Figure 1

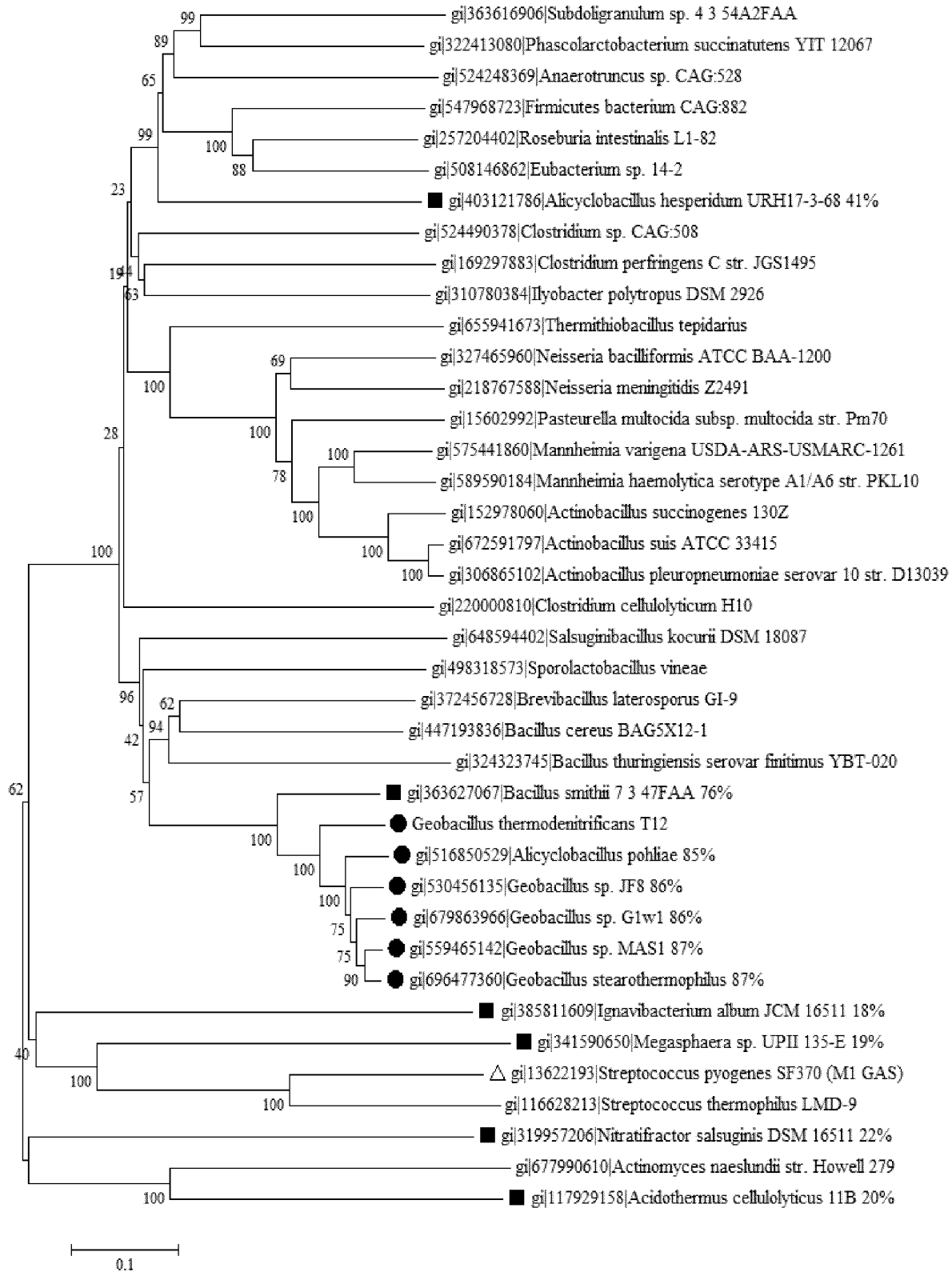

gi|363616906|Subdoligranulum sp. 4 3 54A2FAA
gi|322413080|Phascolarctobacterium succinatutens YIT 12067
gi|524248369|Anaerotruncus sp. CAG:528
gi|547968723|Firmicutes bacterium CAG:882
gi|257204402|Roseburia intestinalis L1-82
gi|508146862|Eubacterium sp. 14-2
gi|403121786|Alicyclobacillus hesperidum URH17-3-68 41%
gi|524490378|Clostridium sp. CAG:508
gi|169297883|Clostridium perfringens C str. JGS1495
gi|310780384|Ilyobacter polytropus DSM 2926
gi|655941673|Thermithiobacillus tepidarius
gi|327465960|Neisseria bacilliformis ATCC BAA-1200
gi|218767588|Neisseria meningitidis Z2491
gi|15602992|Pasteurella multocida subsp. multocida str. Pm70
gi|575441860|Mannheimia varigena USDA-ARS-USMARC-1261
gi|589590184|Mannheimia haemolytica serotype A1/A6 str. PKL10
gi|152978060|Actinobacillus succinogenes 130Z
gi|672591797|Actinobacillus suis ATCC 33415
gi|306865102|Actinobacillus pleuropneumoniae serovar 10 str. D13039
gi|220000810|Clostridium cellulolyticum H10
gi|648594402|Salsuginibacillus kocurii DSM 18087
gi|498318573|Sporolactobacillus vineae
gi|372456728|Brevibacillus laterosporus GI-9
gi|447193836|Bacillus cereus BAG5X12-1
gi|324323745|Bacillus thuringiensis serovar finitimus YBT-020
gi|363627067|Bacillus smithii 7 3 47FAA 76%
Geobacillus thermodenitrificans T12
gi|516850529|Alicyclobacillus pohliae 85%
gi|530456135|Geobacillus sp. JF8 86%
gi|679863966|Geobacillus sp. G1w1 86%
gi|559465142|Geobacillus sp. MAS1 87%
gi|696477360|Geobacillus stearothermophilus 87%
gi|385811609|Ignavibacterium album JCM 16511 18%
gi|341590650|Megasphaera sp. UPII 135-E 19%
gi|13622193|Streptococcus pyogenes SF370 (M1 GAS)
gi|116628213|Streptococcus thermophilus LMD-9
gi|319957206|Nitratifractor salsuginis DSM 16511 22%
gi|677990610|Actinomyces naeslundii str. Howell 279
gi|117929158|Acidothermus cellulolyticus 11B 20%
0.1

