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(71) Demandeurs/Applicants:
HUMABS BIOMED SA, CH;
INSTITUTE FOR RESEARCH IN BIOMEDICINE, CH

(72) Inventeurs/Inventors:
GRASSI, FABIO, CH;
PERRUZZA, LISA, CH;
PIZZUTO, MATTEO, CH;
BENIGNI, FABIO, CH; ...

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(54) Title: ANTIBODIES AGAINST CAMPYLOBACTER SPECIES

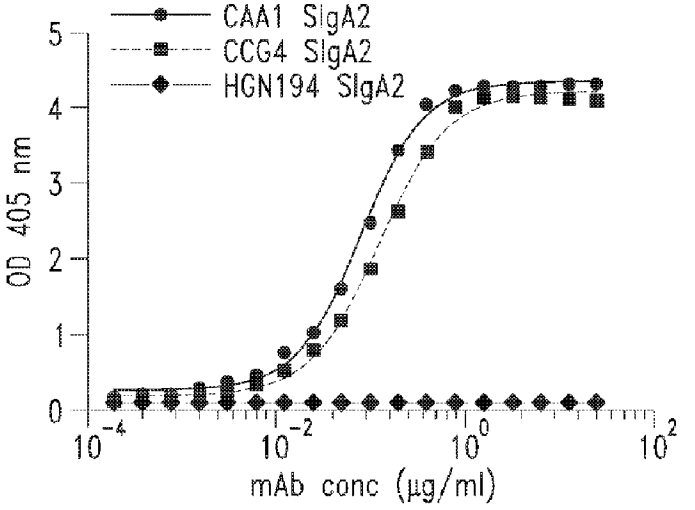

FIG. 7A

(57) Abrégé/Abstract:
The instant disclosure provides antibodies and antigen-binding fragments thereof that are specific for Campylobacter and, in certain embodiments, are capable of neutralizing a Campylobacter infection in a subject. In certain embodiments, the antibody or antigen binding fragment comprises an IgA antibody, such as, for example, a secretory IgA antibody. Also provided are pharmaceutical compositions comprising a disclosed antibody or antigen-binding fragment. Methods of using the antibodies, antigen-binding fragments, and compositions to treat or prevent a Campylobacter infection in a subject are also provided. In certain embodiments, recombinant secretory IgA antibodies of the instant disclosure are administered orally to a subject having or at risk of developing a Campylobacter infection.

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(72) Inventeurs(suite)/Inventors(continued): CORTI, DAVIDE, CH
(74) Agent: GOWLING WLG (CANADA) LLP

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(71) Applicant: **HUMABS BIOMED SA** [CH/CH]; via Mirasole 1, 6500 Bellinzona (CH).

(72) Inventors; and
(71) Applicants: **GRASSI, Fabio** [CH/CH]; Via Vincenzo Vela 6, 6500 Bellinzona (CH). **PERRUZZA, Lisa** [CH/CH]; Via Vincenzo Vela 6, 6500 Bellinzona (CH).

(72) Inventors: **PIZZUTO, Matteo**; via Mirasole 1, 6500 Bellinzona (CH). **BENIGNI, Fabio**; via Mirasole 1, 6500 Bellinzona (CH). **CORTI, Davide**; via Mirasole 1, 6500 Bellinzona (CH).

(74) Agent: **MORGAN, John, A.** et al.; Seed Intellectual Property Law Group LLP, Suite 5400, 701 Fifth Avenue, Seattle, Washington 98104-7064 (US).

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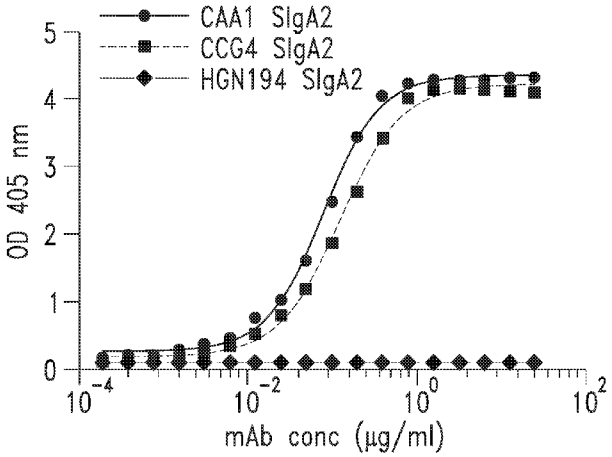

FIG. 7A

(57) **Abstract:** The instant disclosure provides antibodies and antigen-binding fragments thereof that are specific for Campylobacter and, in certain embodiments, are capable of neutralizing a Campylobacter infection in a subject. In certain embodiments, the antibody or antigen binding fragment comprises an IgA antibody, such as, for example, a secretory IgA antibody. Also provided are pharmaceutical compositions comprising a disclosed antibody or antigen-binding fragment. Methods of using the antibodies, antigen-binding fragments, and compositions to treat or prevent a Campylobacter infection in a subject are also provided. In certain embodiments, recombinant secretory IgA antibodies of the instant disclosure are administered orally to a subject having or at risk of developing a Campylobacter infection.

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ANTIBODIES AGAINST CAMPYLOBACTER SPECIES

STATEMENT REGARDING SEQUENCE LISTING

The Sequence Listing associated with this application is provided in text format in lieu of a paper copy, and is hereby incorporated by reference into the specification. The name of the text file containing the Sequence Listing is 470082_406WO_SEQUENCE_LISTING.txt. The text file is 304 KB, was created on July 16, 2019, and is being submitted electronically via EFS-Web.

BACKGROUND

Campylobacter is the most common cause of bacterial gastroenteritis worldwide and has recently been added to the World Health Organization (WHO) list of antibiotic resistant bacteria that pose a potential global threat to human health (*see*, *e.g.*, "WHO publishes list of bacteria for which new antibiotics are urgently needed", World Health Organization news release, February 27 2017; who.int/en/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed) . *Campylobacter* species (*C. jejuni* and *C. coli*) are a significant cause of traveler's diarrhea in developed countries and a major cause of life-threatening acute watery diarrhea in children under the age of 2 in developing countries. Currently, there are no vaccines approved to prevent Campylobacteriosis. Rehydration is the main form of therapy, and although antibiotics have been shown to be beneficial in severe infections, they are often not recommended to avoid the rapid development of resistance.

Accordingly, new therapies for preventing or treating Campylobacter infections are needed.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows cross-reactivity with murine microbiota and breadth of *Campylobacter* ("Campy")-reactive rSIgA of the present disclosure.

FIG. 2 shows the design of a bacterial motility assay examining the ability of Campy-reactive rSIgA of the present disclosure to limit bacteria motility.

FIG. 3 shows results from the experiment shown in FIG. 2. Culture plates were as follows: (left to right) = mock infected; no mAb; ctrl rSIgA; Campy-reactive rSIgA.

FIG. 4A shows FACS analysis of human IgA-coated bacteria in the stools of C57BL/6 mice that received a prophylactic dose of Campy-reactive rSIgA 1h prior to infection with 10^9 CFU of *Campylobacter jejuni* strain 81-176, followed by a second dose of rSIgA at 6h p.i. Stool samples were taken at 4h, 6h, and 9h p.i., as indicated.

FIG. 4B shows anti-HuIgA-coated bacteria in the stools of uninfected (L) versus infected (R) mice.

FIGS. 5A and 5B show Campylobacter shedding in treated and untreated animals at (**A**) 24 hours and (**B**) 72 hours post-infection.

FIG. 6 shows ELISA quantification of Lipocalin-2 at 24, 48 and 72 hours post-infection in animal stools.

FIGS. 7A-7E show *in vitro* characterization of exemplary antibodies CAA1 and CCG4 of the present disclosure (expressed as rSIgA) binding to FliD. **(A)** Binding of CAA1, CCG4 and HGN194 rSIgA to coated recombinant FliD as measured by ELISA. Serial dilutions of the three mAbs were incubated for 1h at RT with FliD pre-coated 96 well ELISA plates. Detection was performed using a biotinylated anti-human SC antibody followed by incubation with Streptavidin-AP. **(B)** Cross-competition studies performed by bio-layer interferometry (BLI). FliD antigen was immobilized on APS sensors and then incubated with CAA1 prior to association with CGG4, CAA1 or PBS with 1% BSA. **(C)** Western blot analysis of CAA1, CCG4 and HGN194 rSIgA binding to FliD antigen (70 KDa) under reducing and denaturing conditions. **(D)** Representative histograms of the *in vitro* binding of the indicated mAbs against pure culture of *C. jejuni* and *C. coli*. One representative experiment out of three is shown. **(E)** Binding of CAA1, CCG4 and HGN194 rSIgA2 to *C. jejuni* as observed in confocal microscopy. Bacteria were stained using Syto BC, whereas the mAbs were detected using anti-human IgA AF647 conjugated.

FIGS. 8A-8D show that C57BL/6 just-weaned mice are highly sensitive to *C. jejuni* infection. **(A-C)** C57BL/6 mice at 12, 21 and 56 days of age were orally infected with 10^8 CFU of *C. jejuni*. **(A)** Bacteria loads (CFU), and **(B)** Lipocalin 2 (LCN2) in

the stools of infected animals were determined at 6 days post-infection. **(C)** Representative H&E sections of the caecum from infected mice and statistical analysis of histopathological scores at 6 days post-infection. White arrows: submucosal inflammation; white asterisk: crypt hyperplasia with decreased number of goblet cells; black asterisk: epithelial desquamation; black arrows: mucosal inflammation. Scale bar: 200 μm. **(D)** Quantification of fecal IgA concentrations in C57BL/6 mice at 12, 21 and 56 days of age. Dots represent individual mice and results are shown as ± SEM. Mann-Whitney test (A–D) was used. $*p < 0.05$, $**p < 0.01$. One representative experiment out of two is shown.

FIGS. 9A-9D show prophylactic activity of orally administered CAA1 and CCG4 rSIgA2 against *C. jejuni* infection in just-weaned mice. **(A-D)** Two hours prior to infection with 10^8 cfu of *C. jejuni*, 21-day-old C57BL/6 mice were orally administered by gavage with 200 μg of the indicated mAbs in PBS. **(A)** Fecal bacterial loads (CFU) at 24h, 48h and 72h post *C.jejuni* infection were determined. **(B)** Lipocalin-2 (LCN) levels in the stools, **(C)** statistical analysis of polymorphonucleated (PMN) cell infiltrates gated as $Gr1^+CD11b^+$, and **(D)** histopathological score in the caecum were determined at 72h post infection in the different treatment conditions. Dots represent individual mice and results are shown as ± SEM. Mann-Whitney test **(A–D)** was used. $*p < 0.05$, $**p < 0.01$, $***p < 0.001$. One representative experiment out of at least two is shown.

FIGS. 10A-10D show that CAA1 SIgA1 and SIgA2 have similar prophylactic activity against *C. jejuni* infection. **(A-D)** Two hours prior to infection with 10^8 CFU of *C. jejuni*, 21-day-old C57BL/6 mice were orally administered via gavage with 200 μg of CAA1 as rSIgA1 or rSIgA2. **(A)** Quantification of the bacterial load (CFU) in the stools of the animals at 24h, 48h and 72h post-infection. **(B)** Representative dot plot and relative quantification of polymorphonucleated cells infiltrated in the caecum gated as $Gr1^+CD11b^+$. **(C)** Quantification of Lipocalin-2 (LCN) in the stools, and **(D)** statistical analysis of histopathological score in the caecum at 72h post infection in the different treatment conditions. Dots represent individual mice and results are shown as

± SEM. Mann-Whitney test **(A–D)** was used. *$p < 0.05$, **$p < 0.01$. One representative experiment out of at least two is shown.

FIGS. 11A-11D show that conversion to IgG reduces oral CAA1 prophylactic activity against *C. jejuni* infection. **(A-D)** 2h prior to infection with 10^8 CFU of *C. jejuni*, 21-day-old C57BL/6 mice were orally administered, via gavage, 200 µg of CAA1 as rSIgA2 or rIgG1. **(A)** Quantification of the bacterial load (CFU) in the stools of the animals at 24h, 48h and 72h post-infection. **(B)** Representative dot plot and relative quantification of polymorphonucleated cells infiltrated in the caecum gated as $Gr1^+CD11b^+$. **(C)** Quantification of Lipocalin-2 (LCN) in the stools, and **(D)** statistical analysis of histopathological score in the caecum at 72h post infection in the different treatment conditions. Dots represent individual mice and results are shown as ± SEM. Mann-Whitney test (A–D) was used. *$p < 0.05$, **$p < 0.01$. One representative experiment out of at least two is shown.

FIG. 12 shows analysis of FliD amino acid sequence conservation. FliD amino acid sequences from *C. jejuni* and *C. coli* isolates were retrieved from GenBank and analyzed using CLC Main Workbench software (Qiagen). The height of each letter in the sequence logo represents the level of conservation of that amino acid at the specific site. The consensus sequence for FliD is shown at top.

FIG. 13 shows frequency of FliD-reactive IgA^+ and IgG^+ memory B cells from different tonsillar samples. Analysis of reactivity against FliD antigen of the IgA^+ (upper panel) and IgG^+ (lower panel) memory B cell repertoire for different tonsillar samples is shown.

FIGS. 14A-14C show cross-reactivity of FliD-reactive mAbs with the murine microbiota and persistence in caecum of C57BL/6 just weaned mice. **(A)** Representative histograms of the specific binding of the indicated mAbs against fecal microbiota of mice mock infected or infected with *C. jejuni* or *C. coli*. One representative experiment out of three is shown. **(B-C)** Pharmacokinetics evaluation by ELISA of HGN194 **(B)** rSIgA and **(C)** rIgG antibody at the indicated time points in the different mouse intestinal sub-compartments. One representative experiment out of at two is shown.

FIGS. 15A-15D provide further data showing prophylactic activity of CAA1 rSIgA at different *C. jejuni* infection doses. **(A-B)** Quantification of the fecal bacterial load (CFU) in 21-day-old C57BL/6 mice administered via gavage with 200 µg of CAA1 rSIgA2 as measured at 24, 72 and 120h post-infection with 10^7 or 10^9 CFU of *C. jejuni*. **(C-D)** Quantification of fecal lipocalin-2 (LCN) in 21-day-old C57BL/6 mice administered via gavage with 200 µg of CAA1 rSIgA2 as measured at 120h post-infection with 10^7 or 10^9 CFU of *C. jejuni*. Dots represent individual mice and results are shown as ± SEM. Mann-Whitney test **(A–D)** was used. *$p < 0.05$, **$p < 0.01$. One representative experiment out of at least two is shown.

FIGS. 16A-16D show that IgA isotype switch affects Igase sensitivity, but not FliD affinity or specificity. **(A)** Denaturing non-reducing gel of CAA1 rSIgA1 and rSIgA2 incubated over-night (18 hours) with PBS or with rIgA protease (IgAse Pro-Pro-Y-Pro) from *Neisseria gonorrhoeae*. (1: SIgA1 + PBS; 2: SIgA2 + PBS; 3: SIgA1+Igase; 4: SIgA2+Igase). **(B)** Binding of rSIgA1 and rSIgA2 CAA1 to FliD, as measured by ELISA. Serial dilutions of the the mAbs were incubated for 1h at RT with FliD pre-coated 96 well ELISA plates. Detection was performed using a biotinylated anti-human SC antibody followed by incubation with Streptavidin-AP. **(C)** Representative histograms of the *in vitro* specific binding of the indicated mAbs against pure culture of *C. jejuni* and *C. coli*. One representative experiment out of three is shown. **(D)** Representative histograms of CAA1 rSIgA1 and rSIgA2 binding to the fecal microbiota of not infected C57BL/6 just-weaned mice.

FIGS. 17A-17D show that conversion to IgG format reduces oral CCG4 prophylactic activity against *C. jejuni* infection. **(A-D)** 2h prior to infection with 10^8 CFU of *C. jejuni*, 21-day-old C57BL/6 mice were orally administered via gavage with 200 µg of CCg4 as rSIgA2 or rIgG1. **(A)** Quantification of the bacterial load (CFU) in the stools of the animals at 24 and 72h post-infection. **(B)** Representative dot plot and relative quantification of polymorphonucleated cells infiltrated in the caecum at 72h post-infection. **(C)** Quantification of Lipocalin-2 (LCN) in the stools, and **(D)** statistical analysis of histopathological score in the caecum at 72h post infection in the different treatment conditions. Dots represent individual mice and results are shown as ± SEM.

Mann-Whitney test **(A–D)** was used. *$p < 0.05$, **$p < 0.01$. One representative experiment out of two is shown.

DETAILED DESCRIPTION

Provided herein are antibodies and antigen-binding fragments specific for *Campylobacter*, compositions comprising the same, and methods of using the antibodies and compositions to treat (*e.g.,* reduce, delay, eliminate, or prevent) a *Campylobacter* infection in a subject. In some embodiments, an antibody of the present disclosure comprises an IgA molecule, such as a dimeric IgA molecule. In certain embodiments, an IgA antibody of the present disclosure is provided in a secretory form (SIgA), as described herein. Administration of antibodies and antigen-binding fragments of the present disclosure, *e.g.*, via oral delivery of a presently disclosed SIgA, can treat infection by *Campylobacter*, such as *Campylobacter* species associated with severe neonatal gastroenteritis.

By way of background, *Campylobacter* is an established cause of diarrhea worldwide and has recently been added to the WHO list of bacteria whose antibiotic resistance might pose a global threat to human health (World Health Organization (WHO), 2017). *Campylobacter*'s epidemiology differs between high-income countries, where the encounter with the bacteria is sporadic, and low- and middle-income countries, in which the infection is almost universal in early childhood, and is a major cause of life-threatening acute watery diarrhea in infants (Riddle and Guerry, *Vaccine,* 34:2903-2906 (2016)).

Considered as a leading zoonosis, *Campylobacter* infection is mainly associated with the consumption of contaminated undercooked animal meat (poultry being the primary bacteria reservoir), water or unpasteurized milk (Kaakoush *et al.,* *Clin.Microbiol.Rev.,* 28:687-720 (2015)). *Campylobacter jejuni* and *C. coli* are major causes of *Campylobacter* enteritis in humans (Man, *Nat.Rev.Gastroenterol.Hepatol.,* 8:669-685 (2011)).

Campylobacteriosis typically results in an acute, gastrointestinal illness characterized by watery or bloody diarrhea, fever, weight loss, and cramps that last on

average 6 days Kaakoush *et al., Clin.Microbiol.Rev.,* 28:687-720 (2015); World Health Organization (WHO) (2013)). Severe dehydration associated with *Campylobacter* enteritis represents a significant cause of death among newborns and children, particularly in developing countries (Platts-Mills *et al., Lancet Glob.Health.,* 3:e564-75 (2015)). Furthermore, *C. jejuni* infection has been consistently linked with the onset of autoimmune conditions such as Guillain-Barré Syndrome (GBS) (Islam *et al., PLoS One,* 7:e43976 (2012); Yuki *et al., Proc.Natl.Acad.Sci.U.S.A.,* 101:11404-11409 (2004)) and Inflammatory Bowel Disease (IBD) (Gradel *et al., Gastroenterology,* 137:495-501 (2009)).

Flagellum-mediated motility is thought to be important for *Campylobacter*'s virulence and pathogenicity, as shown in both experimental animal models and in human healthy volunteer studies (Black *et al., J.Infect.Dis.,* 157:472-479 (1988); Morooka *et al., J.Gen.Microbiol.,* 131:1973-1980 (1985)). But, flagellin (FlaA), the major constituent of the flagellum, does not present a high level of conservation even within the same *C. jejuni* species, and its heavy glycosylation pattern varies greatly depending on the strain and growth phase (Parkhill *et al., Nature,* 403:665-668 (2000); Thibault *et al., J.Biol.Chem.,* 276:34862-34870 (2001)). A recombinant non-glycosylated form of *C. jejuni* flagellin was shown to be poorly immunogenic in clinical trials (Riddle and Guerry, *Vaccine,* 34:2903-2906 (2016)), making FlaA a challenging target for therapy. Moreover, the possibility to use *C. jejuni* in a vaccine has been limited by the risk of GBS development associated with ganglioside mimicry of bacterial lipo-oligosaccharide (LOS) (Riddle and Guerry, *Vaccine,* 34:2903-2906 (2016)).

Due to these shortcomings, there are currently no vaccines approved by a global regulatory authority to prevent *Campylobacter* infection. Rehydration is the main form of therapy, and while antibiotics have been shown to be beneficial in severe infections, they are often not recommended due to the rapid development of antibiotic resistance. Even in the case of recovery from the infection, the continuous exposure of infants in low-income countries to intestinal pathogens, including *Campylobacter*, has been linked to environmental enteropathy (EE)/environmental enteric dysfunction (EED), a

subclinical chronic inflammation of the small intestine associated with malabsorption of nutrients, growth faltering, impaired cognitive development, changes in microbiota, and reduced responsiveness to oral vaccination (Watanabe and Petri, *EBioMedicine,* 10:25-32 (2016)).

The present disclosure provides antibodies and antigen-binding fragments that bind to the *Campylobacter* flagellar-capping protein FliD. Antibodies according to the present disclosure advantageously limit motility of *Campylobacter* and, in an animal model of *Campylobacter* infection described in this disclosure, are capable of boosting *Campylobacter* clearance infection, significantly reducing the levels of inflammation markers associated with epithelial damage and polymorphonuclear (PMN) cells infiltration.

Also provided herein are compositions that comprise a *Campylobacter* FliD-specific antibody or antigen-binding fragment of the present disclosure, polynucleotides that encode the antibody or antigen-binding fragment, vectors that contain the polynucleotide, and host cells that express the antibody or antigen-binding fragment, and/or comprise or contain a polynucleotide or vector of the present disclosure. Methods and uses are also provided for treating a *Campylobacter* infection and/or for reducing an associated symptom.

Also provided are non-human animal models for studying *Campylobacter* infection.

Prior to setting forth this disclosure in more detail, it may be helpful to an understanding thereof to provide definitions of certain terms to be used herein. Additional definitions are set forth throughout this disclosure.

In the present description, any concentration range, percentage range, ratio range, or integer range is to be understood to include the value of any integer within the recited range and, when appropriate, fractions thereof (such as one tenth and one hundredth of an integer), unless otherwise indicated. Also, any number range recited herein relating to any physical feature, such as polymer subunits, size or thickness, are to be understood to include any integer within the recited range, unless otherwise indicated. As used herein, the term "about" means ± 20% of the indicated range, value,

or structure, unless otherwise indicated. It should be understood that the terms "a" and "an" as used herein refer to "one or more" of the enumerated components. The use of the alternative (*e.g.*, "or") should be understood to mean either one, both, or any combination thereof of the alternatives. As used herein, the terms "include," "have," and "comprise" are used synonymously, which terms and variants thereof are intended to be construed as non-limiting.

"Optional" or "optionally" means that the subsequently described element, component, event, or circumstance may or may not occur, and that the description includes instances in which the element, component, event, or circumstance occurs and instances in which they do not.

In addition, it should be understood that the individual constructs, or groups of constructs, derived from the various combinations of the structures and subunits described herein, are disclosed by the present application to the same extent as if each construct or group of constructs was set forth individually. Thus, selection of particular structures or particular subunits is within the scope of the present disclosure.

The term "consisting essentially of" is not equivalent to "comprising" and refers to the specified materials or steps of a claim, or to those that do not materially affect the basic characteristics of a claimed subject matter. For example, a protein domain, region, or module (e.g., a binding domain, hinge region, or linker) or a protein (which may have one or more domains, regions, or modules) "consists essentially of" a particular amino acid sequence when the amino acid sequence of a domain, region, module, or protein includes extensions, deletions, mutations, or a combination thereof (e.g., amino acids at the amino- or carboxy-terminus or between domains) that, in combination, contribute to at most 20% (e.g., at most 15%, 10%, 8%, 6%, 5%, 4%, 3%, 2% or 1%) of the length of a domain, region, module, or protein and do not substantially affect (i.e., do not reduce the activity by more than 50%, such as no more than 40%, 30%, 25%, 20%, 15%, 10%, 5%, or 1%) the activity of the domain(s), region(s), module(s), or protein (e.g., the target binding affinity of a binding protein).

As used herein, "amino acid" refers to naturally occurring and synthetic amino acids, as well as amino acid analogs and amino acid mimetics that function in a manner

similar to the naturally occurring amino acids. Naturally occurring amino acids are those encoded by the genetic code, as well as those amino acids that are later modified, *e.g.*, hydroxyproline, γ-carboxyglutamate, and O-phosphoserine. Amino acid analogs refer to compounds that have the same basic chemical structure as a naturally occurring amino acid, *i.e.*, an α-carbon that is bound to a hydrogen, a carboxyl group, an amino group, and an R group, *e.g.*, homoserine, norleucine, methionine sulfoxide, methionine methyl sulfonium. Such analogs have modified R groups (*e.g.*, norleucine) or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid. Amino acid mimetics refer to chemical compounds that have a structure that is different from the general chemical structure of an amino acid, but that functions in a manner similar to a naturally occurring amino acid.

As used herein, "mutation" refers to a change in the sequence of a nucleic acid molecule or polypeptide molecule as compared to a reference or wild-type nucleic acid molecule or polypeptide molecule, respectively. A mutation can result in several different types of change in sequence, including substitution, insertion or deletion of nucleotide(s) or amino acid(s).

A "conservative substitution" refers to amino acid substitutions that do not significantly affect or alter binding characteristics of a particular protein. Generally, conservative substitutions are ones in which a substituted amino acid residue is replaced with an amino acid residue having a similar side chain. Conservative substitutions include a substitution found in one of the following groups: Group 1: Alanine (Ala or A), Glycine (Gly or G), Serine (Ser or S), Threonine (Thr or T); Group 2: Aspartic acid (Asp or D), Glutamic acid (Glu or Z); Group 3: Asparagine (Asn or N), Glutamine (Gln or Q); Group 4: Arginine (Arg or R), Lysine (Lys or K), Histidine (His or H); Group 5: Isoleucine (Ile or I), Leucine (Leu or L), Methionine (Met or M), Valine (Val or V); and Group 6: Phenylalanine (Phe or F), Tyrosine (Tyr or Y), Tryptophan (Trp or W). Additionally or alternatively, amino acids can be grouped into conservative substitution groups by similar function, chemical structure, or composition (*e.g.*, acidic, basic, aliphatic, aromatic, or sulfur-containing). For example, an aliphatic grouping may include, for purposes of substitution, Gly, Ala, Val, Leu, and Ile. Other conservative

substitutions groups include: sulfur-containing: Met and Cysteine (Cys or C); acidic: Asp, Glu, Asn, and Gln; small aliphatic, nonpolar or slightly polar residues: Ala, Ser, Thr, Pro, and Gly; polar, negatively charged residues and their amides: Asp, Asn, Glu, and Gln; polar, positively charged residues: His, Arg, and Lys; large aliphatic, nonpolar residues: Met, Leu, Ile, Val, and Cys; and large aromatic residues: Phe, Tyr, and Trp. Additional information can be found in Creighton (1984) Proteins, W.H. Freeman and Company.

As used herein, "protein" or "polypeptide" refers to a polymer of amino acid residues. Proteins apply to naturally occurring amino acid polymers, as well as to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid and non-naturally occurring amino acid polymers. Variants of proteins, peptides, and polypeptides of this disclosure are also contemplated. In certain embodiments, variant proteins, peptides, and polypeptides comprise or consist of an amino acid sequence that is at least 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.9% identical to an amino acid sequence of a defined or reference amino acid sequence as described herein.

"Nucleic acid molecule" or "polynucleotide" or "polynucleic acid" refers to a polymeric compound including covalently linked nucleotides, which can be made up of natural subunits (*e.g.*, purine or pyrimidine bases) or non-natural subunits (*e.g.*, morpholine ring). Purine bases include adenine, guanine, hypoxanthine, and xanthine, and pyrimidine bases include uracil, thymine, and cytosine. Nucleic acid molecules include polyribonucleic acid (RNA), which includes mRNA, microRNA, siRNA, viral genomic RNA, and synthetic RNA, and polydeoxyribonucleic acid (DNA), which includes cDNA, genomic DNA, and synthetic DNA, either of which may be single or double stranded. If single-stranded, the nucleic acid molecule may be the coding strand or non-coding (anti-sense) strand. A nucleic acid molecule encoding an amino acid sequence includes all nucleotide sequences that encode the same amino acid sequence. Some versions of the nucleotide sequences may also include intron(s) to the extent that the intron(s) would be removed through co- or post-transcriptional mechanisms. In

other words, different nucleotide sequences may encode the same amino acid sequence as the result of the redundancy or degeneracy of the genetic code, or by splicing.

Variants of nucleic acid molecules of this disclosure are also contemplated. Variant nucleic acid molecules are at least 70%, 75%, 80%, 85%, 90%, and are preferably 95%, 96%, 97%, 98%, 99%, or 99.9% identical a nucleic acid molecule of a defined or reference polynucleotide as described herein, or that hybridize to a polynucleotide under stringent hybridization conditions of 0.015M sodium chloride, 0.0015M sodium citrate at about 65-68°C or 0.015M sodium chloride, 0.0015M sodium citrate, and 50% formamide at about 42°C. Nucleic acid molecule variants retain the capacity to encode a binding domain thereof having a functionality described herein, such as binding a target molecule.

"Percent sequence identity" refers to a relationship between two or more sequences, as determined by comparing the sequences. Preferred methods to determine sequence identity are designed to give the best match between the sequences being compared. For example, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment). Further, non-homologous sequences may be disregarded for comparison purposes. The percent sequence identity referenced herein is calculated over the length of the reference sequence, unless indicated otherwise. Methods to determine sequence identity and similarity can be found in publicly available computer programs. Sequence alignments and percent identity calculations may be performed using a BLAST program (*e.g.*, BLAST 2.0, BLASTP, BLASTN, or BLASTX). The mathematical algorithm used in the BLAST programs can be found in Altschul *et al.*, *Nucleic Acids Res. 25*:3389-3402, 1997. Within the context of this disclosure, it will be understood that where sequence analysis software is used for analysis, the results of the analysis are based on the "default values" of the program referenced. "Default values" mean any set of values or parameters which originally load with the software when first initialized.

The term "isolated" means that the material is removed from its original environment (*e.g.*, the natural environment if it is naturally occurring). For example, a

naturally occurring nucleic acid or polypeptide present in a living animal is not isolated, but the same nucleic acid or polypeptide, separated from some or all of the co-existing materials in the natural system, is isolated. Such nucleic acid could be part of a vector and/or such nucleic acid or polypeptide could be part of a composition (*e.g.*, a cell lysate), and still be isolated in that such vector or composition is not part of the natural environment for the nucleic acid or polypeptide.

The term "gene" means the segment of DNA or RNA involved in producing a polypeptide chain; it includes regions preceding and following the coding region (*e.g.*, 5' untranslated region (UTR) and 3' UTR) as well as intervening sequences (introns) between individual coding segments (exons).

A "functional variant" refers to a polypeptide or polynucleotide that is structurally similar or substantially structurally similar to a parent or reference compound of this disclosure, but differs slightly in composition (e.g., one base, atom or functional group is different, added, or removed), such that the polypeptide or encoded polypeptide is capable of performing at least one function of the parent polypeptide with at least 50% efficiency, preferably at least 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, 99.9%, or 100% level of activity of the parent polypeptide. In other words, a functional variant of a polypeptide or encoded polypeptide of this disclosure has "similar binding," "similar affinity" or "similar activity" when the functional variant displays no more than a 50% reduction in performance in a selected assay as compared to the parent or reference polypeptide, such as an assay for measuring binding affinity (e.g., Biacore® or tetramer staining measuring an association (Ka) or a dissociation (KD) constant).

As used herein, a "functional portion" or "functional fragment" refers to a polypeptide or polynucleotide that comprises only a domain, portion or fragment of a parent or reference compound, and the polypeptide or encoded polypeptide retains at least 50% activity associated with the domain, portion or fragment of the parent or reference compound, preferably at least 55%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, 99.9%, or 100% level of activity of the parent polypeptide, or provides a biological benefit (e.g., effector function). A "functional portion" or

"functional fragment" of a polypeptide or encoded polypeptide of this disclosure has "similar binding" or "similar activity" when the functional portion or fragment displays no more than a 50% reduction in performance in a selected assay as compared to the parent or reference polypeptide (preferably no more than 20% or 10%, or no more than a log difference as compared to the parent or reference with regard to affinity).

As used herein, the term "engineered," "recombinant," or "non-natural" refers to an organism, microorganism, cell, nucleic acid molecule, or vector that includes at least one genetic alteration or has been modified by introduction of an exogenous or heterologous nucleic acid molecule, wherein such alterations or modifications are introduced by genetic engineering (*i.e.*, human intervention). Genetic alterations include, for example, modifications introducing expressible nucleic acid molecules encoding functional RNA, proteins, fusion proteins or enzymes, or other nucleic acid molecule additions, deletions, substitutions, or other functional disruption of a cell's genetic material. Additional modifications include, for example, non-coding regulatory regions in which the modifications alter expression of a polynucleotide, gene, or operon.

As used herein, "heterologous" or "non-endogenous" or "exogenous" refers to any gene, protein, compound, nucleic acid molecule, or activity that is not native to a host cell or a subject, or any gene, protein, compound, nucleic acid molecule, or activity native to a host cell or a subject that has been altered. Heterologous, non-endogenous, or exogenous includes genes, proteins, compounds, or nucleic acid molecules that have been mutated or otherwise altered such that the structure, activity, or both is different as between the native and altered genes, proteins, compounds, or nucleic acid molecules. In certain embodiments, heterologous, non-endogenous, or exogenous genes, proteins, or nucleic acid molecules (*e.g.*, receptors, ligands, etc.) may not be endogenous to a host cell or a subject, but instead nucleic acids encoding such genes, proteins, or nucleic acid molecules may have been added to a host cell by conjugation, transformation, transfection, electroporation, or the like, wherein the added nucleic acid molecule may integrate into a host cell genome or can exist as extra-chromosomal genetic material (*e.g.*, as a plasmid or other self-replicating vector). The term "homologous" or

"homolog" refers to a gene, protein, compound, nucleic acid molecule, or activity found in or derived from a host cell, species, or strain. For example, a heterologous or exogenous polynucleotide or gene encoding a polypeptide may be homologous to a native polynucleotide or gene and encode a homologous polypeptide or activity, but the polynucleotide or polypeptide may have an altered structure, sequence, expression level, or any combination thereof. A non-endogenous polynucleotide or gene, as well as the encoded polypeptide or activity, may be from the same species, a different species, or a combination thereof.

