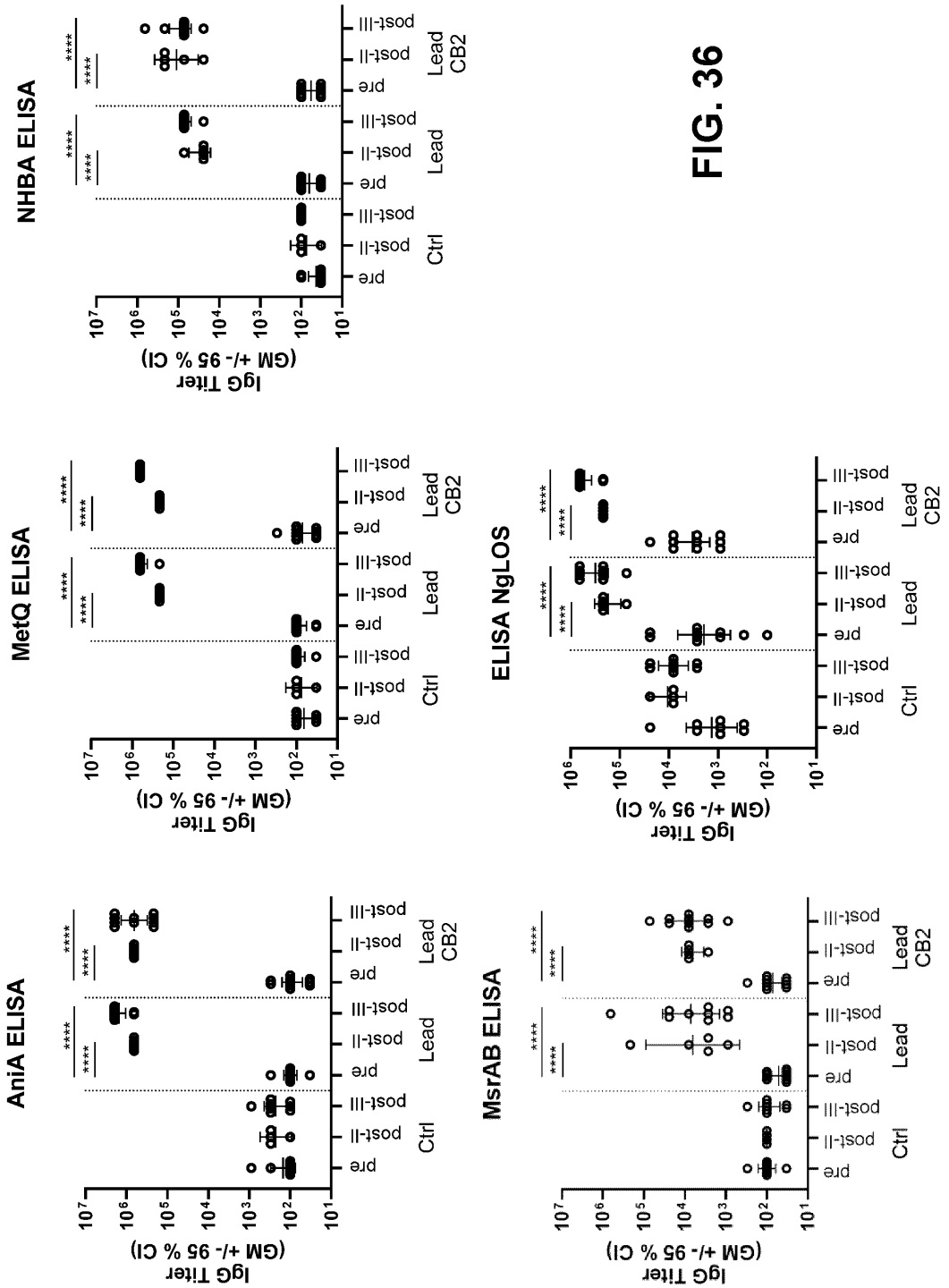

AniA ELISA
MetQ ELISA
NHBA ELISA
ELISA NgLOS
MsrAB ELISA
IgG Titer
(GM +/- 95 % CI)
pre
post-II
post-III
Ctrl
Lead
Lead CB2
****

FIG. 36