Figure 2

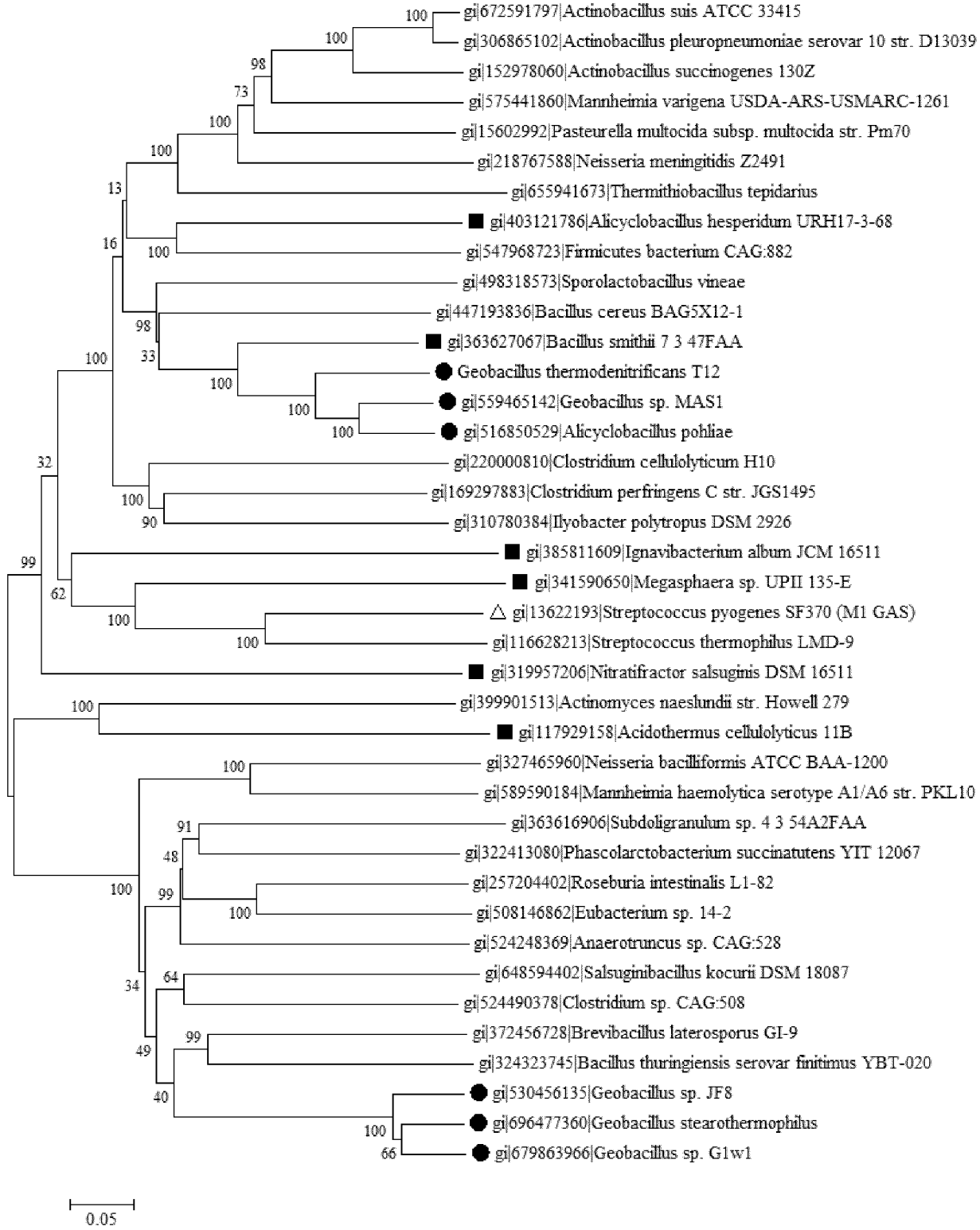

gi|672591797|Actinobacillus suis ATCC 33415
gi|306865102|Actinobacillus pleuropneumoniae serovar 10 str. D13039
gi|152978060|Actinobacillus succinogenes 130Z
gi|575441860|Mannheimia varigena USDA-ARS-USMARC-1261
gi|15602992|Pasteurella multocida subsp. multocida str. Pm70
gi|218767588|Neisseria meningitidis Z2491
gi|655941673|Thermithiobacillus tepidarius
gi|403121786|Alicyclobacillus hesperidum URH17-3-68
gi|547968723|Firmicutes bacterium CAG:882
gi|498318573|Sporolactobacillus vineae
gi|447193836|Bacillus cereus BAG5X12-1
gi|363627067|Bacillus smithii 7 3 47FAA
Geobacillus thermodenitrificans T12
gi|559465142|Geobacillus sp. MAS1
gi|516850529|Alicyclobacillus pohliae
gi|220000810|Clostridium cellulolyticum H10
gi|169297883|Clostridium perfringens C str. JGS1495
gi|310780384|Ilyobacter polytropus DSM 2926
gi|385811609|Ignavibacterium album JCM 16511
gi|341590650|Megasphaera sp. UPII 135-E
gi|13622193|Streptococcus pyogenes SF370 (M1 GAS)
gi|116628213|Streptococcus thermophilus LMD-9
gi|319957206|Nitratifractor salsuginis DSM 16511
gi|399901513|Actinomyces naeslundii str. Howell 279
gi|117929158|Acidothermus cellulolyticus 11B
gi|327465960|Neisseria bacilliformis ATCC BAA-1200
gi|589590184|Mannheimia haemolytica serotype A1/A6 str. PKL10
gi|363616906|Subdoligranulum sp. 4 3 54A2FAA
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gi|257204402|Roseburia intestinalis L1-82
gi|508146862|Eubacterium sp. 14-2
gi|524248369|Anaerotruncus sp. CAG:528
gi|648594402|Salsuginibacillus kocurii DSM 18087
gi|524490378|Clostridium sp. CAG:508
gi|372456728|Brevibacillus laterosporus GI-9
gi|324323745|Bacillus thuringiensis serovar finitimus YBT-020
gi|530456135|Geobacillus sp. JF8
gi|696477360|Geobacillus stearothermophilus
gi|679863966|Geobacillus sp. G1w1
0.05