In certain embodiments, a nucleic acid molecule or portion thereof native to a host cell will be considered heterologous to the host cell if it has been altered or mutated, or a nucleic acid molecule native to a host cell may be considered heterologous if it has been altered with a heterologous expression control sequence or has been altered with an endogenous expression control sequence not normally associated with the nucleic acid molecule native to a host cell. In addition, the term "heterologous" can refer to a biological activity that is different, altered, or not endogenous to a host cell. As described herein, more than one heterologous nucleic acid molecule can be introduced into a host cell as separate nucleic acid molecules, as a plurality of individually controlled genes, as a polycistronic nucleic acid molecule, as a single nucleic acid molecule encoding a fusion protein, or any combination thereof. When

As used herein, the term "endogenous" or "native" refers to a polynucleotide, gene, protein, compound, molecule, or activity that is normally present in a host cell or a subject.

The term "expression", as used herein, refers to the process by which a polypeptide is produced based on the encoding sequence of a nucleic acid molecule, such as a gene. The process may include transcription, post-transcriptional control, post-transcriptional modification, translation, post-translational control, post-translational modification, or any combination thereof. An expressed nucleic acid molecule is typically operably linked to an expression control sequence (e.g., a promoter).

The term "operably linked" refers to the association of two or more nucleic acid molecules on a single nucleic acid fragment so that the function of one is affected by the other. For example, a promoter is operably linked with a coding sequence when it is capable of affecting the expression of that coding sequence (i.e., the coding sequence is under the transcriptional control of the promoter). "Unlinked" means that the associated genetic elements are not closely associated with one another and the function of one does not affect the other.

As described herein, more than one heterologous nucleic acid molecule can be introduced into a host cell as separate nucleic acid molecules, as a plurality of individually controlled genes, as a polycistronic nucleic acid molecule, as a single nucleic acid molecule encoding a fusion protein, or any combination thereof. When two or more heterologous nucleic acid molecules are introduced into a host cell, it is understood that the two or more heterologous nucleic acid molecules can be introduced as a single nucleic acid molecule (*e.g.*, on a single vector), on separate vectors, integrated into the host chromosome at a single site or multiple sites, or any combination thereof. The number of referenced heterologous nucleic acid molecules or protein activities refers to the number of encoding nucleic acid molecules or the number of protein activities, not the number of separate nucleic acid molecules introduced into a host cell.

The term "construct" refers to any polynucleotide that contains a recombinant nucleic acid molecule (or, when the context clearly indicates, a fusion protein of the present disclosure). A (polynucleotide) construct may be present in a vector (e.g., a bacterial vector, a viral vector) or may be integrated into a genome. A "vector" is a nucleic acid molecule that is capable of transporting another nucleic acid molecule. Vectors may be, for example, plasmids, cosmids, viruses, a RNA vector or a linear or circular DNA or RNA molecule that may include chromosomal, non-chromosomal, semi-synthetic or synthetic nucleic acid molecules. Vectors of the present disclosure also include transposon systems (*e.g.*, Sleeping Beauty, *see, e.g., Geurts et al., Mol. Ther. 8*:108, 2003: Mátés *et al., Nat. Genet. 41*:753, 2009). Exemplary vectors are those capable of autonomous replication (episomal vector), capable of delivering a

polynucleotide to a cell genome (e.g., viral vector), or capable of expressing nucleic acid molecules to which they are linked (expression vectors).

As used herein, "expression vector" or "vector" refers to a DNA construct containing a nucleic acid molecule that is operably linked to a suitable control sequence capable of effecting the expression of the nucleic acid molecule in a suitable host. Such control sequences include a promoter to effect transcription, an optional operator sequence to control such transcription, a sequence encoding suitable mRNA ribosome binding sites, and sequences which control termination of transcription and translation. The vector may be a plasmid, a phage particle, a virus, or simply a potential genomic insert. Once transformed into a suitable host, the vector may replicate and function independently of the host genome, or may, in some instances, integrate into the genome itself or deliver the polynucleotide contained in the vector into the genome without the vector sequence. In the present specification, "plasmid," "expression plasmid," "virus," and "vector" are often used interchangeably.

The term "introduced" in the context of inserting a nucleic acid molecule into a cell, means "transfection", "transformation," or "transduction" and includes reference to the incorporation of a nucleic acid molecule into a eukaryotic or prokaryotic cell wherein the nucleic acid molecule may be incorporated into the genome of a cell (*e.g.*, chromosome, plasmid, plastid, or mitochondrial DNA), converted into an autonomous replicon, or transiently expressed (*e.g.*, transfected mRNA).

In certain embodiments, polynucleotides of the present disclosure may be operatively linked to certain elements of a vector. For example, polynucleotide sequences that are needed to effect the expression and processing of coding sequences to which they are ligated may be operatively linked. Expression control sequences may include appropriate transcription initiation, termination, promoter, and enhancer sequences; efficient RNA processing signals such as splicing and polyadenylation signals; sequences that stabilize cytoplasmic mRNA; sequences that enhance translation efficiency (*i.e.*, Kozak consensus sequences); sequences that enhance protein stability; and possibly sequences that enhance protein secretion. Expression control sequences may be operatively linked if they are contiguous with the gene of interest and

expression control sequences that act in *trans* or at a distance to control the gene of interest.

In certain embodiments, the vector comprises a plasmid vector or a viral vector (*e.g.*, a lentiviral vector or a γ-retroviral vector). Viral vectors include retrovirus, adenovirus, parvovirus (*e.g.*, adeno-associated viruses), coronavirus, negative strand RNA viruses such as ortho-myxovirus (*e.g.*, influenza virus), rhabdovirus (*e.g.*, rabies and vesicular stomatitis virus), paramyxovirus (*e.g.*, measles and Sendai), positive strand RNA viruses such as picornavirus and alphavirus, and double-stranded DNA viruses including adenovirus, herpesvirus (*e.g.*, Herpes Simplex virus types 1 and 2, Epstein-Barr virus, cytomegalovirus), and poxvirus (*e.g.*, vaccinia, fowlpox, and canarypox). Other viruses include, for example, Norwalk virus, togavirus, flavivirus, reoviruses, papovavirus, hepadnavirus, and hepatitis virus. Examples of retroviruses include avian leukosis-sarcoma, mammalian C-type, B-type viruses, D type viruses, HTLV-BLV group, lentivirus, spumavirus (Coffin, J. M., Retroviridae: The viruses and their replication, In Fundamental Virology, Third Edition, B. N. Fields et al., Eds., Lippincott-Raven Publishers, Philadelphia, 1996).

"Retroviruses" are viruses having an RNA genome, which is reverse-transcribed into DNA using a reverse transcriptase enzyme, the reverse-transcribed DNA is then incorporated into the host cell genome. "Gammaretrovirus" refers to a genus of the retroviridae family. Examples of gammaretroviruses include mouse stem cell virus, murine leukemia virus, feline leukemia virus, feline sarcoma virus, and avian reticuloendotheliosis viruses.

"Lentiviral vectors" include HIV-based lentiviral vectors for gene delivery, which can be integrative or non-integrative, have relatively large packaging capacity, and can transduce a range of different cell types. Lentiviral vectors are usually generated following transient transfection of three (packaging, envelope, and transfer) or more plasmids into producer cells. Like HIV, lentiviral vectors enter the target cell through the interaction of viral surface glycoproteins with receptors on the cell surface. On entry, the viral RNA undergoes reverse transcription, which is mediated by the viral reverse transcriptase complex. The product of reverse transcription is a double-stranded

linear viral DNA, which is the substrate for viral integration into the DNA of infected cells.

In certain embodiments, the viral vector can be a gammaretrovirus, *e.g.*, Moloney murine leukemia virus (MLV)-derived vectors. In other embodiments, the viral vector can be a more complex retrovirus-derived vector, *e.g.*, a lentivirus-derived vector. HIV-1-derived vectors belong to this category. Other examples include lentivirus vectors derived from HIV-2, FIV, equine infectious anemia virus, SIV, and Maedi-Visna virus (ovine lentivirus). Methods of using retroviral and lentiviral viral vectors and packaging cells for transducing mammalian host cells with viral particles containing transgenes are known in the art and have been previous described, for example, in: U.S. Patent 8,119,772; Walchli *et al.*, *PLoS One 6*:327930, 2011; Zhao *et al.*, *J. Immunol. 174*:4415, 2005; Engels *et al.*, *Hum. Gene Ther. 14*:1155, 2003; Frecha *et al.*, *Mol. Ther. 18*:1748, 2010; and Verhoeyen *et al.*, *Methods Mol. Biol. 506*:97, 2009. Retroviral and lentiviral vector constructs and expression systems are also commercially available. Other viral vectors also can be used for polynucleotide delivery including DNA viral vectors, including, for example adenovirus-based vectors and adeno-associated virus (AAV)-based vectors; vectors derived from herpes simplex viruses (HSVs), including amplicon vectors, replication-defective HSV and attenuated HSV (Krisky *et al.*, *Gene Ther. 5*:1517, 1998).

Other vectors that can be used with the compositions and methods of this disclosure include those derived from baculoviruses and α-viruses. (Jolly, D J. 1999. Emerging Viral Vectors. pp 209-40 in Friedmann T. ed. The Development of Human Gene Therapy. New York: Cold Spring Harbor Lab), or plasmid vectors (such as sleeping beauty or other transposon vectors).

When a viral vector genome comprises a plurality of polynucleotides to be expressed in a host cell as separate transcripts, the viral vector may also comprise additional sequences between the two (or more) transcripts allowing for bicistronic or multicistronic expression. Examples of such sequences used in viral vectors include internal ribosome entry sites (IRES), furin cleavage sites, viral 2A peptide, or any combination thereof.

As used herein, the term "host" refers to a cell or microorganism targeted for genetic modification with a heterologous nucleic acid molecule to produce a polypeptide of interest (*e.g.*, an antibody of the present disclosure).

A host cell may include any individual cell or cell culture which may receive a vector or the incorporation of nucleic acids or express proteins. The term also encompasses progeny of the host cell, whether genetically or phenotypically the same or different. Suitable host cells may depend on the vector and may include mammalian cells, animal cells, human cells, simian cells, insect cells, yeast cells, and bacterial cells. These cells may be induced to incorporate the vector or other material by use of a viral vector, transformation via calcium phosphate precipitation, DEAE-dextran, electroporation, microinjection, or other methods. *See*, for example, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual* 2d ed. (Cold Spring Harbor Laboratory, 1989).

As used herein, "flagellar-capping protein", also referred to as "FliD", and "hook-associated protein 2 (HAP2)", is an approximately 70 kDa protein with high sequence conservation across the *C. jejuni* and *C. coli* species (Chintoan-Uta *et al.*, *Vaccine,* 34:1739-1743 (2016)) (*e.g.*, Figure 12; SEQ ID NOs:43-95). Without wishing to be bound by theory, it is believed that *Campylobacter* FliD oligomers form a cap protein complex located at the tip of the flagellum, which controls the distal growth of the filament by regulating the assembly of the flagellin molecules. Due to its functional role in filament elongation, FliD-deficient mutants exhibit defects in bacterial motility (Song *et al., J.Mol.Biol.*, 429:847-857 (2017)). FliD has been proposed to be involved in cell adherence (Freitag *et al., Cell.Microbiol.,* (2017)) and immunogenicity in chickens during natural infection.

"Antigen" or "Ag", as used herein, refers to an immunogenic molecule that provokes an immune response. This immune response may involve antibody production, activation of specific immunologically-competent cells, activation of complement, antibody dependent cytotoxicicity, or any combination thereof. An antigen (immunogenic molecule) may be, for example, a peptide, glycopeptide, polypeptide, glycopolypeptide, polynucleotide, polysaccharide, lipid, or the like. It is

readily apparent that an antigen can be synthesized, produced recombinantly, or derived from a biological sample. Exemplary biological samples that can contain one or more antigens include tissue samples, stool samples, cells, biological fluids, or combinations thereof. Antigens can be produced by cells that have been modified or genetically engineered to express an antigen. Antigens can also be present in a *Campylobacter*; *e.g.*, a FliD protein or portion thereof.

The term "epitope" or "antigenic epitope" includes any molecule, structure, amino acid sequence, or protein determinant that is recognized and specifically bound by a cognate binding molecule, such as an immunoglobulin, or other binding molecule, domain, or protein. Epitopic determinants generally contain chemically active surface groupings of molecules, such as amino acids or sugar side chains, and can have specific three dimensional structural characteristics, as well as specific charge characteristics. Where an antigen is or comprises a peptide or protein, the epitope can be comprised of consecutive amino acids (*e.g.*, a linear epitope), or can be comprised of amino acids from different parts or regions of the protein that are brought into proximity by protein folding (*e.g.*, a discontinuous or conformational epitope), or non-contiguous amino acids that are in close proximity irrespective of protein folding.

Antibodies, Antigen-Binding Fragments, and Compositions

In one aspect, the present disclosure provides an isolated antibody, or an antigen-binding fragment thereof, that is specific for a *Campylobacter* flagellum capping protein (FliD) epitope. In certain embodiments, the epitope is a conformational epitope. In other embodiments, the epitope is a linear epitope.

An antibody or antigen-binding fragment of the present disclosure is "specific for" a FliD epitope or antigen, meaning that it associates with or unites with the epitope or antigen comprising the epitope, while not significantly associating or uniting with any other molecules or components in a sample. In certain embodiments, an antibody or antigen-binding fragment of the present disclosure associates with or unites (*e.g.*, binds) to FliD, while not significantly associating with other molecules or components (*e.g.*, other antigens or potential antigens, including other *Campylobacter* proteins) present in a sample. In certain embodiments, an antibody or antigen-binding fragment

of the present disclosure that is specific for FliD is capable of binding to the FliD epitope with an EC50 of less than about 0.1μg/mL, or less than about 0.05μg/mL, or less than about 0.03μg/mL, as measured by ELISA. In certain embodiments, the antibody or antigen-binding fragment is capable of binding to the FliD epitope with an EC50 of about 0.03μg/mL, or about 0.025μg/mL, or about 0.020μg/mL.

In certain embodiments, an antibody or antigen-binding fragment of the present disclosure is capable of binding to the FliD epitope with an EC50 of less than about 0.1μg/mL (*i.e.*, less than about 0.1, 0.09, 0.08, 0.07, 0.06, 0.05, 0.04, 0.03, 0.025, or 0.02 μg/mL, or less), as measured by ELISA (*e.g.*, with a readout of OD 450nm). In certain embodiments, an antibody or antigen-binding fragment of the present disclosure is capable of binding to the FliD epitope with an EC50 of less than about 0.05μg/mL, or less than about 0.03μg/mL, as measured by ELISA (*e.g.*, with a readout of OD 450nm).

An exemplary assay for measuring EC50 of an antibody or antigen-binding fragment for FliD includes incubating the antibody or antigen-binding fragment for about 1h at RT with FliD-pre-coated 96-well ELISA plates, and then performing detection using a biotinylated anti-Ig SC antibody followed by incubation with Streptavidin-AP.

As used herein, "specifically binds" refers to an association or union of an antibody or antigen-binding fragment to an antigen with an affinity or K_a (*i.e.*, an equilibrium association constant of a particular binding interaction with units of 1/M) equal to or greater than 10^5 M^{-1} (which equals the ratio of the on-rate [K_{on}] to the off rate [K_{off}] for this association reaction), while not significantly associating or uniting with any other molecules or components in a sample. Alternatively, affinity may be defined as an equilibrium dissociation constant (K_d) of a particular binding interaction with units of M (*e.g.*, 10^{-5} M to 10^{-13} M). Antibodies may be classified as "high-affinity" antibodies or as "low-affinity" antibodies. "High-affinity" antibodies refer to those antibodies having a K_a of at least 10^7 M^{-1}, at least 10^8 M^{-1}, at least 10^9 M^{-1}, at least 10^{10} M^{-1}, at least 10^{11} M^{-1}, at least 10^{12} M^{-1}, or at least 10^{13} M^{-1}. "Low-affinity" antibodies refer to those antibodies having a K_a of up to 10^7 M^{-1}, up to 10^6 M^{-1}, up to

10^5 M^{-1}. Alternatively, affinity may be defined as an equilibrium dissociation constant (K_d) of a particular binding interaction with units of M (*e.g.*, 10^{-5} M to 10^{-13} M).

A variety of assays are known for identifying antibodies of the present disclosure that bind a particular target, as well as determining binding domain or binding protein affinities, such as Western blot, ELISA, analytical ultracentrifugation, spectroscopy, and surface plasmon resonance (Biacore®) analysis (*see, e.g.,* Scatchard *et al.*, *Ann. N.Y. Acad. Sci. 51*:660, 1949; Wilson, *Science 295*:2103, 2002; Wolff *et al.*, *Cancer Res. 53*:2560, 1993; and U.S. Patent Nos. 5,283,173, 5,468,614, or the equivalent). Assays for assessing affinity or apparent affinity or relative affinity are also known. In certain examples, apparent affinity for an immunoglobulin binding protein is measured by assessing binding to various concentrations of tetramers, for example, by flow cytometry using labeled tetramers. In some examples, apparent K_d of an immunoglobulin binding protein is measured using 2-fold dilutions of labeled tetramers at a range of concentrations, followed by determination of binding curves by non-linear regression, apparent K_d being determined as the concentration of ligand that yielded half-maximal binding.

In certain embodiments, an antibody or antigen-binding fragment of the present disclosure is capable of reducing motility of the *Campylobacter* in an *in vitro* cell motility assay. An exemplary motility assay is illustrated schematically in FIG. 2; *see also* Riazi *et al.*, *PLoS One 8(12): e83928* (2013).

In certain embodiments, an antibody of the present disclosure is capable of neutralizing infection by one or more *Campylobacter* sp. As used herein, a "neutralizing antibody" is one that can neutralize, *i.e.*, prevent, inhibit, reduce, impede, or interfere with, the ability of a pathogen to initiate and/or perpetuate an infection in a host. The terms "neutralizing antibody" and "an antibody that neutralizes" or "antibodies that neutralize" are used interchangeably herein.

In any of the presently disclosed embodiments, the *Campylobacter* comprises *Campylobacter jejuni*, *Campylobacter coli*, or both. In certain embodiments, the *Campylobacter* comprises *C. jejuni* 81-176, *C. coli* 10092/ATB, or both.

Terms understood by those in the art of antibody technology are each given the meaning acquired in the art, unless expressly defined differently herein. For example, the term "antibody" refers to an intact antibody comprising at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds, as well as any antigen-binding portion or fragment of an intact antibody that has or retains the ability to bind to the antigen target molecule recognized by the intact antibody, such as an scFv, Fab, or Fab'2 fragment. Thus, the term "antibody" herein is used in the broadest sense and includes polyclonal and monoclonal antibodies, including intact antibodies and functional (antigen-binding) antibody fragments thereof, including fragment antigen binding (Fab) fragments, F(ab')2 fragments, Fab' fragments, Fv fragments, recombinant IgG (rIgG) fragments, single chain antibody fragments, including single chain variable fragments (scFv), and single domain antibodies (*e.g.*, sdAb, sdFv, nanobody) fragments. The term encompasses genetically engineered and/or otherwise modified forms of immunoglobulins, such as intrabodies, peptibodies, chimeric antibodies, fully human antibodies, humanized antibodies, and heteroconjugate antibodies, multispecific, *e.g.*, bispecific antibodies, diabodies, triabodies, tetrabodies, tandem di-scFv, and tandem tri-scFv. Unless otherwise stated, the term "antibody" should be understood to encompass functional antibody fragments thereof. The term also encompasses intact or full-length antibodies, including antibodies of any class or sub-class, including IgG and sub-classes thereof, IgM, IgE, IgA, and IgD.

The terms "V_L" or "VL" and "V_H" or "VH" refer to the variable binding region from an antibody light and heavy chain, respectively. In certain embodiments, a VL is a kappa (κ) class (also "VK" herein). In certain embodiments, a VL is a lambda (λ) class. The variable binding regions are made up of discrete, well-defined sub-regions known as "complementarity determining regions" (CDRs) and "framework regions" (FRs). The terms "complementarity determining region," and "CDR," are synonymous with "hypervariable region" or "HVR," and refer to sequences of amino acids within antibody variable regions, which, in general, confer the antigen specificity and/or binding affinity of the antibody, and are separated from one another by a framework region. There are three CDRs in each variable region (HCDR1, HCDR2, HCDR3;

LCDR1, LCDR2, LCDR3; also referred to as CDRHs and CDRLs, respectively). In certain embodiments, an antibody VH comprises four FRs and three CDRs as follows: FR1-HCDR1-FR2-HCDR2-FR3-HCDR3-FR4; and an antibody VL comprises four FRs and three CDRs as follows: FR1-LCDR1-FR2-LCDR2-FR3-LCDR3-FR4. In general, the VH and the VL together form the antigen-binding site through their respective CDRs.

As used herein, a "variant" of a CDR refers to a functional variant of a CDR sequence having up to 1-3 amino acid substitutions (*e.g.*, conservative or non-conservative substitutions), deletions, or combinations thereof.

Numbering of CDR and framework regions may be according to any known method or scheme, such as the Kabat, Chothia, EU, IMGT, and AHo numbering schemes (*see*, *e.g.*, Kabat *et al.*, "Sequences of Proteins of Immunological Interest, US Dept. Health and Human Services, Public Health Service National Institutes of Health, 1991, 5th ed.; Chothia and Lesk, *J. Mol. Biol. 196*:901-917 (1987)); Lefranc *et al.*, *Dev. Comp. Immunol. 27*:55, 2003; Honegger and Plückthun, *J. Mol. Bio. 309*:657-670 (2001)). Equivalent residue positions can be annotated and for different molecules to be compared using Antigen receptor Numbering And Receptor Classification (ANARCI) software tool (2016, Bioinformatics 15:298-300).

In certain embodiments, an antibody or antigen-binding fragment of the present disclosure comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 amino acid sequences according to: (i) SEQ ID NOs:9-14, respectively; or (ii) SEQ ID NOs:25-30, respectively.

The term "CL" refers to an "immunoglobulin light chain constant region" or a "light chain constant region," *i.e.*, a constant region from an antibody light chain. The term "CH" refers to an "immunoglobulin heavy chain constant region" or a "heavy chain constant region," which is further divisible, depending on the antibody isotype into CH1, CH2, and CH3 (IgA, IgD, IgG), or CH1, CH2, CH3, and CH4 domains (IgE, IgM).

A "Fab" (fragment antigen binding) is the part of an antibody that binds to antigens and includes the variable region and CH1 of the heavy chain linked to the light

chain via an inter-chain disulfide bond. Each Fab fragment is monovalent with respect to antigen binding, *i.e.*, it has a single antigen-binding site. Pepsin treatment of an antibody yields a single large F(ab')2 fragment that roughly corresponds to two disulfide linked Fab fragments having divalent antigen-binding activity and is still capable of cross-linking antigen. Both the Fab and F(ab')2 are examples of "antigen-binding fragments." Fab' fragments differ from Fab fragments by having additional few residues at the carboxy terminus of the CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. F(ab')2 antibody fragments originally were produced as pairs of Fab' fragments that have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

"Fv" is the minimum antibody fragment that contains a complete antigen-recognition and antigen-binding site. This fragment consists of a dimer of one heavy- and one light-chain variable region domain in tight, non-covalent association. From the folding of these two domains emanate six hypervariable loops (three loops each from the H and L chain) that contribute the amino acid residues for antigen binding and confer antigen binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although typically at a lower affinity than the entire binding site.

"Single-chain Fv" also abbreviated as "sFv" or "scFv", are antibody fragments that comprise the V_H and V_L antibody domains connected into a single polypeptide chain. Preferably, the sFv polypeptide further comprises a polypeptide linker between the V_H and V_L domains that enables the sFv to form the desired structure for antigen binding. For a review of sFv, see Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994); Borrebaeck 1995, *infra*.

During antibody development, DNA in the germline variable (V), joining (J), and diversity (D) gene loci may be rearranged and insertions and/or deletions of nucleotides in the coding sequence may occur. Somatic mutations may be encoded by

the resultant sequence, and can be identified by reference to a corresponding known germline sequence. In some contexts, somatic mutations that are not critical to a desired property of the antibody (*e.g.*, specific binding to a *Campylobacter* sp.), or that confer an undesirable property upon the antibody (*e.g.*, an increased risk of immunogenicity in a subject administered the antibody), or both, may be replaced by the corresponding germline-encoded amino acid, or by a different amino acid, so that a desirable property of the antibody is improved or maintained and the undesirable property of the antibody is reduced or abrogated. Thus, in some embodiments, the antibody or antigen-binding fragment of the present disclosure comprises at least one more germline-encoded amino acid in a variable region as compared to a parent antibody or antigen binding fragment, provided that the parent antibody or antigen binding fragment comprises one or more somatic mutations. Variable region amino acid sequences of exemplary anti-*Campylobacter* antibodies of the present disclosure are provided in Table 1 herein, wherein somatic mutations are shown by underlining.

Also provided herein are variant antibodies that comprise one or more amino acid alterations in a variable region (*e.g.*, VH, VL, framework or CDR) as compared to a presently disclosed ("parent") antibody, wherein the variant antibody is capable of specifically binding to a *Campylobacter* FliD epitope with an affinity similar to or stronger than the parent antibody. For example, in some embodiments, an antibody or antigen-binding fragment of the present disclosure comprises a heavy chain variable domain (VH) having at least 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to the amino acid sequence of SEQ ID NO:2 or 22, and a light chain variable domain (VL) having at least 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to the amino acid sequence of SEQ ID NO:4 or 24, provided that the variant antibody or antigen-binding fragment specifically binds a *Campylobacter* FliD epitope with an affinity similar to or better than a parent antibody having a VH according to SEQ ID NO:2 or 22 and a VL according to SEQ ID NO:4 or 24, respectively.

In certain embodiments, the antibody or antigen-binding fragment can comprise: (i) VH having at least 85% (*i.e.*, at least 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97,

98, 99, or more) amino acid identity to SEQ ID NO:2, and a VL having at least 85% (*i.e.*, at least 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or more) amino acid identity to SEQ ID NO:4; or (ii) VH having at least 85% amino acid identity to SEQ ID NO:22, and a VL having at least 85% amino acid identity to SEQ ID NO:24.

In further embodiments, the antibody or antigen-binding fragment comprises: (i) a VH according to SEQ ID NO:2, and a VL according to SEQ ID NO:4; or (ii) a VH according to SEQ ID NO:22, and a VL according to SEQ ID NO:24.

In any of the presently disclosed embodiments, the antibody or antigen-binding fragment is multispecific; *e.g.*, bispecific, trispecific, or the like.

In any of the presently disclosed embodiments, the antibody or antigen-binding fragment is an IgA, IgG, IgD, IgE, or IgM isotype.

In certain embodiments, the antibody or antigen-binding fragment is an IgA isotype. In humans, IgA antibodies are found in monomeric, dimeric, or tetrameric forms. IgA subclasses include IgA1 and IgA2. IgA1 has a longer hinge sequence (between the Fab arms and the Fc) than IgA2. *See*, *e.g.*, Woof and Kerr, *Immunology 113*(2):175-177 (2004)).

Without wishing to be bound by theory, IgA dimers generally comprise two IgA monomers linked together by at least a joining chain ("J-chain") polypeptide formed in IgA-secreting cells. Soluble IgA dimers are generally capable of forming a complex with poly-Ig receptor ("pIgR") proteins found on the basolateral surface of epithelial cells. Following formation, the IgA dimer-pIgR complex is internalized into the epithelial cell and transported to the luminal surface for release into the lumen. Prior to secretion into the lumen, a portion of the pIgR is cleaved, while a portion known as the secretory component or "SC" remains bound to the IgA, forming secretory IgA (SIgA). Without wishing to be bound by theory, the SC is believed to improve stability of the IgA dimer in the vesicular and luminal environments, possibly by protecting proteolytically sensitive sites in the IgA dimer.

In certain embodiments, an antibody or antigen-binding fragment of the present disclosure is an IgA1 isotype or an IgA2 isotype.

In certain embodiments, an antibody or antigen-binding fragment of the present disclosure comprises an IgA dimer molecule.

In certain embodiments, an antibody or antigen-binding fragment of the present disclosure comprises a secretory IgA molecule.

The "Fc" fragment or Fc polypeptide comprises the carboxy-terminal portions (*i.e.*, the CH2 and CH3 domains of IgG) of both antibody H chains held together by disulfides. The effector functions of antibodies are determined by sequences in the Fc region. The Fc domain is the portion of the antibody recognized by cell receptors, such as the FcRs, and to which the complement-activating protein, C1q, binds. As discussed herein, modifications (*e.g.*, amino acid substitutions) may be made to an Fc domain in order to modify (*e.g.*, improve, reduce, or ablate) one or more functionality of an Fc-containing polypeptide (*e.g.*, an antibody of the present disclosure). In any of the presently disclosed embodiments, the antibody or antigen-binding fragment comprises a Fc polypeptide or a fragment thereof, including a CH2 (or a fragment thereof, a CH3 (or a fragment thereof), or a CH2 and a CH3, wherein the CH2, the CH3, or both can be of any isotype and may contain amino acid substitutions or other modifications as compared to a corresponding wild-type CH2 or CH3, respectively. In certain embodiments, a Fc polypeptide of the present disclosure comprises two CH2-CH3 polypeptides that associate to form a dimer.

In certain embodiments, the antibody or antigen-binding fragment of comprises a heavy chain constant region having at least 90% identity (*i.e.*, at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity to any one of SEQ ID NOs:40-42.

In any of the presently disclosed embodiments, the antibody or antigen-binding fragment is monoclonal. The term "monoclonal antibody" (mAb) as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, *i.e.*, individual antibodies comprising the population are identical except for possible naturally occurring mutations that may be present, in some cases in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. Furthermore, in contrast to polyclonal antibody preparations that include different

antibodies directed against different epitopes, each monoclonal antibody is directed against a single epitope of the antigen. In addition to their specificity, the monoclonal antibodies are advantageous in that they may be synthesized uncontaminated by other antibodies. The term "monoclonal" is not to be construed as requiring production of the antibody by any particular method. For example, monoclonal antibodies useful in the present invention may be prepared by the hybridoma methodology first described by Kohler *et al.*, *Nature 256*:495 (1975), or may be made using recombinant DNA methods in bacterial, eukaryotic animal, or plant cells (*see*, *e.g.*, U.S. Pat. No. 4,816,567). Monoclonal antibodies may also be isolated from phage antibody libraries using the techniques described in Clackson *et al.*, *Nature*, *352*:624-628 (1991) and Marks *et al.*, *J. Mol. Biol.*, *222*:581-597 (1991), for example. Monoclonal antibodies may also be obtained using methods disclosed in PCT Publication No. WO 2004/076677A2.

Antibodies and antigen-binding fragments of the present disclosure include "chimeric antibodies" in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical with or homologous to corresponding sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they exhibit the desired biological activity (*see,* U.S. Pat. Nos. 4,816,567; 5,530,101 and 7,498,415; and Morrison *et al.*, Proc. Natl. Acad. Sci. USA, *81*:6851-6855 (1984)). For example, chimeric antibodies may comprise human and non-human residues. Furthermore, chimeric antibodies may comprise residues that are not found in the recipient antibody or in the donor antibody. These modifications are made to further refine antibody performance. For further details, see Jones *et al.*, *Nature* 321:522-525 (1986); Riechmann *et al.*, *Nature* 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol. 2*:593-596 (1992). Chimeric antibodies also include primatized and humanized antibodies.

A "humanized antibody" is generally considered to be a human antibody that has one or more amino acid residues introduced into it from a source that is non-human.

These non-human amino acid residues are typically taken from a variable domain. Humanization may be performed following the method of Winter and co-workers (Jones *et al.*, *Nature*, 321:522-525 (1986); Reichmann *et al.*, *Nature*, 332:323-327 (1988); Verhoeyen *et al.*, *Science*, 239:1534-1536 (1988)), by substituting non-human variable sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Pat. Nos. 4,816,567; 5,530,101 and 7,498,415) wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In some instances, a "humanized" antibody is one which is produced by a non-human cell or animal and comprises human sequences, *e.g.*, H_C domains.

A "human antibody" is an antibody containing only sequences that are present in an antibody that is produced by a human. However, as used herein, human antibodies may comprise residues or modifications not found in a naturally occurring human antibody (*e.g.*, an antibody that is isolated from a human), including those modifications and variant sequences described herein. These are typically made to further refine or enhance antibody performance. In some instances, human antibodies are produced by transgenic animals. For example, *see* U.S. Pat. Nos. 5,770,429; 6,596,541 and 7,049,426.

In certain embodiments, an antibody or antigen-binding fragment of the present disclosure is chimeric, humanized, or human.

Also provided herein are compositions that comprise any antibody or antigen-binding fragment as disclosed herein, and a pharmaceutically acceptable carrier, excipient, or diluent. Pharmaceutically acceptable components for use in such compositions are discussed further herein.

In another aspect, the present disclosure provides kits, wherein a kit, comprises: (i) a first antibody or an antigen-binding fragment thereof, which is specific for a Campylobacter flagellum capping protein (FliD) linear epitope; and (ii) a second antibody or an antigen-binding fragment thereof, which is which is specific for a Campylobacter flagellum capping protein (FliD) conformational epitope.

In certain embodiments, (i) the first antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 sequences according to SEQ ID NOs:9-14, respectively; and (ii) the second antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 sequences according to SEQ ID NOs:25-30, respectively.

In certain embodiments, (i) the first antibody or antigen-binding fragment comprises a VH having at least 85% amino acid identity to SEQ ID NO:2, and a VL having at least 85% amino acid identity to SEQ ID NO:4; and (ii) the second antibody or antigen-binding fragment comprises a VH having at least 85% amino acid identity to SEQ ID NO:22, and a VL having at least 85% amino acid identity to SEQ ID NO:24. In further embodiments: (i) the first antibody or antigen-binding fragment comprises a VH according to SEQ ID NO:2, and a VL according to SEQ ID NO:4; and (ii) the second antibody or antigen-binding fragment comprises a VH according to SEQ ID NO:22, and a VL according to SEQ ID NO:24.

In certain embodiments, the first antibody or antigen-binding fragment and the second antibody or antigen-binding fragment of a kit are each a same isotype. In particular embodiments, the first antibody or antigen-binding fragment and the second antibody or antigen-binding fragment are each a secreted IgA.

In certain embodiments, a kit further comprises directions or instructions on using the first and second antibodies or antigen-binding fragments; *e.g.*, to treat or diagnose a *Campylobacter* infection in a subject.

Polynucleotides, Vectors, and Host cells

In another aspect, the present disclosure provides isolated polynucleotides that encode any of the presently disclosed antibodies or an antigen-binding fragment thereof. In certain embodiments, the polynucleotide is codon-optimized for expression in a host cell. Once a coding sequence is known or identified, codon optimization can be performed using known techniques and tools, *e.g.*, using the GenScript® OptimiumGene™ tool; *see also* Scholten *et al.*, *Clin. Immunol. 119*:135, 2006). Codon-optimized sequences include sequences that are partially codon-optimized (*i.e.*,

one or more codon is optimized for expression in the host cell) and those that are fully codon-optimized.

It will also be appreciated that polynucleotides encoding antibodies and antigen-binding fragments of the present disclosure may possess different nucleotide sequences while still encoding a same antibody or antigen-binding fragment due to, for example, the degeneracy of the genetic code, splicing, and the like.

In certain embodiments, an isolated polynucleotide encoding a FliD-specific antibody or antigen-binding fragment comprises: (i) a VH-encoding polynucleotide having at least 75% identity (*i.e.*, at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or at least 99% sequence identity) to the nucleotide sequence set forth in any one of SEQ ID NOs:1, 5, 7, 8, 21, 37, or 38; (ii) a VL-encoding polynucleotide having at least 75% identity to the nucleotide sequence set forth in SEQ ID NO:3, 6, 23, or 39; and/or (iii) HCDR1-, HCDR2-, HCDR3-, LCDR1-, LCDR2-, and LCDR3-encoding sequences having at least 90% identity to the nucleotide sequences set forth in SEQ ID NOs:15-20, respectively, or in SEQ ID NOs:31-36, respectively.

Vectors are also provided, wherein the vectors comprise or contain a polynucleotide as disclosed herein (*i.e.*, a polynucleotide that encodes a FliD-specific antibody or antigen-binding fragment). A vector can comprise any one or more of the vectors disclosed herein.

In a further aspect, the present disclosure also provides a host cell expressing an antibody or antigen-binding fragment according to the present disclosure; or comprising or containing a vector or polynucleotide according the present disclosure.

Examples of such cells include but are not limited to, eukaryotic cells, *e.g.*, yeast cells, animal cells, insect cells, plant cells; and prokaryotic cells, including *E. coli*. In some embodiments, the cells are mammalian cells. In certain such embodiments, the cells are a mammalian cell line such as CHO cells (*e.g.*, DHFR- CHO cells (Urlaub *et al., PNAS 77*:4216 (1980)), human embryonic kidney cells (*e.g.*, HEK293T cells), PER.C6 cells, Y0 cells, Sp2/0 cells. NS0 cells, human liver cells, e.g. Hepa RG cells, myeloma cells or hybridoma cells. Other examples of mammalian host cell lines

include mouse sertoli cells (*e.g.*, TM4 cells); monkey kidney CV1 line transformed by SV40 (COS-7); baby hamster kidney cells (BHK); African green monkey kidney cells (VERO-76); monkey kidney cells (CV1); human cervical carcinoma cells (HELA); human lung cells (W138); human liver cells (Hep G2); canine kidney cells (MDCK; buffalo rat liver cells (BRL 3A); mouse mammary tumor (MMT 060562); TRI cells; *MRC* 5 cells; and FS4 cells. Mammalian host cell lines suitable for antibody production also include those described in, for example, Yazaki and Wu, *Methods in Molecular Biology*, Vol. 248 (B. K. C. Lo, ed., Humana Press, Totowa, N.J.), pp. 255-268 (2003).

In certain embodiments, a host cell is a prokaryotic cell, such as an *E. coli*. The expression of peptides in prokaryotic cells such as *E. coli* is well established (*see*, *e.g.*, Pluckthun, A. *Bio/Technology 9:*545-551 (1991). For example, antibodies may be produced in bacteria, in particular when glycosylation and Fc effector function are not needed. For expression of antibody fragments and polypeptides in bacteria, *see, e.g.*, U.S. Pat. Nos. 5,648,237; 5,789,199; and 5,840,523.

In particular embodiments, the cell may be transfected with a vector according to the present description with an expression vector. The term "transfection" refers to the introduction of nucleic acid molecules, such as DNA or RNA (e.g. mRNA) molecules, into cells, such as into eukaryotic cells. In the context of the present description, the term "transfection" encompasses any method known to the skilled person for introducing nucleic acid molecules into cells, such as into eukaryotic cells, including into mammalian cells. Such methods encompass, for example, electroporation, lipofection, *e.g.*, based on cationic lipids and/or liposomes, calcium phosphate precipitation, nanoparticle based transfection, virus based transfection, or transfection based on cationic polymers, such as DEAE-dextran or polyethylenimine, *etc*. In certain embodiments, the introduction is non-viral.

Moreover, host cells of the present disclosure may be transfected stably or transiently with a vector according to the present disclosure, *e.g.* for expressing an antibody, or an antigen-binding fragment thereof, according to the present disclosure. In such embodiments, the cells may be stably transfected with the vector as described

herein. Alternatively, cells may be transiently transfected with a vector according to the present disclosure encoding an antibody or antigen-binding fragment as disclosed herein. In any of the presently disclosed embodiments, a polynucleotide may be heterologous to the host cell.

Accordingly, the present disclosure also provides recombinant host cells that heterologously express an antibody or antigen-binding fragment of the present disclosure. For example, the cell may be of a species that is different to the species from which the antibody was fully or partially obtained (*e.g.*, CHO cells expressing a human antibody or an engineered human antibody). In some embodiments, the cell type of the host cell does not express the antibody or antigen-binding fragment in nature. Moreover, the host cell may impart a post-translational modification (PTM; *e.g.*, glysocylation or fucosylation) on the antibody or antigen-binding fragment that is not present in a native state of the antibody or antigen-binding fragment (or in a native state of a parent antibody from which the antibody or antigen binding fragment was engineered or derived). Such a PTM may result in a functional difference (*e.g.*, reduced immunogenicity). Accordingly, an antibody or antigen-binding fragment of the present disclosure that is produced by a host cell as disclosed herein may include one or more post-translational modification that is distinct from the antibody (or parent antibody) in its native state (*e.g.*, a human antibody produced by a CHO cell can comprise a more post-translational modification that is distinct from the antibody when isolated from the human and/or produced by the native human B cell or plasma cell).

Insect cells useful expressing a binding protein of the present disclosure are known in the art and include, for example, *Spodoptera frugipera* Sf9 cells, Trichoplusia ni BTI-TN5B1-4 cells, and *Spodoptera frugipera* SfSWT01 "Mimic^{TM}" cells. *See*, *e.g.*, Palmberger *et al.*, *J. Biotechnol. 153*(3-4):160-166 (2011). Numerous baculoviral strains have been identified which may be used in conjunction with insect cells, particularly for transfection of *Spodoptera frugiperda* cells.

Eukaryotic microbes such as filamentous fungi or yeast are also suitable hosts for cloning or expressing protein-encoding vectors, and include fungi and yeast strains with "humanized" glycosylation pathways, resulting in the production of an antibody

with a partially or fully human glycosylation pattern. *See* Gerngross, *Nat. Biotech.* 22:1409-1414 (2004); Li *et al.*, *Nat. Biotech.* 24:210-215 (2006).

Plant cells can also be utilized as hosts for expressing a binding protein of the present disclosure. For example, PLANTIBODIES™ technology (described in, for example, U.S. Pat. Nos. 5,959,177; 6,040,498; 6,420,548; 7,125,978; and 6,417,429) employs transgenic plants to produce antibodies.

In certain embodiments, the host cell comprises a mammalian cell. In particular embodiments, the host cell is a CHO cell, a HEK293 cell, a PER.C6 cell, a Y0 cell, a Sp2/0 cell, a NS0 cell, a human liver cell, a myeloma cell, or a hybridoma cell.

In a related aspect, the present disclosure provides methods for producing an antibody, antigen binding fragment, wherein the methods comprise culturing a host cell of the present disclosure under conditions and for a time sufficient to produce the antibody, or the antigen-binding fragment. Methods useful for isolating and purifying recombinantly produced antibodies, by way of example, may include obtaining supernatants from suitable host cell/vector systems that secrete the recombinant antibody into culture media and then concentrating the media using a commercially available filter. Following concentration, the concentrate may be applied to a single suitable purification matrix or to a series of suitable matrices, such as an affinity matrix or an ion exchange resin. One or more reverse phase HPLC steps may be employed to further purify a recombinant polypeptide. These purification methods may also be employed when isolating an immunogen from its natural environment. Methods for large scale production of one or more of the isolated/recombinant antibody described herein include batch cell culture, which is monitored and controlled to maintain appropriate culture conditions. Purification of soluble antibodies may be performed according to methods described herein and known in the art and that comport with laws and guidelines of domestic and foreign regulatory agencies.

Model of Campylobacter infection

In yet another aspect, the present disclosure provides animal models for investigating *Campylobacter* infection and pathogenesis, as well as potential therapies and research reagents.

Briefly, existing animal models for studying *Campylobacter* pathogensis have numerous drawbacks, such as high cost and intensive care settings (*e.g.*, gnotobiotic or germ-free animals), resistance to intestinal colonization by *Campylobacter* (*e.g.*, laboratory mice), and unpredictable or deleterious effects of transgenic animals (*e.g.*, SIGIRR or IL10$^{-/-}$ mice). As described in the Examples, it was found that recently weaned animals (mice 21 days of age) that are no longer receiving maternal antibodies but do not possess a mature gastrointestinal immune system, and have a depleted intestinal flora, are surprisingly susceptible to infection by *Campylobacter*; thus, providing an improved model for studying *Campylobacter* pathogenesis and potential treatments thereof.

In certain embodiments, a non-human mammal is provided, wherein the non-human mammal comprises a weaned mammal that: (i) does not have a mature gastrointestinal immune system, and (ii) has a depleted intestinal flora, wherein the depletion is caused by an antibiotic agent. In certain embodiments, the non-human mammal further comprises a *Campylobacter* infection.

In certain embodiments, a non-human mammal of the present disclosure is or comprises a mouse (*e.g.*, a C57BL/6 mouse), a rat, a pig, a rabbit, a dog, a cat, a guinea pig, a hamster, a non-human primate (*e.g.*, cynomolgus), or the like. A non-human mammal that has been weaned is no longer receiving nutrients via milk from a mother mammal (*i.e.*, the mother that gave birth to the non-human mammal, or a surrogate mother).

A mature gastrointestinal immune system according to the present disclosure is one that is capable of a functional endogenous immune activity (*e.g.*, mucosal protection) against an antigen or pathogen. For example, a mature gastrointestinal immune system processes antigens from via microfold cells, dendritic cells, and macrophages for presentation to T cells in the gut-associated lymphoid tissue, and produces antigen-neutralizing IgA immunoglobulins by via B cells. *See*, *e.g.*, Gutzeit *et al.*, *Immunol. Rev. 260*(2):76-85 (2014). In certain embodiments, a non-human mammal as disclosed herein does not endogenously produce IgA immunoglobulins, or produces a reduced amount of IgA immunoglobulins as compared to a reference healthy

non-human mammal (*i.e.*, of the same species) that is of an age and/or developmental stage at which the gastrointestinal immune system is considered to be mature and functional. A mature gastrointestinal immune system typically arises naturally with age in a healthy animal; *e.g.*, healthy adult mice (56 days) have a mature gastrointestinal immune system.

It is understood that commensal bacteria (also referred collectively to as the "flora" or "microbiota") inhabit the intestine, conferring upon the host various defensive and metabolic capabilities (*see* Gutzeit *et al.*, *Immunol. Rev. 260*(2):76-85 (2014)). The flora may prevent or inhibit colonization by pathogens, such as *Campylobacter*. A depleted intestinal flora is one that has a statistically significant reduction in one or more of the following: the overall number of bacteria; a growth rate of one or more of the bacteria; a metabolic function of the bacteria; a defensive function of the bacteria; and/or a diversity of bacteria, as compared to an intestinal flora of a healthy reference non-human mammal (*i.e.*, of the same species and the same age, or of about the same age).

The age or developmental stage at which such a non-human mammal may be weaned by separation from the mother will be in accordance with the relevant animal care standards and the known biology of the organism. For example, mice may be weaned at about 15 days, about 16 days, about 17 days, about 18 days, about 19 days, about 20 days, about 21 days, about 22 days, about 23 days, about 24 days, about 25 days, about 26 days, about 27 days, about 28 days, about 29 days, or about 30 days after birth, or later. In certain embodiments, a weaned mouse is 18 days, 19 days, 20 days, 21 days, 22 days, 23 days, or 24 days old, or older. In certain embodiments, a non-human mammal is selected at an age or developmental stage that is less than the age, or is of an earlier developmental stage, respectively, than the age or developmental stage by which the non-human mammal will possess a mature gastrointestinal immune system. In other embodiments, a non-human mammal may be manipulated (*e.g.*, genetically or otherwise) to delay or prevent development of a mature gastrointestinal immune system. It will be understood that a gastrointestinal immune system may mature over time; accordingly, in preferred embodiments, a non-human mammal is

recently weaned. A recently weaned mammal is a mammal that has been weaned for from about 1 to about 10 days.

A non-human mammal according to the present disclosure has a depleted intestinal flora. Bacteria number, growth rate, metabolic function, defensive function, and diversity can be determined, and compared to a reference, using methods known to a person of ordinary skill in the art.

Intestinal flora can be depleted, for example, by administration of antibiotic agent. Exemplary antibiotic agents include vancomycin and other glycopeptide antibiotics, trimethoprim, ampicillin, metronidazole, and streptomycin, and analogs thereof, and combinations thereof. In preferred embodiments, the antibiotic agent is or comprises an agent to which *Campylobacter* have resistance; *e.g.*, vancomycin or an analog thereof. Dosing and administration of an antibiotic agent to deplete an intestinal flora can be determined in accordance with known principles, accounting for, *e.g.*, the age, size, and/or health of the non-human mammal, and the desired effect.

In further embodiments, the non-human mammal further comprises a *Camplyobacter* (*e.g.*, a *Camplyobacter* of interest, such as a *C. jejuni*, a *C. coli*, or both). *Campylobacter* can be administered, for example, orally (*e.g.*, via gavage), in an amount sufficient to form colonies in the intestine. For example, mice aged 12, 21, or 56 days are innoculated with 10^8 to 10^9 *Campylobacter*. In certain embodiments, the *Campylobacter* introduced to the non-human mammal comprises about 10^5, about 5 x 10^5, about 10^6, about 5 x 10^6, about 10^7, about 5 x 10^7, about 10^8, about 5 x 10^8, about 10^9, about 5 x 10^9, about 10^{10}, about 5 x 10^5, about 10^{11}, about 5 x 10^{11}, or about 10^{12} *Campylobacter*, or more. Once administered, the number of *Campylobacter* may grow to a greater number in the non-human mammal host.

In a related aspect, methods are provided that comprise administering to or inoculating a weaned non-human mammal that (i) does not have a mature gastrointestinal immune system, and (ii) has a depleted intestinal flora with a *Camplyobacter* in an amount sufficient to cause an intestinal infection in the non-human mammal.

In another aspect, methods are provided that comprise administering to a non-human mammal that (i) is weaned, and (ii) does not have a mature gastrointestinal immune system, an agent that depletes an intestinal flora of the non-human mammal. In certain embodiments, the agent comprises an antibiotic agent as disclosed herein, such as, for example, vancomycin or an analog thereof. In certain embodiments, the method further comprises adminsistering to the non-human mammal, or inoculating the non-human mammal with, a *Camplyobacter* in an amount sufficient to cause an intestinal infection comprising *Campylobacter* in the non-human mammal.

Methods and Uses

Also provided herein are methods of treating a subject using an antibody or antigen-binding fragment of the present disclosure, or a composition comprising the same, wherein the subject has, is believed to have, or is at risk for having an infection by a *Campylobacter* sp. "Treat," "treatment," or "ameliorate" refers to medical management of a disease, disorder, or condition of a subject (*e.g.*, a human or non-human mammal, such as a primate, horse, cat, dog, goat, mouse, or rat). In general, an appropriate dose or treatment regimen comprising an antibody or composition of the present disclosure is administered in an amount sufficient to elicit a therapeutic or prophylactic benefit. Therapeutic or prophylactic/preventive benefit includes improved clinical outcome; lessening or alleviation of symptoms associated with a disease; decreased occurrence of symptoms; improved quality of life; longer disease-free status; diminishment of extent of disease, stabilization of disease state; delay of disease progression; remission; survival; prolonged survival; or any combination thereof.

A "therapeutically effective amount" or "effective amount" of an antibody, antigen-binding fragment, or composition of this disclosure refers to an amount of the composition or molecule sufficient to result in a therapeutic effect, including improved clinical outcome; lessening or alleviation of symptoms associated with a disease; decreased occurrence of symptoms; improved quality of life; longer disease-free status; diminishment of extent of disease, stabilization of disease state; delay of disease progression; remission; survival; or prolonged survival in a statistically significant manner. When referring to an individual active ingredient, administered alone, a

therapeutically effective amount refers to the effects of that ingredient or cell expressing that ingredient alone. When referring to a combination, a therapeutically effective amount refers to the combined amounts of active ingredients or combined adjunctive active ingredient with a cell expressing an active ingredient that results in a therapeutic effect, whether administered serially, sequentially, or simultaneously. A combination may comprise, for example, two different antibodies that specifically bind a *Campylobacter* sp. epitope (*e.g.*, a FliD epitope), which in certain embodiments, may be the same or different *Campylobacter* sp., and/or can comprise the same or different epitopes.

Accordingly, in certain embodiments, methods are provided for treating a *Campylobacter* infection in a subject, wherein the methods comprise administering to the subject an effective amount of an antibody, antigen-binding fragment, or composition as disclosed herein.

In certain embodiments, methods are provided for reducing (*i.e.*, reducing or completely abrogating) intestinal inflammation in a subject having a *Campylobacter* infection, wherein the methods comprise administering to the subject an effective amount of an antibody, antigen-binding fragment, or composition as disclosed herein.

In certain embodiments, methods are provided for increasing intestinal shedding of a *Campylobacter* by a subject having a *Campylobacter* infection, wherein the methods comprise administering to the subject an effective amount of an antibody, antigen-binding fragment, or composition as disclosed herein.

In any of the presently disclosed embodiments, the antibody or antigen-binding fragment comprises a secretory IgA molecule.

Subjects that can be treated by the present disclosure are, in general, human and other primate subjects, such as monkeys and apes for veterinary medicine purposes. Other model organisms, such as mice and rats, may also be treated according to the present disclosure. In any of the aforementioned embodiments, the subject may be a human subject. The subjects can be male or female and can be any suitable age, including infant, juvenile, adolescent, adult, and geriatric subjects.

Typical routes of administering the presently disclosed compositions thus include, without limitation, oral, topical, transdermal, inhalation, parenteral, sublingual, buccal, rectal, vaginal, and intranasal. The term "parenteral", as used herein, includes subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques. In certain embodiments, administering comprises administering by a route that is selected from oral, intravenous, parenteral, intragastric, intrapleural, intrapulmonary, intrarectal, intradermal, intraperitoneal, intratumoral, subcutaneous, topical, transdermal, intracisternal, intrathecal, intranasal, and intramuscular. In particular embodiments, a method comprises orally administering the antibody, antigen-binding fragment, or composition to the subject.

Pharmaceutical compositions according to certain embodiments of the present invention are formulated so as to allow the active ingredients contained therein to be bioavailable upon administration of the composition to a patient. Compositions that will be administered to a subject or patient may take the form of one or more dosage units, where for example, a tablet may be a single dosage unit, and a container of a herein described an antibody or antigen-binding in aerosol form may hold a plurality of dosage units. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, *see* Remington: The Science and Practice of Pharmacy, 20th Edition (Philadelphia College of Pharmacy and Science, 2000). The composition to be administered will, in any event, contain an effective amount of an antibody or antigen-binding fragment thereof of the present disclosure, for treatment of a disease or condition of interest in accordance with teachings herein.

A composition may be in the form of a solid or liquid. In some embodiments, the carrier(s) are particulate, so that the compositions are, for example, in tablet or powder form. The carrier(s) may be liquid, with the compositions being, for example, an oral oil, injectable liquid or an aerosol, which is useful in, for example, inhalatory administration. When intended for oral administration, the pharmaceutical composition is preferably in either solid or liquid form, where semi solid, semi liquid, suspension and gel forms are included within the forms considered herein as either solid or liquid.

As a solid composition for oral administration, the pharmaceutical composition may be formulated into a powder, granule, compressed tablet, pill, capsule, chewing gum, wafer or the like. Such a solid composition will typically contain one or more inert diluents or edible carriers. In addition, one or more of the following may be present: binders such as carboxymethylcellulose, ethyl cellulose, microcrystalline cellulose, gum tragacanth or gelatin; excipients such as starch, lactose or dextrins, disintegrating agents such as alginic acid, sodium alginate, Primogel, corn starch and the like; lubricants such as magnesium stearate or Sterotex; glidants such as colloidal silicon dioxide; sweetening agents such as sucrose or saccharin; a flavoring agent such as peppermint, methyl salicylate or orange flavoring; and a coloring agent. When the composition is in the form of a capsule, for example, a gelatin capsule, it may contain, in addition to materials of the above type, a liquid carrier such as polyethylene glycol or oil.

The composition may be in the form of a liquid, for example, an elixir, syrup, solution, emulsion or suspension. The liquid may be for oral administration or for delivery by injection, as two examples. When intended for oral administration, preferred compositions contain, in addition to the present compounds, one or more of a sweetening agent, preservatives, dye/colorant and flavor enhancer. In a composition intended to be administered by injection, one or more of a surfactant, preservative, wetting agent, dispersing agent, suspending agent, buffer, stabilizer and isotonic agent may be included.

Liquid pharmaceutical compositions, whether they be solutions, suspensions or other like form, may include one or more of the following adjuvants: sterile diluents such as water for injection, saline solution, preferably physiological saline, Ringer's solution, isotonic sodium chloride, fixed oils such as synthetic mono or diglycerides which may serve as the solvent or suspending medium, polyethylene glycols, glycerin, propylene glycol or other solvents; antibacterial agents such as benzyl alcohol or methyl paraben; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The

parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic. Physiological saline is a preferred adjuvant. An injectable pharmaceutical composition is preferably sterile.

A liquid composition intended for either parenteral or oral administration should contain an amount of an antibody or antigen-binding fragment as herein disclosed such that a suitable dosage will be obtained. Typically, this amount is at least 0.01% of the antibody or antigen-binding fragment in the composition. When intended for oral administration, this amount may be varied to be between 0.1 and about 70% of the weight of the composition. Certain oral pharmaceutical compositions contain between about 4% and about 75% of the antibody or antigen-binding fragment. In certain embodiments, pharmaceutical compositions and preparations according to the present invention are prepared so that a parenteral dosage unit contains between 0.01 to 10% by weight of antibody or antigen-binding fragment prior to dilution.

The composition may be intended for topical administration, in which case the carrier may suitably comprise a solution, emulsion, ointment or gel base. The base, for example, may comprise one or more of the following: petrolatum, lanolin, polyethylene glycols, bee wax, mineral oil, diluents such as water and alcohol, and emulsifiers and stabilizers. Thickening agents may be present in a composition for topical administration. If intended for transdermal administration, the composition may include a transdermal patch or iontophoresis device. The pharmaceutical composition may be intended for rectal administration, in the form, for example, of a suppository, which will melt in the rectum and release the drug. The composition for rectal administration may contain an oleaginous base as a suitable nonirritating excipient. Such bases include, without limitation, lanolin, cocoa butter and polyethylene glycol.

A composition may include various materials which modify the physical form of a solid or liquid dosage unit. For example, the composition may include materials that form a coating shell around the active ingredients. The materials that form the coating shell are typically inert, and may be selected from, for example, sugar, shellac, and other enteric coating agents. Alternatively, the active ingredients may be encased in a gelatin capsule. The composition in solid or liquid form may include an agent that

binds to the antibody or antigen-binding fragment of the disclosure and thereby assists in the delivery of the compound. Suitable agents that may act in this capacity include monoclonal or polyclonal antibodies, one or more proteins or a liposome. The composition may consist essentially of dosage units that can be administered as an aerosol. The term aerosol is used to denote a variety of systems ranging from those of colloidal nature to systems consisting of pressurized packages. Delivery may be by a liquefied or compressed gas or by a suitable pump system that dispenses the active ingredients. Aerosols may be delivered in single phase, bi phasic, or tri phasic systems in order to deliver the active ingredient(s). Delivery of the aerosol includes the necessary container, activators, valves, subcontainers, and the like, which together may form a kit. One of ordinary skill in the art, without undue experimentation, may determine preferred aerosols.

The pharmaceutical compositions may be prepared by methodology well known in the pharmaceutical art. For example, a composition intended to be administered by injection can be prepared by combining a composition that comprises an antibody, antigen-binding fragment thereof, or antibody conjugate as described herein and optionally, one or more of salts, buffers and/or stabilizers, with sterile, distilled water so as to form a solution. A surfactant may be added to facilitate the formation of a homogeneous solution or suspension. Surfactants are compounds that non-covalently interact with the peptide composition so as to facilitate dissolution or homogeneous suspension of the antibody or antigen-binding fragment thereof in the aqueous delivery system.

In general, an appropriate dose and treatment regimen provide the composition(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit (such as described herein, including an improved clinical outcome (*e.g.*, a decrease in frequency, duration, or severity of diarrhea or associated dehydration, or inflammation, or longer disease-free and/or overall survival, or a lessening of symptom severity). For prophylactic use, a dose should be sufficient to prevent, delay the onset of, or diminish the severity of a disease associated with disease or disorder. Prophylactic benefit of the compositions administered according to the methods

described herein can be determined by performing pre-clinical (including *in vitro* and *in vivo* animal studies) and clinical studies and analyzing data obtained therefrom by appropriate statistical, biological, and clinical methods and techniques, all of which can readily be practiced by a person skilled in the art.

Compositions are administered in an effective amount (*e.g.*, to treat a *Campylobacter* infection), which will vary depending upon a variety of factors including the activity of the specific compound employed; the metabolic stability and length of action of the compound; the age, body weight, general health, sex, and diet of the subject; the mode and time of administration; the rate of excretion; the drug combination; the severity of the particular disorder or condition; and the subject undergoing therapy. In certain embodiments, tollowing administration of therapies according to the formulations and methods of this disclosure, test subjects will exhibit about a 10% up to about a 99% reduction in one or more symptoms associated with the disease or disorder being treated as compared to placebo-treated or other suitable control subjects.

Generally, a therapeutically effective daily dose is (for a 70 kg mammal) from about 0.001 mg/kg (*i.e.*, 0.07 mg) to about 100 mg/kg (*i.e.*, 7.0 g); preferably a therapeutically effective dose is (for a 70 kg mammal) from about 0.01 mg/kg (*i.e.*, 0.7 mg) to about 50 mg/kg (*i.e.*, 3.5 g); more preferably a therapeutically effective dose is (for a 70 kg mammal) from about 1 mg/kg (*i.e.*, 70 mg) to about 25 mg/kg (*i.e.*, 1.75 g).

In certain embodiments, a method comprises administering the antibody, antigen-binding fragment, or composition to the subject at 2, 3, 4, 5, 6, 7, 8, 9, 10 times, or more.

In certain embodiments, a method comprises administering the antibody, antigen-binding fragment, or composition to the subject a plurality of times, wherein a second or successive administration is performed at about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 24, about 48, about 74, about 96 hours, or more, following a first or prior administration, respectively.

In certain embodiments, a method comprises administering the antibody, antigen-binding fragment, or composition at least one time prior to the subject being infected by the *Campylobacter*.

In any of the presently disclosed methods, following the administering, a stool sample from the subject comprises an increased number of Campylobacter colony-forming units (CFUs) as compared to a stool sample from the subject prior to being administered an effective amount of the antibody, antigen-binding fragment, or composition.

Lipocalin-2 (LCN2) is a marker of intestinal inflammation and is linked to epithelial damage and neutrophil infiltration. In any of the presently disclosed methods,following the administering, a stool sample from the subject comprises a reduced amount of LCN2 as compared to a stool sample from the subject prior to being administered an effective amount of the antibody, antigen-binding fragment, or composition. LCN2 can be measured, for example, using anti-LCN2 antibody and performing an ELISA assay.

In any of the presently disclosed methods, following the administering, the subject comprises a reduced amount of polymorphonucleated (PMN) cell infiltrate in the subject's caecum as compared to the subject prior to being administered an effective amount of the antibody, antigen-binding fragment, or composition, wherein the PMN cells are $Gr1^{+}CD11b^{+}$.

In any of the presently disclosed methods, following the administering, the subject has an improved caecum histology as compared to the subject prior to being administered an effective amount of the antibody, antigen-binding fragment, or composition. Standard histology analysis and scoring techniques may be employed to score a tissue (*e.g.*, caecum) for damage, inflammation, or other indicia of a *Campylobacter* infection.

In any of the presently disclosed methods, following the administering, the antibody or antigen-binding fragment is present in the caecum and/or in feces of the subject for at least 4 hours or for at least 8 hours following the administration.

Compositions comprising an antibody or antigen-binding fragment of the present disclosure may also be administered simultaneously with, prior to, or after administration of one or more other therapeutic agents. Such combination therapy may include administration of a single pharmaceutical dosage formulation which contains a compound of the invention and one or more additional active agents, as well as administration of compositions comprising an antibody or antigen-binding fragment of the disclosure and each active agent in its own separate dosage formulation. For example, an antibody or antigen-binding fragment thereof as described herein and the other active agent can be administered to the patient together in a single oral dosage composition such as a tablet or capsule, or each agent administered in separate oral dosage formulations. Similarly, an antibody or antigen-binding fragment as described herein and the other active agent can be administered to the subject together in a single parenteral dosage composition such as in a saline solution or other physiologically acceptable solution, or each agent administered in separate parenteral dosage formulations. Where separate dosage formulations are used, the compositions comprising an antibody or antigen-binding fragment and one or more additional active agents can be administered at essentially the same time, *i.e.*, concurrently, or at separately staggered times, *i.e.*, sequentially and in any order; combination therapy is understood to include all these regimens.

In a related aspect, uses of the presently disclosed antibodies, antigen-binding fragments, and compositions are provided.

In certain embodiments, an antibody, antigen-binding fragment, or composition is provided for use in a method of: (a) treating a Campylobacter infection in a subject; (b) reducing intestinal inflammation in a subject having a Campylobacter infection; and/or (c) increasing intestinal shedding of a Campylobacter by a subject having a Campylobacter infection. It will be appreciated that treatment, reduction of inflammation, and increased intestinal shedding are as described herein.

In certain embodiments, an antibody, antigen-binding fragment, or composition is provided for use in a method of manufacturing or preparing a medicament for: (a)treating a *Campylobacter* infection in a subject; (b) reducing intestinal inflammation

in a subject having a *Campylobacter* infection; and/or (c) increasing intestinal shedding of a *Campylobacter* by a subject having a Campylobacter infection. In certain embodiments, the medicament is formulated for oral administration.

EXAMPLES

EXAMPLE 1

EXPERIMENTAL METHODS

Immunoglobulins against select *Campylobacter* antigens associated with bacterial motility, adhesion, or mucosa invasion were isolated and tested for potency, selectivity, and breadth *in vitro* and *ex-vivo*. The corresponding recombinant SIgA (rSIgA) were expressed via co-transfection in mammalian cells and purified using affinity column chromatography.

rSIgA ability to curb *Campylobacter* motility was appraised *in vitro* by motility assay (Riazi *et al.*, *PLoS One* 2013), whereas breadth and cross-reactivity of the rSIgA with the murine microbiota was evaluated by incubating the mAbs with the stools of infected or mock infected mice followed by FACS analysis of human IgA coated bacteria.

The prophylactic activity of orally administered rSIgA was tested in C57BL/6 mouse model for *Campylobacter* infection. In a first experiment, C57/BL6 mice were pre-treated 3 times via oral gavage with vancomycin 48 hours before mAbs administration. Next, after 1 hour the animals were infected with 10^9 CFU of *Campylobacter jejuni* strain 81-176 (collection number ATCC BAA-2151) and then administered again twice with the antibodies at 6-hour intervals. In another experiment, C57BL/6 female mice (21 days old) were pre-treated with 10 mg of vancomycin (Sigma-Aldrich) in 200µl PBS 48, 24 and 12h prior to mAbs administration. Mice then received a single oral administration of 200 µg of FliD-reactive mAbs in 200 µl PBS 2 hours before being infected by oral gavage with 10^8 CFU of *C. jejuni* 81-176 (collection number ATCC BAA-2151). This infection can also be done with other *Campylobacter*

species, such as *Campylobacter coli* strain 10092/ATB (collection number NCTC 11437). Bacterial shedding in animal stools was monitored throughout the experiment. Lipocalin-2, a marker of intestinal inflammation, was measured by ELISA in stool samples and histological evaluation on the caecum was performed to investigate bacterial invasion and changes of the mucosal epithelium.