Figure 3

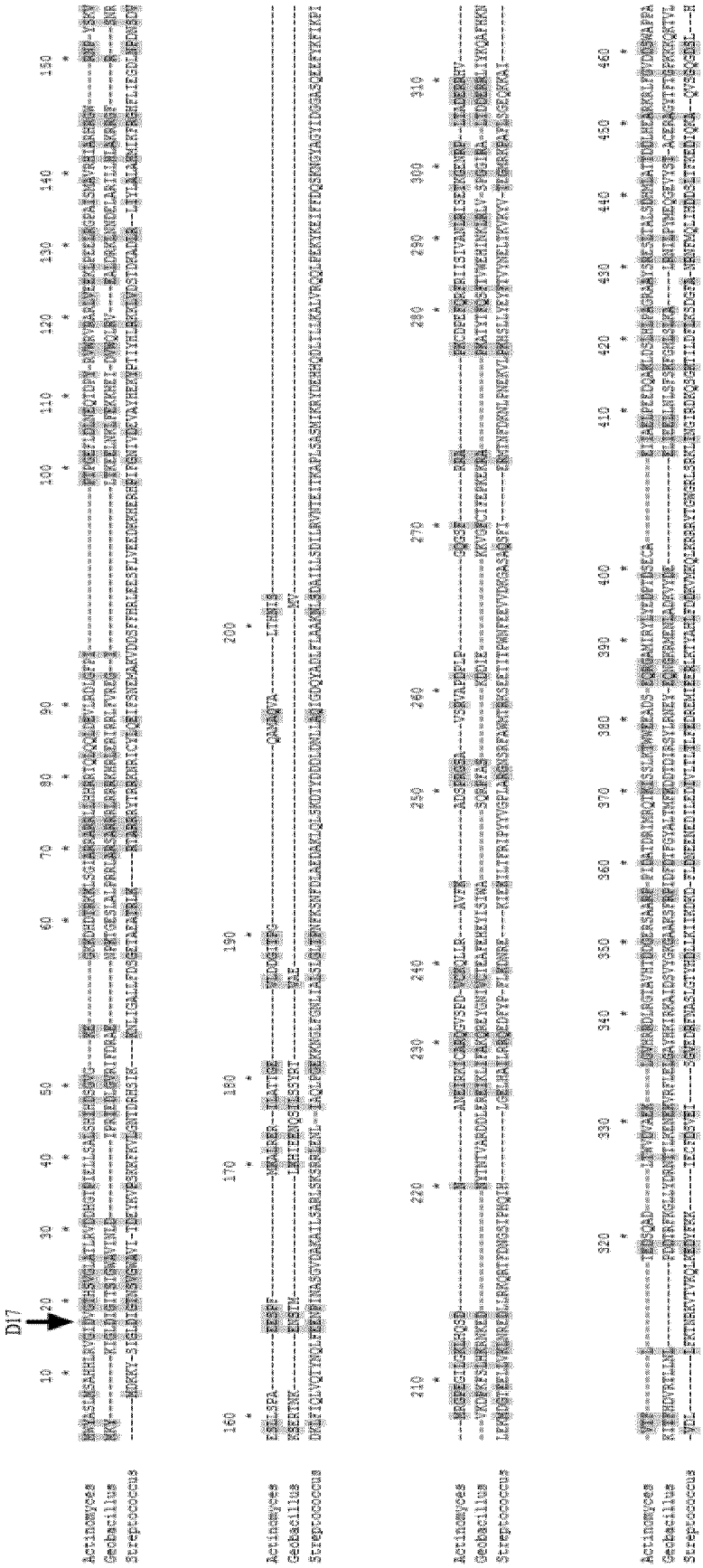


Figure 3 (continued)