EXAMPLE 2

GENERATION OF A CAMPYLOBACTER-SPECIFIC MONOCLONAL IGA ANTIBODIES

Campylobacter flagellar capping protein (FliD) has not been assessed to-date as a potential target for therapeutic monoclonal antibodies. FliD was selected as antigen for mAb development. The frequencies of IgG+ and IgA+ FliD-reactive memory B cells in 50 tonsillar samples of Swiss origin were evaluated using the Antigen-specific-Memory-B-cell-Repertoire-Analysis (AMBRA) (Pinna *et al., Eur.J.Immunol.*, 39:1260-1270 (2009)) (Figure 13). IgG+ and IgA+ memory B cells from selected tonsils were then immortalized (Traggiai *et al., Nat.Med.*, 10:871-875 (2004)), and culture supernatants screened using a 384 well plate-based high-throughput platform to identify cell clones expressing FliD-reactive antibodies.

Memory B cell clones producing human monoclonal antibodies "CAA" and "CCG4" were isolated and selected based on their specificity and affinity for FliD antigen. CAA1 was isolated as an IgA1 encoded by V_H3-48/D2-15/J_H3 with a 21-amino acid HCDR3 and V_K1-39/J_K5. CCG4 was isolated as an IgG3 encoded by V_H3-9/D1-7/J_H1 bearing a shorter (11 amino acids) HCDR3 and V_L3-27/J_L3. Nucleic acid and amino acid sequences of variable regions from exemplary mAbs are provided in Table 1.

Humans present two IgA isotype subclasses that differ mainly in the length and glycosylation of the hinge region. IgA1 possesses a hinge that is 13 amino acids longer than that of IgA2 and contains up to five O-linked glycans at serine and threonine residues. The longer hinge of IgA1 is believed to confer greater flexibility and a longer Fab reach, but may also contribute to sensitivity of IgA1 to IgA1 proteases. IgA2 has a shorter hinge region that lacks proline-serine and/or proline-threonine peptide bonds,

and is resistant to IgA1 proteases (Plaut, *Annu.Rev.Microbiol.*, 37:603-622 (1983)). In addition, the IgA2 isotype can undergo reverse transcytosis by contacting Dectin-I receptor on the surface of PPs M cells (Rochereau *et al.*, *PLoS Biol.*, 11:e1001658 (2013)). IgG, IgM, and IgA1 isotypes are not believed to have this ability. Both the Cα1 region and the glycosylation pattern of IgA2 are thought to be important for interaction with Dectin-I receptor, which may boost adaptive immunity against pathogens (Rochereau *et al.*, *Eur.J.Immunol.*, 45:773-779 (2015)).

The IgA2 scaffold was initially selected over IgA1 for further studies, and both CAA1 and CCG4 were produced as rSIgA2 before further *in vitro* characterization. For a control antibody non-reactive with the antigen, HGN194 mAb (Corti *et al.*, *PLoS One*, 5:e8805 (2010)), which targets an HIV glycoprotein, was also expressed as rSIgA2. Antibodies were expressed as rSIgA2 via plasmid co-transfection in mammalian cells and purified using CaptureSelect IgA affinity columns.

Structural and functional characterization of purified rSIgA was performed using ELISA and UPLC analysis. *Campylobacter* -reactive rSIgA was able to recognize and bind the most common Campylobacter species associated with severe infections, including recent clinical isolates (FIG. 1), displaying limited cross-reactivity with the murine microbiota, which might be due to modest level of homology with similar antigens in the flagella of commensal species or to non-Fab mediated interactions.

Table 1 provides sequences of exemplary anti-FliD mAbs according to the present disclosure, as well as sequences of exemplary FliD proteins. Antibody CDR sequences (amino acid and nucleotide) are shown in bold. Antibody residues that arose from somatic mutation are underlined.

Table 1. Sequences

Sequence Description	SEQ ID NO.	Sequence
CAA1 (VH, codon optimized for IgA2m2)	1	gaagcacagctggtggagagcggcggcggcctgatcc agccaggcggctctctgagactgagctgtgaggcctctg gcttcagcctgagctcccacgagatgaactgggtgagac aggcacctggcaagggactggagtggctgagctacatct ccacctctggcatcacaatctactatgcagactccgtgcg gggccggttcaccatcagcagggatacagccaagaact

Sequence Description	SEQ ID NO.	Sequence
		ccctgtacctgcagatgaattctctgagggccgaggacac cgccctgtatcactgtgcccgcgatctgggcggctactgc tctggcggcctgtgctatcctcgcggcgccctggacctgt ggggacagggaaccacagtgaccgtgtctagcg
CAA1 (VH)	2	EAQLVESGGGLIQPGGSLRLSCEAS**G FSLSSHE**MNWVRQAPGKGLEWLSY**I STSGITI**YYADSVRGRFTISRDTAKNS LYLQMNSLRAEDTALYHC**ARDLGG YCSGGLCYPRGALDL**WGQGTTVTV SS
CAA1 (VK, codon optimized)	3	gacatcctgatgacacagtctcctagctccctgtctgcctct gtgggcgatagggtgaccatcacatgccgcgcctcccag acaatccggacctacgtgaactggtatcagcagaagccc ggcgagacacctaggctgctgatctacgcagcaaccatc ctgcagcggggcgtgccatccagattctccggctctggc agcggcacagactttaccctgacaatcacctctctgcagc ccgaggatttcggcacctactattgtcagcagaattataag acattcctgacctttggccagggcacccggctggagatca agc
CAA1 (VK)	4	DILMTQSPSSLSASVGDRVTITCRAS**Q TIRTY**VNWYQQKPGETPRLLIY**AATI** LQRGVPSRFSGSGSGTDFTLTITSLQP EDFGTYYC**QQNYKTFLT**FGQGTRLE IK
CAA1 (VH, native)	5	GAGGCGCAGCTGGTGGAGTCTGGG GGAGGCCTGATACAGCCTGGAGGG TCCCTGAGACTCTCCTGTGAAGCCT CT**GGCTTCTCCCTCAGTTCTCATG AA**ATGAATTGGGTCCGCCAGGCTC CAGGGAAGGGGCTGGAGTGGCTTT CATAT**ATTAGTACTAGTGGTATTA CAATA**TATTACGCGGACTCTGTGA GGGGCCGATTCACCATCTCCAGAG ACACCGCCAAGAACTCACTGTATCT GCAAATGAACAGCCTGAGAGCCGA GGACACGGCTCTTTATCACTGT**GCG AGAGATCTTGGCGGTTATTGTAG TGGTGGTTTGTGCTACCCGAGGG GTGCCTTGGATCTC**TGGGGCCAAG GGACAACGGTCACCGTCTCGTCAG
CAA1 (VK, native)	6	GACATCCTGATGACCCAGTCTCCAT CCTCCCTGTCTGCATCTGTCGGAGA CAGAGTCACCATCACTTGCCGGGC AAGT**CAGACCATTCGCACCTAT**GT

Sequence Description	SEQ ID NO.	Sequence
		AAATTGGTATCAGCAGAAGCCAGG GGAAACCCCAAGACTCCTTATCTAT **GCTGCAACC**ATTTTGCAGAGAGGG GTCCCATCAAGGTTCAGTGGCAGTG GATCTGGGACAGATTTCACTCTCAC CATTACCAGTCTGCAACCTGAAGAT TTTGGAACTTACTACTGT**CAACAGA ACTACAAAACCTTTCTCACC**TTCG GCCAAGGGACACGACTGGAGATTA AAG
CAA1 (VH, codon optimized for IgA1 backbone)	7	GAAGCACAGCTGGTGGAGAGCGGC GGCGGCCTGATCCAGCCAGGCGGC TCTCTGAGACTGAGCTGTGAGGCAT CTGGCTTCAGCCTGAGCTCCCACGA GATGAACTGGGTGAGACAGGCACC TGGCAAGGGCCTGGAGTGGCTGAG CTACATCTCCACCTCTGGCATCACA ATCTACTATGCAGACTCCGTGCGGG GCCGGTTCACCATCAGCAGGGATA CAGCCAAGAACTCCCTGTACCTGCA GATGAATTCTCTGAGGGCCGAGGA CACCGCCCTGTATCACTGTGCCCGC GATCTGGGCGGCTACTGCAGCGGC GGCCTGTGCTATCCTCGCGGCGCCC TGGACCTGTGGGGACAGGGAACCA CAGTGACCGTGTCTAGCGCCTCCCC AACATCTCCCAAGGTGTTCCCCCTG AGCCTGTGCTCCACACAGCCTGATG GCAACGTGGTCATCGCCTGTCTGGT GCAGGGCTTCTTTCCTCAGGAGCCA CTGTCTGTGACATGGTCTGAGTCTG GACAGGGAGTGACAGCACGGAATT TTCCCCCTTCCCAGGACGCCTCTGG CGATCTGTAT
CAA1 (VH codon optimized for IgG1 backbone)	8	GAGGCCCAGCTGGTGGAAAGCGGC GGCGGCCTGATTCAGCCCGGCGGC TCTCTGAGACTGAGCTGTGAGGCAT CTGGCTTCTCCCTGAGCTCCCACGA GATGAACTGGGTGAGACAGGCACC TGGCAAGGGCCTGGAGTGGCTGTC CTACATCTCCACCTCTGGCATCACA ATCTACTATGCCGACTCTGTGCGGG GCCGGTTCACCATCTCCAGGGATAC AGCCAAGAACTCTCTGTACCTGCAG ATGAATAGCCTGAGGGCCGAGGAC ACCGCCCTGTATCACTGTGCACGCG ATCTGGGCGGCTACTGCAGCGGCG

Sequence Description	SEQ ID NO.	Sequence
		GCCTGTGCTATCCAAGAGGCGCCCT GGACCTGTGGGGACAGGGAACCAC AGTGACAGTGTCTAGC
CAA1 (HCDR1)	9	**GFSLSSHE**
CAA1 (HCDR2)	10	**ISTSGITI**
CAA1 (HCDR3)	11	**ARDLGGYCSGGLCYPRGALDL**
CAA1 (LCDR1)	12	**QTIRTY**
CAA1 (LCDR2)	13	**AAT**
CAA1 (LCDR3)	14	**QQNYKTFLT**
CAA1 (HCDR1; native)	15	GGCTTCTCCCTCAGTTCTCATGAA
CAA1 (HCDR2; native)	16	ATTAGTACTAGTGGTATTACAATA
CAA1 (HCDR3; native)	17	GCGAGAGATCTTGGCGGTTATTGTA GTGGTGGTTTGTGCTACCCGAGGGG TGCCTTGGATCTC
CAA1 (LCDR1; native)	18	CAGACCATTCGCACCTAT
CAA1 (LCDR2; native)	19	GCTGCAACC
CAA1 (LCDR3; native)	20	CAACAGAACTACAAAACCTTTCTCA CC
CCG4 (VH, native)	21	GAAGTGCAGCTGGTGGAGTCTGGG GGAGGCTTGGTACAGCCTGGCAGG TCCCTGAGACTCTCCTGCGCAGCCT CT**GGAATCACCTTTGATGAATATG CC**ATGTACTGGGTCCGGCAAGCTC CAGGGAAGGGCCTGGAGTGGGTCT CAGGT**ATTAGTTGGAACAGTGCT AATATA**GGCTATGCGGACTCTGTG AAGGGCCGATTCACCATCTCCAGA GACAACGCCAAGAAGTCCCTCTAT

Sequence Description	SEQ ID NO.	Sequence
		CTGCAAATGAATAGTCTGAGAGCT GAAGACACGGCCTTGTATTACTGT**T CAGGTATAACTGGGACTACGGGG ATACAGTAC**TGGGGCCAGGGAACC CTGGTCACCGTCTCCTCAG
CCG4 (VH)	22	EVQLVESGGGLVQPGRSLRLSCAAS **GITFDEYA**MYWVRQAPGKGLEWVS G**ISWNSANI**GYADSVKGRFTISRDNA KKSLYLQMNSLRAEDTALYYC**SGIT GTTGIQY**WGQGTLVTVSS
CCG4 (VL, native)	23	TCCTATGAGCTGACACAGCCATCCT CAGTGTCAGTGTCTCCGGGACAGA CAGCCAGGATCACCTGCTCAGGAG AT**GTATTGGCAAATACATAT**GCTC GGTGGTTCCAGCAGAAGCCAGGCC AGGCCCCTGTACTGGTGATTTAT**AA AGACAGT**GAGCGGCCCTCAGGGAT CCCTGAGCGATTCTCCGGCTCCAGC TCAGGGACCACAGTCACCTTGATCA TCAGGGGGGCCCAGGTTGAGGATG AGGCTGACTATTACTGT**TACTCTG CGGCTGACAACAATCGGAGGGTG** TTCGGCGGAGGGACCAAGCTGACC GTCCTAG
CCG4 (VL)	24	SYELTQPSSVSVSPGQTARITCSGD**VL ANTY**ARWFQQKPGQAPVLVIY**KDS**E RPSGIPERFSGSSSGTTVTLIIRGAQVE DEADYYC**YSAADNNRRV**FGGGTKL TVL
CCG4 (HCDR1)	25	**GITFDEYA**
CCG4 (HCDR2)	26	**ISWNSANI**
CCG4 (HCDR3)	27	**SGITGTTGIQY**
CCG4 (LCDR1)	28	**VLANTY**
CCG4 (LCDR2)	29	**KDS**
CCG4 (LCDR3)	30	**YSAADNNRRV**

Sequence Description	SEQ ID NO.	Sequence
CCG4 (HCDR1; native)	31	**GGAATCACCTTTGATGAATATGCC**
CCG4 (HCDR2; native)	32	**ATTAGTTGGAACAGTGCTAATATA**
CCG4 (HCDR3; native)	33	**TCAGGTATAACTGGGACTACGGGGATACAGTAC**
CCG4 (LCDR1; native)	34	**GTATTGGCAAATACATAT**
CCG4 (LCDR2; native)	35	**AAAGACAGT**
CCG4 (LCDR3; native)	36	**TACTCTGCGGCTGACAACAATCGGAGGGTG**
CCG4 (VH, codon optimized for IgA2M2 backbone)	37	gaggtgcagctggtggaaagcggcggcggcctggtgcagccaggccggtctctgagactgtcttgtgcagcatctggaatcaccttcgacgagtatgcaatgtattgggtgcggcaggcaccaggcaagggactggagtgggtgtccggcatctctggaacagcgccaatatcggctacgccgactccgtgaaggcaggtttacaatctcccgcgataacgccaagaagtctctgtatctgcagatgaatagcctgagggccgaggataccgccctgtactattgctctggcatcacaggcaccacaggcatccagtactggggccagggcaccctggtgacagtgagctccgcctccccaacctctcccaaggtgttccccctgagcctggactccacacctcaggatggcaacgtggtggtggcctgtctggtgcagggcttctttcctcaggagccactgagcgtgacctggtctgagagcggccagaacgtgacagcccggaattttccccttctcaggacgccagcggcgatctgtatacc
CCG4 (VH, codon optimized for IgG1 backbone)	38	gaggtgcagctggtggaaagcggcggcggcctggtgcagcctggccggagcctgagactgtcttgtgcagcatctggaatcaccttcgacgagtacgccatgtattgggtgcggcaggcacctggcaagggcctggagtgggtgtctggcatcagctggaactccgccaatatcggctacgccgactctgtgaaggcaggtttacaatctctcgcgataacgccaagaagagcctgtatctgcagatgaattccctgagggccgaggataccgccctgtactattgtagcggcatcacaggcaccacaggcatccagtactggggccagggcaccctggtgacagtgagctcc
CCG4 (VL, codon optimized)	39	agctacgagctgacccagcctagctccgtgtctgtgagccctggacagacagcaagaatcacatgctctggcgacgtgctggccaacacatacgccaggtggtttcagcagaagcctggacaggcccccgtgctggtcatctacaaggattccgagaggccatctggcattcctgagcggttcagcggctctagctccggcaccacagtgaccctgatcattagaggcgcccaggt

Sequence Description	SEQ ID NO.	Sequence
		ggaggatgaggcagattactattgttatagcgccgccgac aacaatcggagagtgttcggcggcggaaccaagctgac agtgctg
IgA1 - heavy chain constant region	40	asptspkvfplslcstqpdgnvviaclvqgffpqeplsvt wsesgqgvtarnfppsqdasgdlyttssqltlpatqclag ksvtchvkhytnpsqdvtvpcpvpstpptpspstpptp spscchprlslhrpaledlllgseanltctltglrdasgvtft wtpssgksavqgpperdlcgcysvssvlpgcaepwnh gktftctaaypesktpltatlsksgntfrpevhllpppseel alnelvtltclargfspkdvlvrwlqgsqelprekyltwa srqepsqgtttfavtsilrvaaedwkkgdtfscmvghea lplaftqktidrlagkpthvnvsvvmaevdgtcy
IgA2(m1) - heavy chain constant region	41	asptspkvfplsldstpqdgnvvvaclvqgffpqeplsv twsesgqnvtarnfppsqdasgdlyttssqltlpatqcpd gksvtchvkhytnpsqdvtvpcpvpppppcchprlsl hrpaledlllgseanltctltglrdasgatftwtpssgksav qgpperdlcgcysvssvlpgcaqpwnhgetftctaahp elktpltanitksgntfrpevhllpppseelalnelvtltcla rgfspkdvlvrwlqgsqelprekyltwasrqepsqgtttf avtsilrvaaedwkkgdtfscmvghealplaftqktidrl agkpthvnvsvvmaevdgtcy
IgA2(m2) - heavy chain constant region	42	asptspkvfplsldstpqdgnvvvaclvqgffpqeplsv twsesgqnvtarnfppsqdasgdlyttssqltlpatqcpd gksvtchvkhytnssqdvtvpcrvpppppcchprlslh rpaledlllgseanltctltglrdasgatftwtpssgksavq gpperdlcgcysvssvlpgcaqpwnhgetftctaahpe lktpltanitksgntfrpevhllpppseelalnelvtltclar gfspkdvlvrwlqgsqelprekyltwasrqepsqgttty avtsilrvaaedwkkgetfscmvghealplaftqktidr magkpthinvsvvmaeadgtcy
Campylobacter jejuni subsp. jejuni serotype O:23/36 (strain 81-176) Flagellar hook-associated protein 2 (Uniprot A0A0H3PIU8)	43	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsf qtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskgla ndsgfinanl tgttdltffs ngkeytvtvd knttyrelad kineasggei vakivntgek gtpyrltlts ketgedsais fyagkkdsng kytsdseaet ifknlgweld ttssidpakd kkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdf egvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvv dgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitk yedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdftiv fnnqtydlsk nsdgtnfklt gkteeellqn lanhinskgi eglkvkvesy

Sequence Description	SEQ ID NO.	Sequence
		dqngvkgfkl nfsgdgssdf sikgnatilk elglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltnniks lntskdstqa midtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
Campylobacter jejuni subsp. jejuni serotype O:2 (strain ATCC 700819 / NCTC 11168) (Uniprot Q9PHW6)	44	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsf qtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskgla ndggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgek gtpyrltlts ketgedsais fyagkkdsng kyqkdinaek ifddlgwgld vsasidpdkd kkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdf egvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvv dgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitk yedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfklt gkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilk elglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqa midtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar hook-associated protein 2 [Campylobacter jejuni subsp. jejuni NCTC 11168 = ATCC 700819] NCBI Reference Sequence: YP_002343979.1	45	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsf qtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskgla ndggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgek gtpyrltlts ketgedsais fyagkkdsng kyqkdinaek ifddlgwgld vsasidpdkd kkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdf egvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvv dgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitk yedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfklt gkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilk elglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqa midtrydtma nqwlqyesil nklnqqlntv tnminaanns nn

Sequence Description	SEQ ID NO.	Sequence
flagellar filament capping protein FliD [Campylobacter jejuni] NCBI Reference Sequence: WP_038400380.1	46	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandsgfinanl agttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyksdleaek ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl afkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdgsilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar hook-associated protein FliD [Campylobacter jejuni subsp. jejuni 81-176] GenBank: EAQ73028.1	47	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeytvtvd knttyrelad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kytsdseaet ifknlgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy dqngvkgfkl nfsgdgssdf sikgnatilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltnniks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter jejuni]	48	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad

Sequence Description	SEQ ID NO.	Sequence
NCBI Reference Sequence: WP_010790846.1		kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld asasidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlnfdsskf eqkvkedpds aesffsnitkyedinhtgei iktgslskyl nsnggntngl dfkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy dqnnvkgfkl nfsgdgssdf sikgdasilkelglpdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
MULTISPECIES: flagellar filament capping protein FliD [Campylobacter] NCBI Reference Sequence: WP_004316510.1	49	mafgslaslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnanl ngtadltffs ngkeytvtvd rnttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdang aykndpnaet ifknlgweld atssidlakdkkgygikdts lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdginfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlstv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter jejuni] NCBI Reference Sequence: WP_004306838.1	50	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyksdleaek ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn

Sequence Description	SEQ ID NO.	Sequence
		lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf ekkvkedpds aesffsnitkyedinhtgev iktgslskyl nsnggsangl dfkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy dqnnvkgfkl nfsgdgssdf sikgdanilkelglsdvnis skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstq vmidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter jejuni] NCBI Reference Sequence: WP_002935293.1	51	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsf qtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgweld vsasidpdkdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgyftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter jejuni] NCBI Reference Sequence: WP_002928464.1	52	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld asasidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlnfdsskf eqkvkedpds aesffsnitkyedinhtgei iktgslskyl nsnggntngl dfkpgdftiv fnnqtydlsk

Sequence Description	SEQ ID NO.	Sequence
		nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy dqnnvkgfkl nfsgdgssdf sikgdasilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter jejuni] NCBI Reference Sequence: WP_002924910.1	53	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnakl ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdvqg qyksdseaek ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter jejuni] NCBI Reference Sequence: WP_002921586.1	54	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekdtpyrltlts ketgedsais fyagkkdsng kytsdseaet ifknlgweld ttssidpakd kkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy dqngvkgfkl nfsgdgssdf sikgnatilqelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil

Sequence Description	SEQ ID NO.	Sequence
		nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter jejuni] NCBI Reference Sequence: WP_002908989.1	55	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld vsasidpdkdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfkl nfsgdgssdf sikgnasilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter jejuni] NCBI Reference Sequence: WP_002901368.1	56	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kytsdleakt ifknlgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
MULTISPECIES: flagellar filament capping protein FliD	57	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs

Sequence Description	SEQ ID NO.	Sequence
[Campylobacter] NCBI Reference Sequence: WP_002892358.1		mninvtqlaq kdvyqskglandggfinanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng aykndpnaet ifknlgweld tttqtidpakdkkgygikda slhiqtaqna eftldgikmf rssntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdayndlvt nlnaatdyns etgtkgtlqg isevnsirss iladlfdsqvvdgttedang nkvntkvmls mqdfglslnd agtlsfdssk feqkvkedpd stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg ldfkpgdfti vfnnqtydls knsdgtnfkltgkteeellq nlanhinskg ieglkvkves ydqngvkgfk lnfsgdgssd fsikgnatilqelglsdvni tskpiegkgi fsklkatlqe mtgkdgsitk ydesltndik slntskdstqamidtrydtm anqwlqyesi lnklnqqlnt vtnminaann snn
flagellar filament capping protein FliD [Campylobacter jejuni] NCBI Reference Sequence: WP_002874097.1	58	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnakl ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyksdseaek ifkslgweld ttssidpakdkkgysikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter jejuni] NCBI Reference Sequence: WP_002873395.1	59	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld vsasidpakdkkgygikdas lhiqtaqnae

Sequence Description	SEQ ID NO.	Sequence
		ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar hook-associated protein FliD [Campylobacter jejuni subsp. jejuni 305] GenBank: EFV08769.1	60	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdinaek ifddlgwgld vsasidpdkdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar hook-associated protein FliD [Campylobacter jejuni subsp. jejuni 327] GenBank: EFV10698.1	61	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfvnanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyqsdpeaen ifsnlgweld kttqtidpakdkkgygikda slhiqtaqna eftldgikmf rssntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdayndlvt nlnaatdyns etgtkgtlqg isevnsirss iladlfdsqvvdgttedang nkvntkvmls mqdfglslnd agtlsfdssk feqkvkedpd

Sequence Description	SEQ ID NO.	Sequence
		stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg ldfkpgdfti vfnnqtydls knsdgtnfkltgkteeellq nlanhinskg ieglkvkves ydqngvkgfk lnfsgdgssd fsikgnatilqelglsdvni tskpiegkgi fsklkatlqe mtgkdgsitk ydesltndik slntskdstqamidtrydtm anqwlqyesi lnklnqqlnt vtnminaann snn
flagellar hook-associated protein FliD [Campylobacter jejuni subsp. jejuni 84-25]	62	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandsgfinanl agttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyqsdpeaek ifsnlgweld kttqtidpakdkkgygikda slhiqtaqna eftldgikmf rssntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdayndlvt nlnaatdyns etgtkgtlqg isevnsirss iladlfdsqvvdgttedang nkvntkvmls mqdfglslnd agtlsfdssk feqkvkedpd stesffsnitkyedinhtge viktgslsky lnsnggntng lefkpgdfti vfnnqtydls knsdgtnfkltgkteeellq nlanhinskg ieglkvkves ynqnnvtgfr lnfsgdgssd fsikgdanilkelglsdvni tskpiegkgi fsklkatlqe mtgkdgsitk ydesltndik slntskdstqamidtrydtm anqwlqyesi lnklnqqlnt vtnminaann snn
flagellar hook-associated protein FliD [Campylobacter jejuni subsp. jejuni HB93-13] GenBank: EAQ60315.1	63	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeytvtvd ksttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqgqyksdseaekifsnlgweldkttqtidp akdkkgygikda slhiqtaqna eftldgikmf rssntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdayndlvt nlnaatdyns etgtkgtlqg isevnsirss iladlfdsqvvdgttedang nkvntkvmls mqdfglslnd agtlsfdssk feqkvkedpd stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg lefkpggfti vfnnqtydls knsdgtnfkltgkteeellq nlanhinskg ieglkvkves ydqngvkgfk lnfsgdgssd fsikgdanilkelglsdvni tskpiegkgi fsklkatlqe

Sequence Description	SEQ ID NO.	Sequence
		mtgkdgsitk ydesltndik slntskdstqamidtrydtm anqwlqyesi lnklnqqlnt vtnminaann snn
flagellar hook-associated protein FliD [Campylobacter jejuni subsp. jejuni 260.94] GenBank: EAQ58732.1	64	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld asasidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlnfdsskf eqkvkedpds aesffsnitkyedinhtgei iktgnlskyl nsnggntngl dfkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy dqnnvkgfkl nfsgdgssdf sikgdasilkelglsdvnii skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar hook-associated protein FliD [Campylobacter jejuni subsp. jejuni CF93-6] GenBank: EAQ57731.1	65	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdinaek ifddlgwgld vsasidpdkdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
Flagellar hook-	66	mafgslsslg fgsgvltqdt idklkeaeqk

Sequence Description	SEQ ID NO.	Sequence
associated protein FliD [Campylobacter jejuni 4031] GenBank: CDH62398.1		aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnakl ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyksdseaek ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
Flagellar hook-associated protein 2 [Campylobacter jejuni subsp. jejuni M1] GenBank: ADN90737.1	67	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfvnanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyqsdpeaen ifsnlgweld kttqtidpakdkkgygikda slhiqtaqna eftldgikmf rssntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdayndlvt nlnaatdyns etgtkgtlqg isevnsirss iladlfdsqvvdgttedang nkvntkvmls mqdfglslnd agtlsfdssk feqkvkedpd stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg ldfkpgdfti vfnnqtydls knsdgtnfkltgkteeellq nlanhinskg ieglkvkves ydqngvkgfk lnfsgdgssd fsikgnatilqelglsdvni tskpiegkgi fsklkatlqe mtgkdgsitk ydesltndik slntskdstqamidtrydtm anqwlqyesi lnklnqqlnt vtnminaann snn
flagellar filament cap protein FliD [Campylobacter jejuni subsp. jejuni str. RM3420]	68	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeytvtvd ksttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais

Sequence Description	SEQ ID NO.	Sequence
GenBank: AOW96893.1		fyagkkdaqg qyksdseaek ifsnlgweld kttqtidpakdkkgygikda slhiqtaqna eftldgikmf rssntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdayndlvt nlnaatdyns etgtkgtlqg isevnsirss iladlfdsqvvdgttedang nkvntkvmls mqdfglslnd agtlsfdssk feqkvkedpd stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg lefkpggfti vfnnqtydls knsdgtnfkltgkteeellq nlanhinskg ieglkvkves ydqngvkgfk lkfsgdgssd fsikgdanilkelglsdvni tskpiegkgi fsklkatlqe mtgkdgsitk ydesltndik slntskdstqamidtrydtm anqwlqyesi lnklnqqlnt vtnminaann snn
flagellar filament cap protein FliD [Campylobacter jejuni subsp. jejuni] GenBank: AON66729.1	69	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnakl ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyksdpeaek ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgikgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament cap protein FliD [Campylobacter jejuni subsp. jejuni] GenBank: AON65179.1	70	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandsgfinanl agttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyqsdpeaek ifsnlgweld kttqtidpakdkkgygikda slhiqtaqna eftldgikmf rssntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdayndlvt nlnaatdyns etgtkgtlqg isevnsirss

Sequence Description	SEQ ID NO.	Sequence
		iladlfdsqvvdgttedang nkvntkvmls mqdfglslnd agtlsfdssk feqkvkedpd stesffsnitkyedinhtge viktgslsky lnsnggntng lafkpgdfti vfnnqtydls knsdgtnfkltgkteeellq nlanhinskg ieglkvkves ynqnnvtgfr lnfsgdgssd fsikgdgsilkelglsdvni tskpiegkgi fsklkatlqe mtgkdgsitk ydesltndik slntskdstqamidtrydtm anqwlqyesi lnklnqqlnt vtnminaann snn
flagellar filament cap protein [Campylobacter jejuni subsp. jejuni] GenBank: AOH51565.1	71	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng qyqsdseaen ifsnlgweld ktssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev intgslskyl npngldfkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlanhi nskgieglkv kvesynqnnv tgfrlnfsgd gssdfsikgn atilkelglsdvnitskpie gkgifsklka tlqemtgkdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklnq qlntvtnmin aannsnn
flagellar filament cap protein FliD [Campylobacter jejuni subsp. jejuni] GenBank: ALF93210.1	72	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld asasidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlnfdsskf eqkvkedpds aesffsnitkyedinhtgei iktgnlskyl nsnggntngl dfkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi

Sequence Description	SEQ ID NO.	Sequence
		eglkvkvesy dqnnvkgfkl nfsgdgssdf sikgdasilkelglsdvnii skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
Flagellar hook-associated protein 2 [Campylobacter jejuni subsp. jejuni] GenBank: AJP35034.1	73	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyesdseaek ifkslgweld ttssinpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efqpgnftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy dqngvkgfrl nfsgdgssdf sikgdanilkdlglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament cap protein [Campylobacter jejuni subsp. jejuni] GenBank: AOH51565.1	74	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng qyqsdseaen ifsnlgweld ktssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev intgslskyl npngldfkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlanhi nskgieglkv kvesynqnnv tgfrlnfsgd gssdfsikgn atilkelglsdvnitskpie gkgifsklka tlqemtgkdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklnq qlntvtnmin aannsnn

Sequence Description	SEQ ID NO.	Sequence
flagellar capping protein [Campylobacter jejuni subsp. jejuni CG8421] GenBank: AHY39787.1	75	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandsgfinanl agttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyksdleaek ifkslgweld ttssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl afkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdgsilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar cap protein FliD [Campylobacter jejuni 32488] GenBank: AGQ95247.1	76	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqsqglandggfvnakl ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdvqg qyksdseaek ifkslgweld ttssidpakd kkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar capping protein [Campylobacter jejuni subsp. jejuni IA3902]	77	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad

Sequence Description	SEQ ID NO.	Sequence
GenBank: ADC28162.1		kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdinaek ifddlgwgld vsasidpdkdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar hook-associated protein FliD [Campylobacter jejuni subsp. jejuni 81116] GenBank: ABV52108.1	78	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfvnanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyqsdpeaen ifsnlgweld kttqtidpakdkkgygikda slhiqtaqna eftldgikmf rssntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdayndlvt nlnaatdyns etgtkgtlqg isevnsirss iladlfdsqvvdgttedang nkvntkvmls mqdfglslnd agtlsfdssk feqkvkedpd stesffsnitkyedinhtge vikqgslnqy ldssgtgnkg ldfkpgdfti vfnnqtydls knsdgtnfkltgkteeellq nlanhinskg ieglkvkves ydqngvkgfk lnfsgdgssd fsikgnatilqelglsdvni tskpiegkgi fsklkatlqe mtgkdgsitk ydesltndik slntskdstqamidtrydtm anqwlqyesi lnklnqqlnt vtnminaann snn
flagellar hook-associated protein FliD [Campylobacter jejuni RM1221] GenBank: AAW35835.1	79	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdaqg qyksdseaee ifkslgweld tassidpakd kkgygikdps lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn

Sequence Description	SEQ ID NO.	Sequence
		lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl tnglefkpgd ftivfnnqty dlsknsdgtn fkltgkteeellqnlanhin skgieglkvk vesynqnnvt gfrlnfsgdg ssdfsikgna silkelglsdvnitskpieg kgifsklkat lqemtgkdgs itkydesltn dikslntskd stqamidtrydtmanqwlqy esilnklnqq lntvtnmina annsnn
flagellar cap protein FliD [Campylobacter coli RM5611] GenBank: AHK75426.1	80	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng qyqsdseaen ifsnlgweld ktssidpakdkkgygikdts lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgnasilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar cap protein FliD [Campylobacter coli RM4661] GenBank: AHK76446.1	81	mafgslsslg fgsgvltqdt idklkeaeqk arinpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqn mninvtqlaq kdvyqskglandsgfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgapyrltlts ketgedsais fyagkkdssg kytsdsnaet ifknlgweld ttssidpdkdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedvngn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev intgslskyl npngldfkqg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlanhi

Sequence Description	SEQ ID NO.	Sequence
		nskgieglkv kvesynqngv kgfklnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgkdg sitkydeslt ndikslntsk dstqamidtr ydtmanqwlq yesilnklnq qlntvtnmin aannssn
Flagellar hook-associated protein FliD [Campylobacter coli 15-537360] GenBank: AGZ21001.1	82	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng qyqsdseaen ifsnlgweld ktssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter coli] NCBI Reference Sequence: WP_004284951.1	83	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglvndggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld vsasidpakdkkgygikdts lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfnsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlanhi nskgieglkv kvesynqnnv tgfrlnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgkdg sitkydeslt ndikslntsk dstqamidtr ydtmanqwlq yesilnklnq qlntvtnmin aannsnn

Sequence Description	SEQ ID NO.	Sequence
Flagellar hook-associated protein 2 [Campylobacter coli] GenBank: AJW57994.1	84	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld vsasidpakdkkgygikdts lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfnsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlanhi nskgieglkv kvesynqnnv tgfrlnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgkdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklnq qlntvtnmin aannsnn
Flagellar hook-associated protein 2 [Campylobacter coli] GenBank: ALV00075.1	85	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kytsdseaet ifknlgweld kttqtidpakdkkgygikda slhiqtaqna eftldgikmf rssntvtdlg vgmtltlnkt geinfdvqqdfegvtkamqd lvdayndlvt nlnaatdyns etgtkgtlqg isevnsirss iladlfdsqvvdgttedang nkvntkvmls mqdfglslnd agtlsfdssk feqkvkedpd stesffsnitkyedinhtge viktgslsky lnsnglefkp gdftivfnnq tydlsknsdg tnfkltgkteeellqnlanh inskgieglk vkvesynqnn vtgfrlnfsg dgssdfsikg nasilkelglsdvnitskpi egkgifsklk atlqemtgkd gsitkydesltndikslntskdstqamidtrydtmanqw l qyesilnkln qqlntvtnmi naannsnn
Flagellar hook-associated protein FliD [Campylobacter coli IPSID-1] GenBank:	86	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais

Sequence Description	SEQ ID NO.	Sequence
CDL88777.1		fyagkkdsng kytsdseaetifknlgweldttssidpakdkkgygikda s lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev ikqgslnqyl dssgtgnkgl dfkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy dqngvkgfkl nfsgdgssdf sikgnatilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar hook-associated protein 2 (fliD), putative [Campylobacter coli RM2228] GenBank: EAL57379.1	87	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld vsasidpakdkkgygikdts lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfnsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlanhi nskgieglkv kvesynqnnv tgfrlnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgkdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklnq qlntvtnmin aannsnn
flagellar filament capping protein FliD [Campylobacter coli] NCBI Reference Sequence: WP_002842748.1	88	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld vsasidpakdkkgygikdts lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm

Sequence Description	SEQ ID NO.	Sequence
		qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlanhi nskgieglkv kvesynqnnv tgfrlnfsgd gssdfsikgn asilkelglsdvnisskpie gkgifsklka tlqemtgkdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklnq qlntvtnmin aannsnn
flagellar filament capping protein FliD [Campylobacter coli] NCBI Reference Sequence: WP_002833936.1	89	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng qyqsdseaen ifsnlgweld ktssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfnsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlanhi nskgieglkv kvesynqnnv tgfrlnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgkdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklnq qlntvtnmin aannsnn
flagellar hook-associated protein 2 [Campylobacter coli JV20] GenBank: EFM36457.1	90	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglvndggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng kyqkdtnaek ifddlgwgld vsasidpakdkkgygikdts lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfnsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnglefkpg dftivfnnqt ydlsknsdgt nfkltgkteeellqnlanhi nskgieglkv kvesynqnnv tgfrlnfsgd gssdfsikgn asilkelglsdvnitskpie gkgifsklka tlqemtgkdg sitkydeslt ndikslntsk dstqamidtrydtmanqwlq yesilnklnq

Sequence Description	SEQ ID NO.	Sequence
		qlntvtnmin aannsnn
flagellar filament capping protein FliD [Campylobacter coli] NCBI Reference Sequence: WP_002832776.1	91	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandggfvnaql ngtadltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng qyqsdsgaen ifsnlgweld ktssidpakdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgnlskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdanilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter coli] NCBI Reference Sequence: WP_002825071.1	92	mafgslsslg fgsgvltqdt idklkeaeqk arinpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeytvtvd ksttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdssg kytsdsnaet ifknlgweld ttssidpdkdkkgygikdas lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedvngn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev intgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgnasilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter coli]	93	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs

Sequence Description	SEQ ID NO.	Sequence
NCBI Reference Sequence: WP_002804771.1		mninvtqlaq kdvyqskglandsgfinanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng qyqsdseaen ifsnlgweld ktssidpakdkkgygikdts lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgnasilkelglsdvnit skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter coli] NCBI Reference Sequence: WP_002793506.1	94	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfvnanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdsng qyqsdseaen ifsnlgweld ktssidpakdkkgygikdts lhiqtaqnae ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdasilkelglsdvnis skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn
flagellar filament capping protein FliD [Campylobacter coli] NCBI Reference Sequence: WP_002791831.1	95	mafgslsslg fgsgvltqdt idklkeaeqk aridpytkki eenttkqkdl teiktkllsfqtavsslada tvfakrkvvg sisdnppasl tvnsgvalqs mninvtqlaq kdvyqskglandsgfvsanl tgttdltffs ngkeytvtvd knttyrdlad kineasggei vakivntgekgtpyrltlts ketgedsais fyagkkdssg kytsdsnaet ifknlgweld ktssidpakdkkgygikdts lhiqtaqnae

Sequence Description	SEQ ID NO.	Sequence
		ftldgikmfr ssntvtdlgv gmtltlnktg einfdvqqdfegvtkamqdl vdayndlvtn lnaatdynse tgtkgtlqgi sevnsirssi ladlfdsqvvdgttedangn kvntkvmlsm qdfglslnda gtlsfdsskf eqkvkedpds tesffsnitkyedinhtgev iktgslskyl nsnggntngl efkpgdftiv fnnqtydlsk nsdgtnfkltgkteeellqn lanhinskgi eglkvkvesy nqnnvtgfrl nfsgdgssdf sikgdasilkelglsdvnis skpiegkgif sklkatlqem tgkdgsitky desltndiks lntskdstqamidtrydtma nqwlqyesil nklnqqlntv tnminaanns nn

EXAMPLE 3

CAMPYLOBACTER-SPECIFIC ANTIBODIES IN RSIGA2 BIND TO FLID

In the SIgA2 format, CAA1 and CCG4 maintained the original FliD binding activity, displaying similar EC50 for the flagellar protein (Figure 7A). The EC50 of CAA1 SIgA2 was 0.02372, and the EC50 of CCG4 SIgA2 was 0.02954. Epitope binning showed that the binding of one antibody to the antigen did not prevent the binding of the other mAb (Figure 7B), thus indicating the recognition of two different epitopes. Western blot analysis in denaturing reducing conditions indicated that the two mAbs bind structurally different antigenic determinants, with CAA1 targeting a linear epitope and CCG4 a conformational one (Figure 7C). The accessibility of the antibodies to these epitopes in the flagella of *C. jejuni* and *C. coli* historical isolates was confirmed by flow cytometry and by confocal imaging (Figures 7D, 7E).

EXAMPLE 4

RSIGA INHIBITS MOTILITY OF CAMPYLOBACTER *IN VITRO*

A motility assay is shown schematically in Figure. 2. Results are provided in FIG. 3. Binding of CAA1 (rSIgA2) to the Campylobacter flagella reduced bacteria motility, a condition required to maximize infection and invasiveness. The control rSIgA2 HGN194, directed against HIV-1 gp120, was unable to curb bacteria diffusion

in the motility assay, indicating that that the inhibition of bacterial motility was not resulting from "innate" cross-reactivity of the highly glycosylated structure of SIgA.

EXAMPLE 5

MOUSE MODEL OF CAMPYLOBACTER INFECTION

Genetically manipulated animals characterized by an exacerbated inflammatory responses to bacteria, such as SIGIRR or IL10$^{-/-}$ mice, have been proposed as models to study *Campylobacter* pathogenesis (Heimesaat *et al., Front.Cell.Infect.Microbiol.*, 4:77 (2014); Stahl *et al., PLoS Pathog.*, 10:e1004264 (2014)). However, these mutations dramatically alter the murine immune system to an extent that even the presence of commensal microbes can potentially result in spontaneous enterocolitis (Mansfield *et al., Infect.Immun.*, 75:1099-1115 (2007)).

Moreover, the murine intestine has been shown to be highly resistant to *Campylobacter* due to colonization resistance and a certain level of tolerance, which limits inflammation (Bereswill *et al., PLoS One,* 6:e20953 (2011); Chang and Miller, *Infect.Immun.*, 74:5261-5271 (2006); Masanta *et al., Clin.Dev.Immunol.*, 2013:526860 (2013)). To overcome the potential effects of the resident microbiota, pre-treatment via oral gavage with vancomycin, for which *Campylobacter* species are inherently resistant (Taylor and Courvalin, *Antimicrob.Agents Chemother.*, 32:1107-1112 (1988)), was adopted. Although the pretreatment allows robust bacterial colonization in the caecum, it does not appear to enhance the pathology in adult wild type mice, as minimal signs of inflammation were observed (Stahl *et al., PLoS Pathog.*, 10:e1004264 (2014)).

Higher susceptibility to *C. jejuni* infection of infant wild type mice in comparison to adult animals has been previously reported and linked to significant differences in the microbiota composition (Haag *et al., Eur.J.Microbiol.Immunol.(Bp),* 2:2-11 (2012)). To set up a model that could recapitulate the disease in newborn and infants under immunocompetent conditions, the sensitivity to *C. jejuni* 81-176 infection of was evaluated in pups (12 day-old), just-weaned (21 day-old) and adult (56 day-old) C57BL/6 mice. Animals were pre-treated with vancomycin via oral gavage to deplete the murine microbiota before being infected with C. jejuni 81-176 at 10^9 CFU/mouse.

Campylobacter isolation from stools at 6 days post-infection revealed almost 2-log-higher shedding from 21-day-old animals than from 12 and 56- day-old mice (Figure 8A). In-line with these results, just-weaned mice displayed significantly higher intestinal inflammation as measured by the levels of lipocalin-2 in the stools and histological score values in the caecum in comparison to pups and adult mice (Figures 8B-8C).

Since the antibiotic pre-treatment is expected to provide comparable ecological niches for infection in the different animals, other factors could account for the different sensitivity to *C. jejuni* infection displayed by the three groups of mice. Analysis of murine IgA in the stools of 12, 21 and 56- day-old mice revealed different concentrations among the groups (Figure 8D). Notably, just-weaned mice presented negligible levels of IgA in the stools in comparison to both pups and adult mice. Without wishing to be bound by theory, this observation may be consistent with the transition between the exogenous supply of maternal antibodies provided with milk (12 days-old mice) and the beginning of the endogenous production that is established in adult animals (56 days-old mice). Therefore, a factor in the susceptibility of just-weaned mice to C. *jejuni* infection may be a lower concentration of secretory IgA due to the relative immaturity of intestinal immune system and the depletion of maternal antibodies in these animals. Based on these data, just-weaned mice were selected as an immune competent mouse model to study the prophylactic activity of FliD-reactive mAbs.

Off-target binding by CAA1 and CCG4 to the murine microbiota could result in reduced mAb availability and thus, reduced activity against pathogens in a prophylactic setting. To investigate this, potential cross-reactivity of the rSIgAs with the microbiota of just-weaned mice was evaluated. Stools from animals orally infected with *C. jejuni*, *C. coli* or PBS (mock infected) were collected 24 hours post-infection and incubated with the two FliD-reactive mAbs and the control rSIgA HGN194. Analysis of human-IgA coated bacteria from stools of mock and infected animals revealed that both Campylobacter-reactive rSIgA were able to recognize and bind the most common

species associated with severe infections, displaying limited cross-reactivity with the murine microbiota (Figure 14A).

To set-up the conditions for testing the prophylactic efficacy of the antibodies, the pharmacokinetics of orally administered SIgA in different gastrointestinal tracts of just weaned mice were evaluated. The *Campylobacter*-irrelevant HGN194 rSIgA2, which displayed no cross-reactivity with the murine microbiota (Figure 14A), was administered as a single oral gavage of 150 ug in PBS (≈15 mg/Kg) and its concentration in the different intestinal sub-compartments was measured at 2, 4 and 8 h post-administration (Figure 14B). HGN194 rSIgA concentration in the caecum was maintained almost constant within the first 4 hours post-administration and then tended to dramatically decrease by 8 hours (Figure 14B). The human antibody was not detectable at 12- or 24-hours post-administration (data not shown).

EXAMPLE 6

PROPHYLACTIC EFFECT OF ORALLY ADMINISTERED RSIGA

Just-weaned animals (21d) were treated with vanocmycin and then administered a single oral gavage of 200 μg/mouse of rSIgA2 CAA1, CCG4, HGN194 or PBS two hours before oral infection with 10^8 CFU/mouse of *C. jejuni* 81-176. Treated animals and the corresponding control groups were monitored for 72 hours, during which the severity of infection and degree of inflammation were recorded. Analysis of the stools from treated mice revealed a trend characterized by higher *Campylobacter* shedding at 24 hours post-infection followed by a significant decrease over time. Conversely, untreated and HGN194-treated groups presented lower shedding at early time points followed by a consistent CFU increase at 48 hours post-infection (Figure 9A). Figures 5A and 5B show data from a separate experiment in which mice were administered 200 μg mAb once before infection, and twice after infection, with 10^9 CFU/mouse of *C. jejuni* 81-176.

These results suggest that CAA1 and CCG4 may prevent or reduce the ability of the pathogen to adhere to the surface of the mucosal epithelium, thus facilitating the clearance of bacteria via peristalsis or mucocilliary activity at early stages post-

infection. This hypothesis was further supported by significantly lower levels of lipocalin-2, a marker of intestinal inflammation linked to epithelial damage and neutrophil infiltration, recorded at 72 hours post-infection in the stools of CAA1 and CCG4 treated animals in comparison to the control groups (infected/non-treated and infected/HGN194 treated groups) (Figure 9B). Figure 6 shows data from a separate experiment in which mice were administered 200 μg mAb once before infection, and twice after infection, with 10^9 CFU/mouse of *C. jejuni* 81-176.

Similar findings were observed in animals administered with higher or lower *Campylobacter* inoculum (10^7 or 10^9 CFU/mouse; Figures 15A, 15B). In addition, animals treated with a single administration of FliD-reactive mAbs presented levels of PMN cells infiltration and histological score values in the caecum that were comparable with non-infected mice and significantly lower than the HGN194-treated group, hence supporting *in vivo* efficacy that is not driven by the "innate activity" (Kaetzel, *Immunol.Rev.*, 206:83-99 (2005); Phalipon *et al.*, *Immunity*, 17:107-115 (2002)), associated with the highly glycosylated SIgA (Figures 9C, 9D).

These results indicate that FliD-specific antibodies of the present disclosure in rSIgA2 format protect against *Campylobacter* infection and inflammation following oral delivery by accelerating bacterial clearance at early stages after infection.

EXAMPLE 7

IGA ISOTYPE SWITCH DOES NOT AFFECT CAA1 PROPHYLACTIC ACTIVITY

Since IgA1 and IgA2 can have differences in Fab reach, flexibility, and glycosylation that might affect the cross-linking ability and/or persistence of the polymeric Ig in the intestine, the following experiments were performed to determine whether the two IgA isotypes may exert different prophylactic activities in the herein-described immunocompetent mouse model of *Campylobacter* infection.

FliD-reactive CAA1 was recombinantly produced as SIgA1 and SIgA2. Proper assembly of the two subclasses was confirmed by analytical methods and by digestion with IgA1 proteases from *Neisseria gonhorrehoeae* (Figure 16A). CAA1 SIgA1 and SIgA2 displayed comparable binding to FliD (Figure 16B) and no significant

differences in reactivity to *Campylobacter* species *in vitro* or with murine microbiota *ex vivo* were observed between the two formats (Figures 16C, 16D).

The prophylactic activity of the two subclasses was then tested in the murine model of *Campylobacter* infection. In line with previous findings, animals administered the FliD-reactive mAbs displayed higher *Campylobacter* shedding at early timepoints post-infection followed by a decrease over time, while infected non-treated animals produced an opposite trend (Figure 10A). Although CAA1 rSIgA2 accelerated shedding faster than rSIgA1, both subclasses were equally capable of limiting inflammation in infected animals, as shown by the levels of lipocalin-2 in the stools, the PMN infiltration and the corresponding histological score in the caecum at 72 hours post-infection (Figures 10B-10D).

These results indicate that structural differences between IgA1 and IgA2 do not result in differences in prophylactic activity exerted by these two CAA1 formats in the *in-vivo* model.

EXAMPLE 8

MABS CAA1 AND CCG4 HAVE REDUCED ORAL PROPHYLACTIC ACTIVITY WHEN EXPRESSED AS IGG

Although SIgAs are thought to be the most abundant antibodies expressed in association with the intestinal mucosa and may be the first line of defense against enteric pathogens, they are characterized by a complex protein structure and their development as drugs may present challenges in comparison to IgG-based monoclonal antibodies. Since the activity of the *Campylobacter*-reactive mAbs was shown to be dependent on specificity for FliD, CAA1, CCG4 and the *Campylobacter*-irrelevant antibody HGN194 were generated as rIgG1 and evaluated for prophylactic activity in comparison to their corresponding SIgA2 counterparts.

Since glycosylation might affect the ability of mAbs to interact with mucin on the mucosal surface, the localization and persistence of control mAb HGN194 as rIgG1 in the murine intestinal tract was appraised by administering the antibody be a single oral gavage to 21-day old mice and then by measuring its concentration in the different

intestinal sub-compartments after 2, 4 and 8 h (Figure 14C). As with HGN194 rSIgA2, at every time-point, the highest concentration of the rIgG1 was detected in the caecum; however, in this intestinal sub-compartment the rIgG1 concentration tended to decrease faster than rSIgA2, with a significant reduction observed by 4 hours post-administration (Figures 14B, 14C).

The prophylactic activity of the FliD-reactive mAbs CAA1 and CCG4 as rIgG1 or SIgA2 was also evaluated. MAbs were administered orally to just-weaned mice 2 hours before infection with *C. jejuni* 81-176. Interestingly, while animals treated with SIgA2 antibodies displayed the previously observed pattern characterized by higher shedding at 24 hours post-infection followed by a significant decrease at 48 and 72 h, the groups treated with the IgG version of the same antibodies revealed trends similar to the non-treated groups (Figures 11A and 17A). The importance of the SIgA format for *in vivo* efficacy was further confirmed by the lower ability of CAA1 and CCG4 IgG to limit inflammation in comparison to their polymeric counterparts, as shown by PMN cells infiltration in the caecum and lipocalin-2 levels in the stools of the infected animals at 72 post-infection (Figures 11B, C and 17B, 17C). Overall, no significant differences in the histological scores were observed between the mice treated with the FliD-reactive IgG antibodies and the non-treated animals. Conversely, the SIgA versions of the antibodies were able to replicate the beneficial effect previously observed, maintaining the histological score in the caecum to values significantly lower than both non-treated and IgG treated mice (Figure 11D and 17D).

These data indicate that CAA1 and CCG4 IgGs have limited prophylactic activity when orally administered prior to *Campylobacter* infection, as compared to the same antibodies expressed as SIgA. Without wishing to be bound by theory, the lack of activity of orally administered CAA1 and CCG4 IgGs might rely both on a lower persistence in the gastrointestinal tract and on different cross-linking properties associated with the SIgA format.

The various embodiments described above can be combined to provide further embodiments. All of the U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications

referred to in this specification and/or listed in the Application Data Sheet, including U.S. Provisional Patent Application No. 62/699,573, filed July 17, 2018, are incorporated herein by reference, in their entirety. Aspects of the embodiments can be modified, if necessary to employ concepts of the various patents, applications and publications to provide yet further embodiments.

These and other changes can be made to the embodiments in light of the above-detailed description. In general, in the following claims, the terms used should not be construed to limit the claims to the specific embodiments disclosed in the specification and the claims, but should be construed to include all possible embodiments along with the full scope of equivalents to which such claims are entitled. Accordingly, the claims are not limited by the disclosure.

CLAIMS

What is claimed is:

1. An isolated antibody, or an antigen-binding fragment thereof, that is specific for a *Campylobacter* flagellum capping protein (FliD) epitope.

2. The antibody, or an antigen-binding fragment of claim 1, wherein the epitope is a conformational epitope.

3. The antibody, or an antigen-binding fragment of claim 1, wherein the epitope is a linear epitope.

4. The antibody or antigen-binding fragment of any one of claims 1-3, wherein the antibody or antigen-binding fragment is capable of binding to the FliD epitope with an EC50 of less than about 0.1μg/mL, or less than about 0.05μg/mL, or less than about 0.03μg/mL, as measured by ELISA.

5. The antibody or antigen-binding fragment of any one of claims 1-4, wherein the antibody or antigen-binding fragment is capable of reducing motility of the *Campylobacter* in an *in vitro* cell motility assay.

6. The antibody or antigen-binding fragment of any one of claims 1-5, wherein the antibody or antigen-binding fragment is capable of neutralizing a *Campylobacter* infection in a subject.

7. The antibody or antigen-binding fragment of any one of claims 1-6, wherein the *Campylobacter* comprises *Campylobacter jejuni*, *Campylobacter coli*, or both.

8. The antibody or antigen-binding fragment of any one of claims 1-7, wherein the *Campylobacter* comprises *C. jejuni* 81-176, *C. coli* 10092/ATB, or both.

9. The antibody or antigen-binding fragment of any one of claims 1-8, wherein the antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 amino acid sequences according to:

(i) SEQ ID NOs:9-14, respectively; or

(ii) SEQ ID NOs:25-30, respectively.

10. The antibody or antigen-binding fragment of any one of claims 1-9, wherein the antibody or antigen-binding fragment comprises at least one more germline-encoded amino acid in a variable region as compared to a parent antibody or antigen binding fragment, provided that the parent antibody or antigen binding fragment comprises one or more somatic mutations.

11. The antibody or antigen-binding fragment of any one of claims 1-10, wherein the antibody or antigen-binding fragment comprises:

(i) VH having at least 85% amino acid identity to SEQ ID NO:2, and a VL having at least 85% amino acid identity to SEQ ID NO:4; or

(ii) VH having at least 85% amino acid identity to SEQ ID NO:22, and a VL having at least 85% amino acid identity to SEQ ID NO:24.

12. The antibody or antigen-binding fragment of claim 11, wherein the antibody or antigen-binding fragment comprises:

(i) a VH according to SEQ ID NO:2, and a VL according to SEQ ID NO:4; or

(ii) a VH according to SEQ ID NO:22, and a VL according to SEQ ID NO:24.

13. The antibody or antigen-binding fragment of any one of claims 1-12, wherein the antibody or antigen-binding fragment is an IgA, IgG, IgD, IgE, or IgM isotype.

14. The antibody or antigen-binding fragment of claim 13, wherein the antibody or antigen-binding fragment is an IgA isotype.

15. The antibody or antigen-binding fragment of claim 14, wherein the antibody or antigen-binding fragment is an IgA1 isotype.

16. The antibody or antigen-binding fragment of claim 14, wherein the antibody or antigen-binding fragment is an IgA2 isotype.

17. The antibody or antigen-binding fragment of any one of claims 1-16, wherein the antibody or antigen-binding fragment comprises a Fc polypeptide or a fragment thereof.

18. The antibody or antigen-binding fragment of claim 17, comprising a heavy chain constant region having at least 90% identity to any one of SEQ ID NOs:40-42.

19. The antibody or antigen-binding fragment of any one of claims 14-18, wherein the antibody or antigen-binding fragment comprises an IgA dimer molecule.

20. The antibody or antigen-binding fragment of any one of claims 14-19, wherein the antibody or antigen binding fragment comprises a secretory IgA molecule.

21. The antibody or antigen-binding fragment of any one of claims 1-20, wherein the antibody or antigen binding fragment is monoclonal.

22. The antibody or antigen-binding fragment of any one of claims 1-21, wherein the antibody or antigen binding fragment is chimeric, humanized, or human.

23. A composition, comprising the antibody or antigen-binding fragment of any one of claims 1-22, and a pharmaceutically acceptable carrier, excipient, or diluent.

24. A kit, comprising:

(i) a first antibody or an antigen-binding fragment thereof, which is specific for a *Campylobacter* flagellum capping protein (FliD) linear epitope; and

(ii) a second antibody or an antigen-binding fragment thereof, which is specific for a *Campylobacter* flagellum capping protein (FliD) conformational epitope.

25. The kit of claim 24, wherein:

(i) the first antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 sequences according to SEQ ID NOs:9-14, respectively; and

(ii) the second antibody or antigen-binding fragment comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 sequences according to SEQ ID NOs:25-30, respectively.

26. The kit of claim 24 or 25, wherein:

(i) the first antibody or antigen-binding fragment comprises a VH having at least 85% amino acid identity to SEQ ID NO:2, and a VL having at least 85% amino acid identity to SEQ ID NO:4; and

(ii) the second antibody or antigen-binding fragment comprises a VH having at least 85% amino acid identity to SEQ ID NO:22, and a VL having at least 85% amino acid identity to SEQ ID NO:24.

27. The kit of claim 26, wherein:

(i) the first antibody or antigen-binding fragment comprises a VH according to SEQ ID NO:2, and a VK according to SEQ ID NO:4; and

(ii) the second antibody or antigen-binding fragment comprises a VH according to SEQ ID NO:22, and a VL according to SEQ ID NO:24.

28. The kit of any one of claims 24-27, wherein the first antibody or antigen-binding fragment and the second antibody or antigen-binding fragment are each a same isotype.

29. The kit of claim 28, wherein the first antibody or antigen-binding fragment and the second antibody or antigen-binding fragment are each a secreted IgA.

30. An isolated polynucleotide encoding the antibody or antigen-binding fragment of any one of claims 1-22.

31. The isolated polynucleotide of claim 30, wherein the polynucleotide is codon-optimized for expression in a host cell.

32. The isolated polynucleotide of claim 30 or 31, comprising:

(i) a VH-encoding polynucleotide having at least 75% identity to the nucleotide sequence set forth in any one of SEQ ID NOs:1, 5, 7, 8, 21, 37, or 38;

(ii) a VL-encoding polynucleotide having at least 75% identity to the nucleotide sequence set forth in SEQ ID NO:3, 6, 23, or 39; and/or

(iii) HCDR1-, HCDR2-, HCDR3-, LCDR1-, LCDR2-, and LCDR3-encoding sequences having at least 90% identity to the nucleotide sequences set forth in SEQ ID NOs:15-20, respectively, or in SEQ ID NOs:31-36, respectively.

33. A vector, comprising the polynucleotide of any one of claims 30-32.

34. A recombinant host cell, comprising the isolated polynucleotide of any one of claims 30-32, or the vector of claim 33.

35. The recombinant host cell of claim 34, wherein the host cell comprises a mammalian cell.

36. The recombinant host cell of claim 35, wherein the host cell is a CHO cell, a HEK293 cell, a PER.C6 cell, a Y0 cell, a Sp2/0 cell, a NS0 cell, a human liver cell, a myeloma cell, or a hybridoma cell.

37. A method of making the antibody or antigen-binding fragment of any one of claims 1-22, the method comprising culturing the recombinant host cell of any one of claims 34-36 under conditions and for a time suitable to express the antibody or antigen-binding fragment.

38. A method for treating a Campylobacter infection in a subject, the method comprising administering to the subject an effective amount of the antibody or antigen-binding fragment of any one of claims 1-22, or of the composition of claim 23.

39. A method for reducing intestinal inflammation in a subject having a *Campylobacter* infection, the method comprising administering to the subject an effective amount of the antibody or antigen-binding fragment of any one of claims 1-22, or of the composition of claim 23.

40. A method for increasing intestinal shedding of a *Campylobacter* by a subject having a *Campylobacter* infection, the method comprising administering to the subject an effective amount of the antibody or antigen-binding fragment of any one of claims 1-22, or of the composition of claim 23.

41. The method of any one of claims 38-40, wherein the antibody or antigen-binding fragment comprises a secretory IgA molecule.

42. The method of any one of claims 38-41, wherein the administering comprises oral administration of the antibody, antigen-binding fragment, or composition.

43. The method of claim any one of claims 38-42, wherein the administering comprises administering the antibody, antigen-binding fragment, or composition to the subject at 2, 3, 4, 5, 6, 7, 8, 9, 10 times, or more.

44. The method of any one of claims 38-43, wherein the method comprises administering the antibody, antigen-binding fragment, or composition to the subject a plurality of times, wherein a second or successive administration is performed at about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 24, about 48, about 74, about 96 hours, or more, following a first or prior administration, respectively.

45. The method of any one of claims 38-44, wherein the antibody, antigen-binding fragment, or composition is administered to the subject at least one time prior to the subject being infected by the *Campylobacter*.

46. The method of any one of claims 38-45, wherein following the administering, a stool sample from the subject comprises an increased number of *Campylobacter* colony-forming units (CFUs) as compared to a stool sample from the subject prior to being administered an effective amount of the antibody, antigen-binding fragment, or composition.

47. The method of any one of claims 38-46, wherein following the administering, a stool sample from the subject comprises a reduced amount of lipocalin-

2 (LCN2) as compared to a stool sample from the subject prior to being administered an effective amount of the antibody, antigen-binding fragment, or composition.

48. The method of any one of claims 38-47, wherein following the administering, the subject comprises a reduced amount of polymorphonucleated (PMN) cell infiltrate in a caecum as compared to the subject prior to being administered an effective amount of the antibody, antigen-binding fragment, or composition, wherein the PMN cells are $Gr1^{+}CD11b^{+}$.

49. The method of any one of claims 38-48, wherein following the administering, the subject has an improved caecum histology as compared to the subject prior to being administered an effective amount of the antibody, antigen-binding fragment, or composition.

50. The method of any one of claims 38-49, wherein following the administering, the antibody or antigen-binding fragment is present in the caecum and/or in feces of the subject for at least 4 hours or for at least 8 hours following the administration.

51. The antibody or antigen-binding fragment of any one of claims 1-22, or the composition of claim 22, for use in a method of:

(a) treating a *Campylobacter* infection in a subject;

(b) reducing intestinal inflammation in a subject having a *Campylobacter* infection; and/or

(c) increasing intestinal shedding of a *Campylobacter* by a subject having a Campylobacter infection.

52. The antibody or antigen-binding fragment of any one of claims 1-22, or the composition of claim 23, for use in a method of manufacturing or preparing a medicament for:

(a) treating a *Campylobacter* infection in a subject;

(b) reducing intestinal inflammation in a subject having a *Campylobacter* infection; and/or

(c) increasing intestinal shedding of a *Campylobacter* by a subject having a Campylobacter infection.

53. The antibody or antigen-binding fragment, or composition for use according to claim 52, wherein the medicament is formulated for oral administration.

54. A weaned non-human mammal that:

(i) does not have a mature gastrointestinal immune system; and

(iii) has a depleted intestinal flora, wherein the depletion is caused by an antibiotic agent.

55. The weaned non-human mammal of claim 54, wherein the weaned non-human mammal further comprises a *Camplyobacter* infection.

56. The weaned non-human mammal of claim 54 or 55, wherein the non-human mammal is a mouse or a rat.

57. The weaned non-human mammal of claim 56, wherein the non-human mammal is a mouse of about 18 to about 24 days old.

58. The weaned non-human mammal of any one of claims 54-57, wherein the mammal is rencetly weaned.

59. The weaned non-human mammal of any one of claims 54-58, wherein the antibiotic agent comprises vancomycin or an analog thereof.