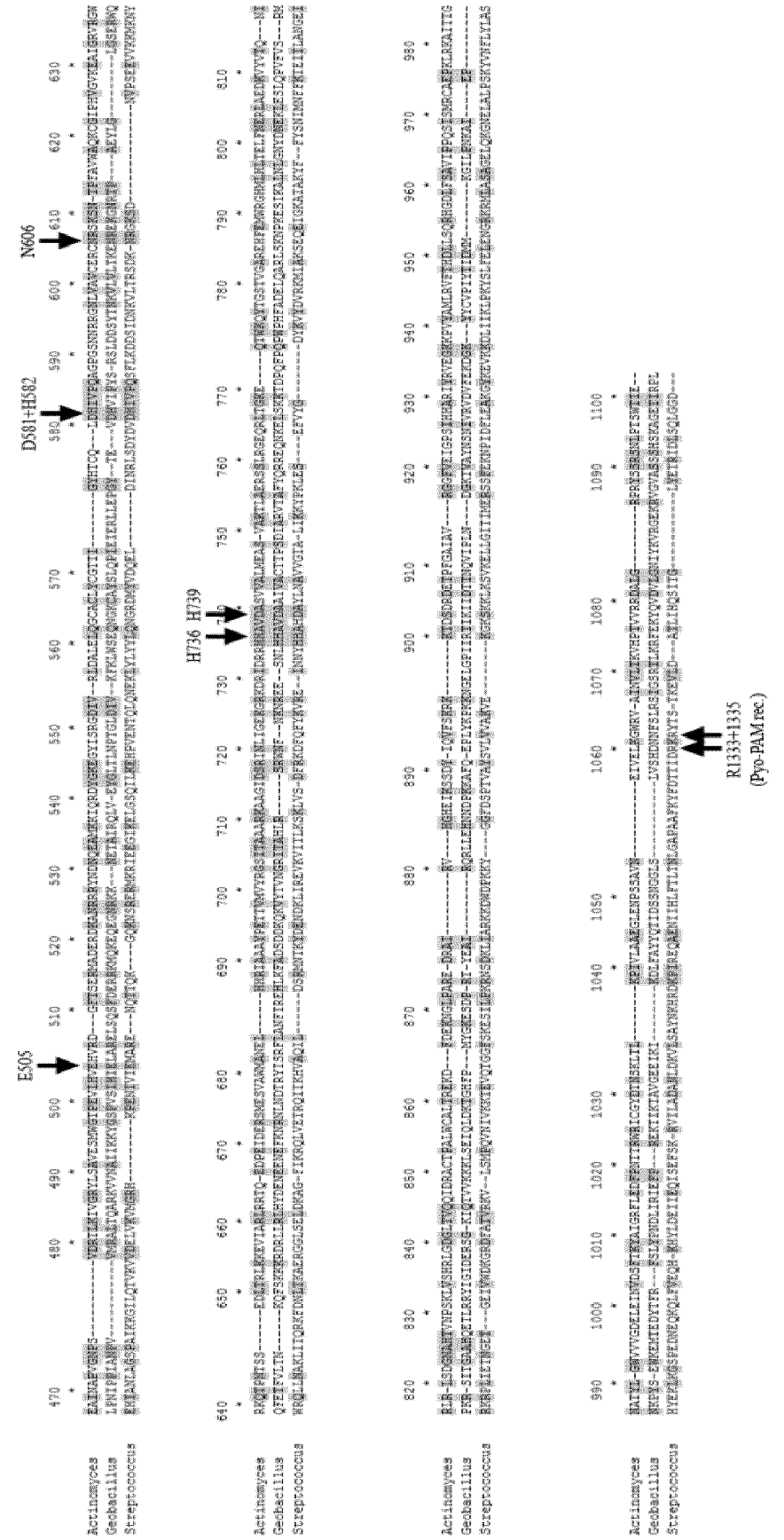


Figure 4

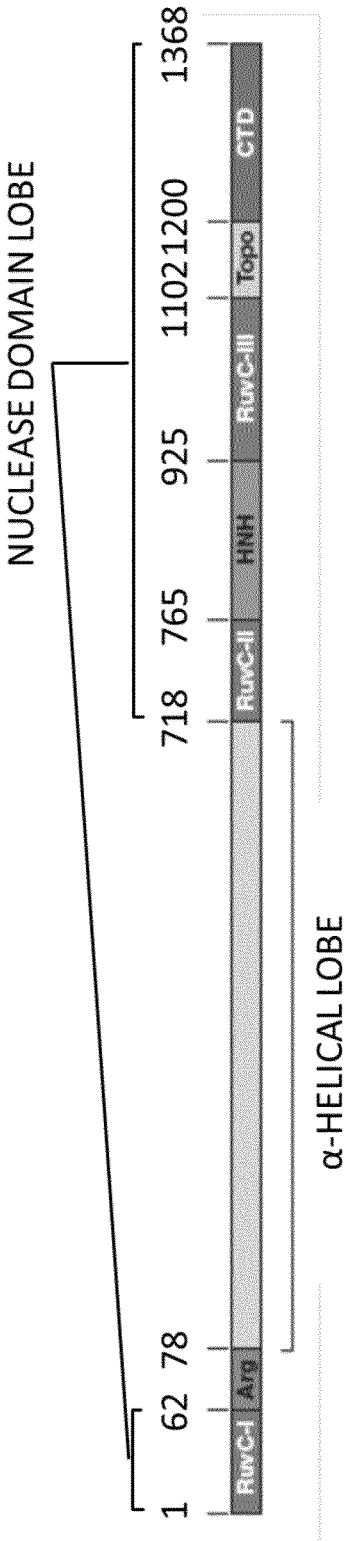
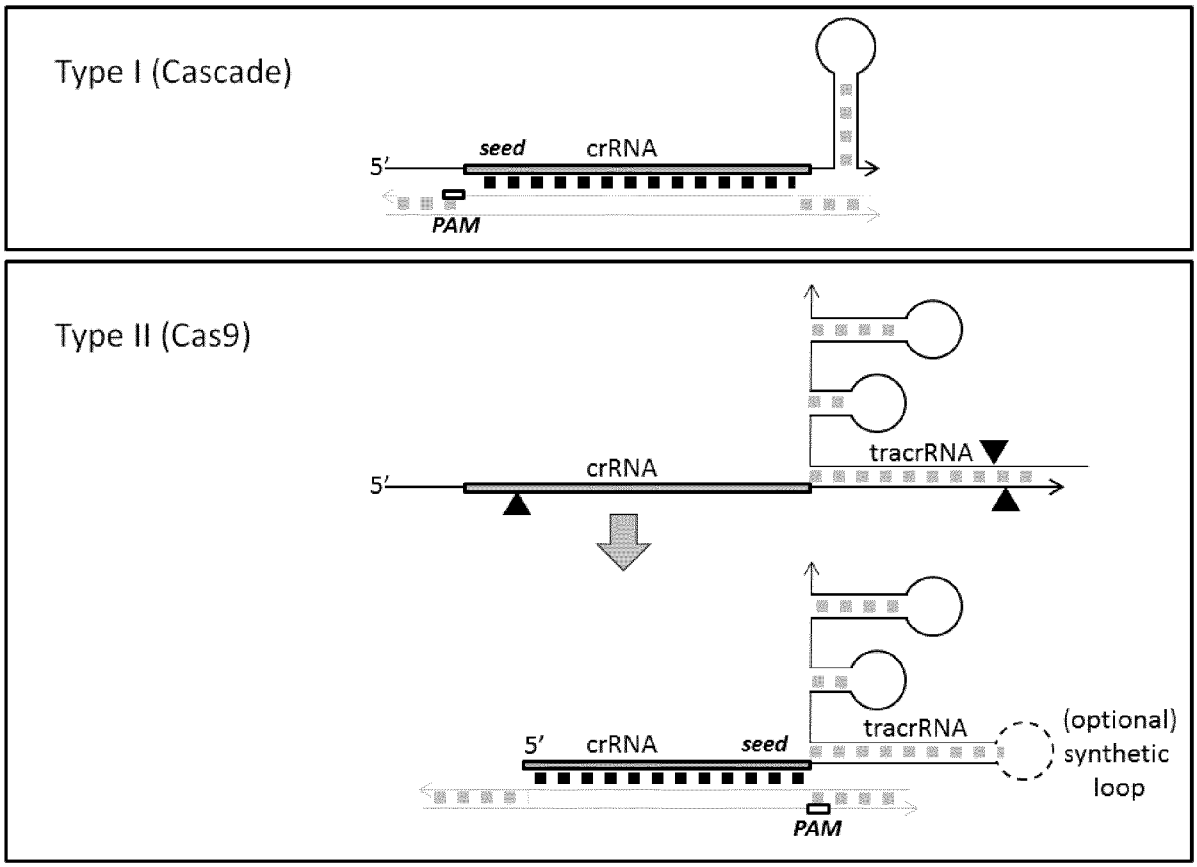

NUCLEASE DOMAIN LOBE
α-HELICAL LOBE
1
62
78
718
765
925
1102
1200
1368
RuvC-I
Arg
RuvC-II
HNH
RuvC-III
Topo
CTD

Figure 5


Type I (Cascade)
5′
seed
crRNA
PAM
Type II (Cas9)
5′
crRNA
tracrRNA
5′
crRNA
seed
tracrRNA
(optional)
synthetic
loop
PAM