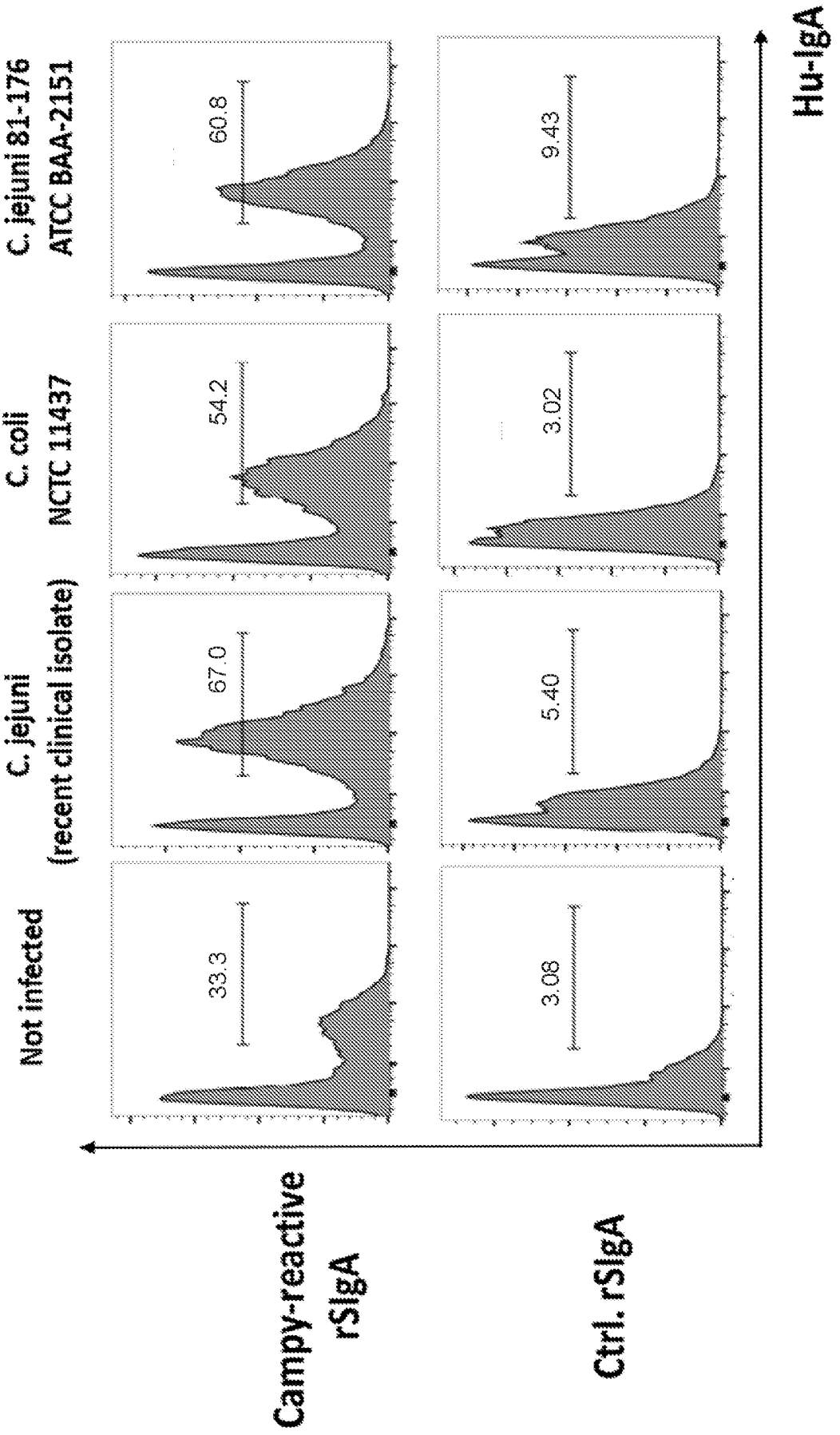

Not infected
C. jejuni (recent clinical isolate)
C. coli NCTC 11437
C. jejuni 81-176 ATCC BAA-2151
Hu-IgA
Campy-reactive rSIgA
Ctrl. rSIgA
33.3
67.0
54.2
60.8
3.08
5.40
3.02
9.43

FIG. 1

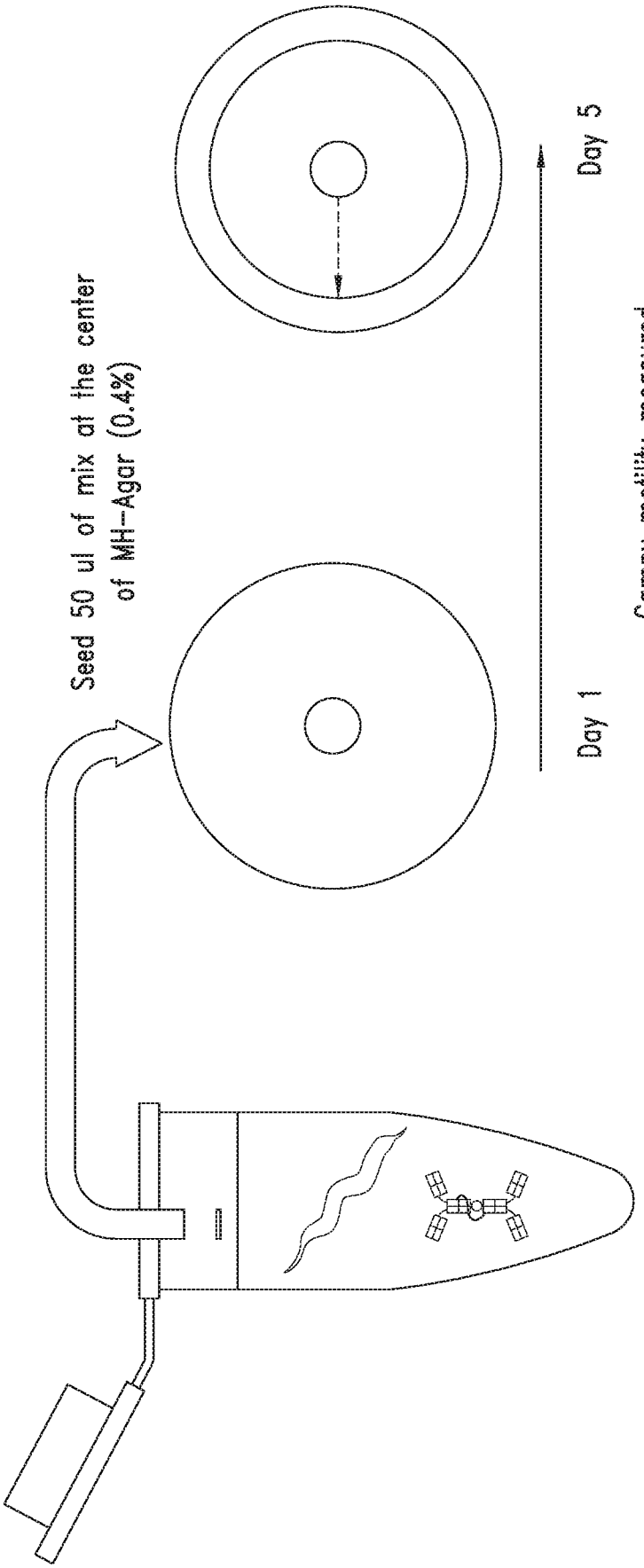

Mix and incubate 30 min @ RT
C. jejuni – conc. 10^7 cfu/ml
CAA1.54 – conc. 300 ug/ml
Seed 50 ul of mix at the center of MH-Agar (0.4%)
Day 1
Day 5
Campy motility measured 5 days post-seeding

FIG. 2

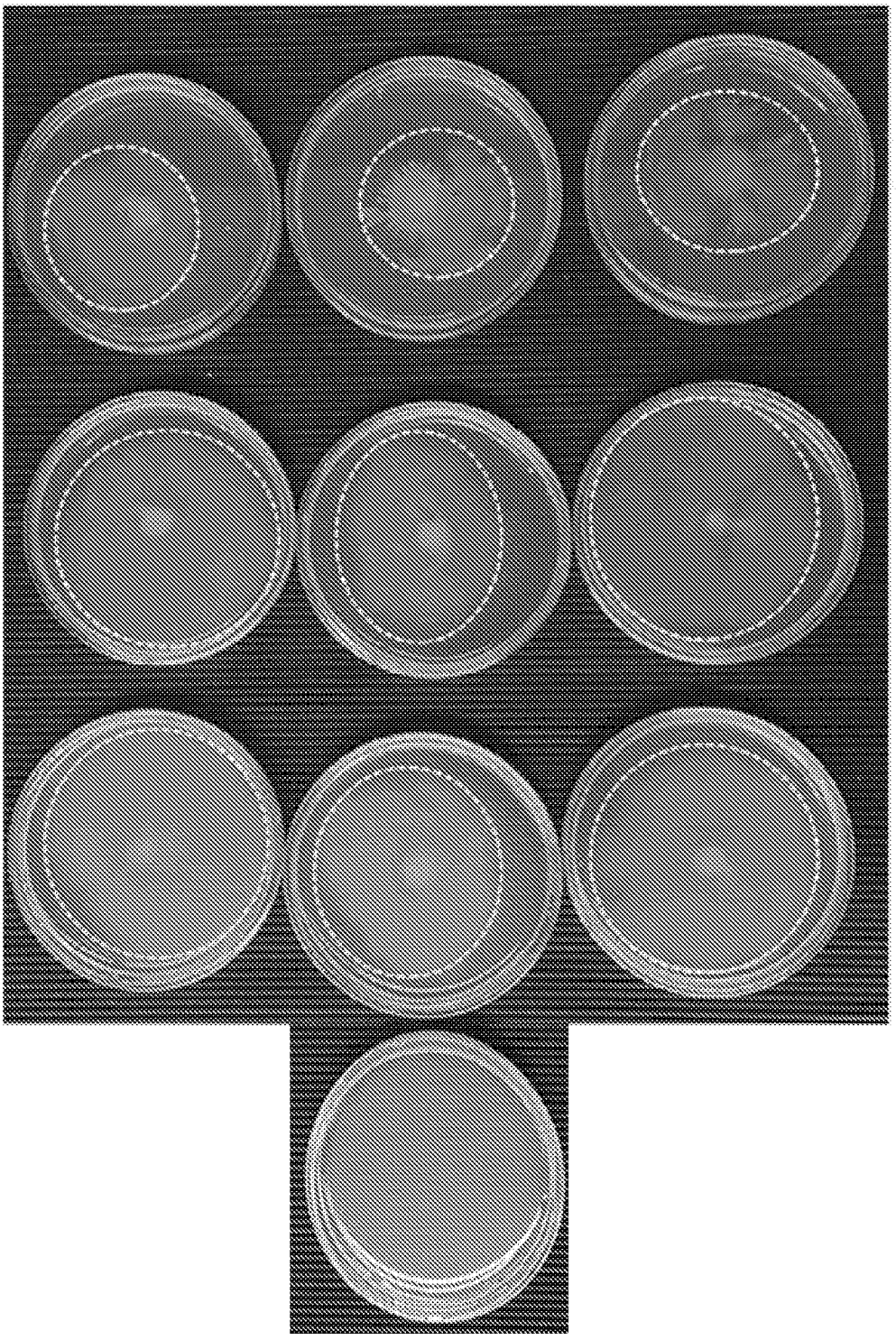


FIG. 3

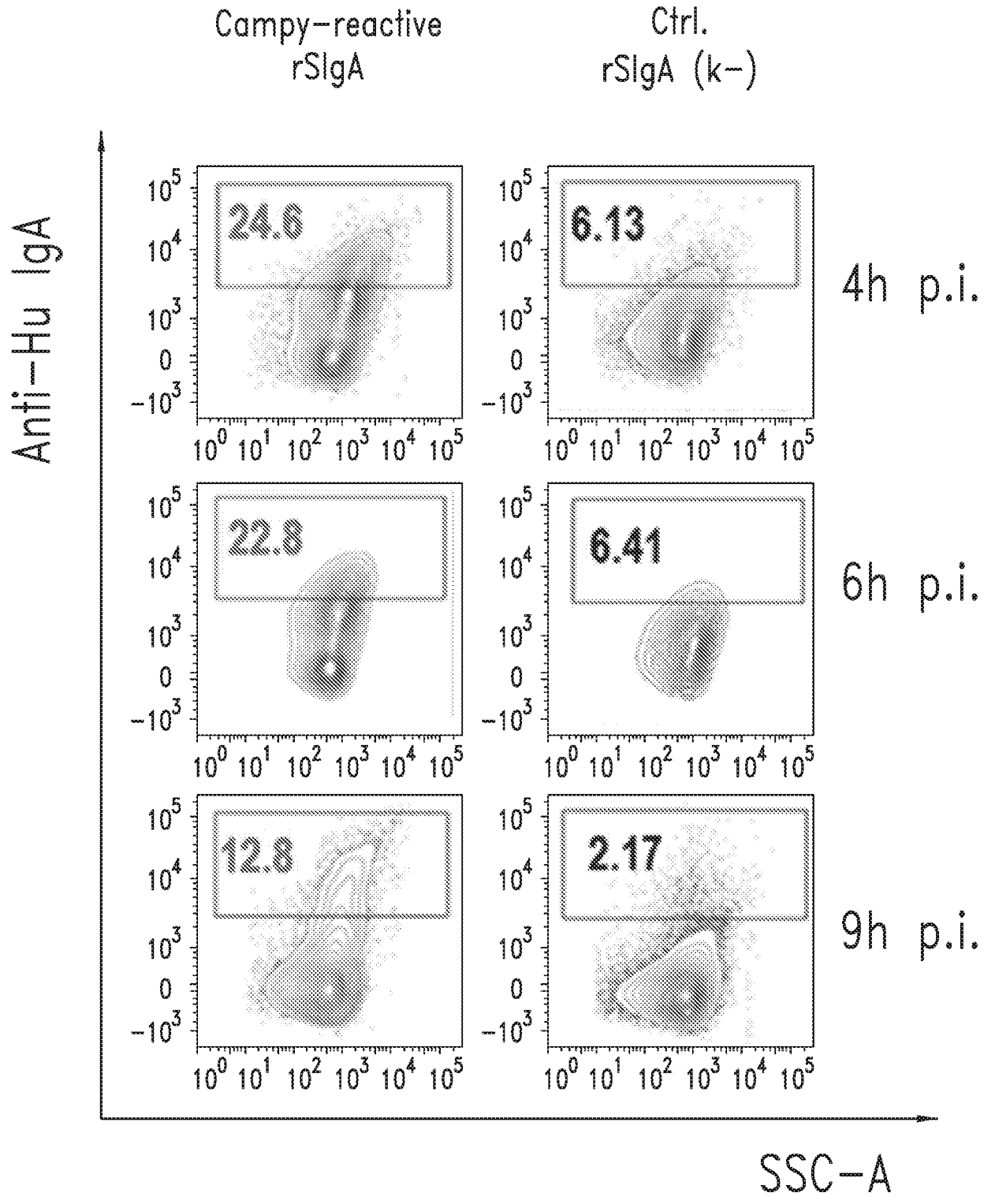

Campy-reactive rSIgA
Ctrl. rSIgA (k-)
Anti-Hu IgA
SSC-A
24.6
6.13
22.8
6.41
12.8
2.17
4h p.i.
6h p.i.
9h p.i.

FIG. 4A

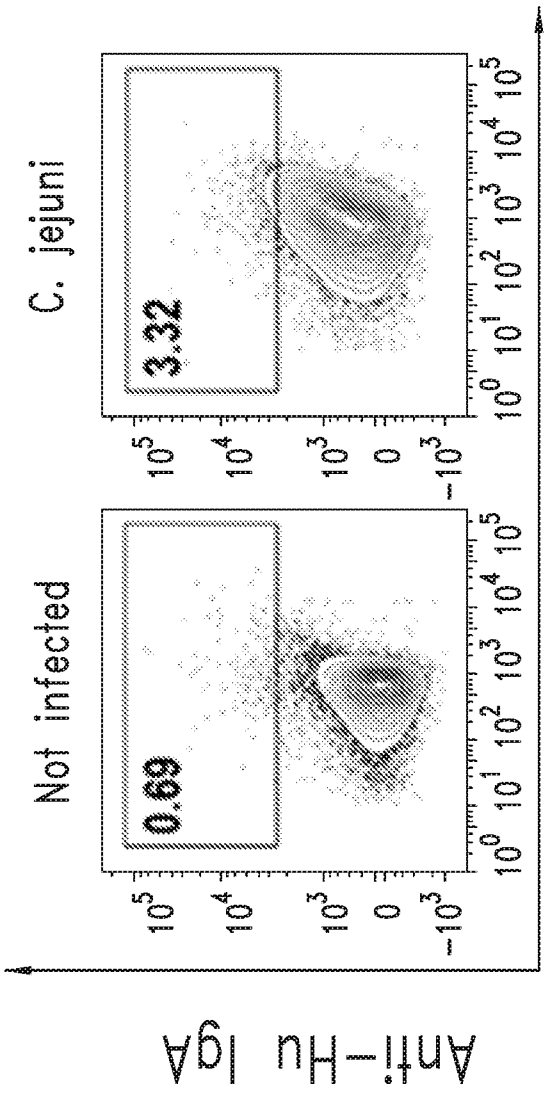


FIG. 4B

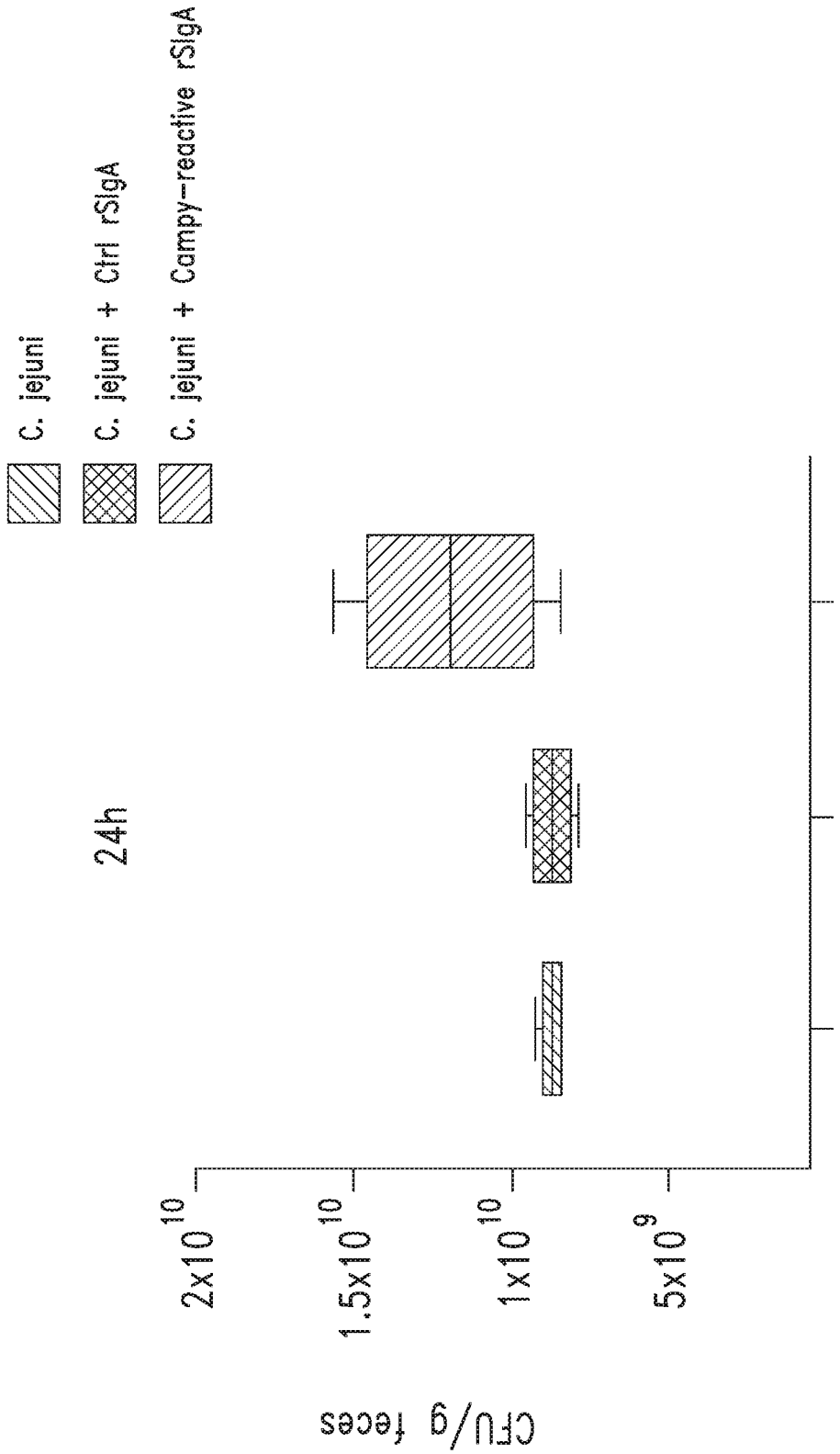

C. jejuni
C. jejuni + Ctrl rSIgA
C. jejuni + Campy-reactive rSIgA
24h
CFU/g feces
2x10^10
1.5x10^10
1x10^10
5x10^9

FIG. 5A

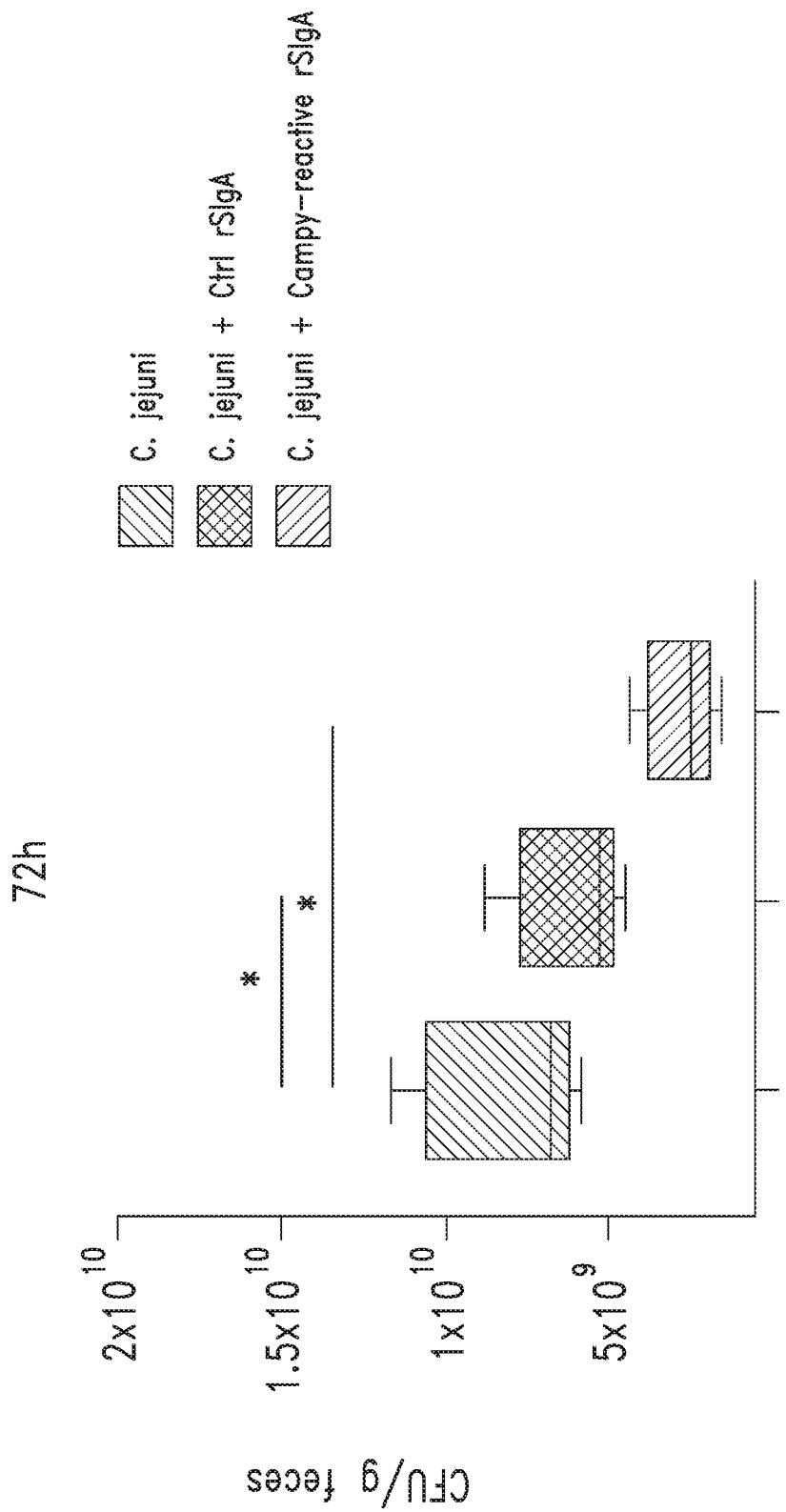

C. jejuni
C. jejuni + Ctrl rSIgA
C. jejuni + Campy-reactive rSIgA
72h
*
*
2x10^10
1.5x10^10
1x10^10
5x10^9
CFU/g feces

FIG. 5B

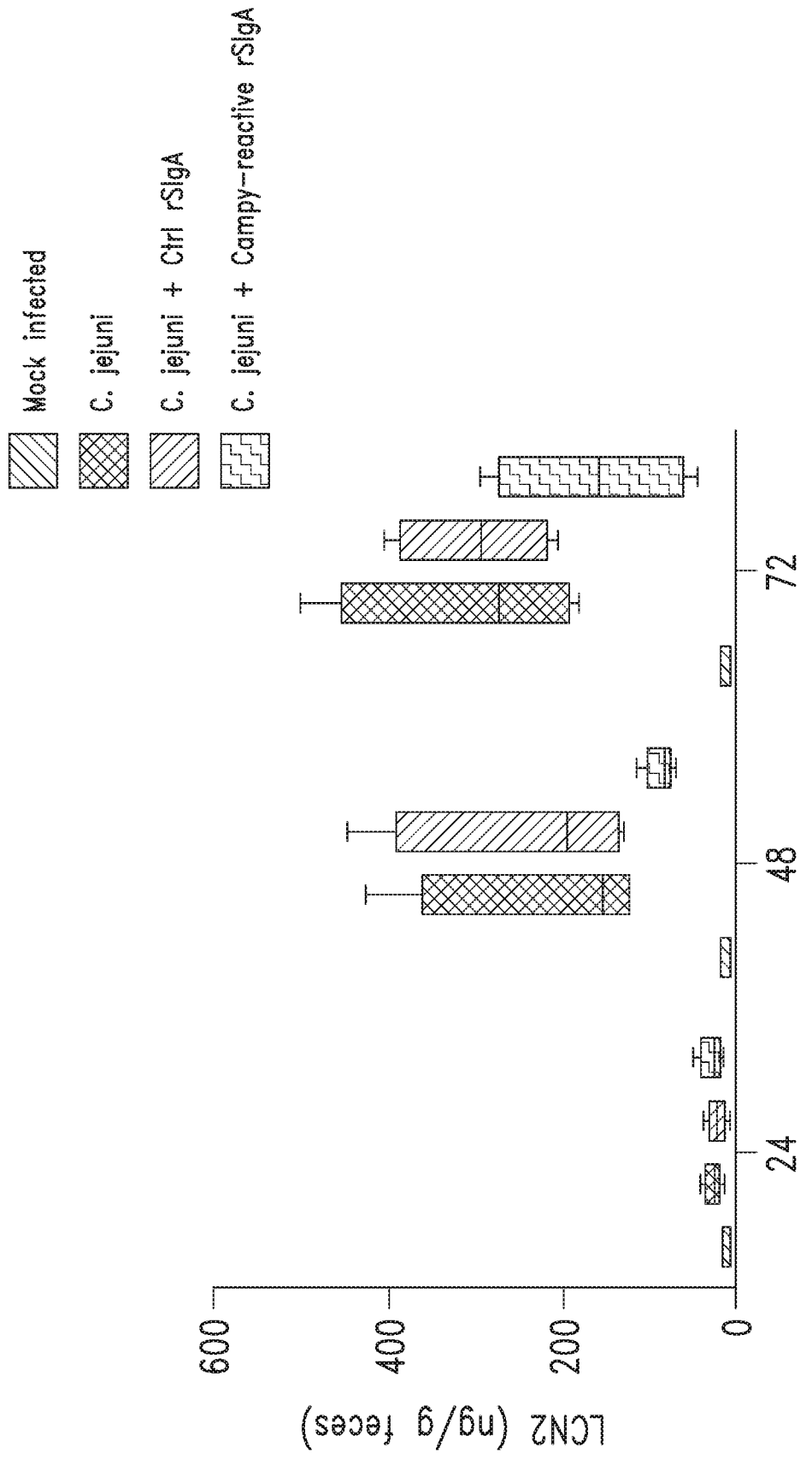

Mock infected
C. jejuni
C. jejuni + Ctrl rSIgA
C. jejuni + Campy-reactive rSIgA
LCN2 (ng/g feces)
600
400
200
0
24
48
72
Time (h.p.i.)

FIG. 6

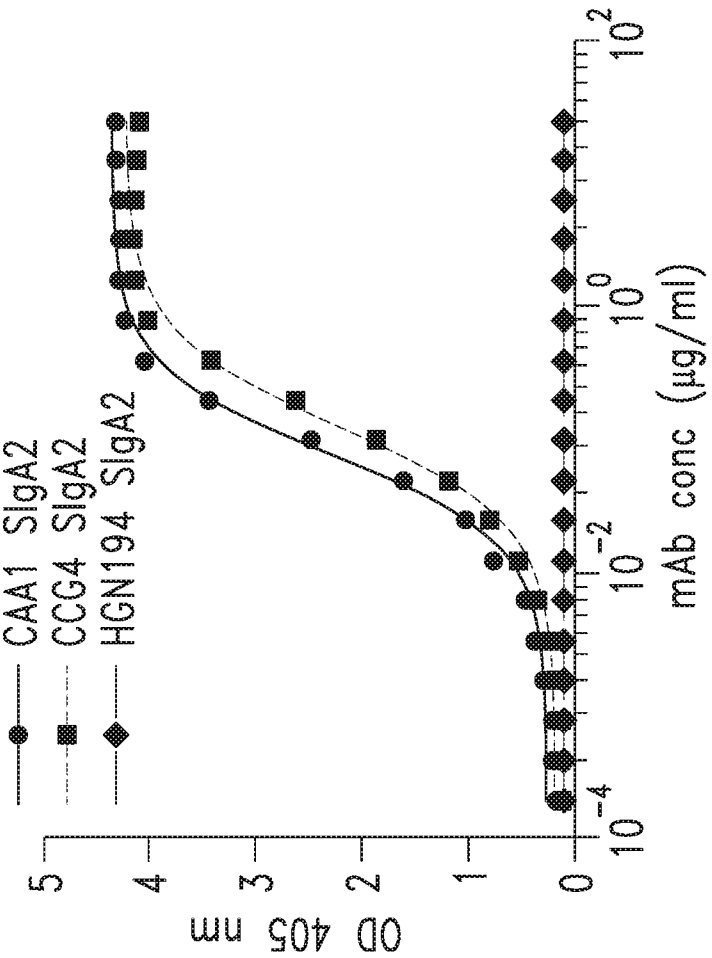

CAA1 SIgA2
CCG4 SIgA2
HGN194 SIgA2
OD 405 nm
0
1
2
3
4
5
10^{-4}
10^{-2}
10^{0}
10^{2}
mAb conc (µg/ml)

FIG. 7A

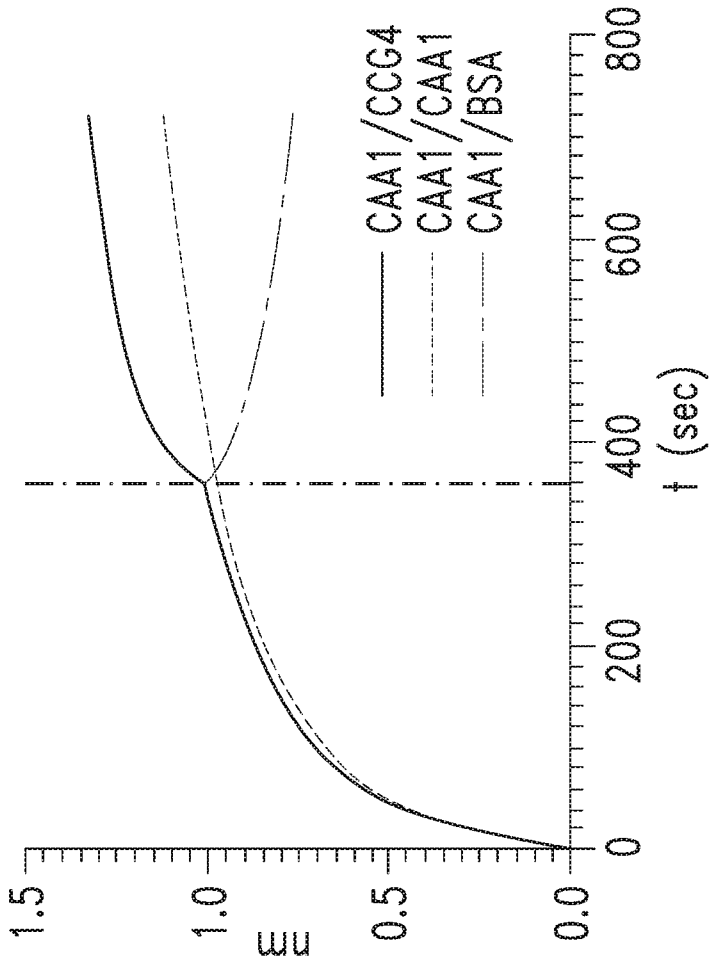

CAA1/CCG4
CAA1/CAA1
CAA1/BSA
t (sec)
0
200
400
600
800
nm
1.5
1.0
0.5
0.0

FIG. 7B

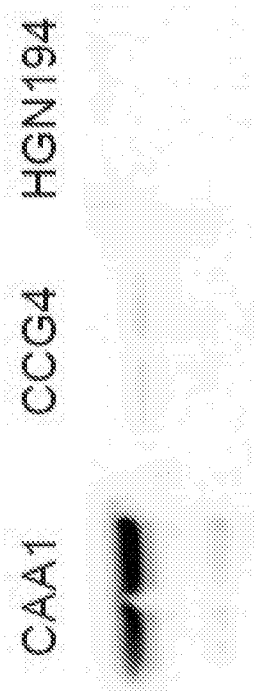


FIG. 7C

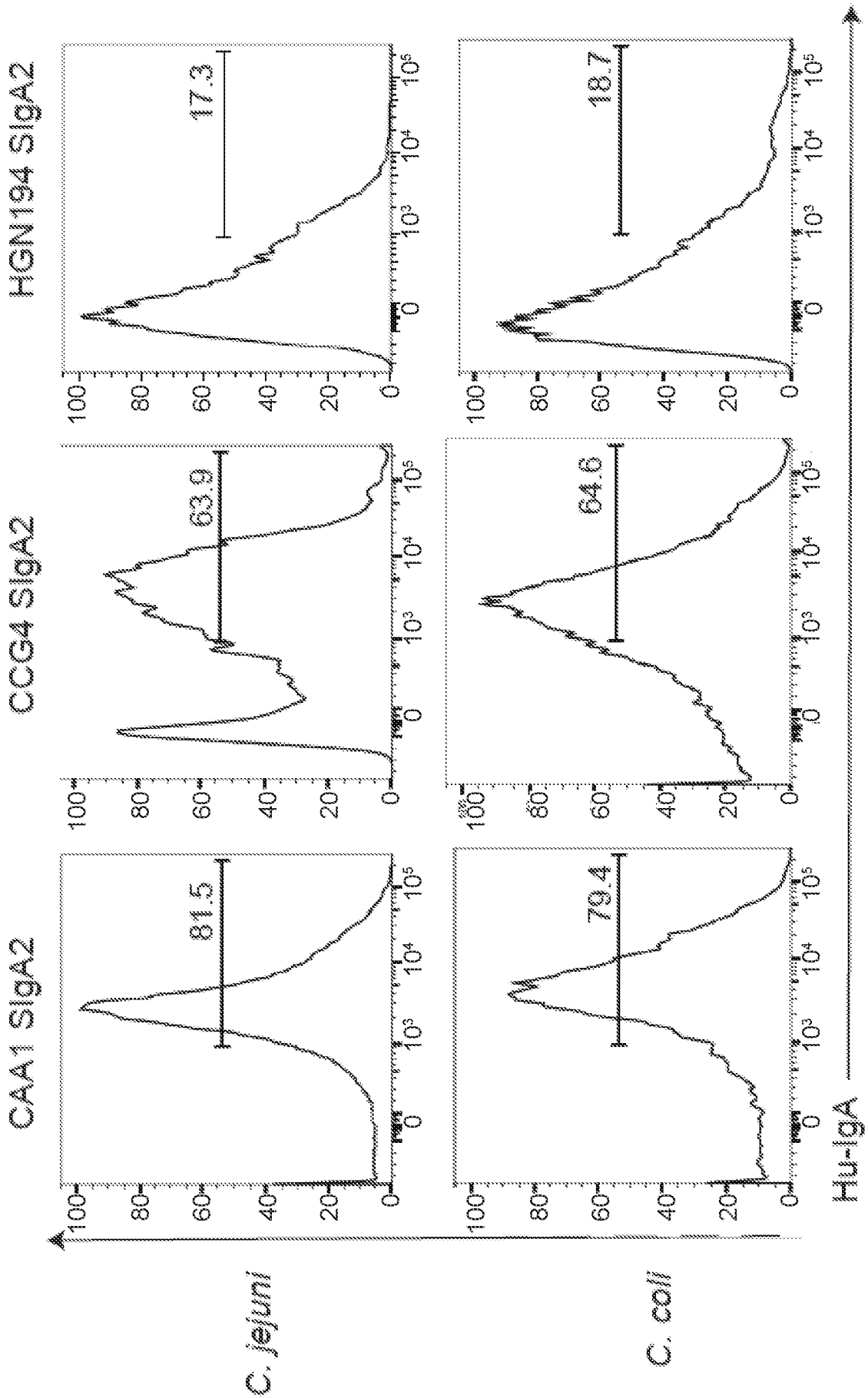

CAA1 SIgA2
CCG4 SIgA2
HGN194 SIgA2
C. jejuni
C. coli
81.5
63.9
17.3
79.4
64.6
18.7
Hu-IgA

FIG. 7D

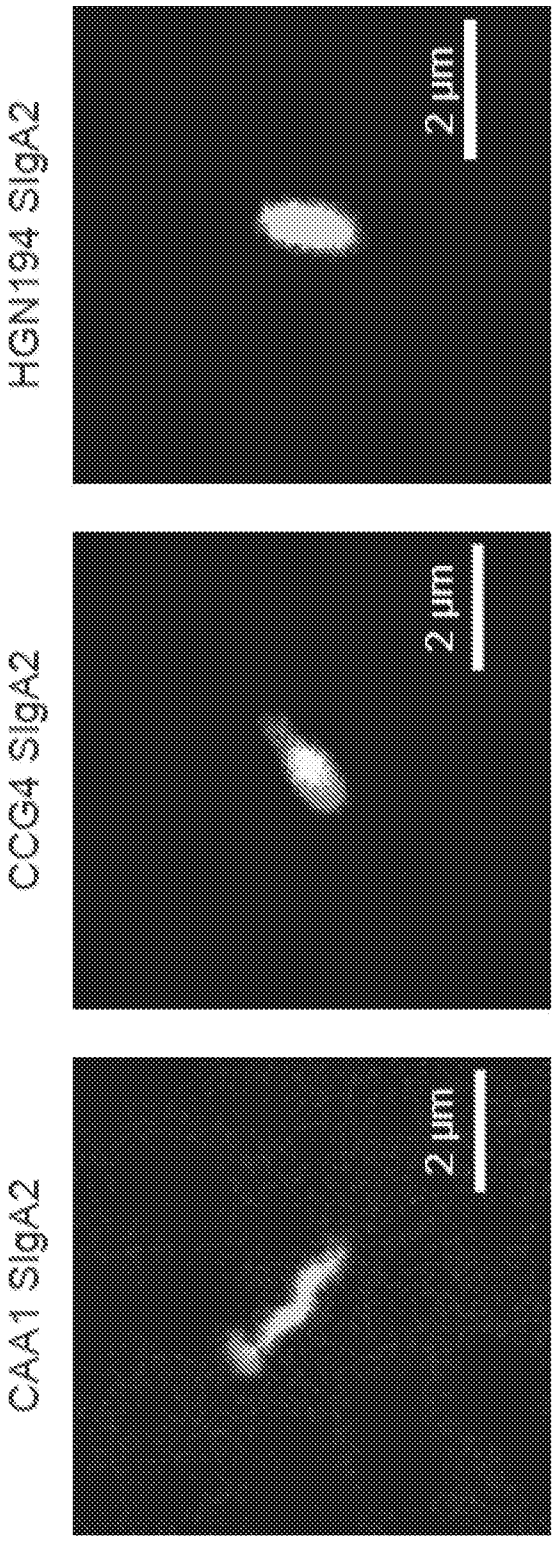


FIG. 7E

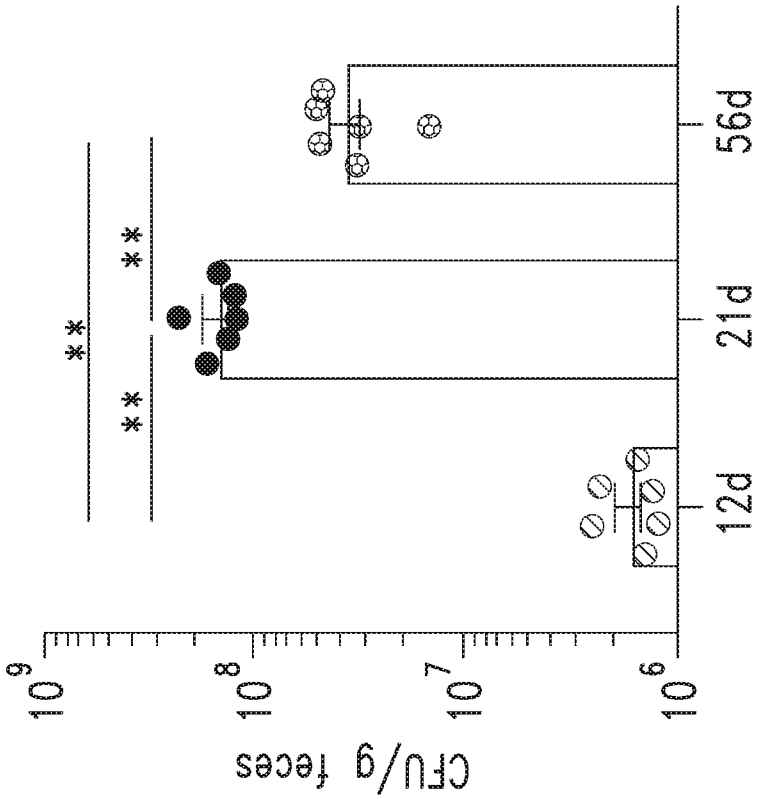


FIG. 8A

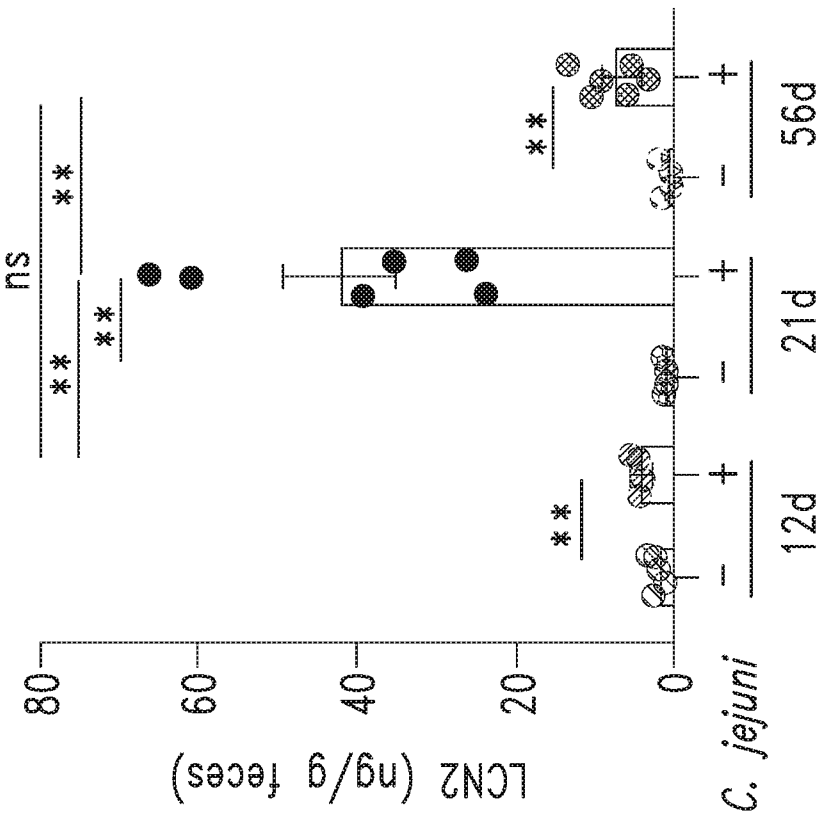


FIG. 8B

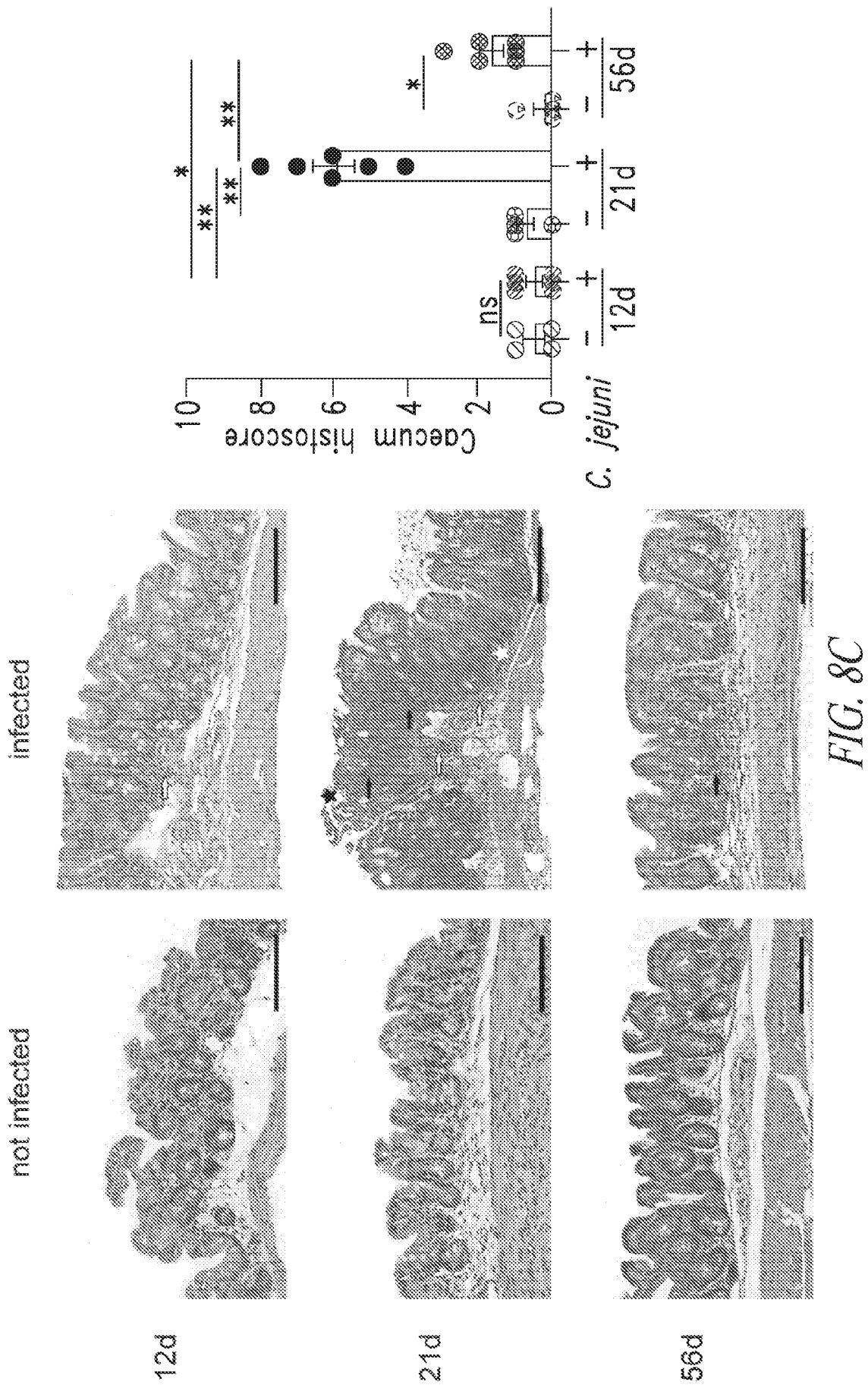

Caecum histoscore
10
8
6
4
2
0
ns
*
**
**
**
*
C. jejuni
– + – + – +
12d 21d 56d
not infected
infected
12d
21d
56d

FIG. 8C

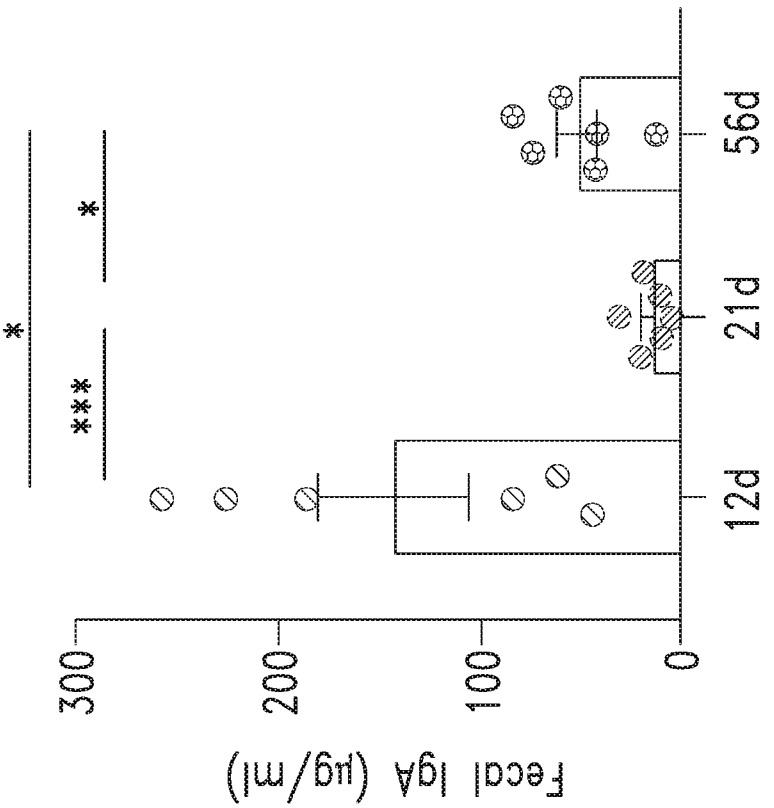


FIG. 8D

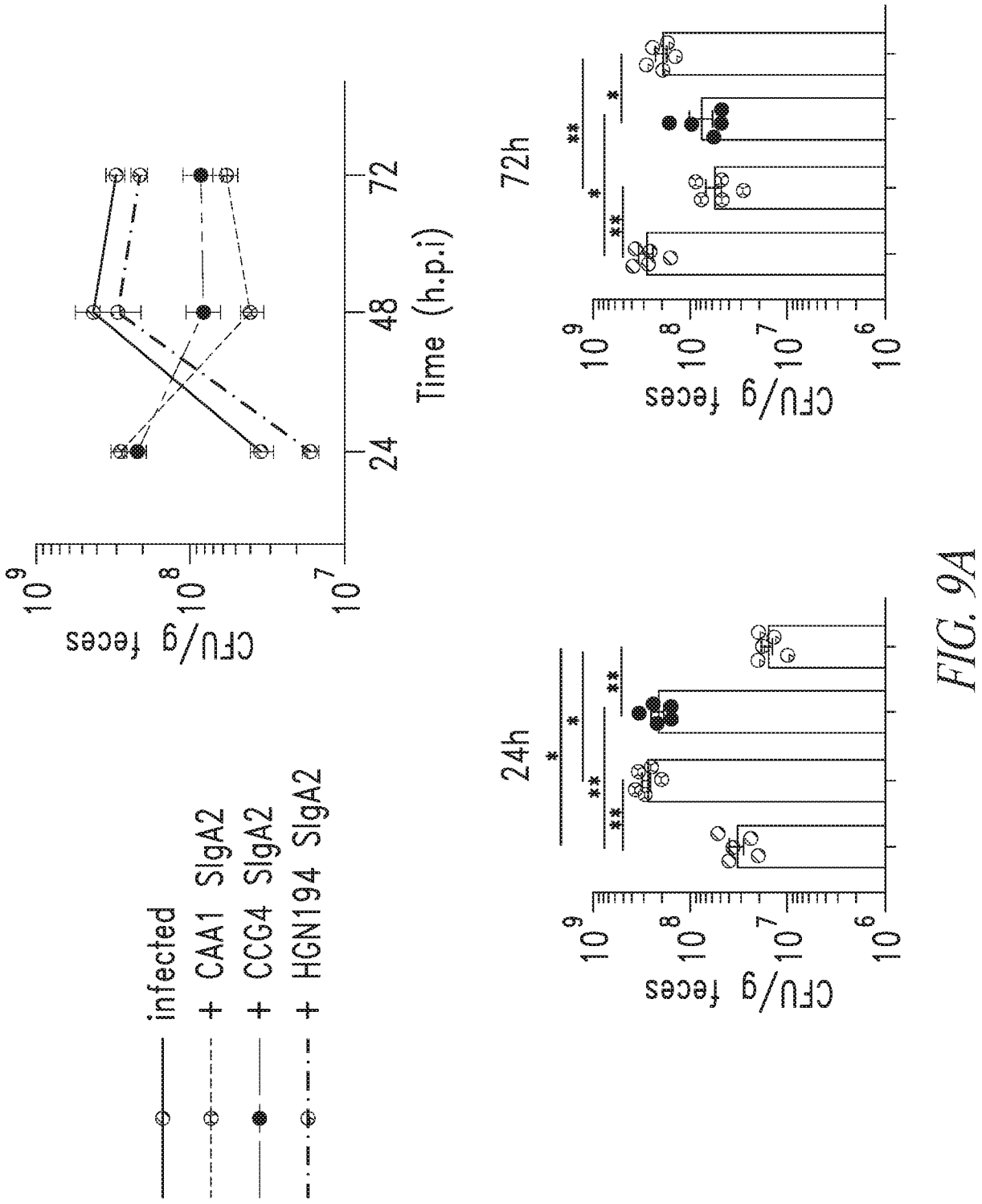

infected
+ CAA1 SIgA2
+ CCG4 SIgA2
+ HGN194 SIgA2
CFU/g feces
Time (h.p.i)
24
48
72
24h
72h

FIG. 9A

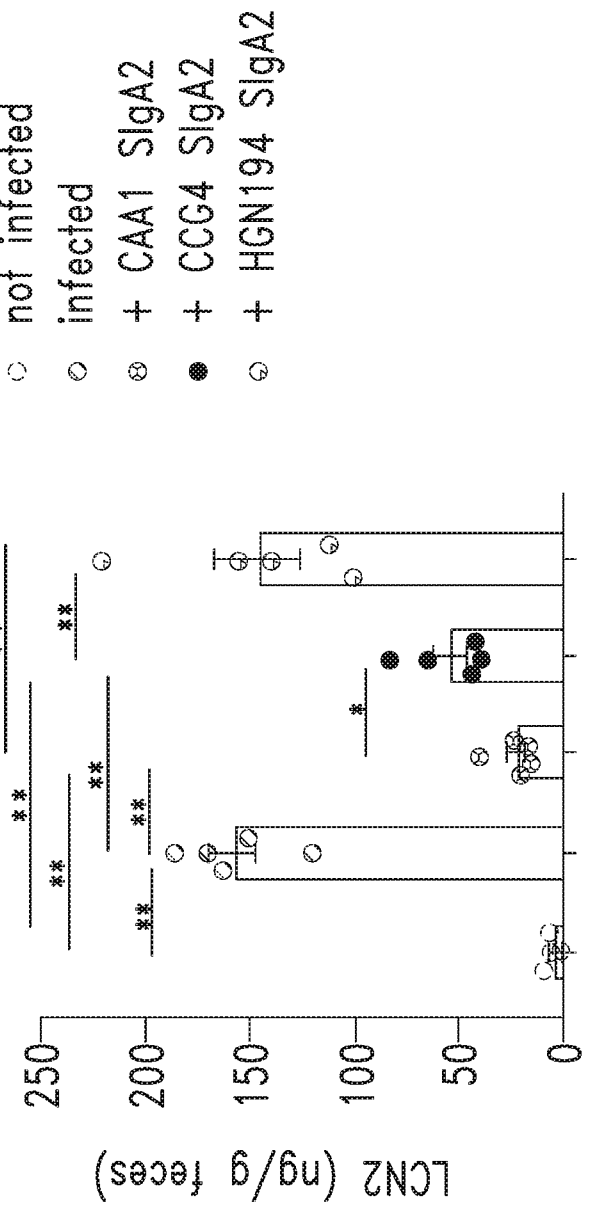

not infected
infected
+ CAA1 SIgA2
+ CCG4 SIgA2
+ HGN194 SIgA2
LCN2 (ng/g feces)
250
200
150
100
50
0
**
**
**
**
**
**
*

FIG. 9B

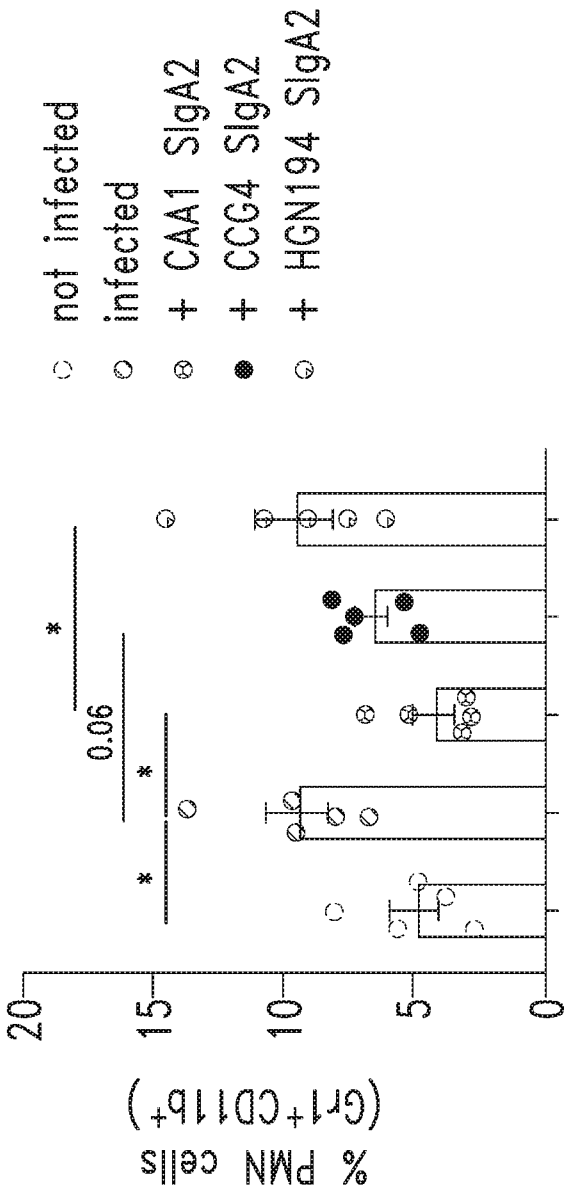

not infected
infected
+ CAA1 SIgA2
+ CCG4 SIgA2
+ HGN194 SIgA2
0.06
*
*
*
20
15
10
5
0
% PMN cells
(Gr1+CD11b+)

FIG. 9C

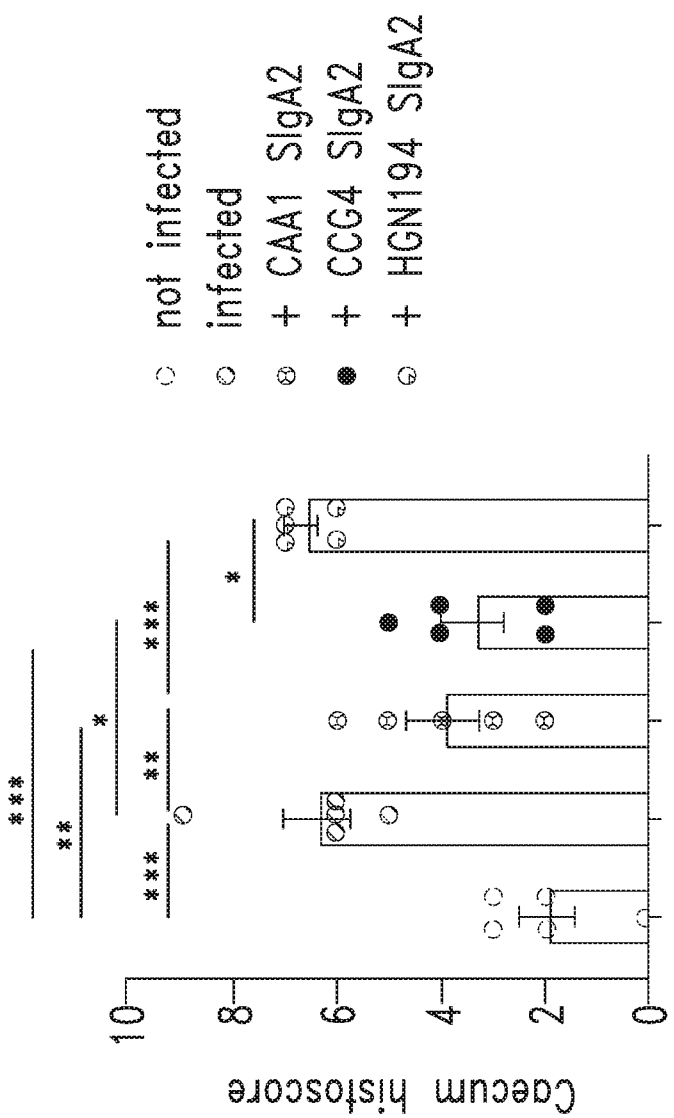

not infected
infected
+ CAA1 SIgA2
+ CCG4 SIgA2
+ HGN194 SIgA2
Caecum histoscore
0
2
4
6
8
10
***
**
*
***
**
*
***

FIG. 9D

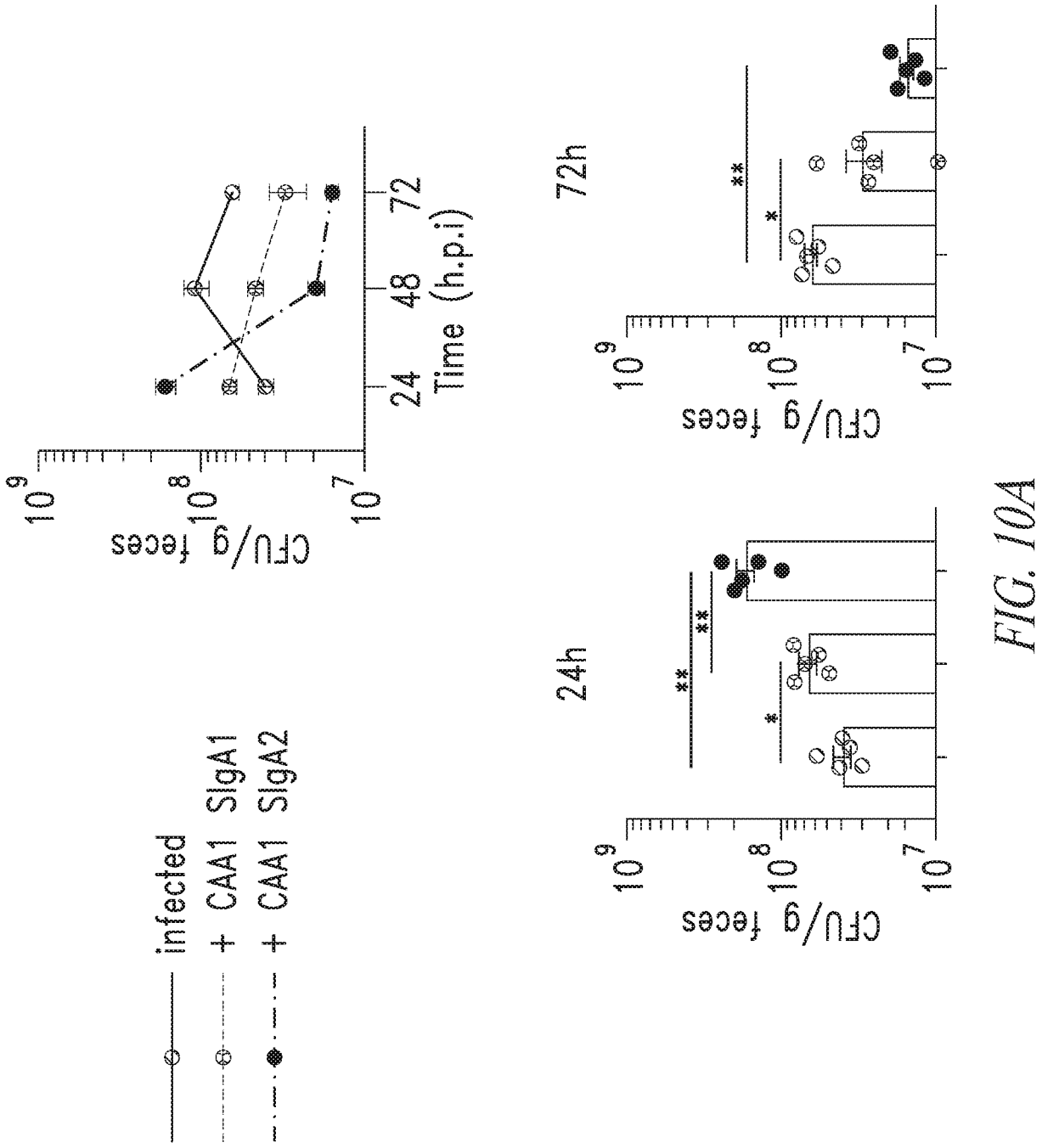
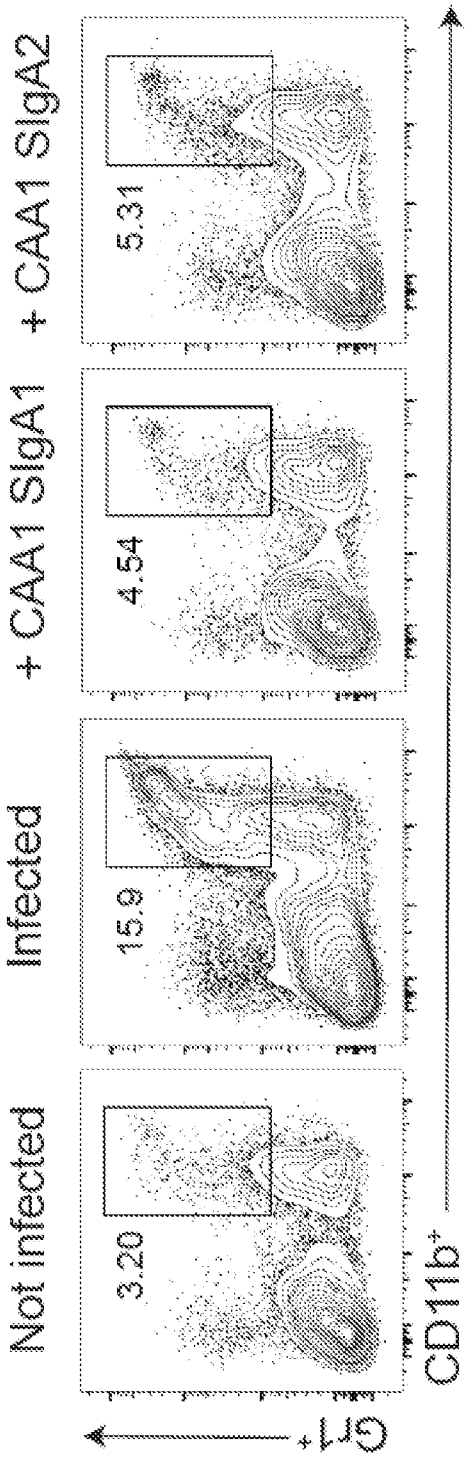

infected
+ CAA1 SIgA1
+ CAA1 SIgA2
CFU/g feces
Time (h.p.i)
24
48
72
24h
72h
*
**

FIG. 10A


Not infected
Infected
+ CAA1 SIgA1
+ CAA1 SIgA2
3.20
15.9
4.54
5.31
Gr1+
CD11b+

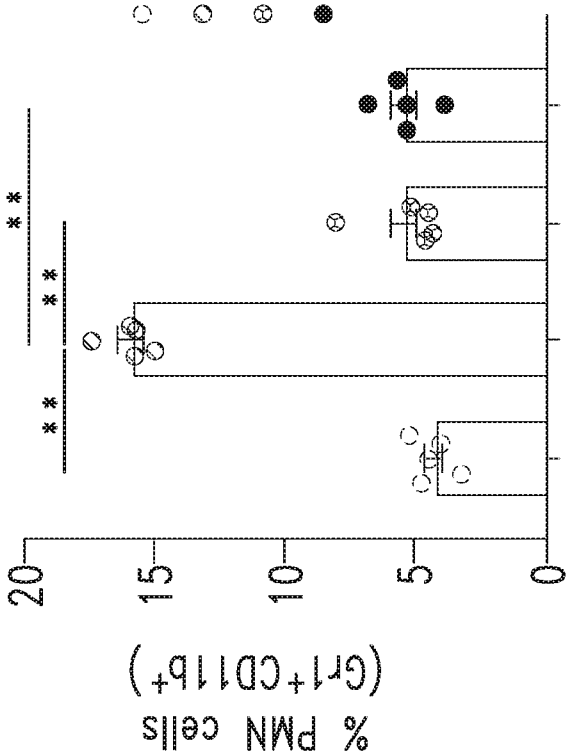

not infected
infected
+ CAA1 SIgA1
+ CAA1 SIgA2
% PMN cells
(Gr1+CD11b+)
20
15
10
5
0
**
**
**
**

FIG. 10B

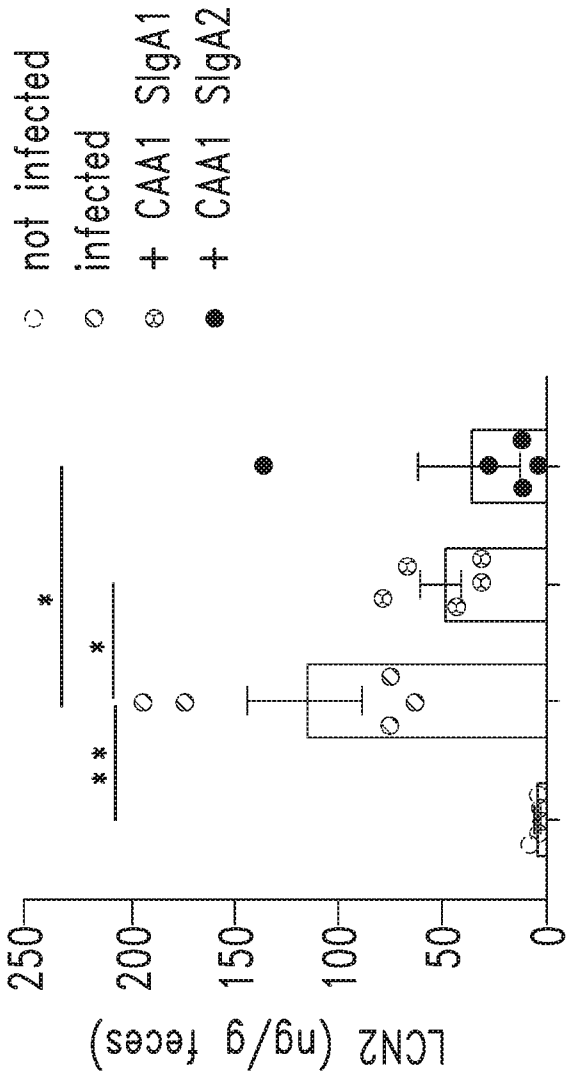

not infected
infected
+ CAA1 SIgA1
+ CAA1 SIgA2
LCN2 (ng/g feces)
250
200
150
100
50
0
*
*
**

FIG. 10C

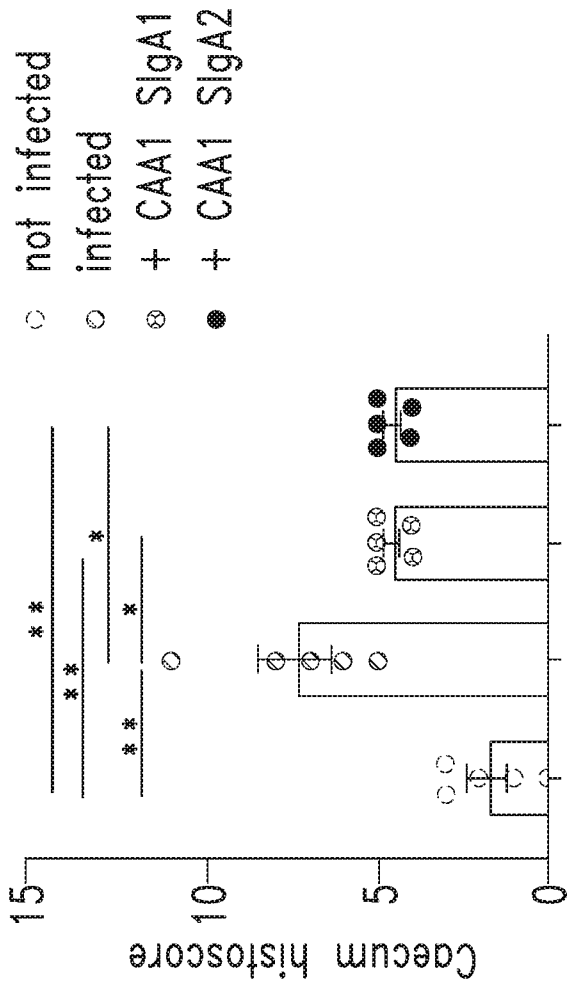

not infected
infected
+ CAA1 SIgA1
+ CAA1 SIgA2
Caecum histoscore
15
10
5
0
**
**
**
*
*

FIG. 10D

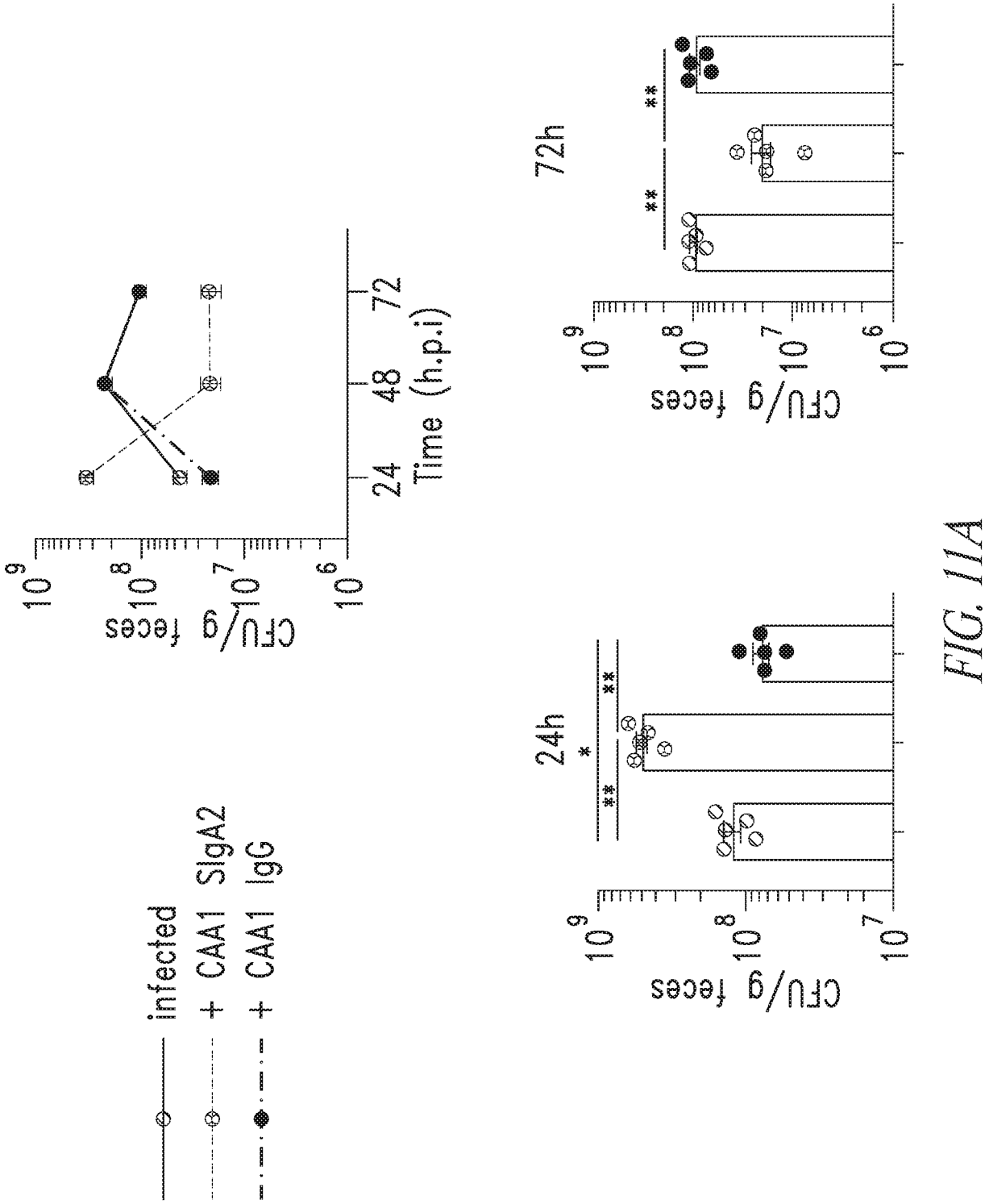

infected
+ CAA1 SIgA2
+ CAA1 IgG
CFU/g feces
Time (h.p.i)
24
48
72
24h
72h
*
**

FIG. 11A

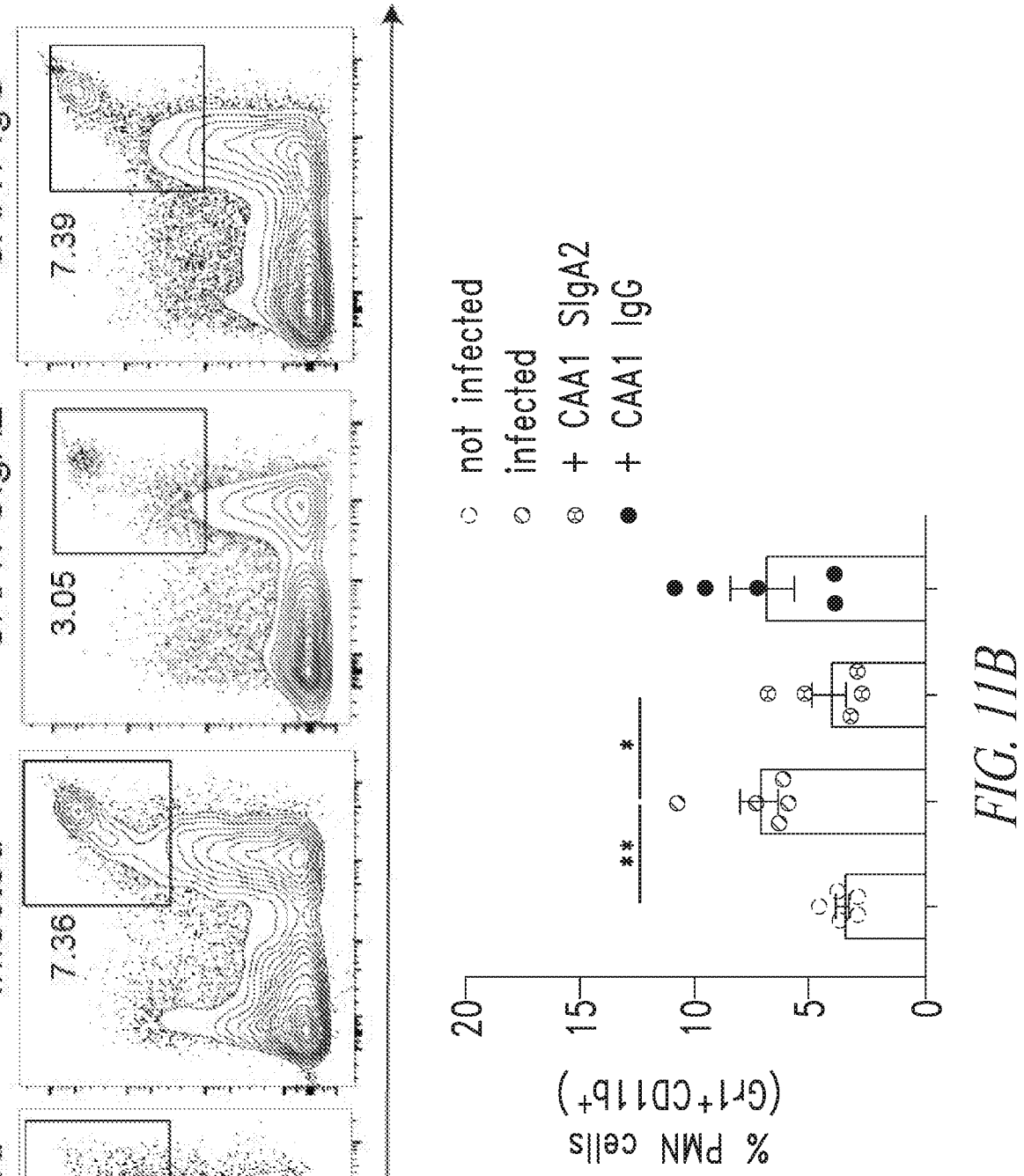

Not infected
Infected
+ CAA1 SIgA2
+ CAA1 IgG
3.88
7.36
3.05
7.39
Gr1+
CD11b+
not infected
infected
+ CAA1 SIgA2
+ CAA1 IgG
% PMN cells
(Gr1+CD11b+)
20
15
10
5
0
**
*
*

FIG. 11B

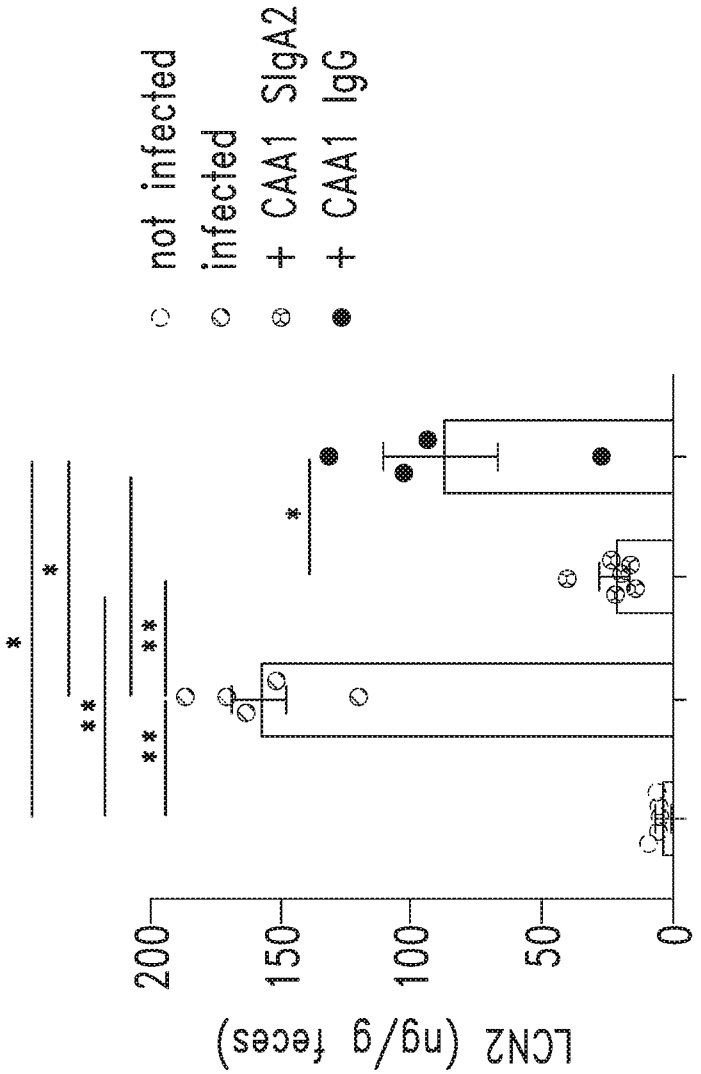

not infected
infected
+ CAA1 SIgA2
+ CAA1 IgG
LCN2 (ng/g feces)
200
150
100
50
0
*
*
**
**
**
**
*

FIG. 11C

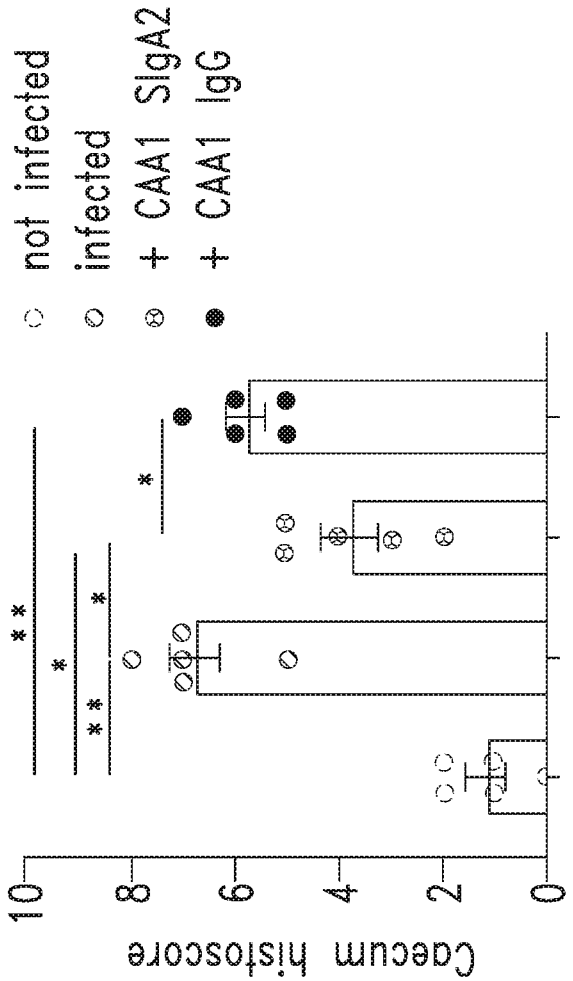

not infected
infected
+ CAA1 SIgA2
+ CAA1 IgG
Caecum histoscore
10
8
6
4
2
0
**
*
**
*
*

FIG. 11D

20
40
Consensus MAFGSLSSLGFGSGVLTQDTIDKLKEAEQKARIDPYTKKI
YP_002343979.1
WP_038400380.1
EAQ73028.1
WP_010790846.1
WP_004316510.1 A
WP_004306838.1
WP_002935293.1
WP_002928464.1
WP_002924910.1
WP_002921586.1
WP_002908989.1
WP_002901368.1
WP_002892358.1
WP_002874097.1
WP_002873395.1
EFV08769.1
EFV10698.1
EAQ94619.1
EAQ60315.1
EAQ58732.1
EAQ57731.1
CDH62398.1
ADN90737.1
APA80830.1
AOW96893.1
AON66729.1
AON65179.1
AOH51565.1

FIG. 12

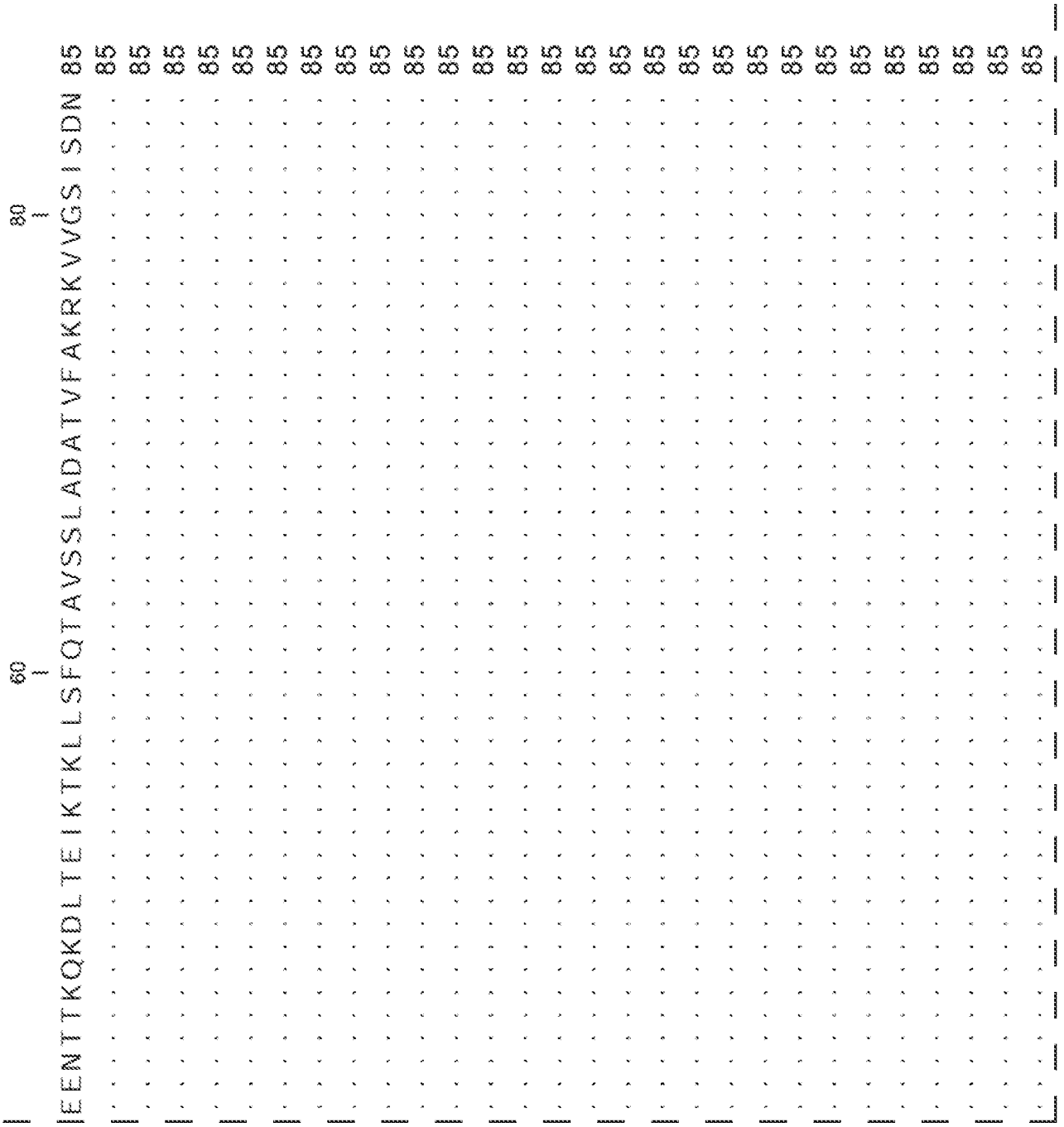


FIG. 12
(Continued)

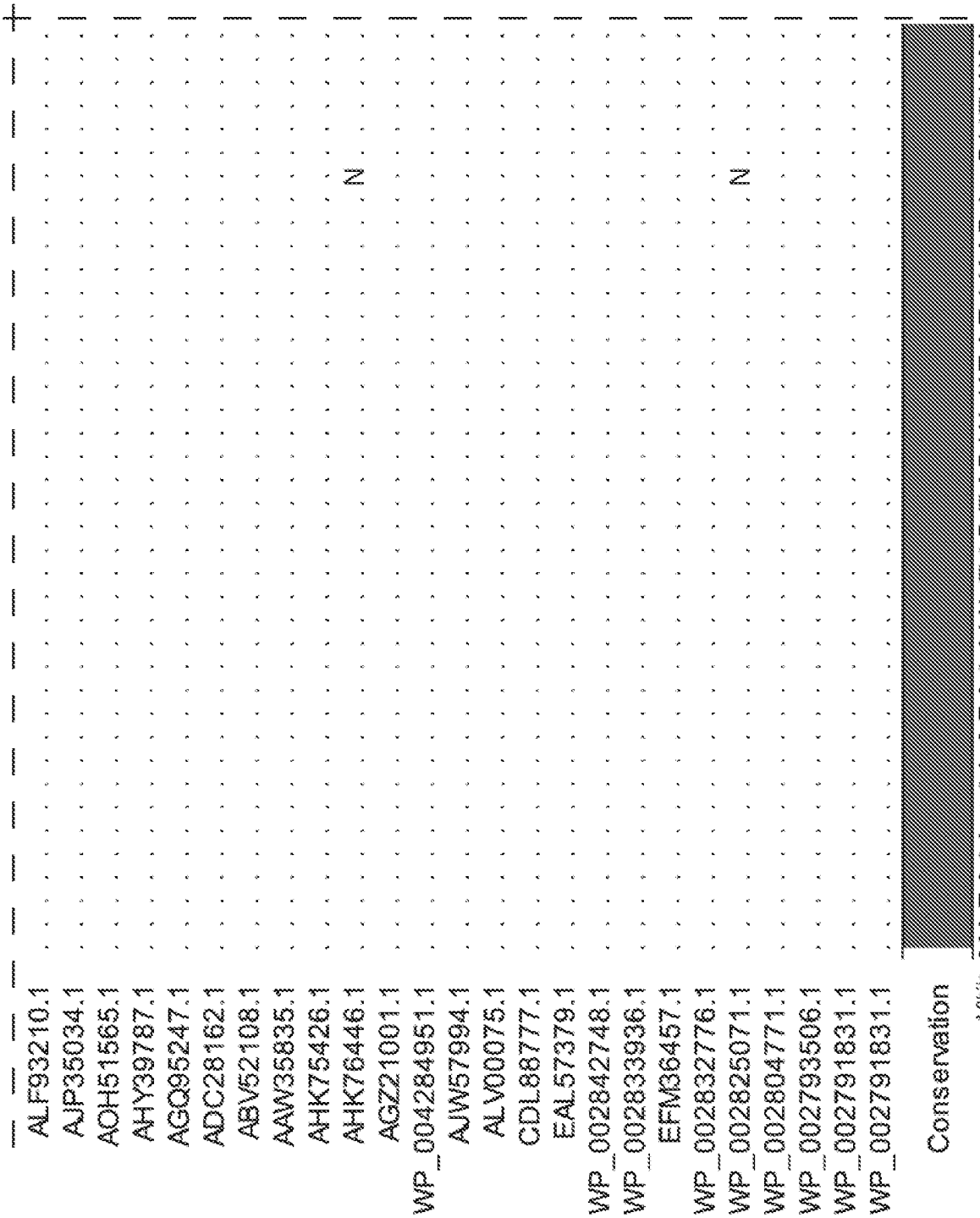


FIG. 12
(Continued)

FIG. 12
(Continued)

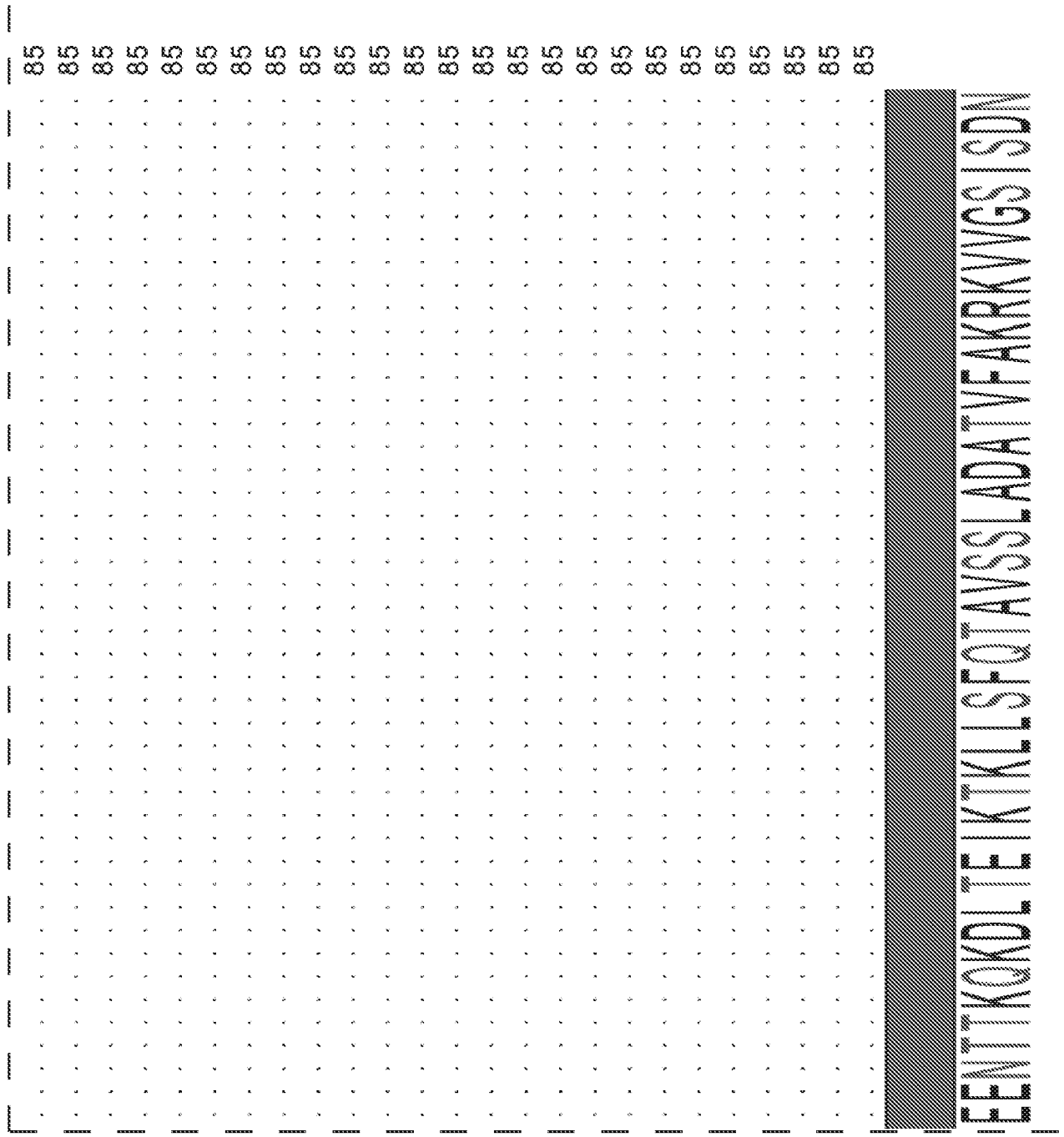


FIG. 12 (Continued)

```
ADLTFFSNGKEYTVTVDKNTTYRDLADKINEASGGEI 170
..................................... 170
T.................................... 170
T......................E............. 170
..................................... 170
.................R................... 170
..................................... 170
..................................... 170
..................................... 170
..................................... 170
T.................................... 170
..................................... 170
T.................................... 170
T.................................... 170
..................................... 170
..................................... 170
..................................... 170
T.................................... 170
T.................................... 170
T.................S.................. 170
..................................... 170
..................................... 170
..................................... 170
T.................................... 170
T.................................... 170
T.................S.................. 170
..................................... 170
T.................................... 170
..................................... 170
```

FIG. 12
(Continued)

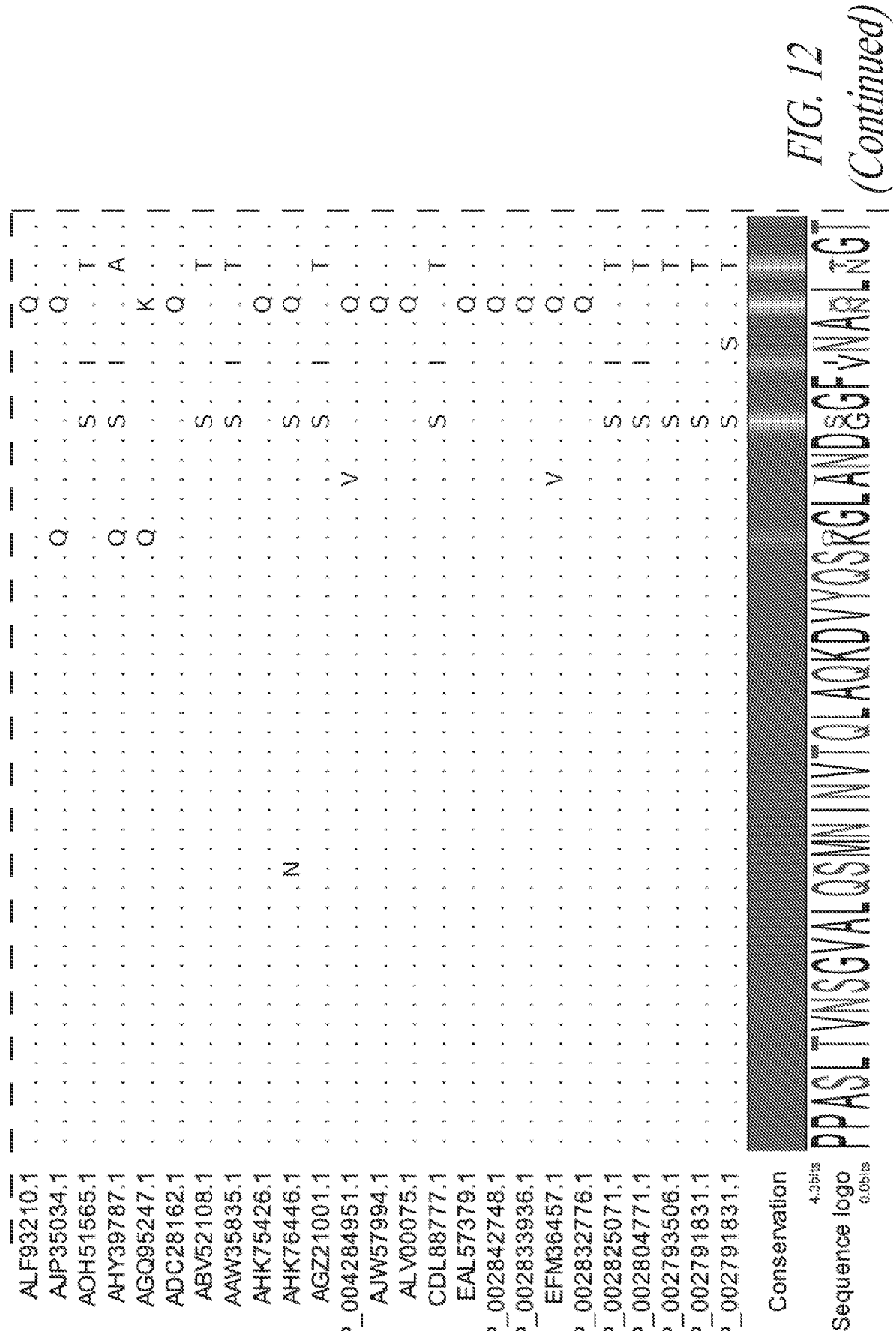


FIG. 12
(Continued)

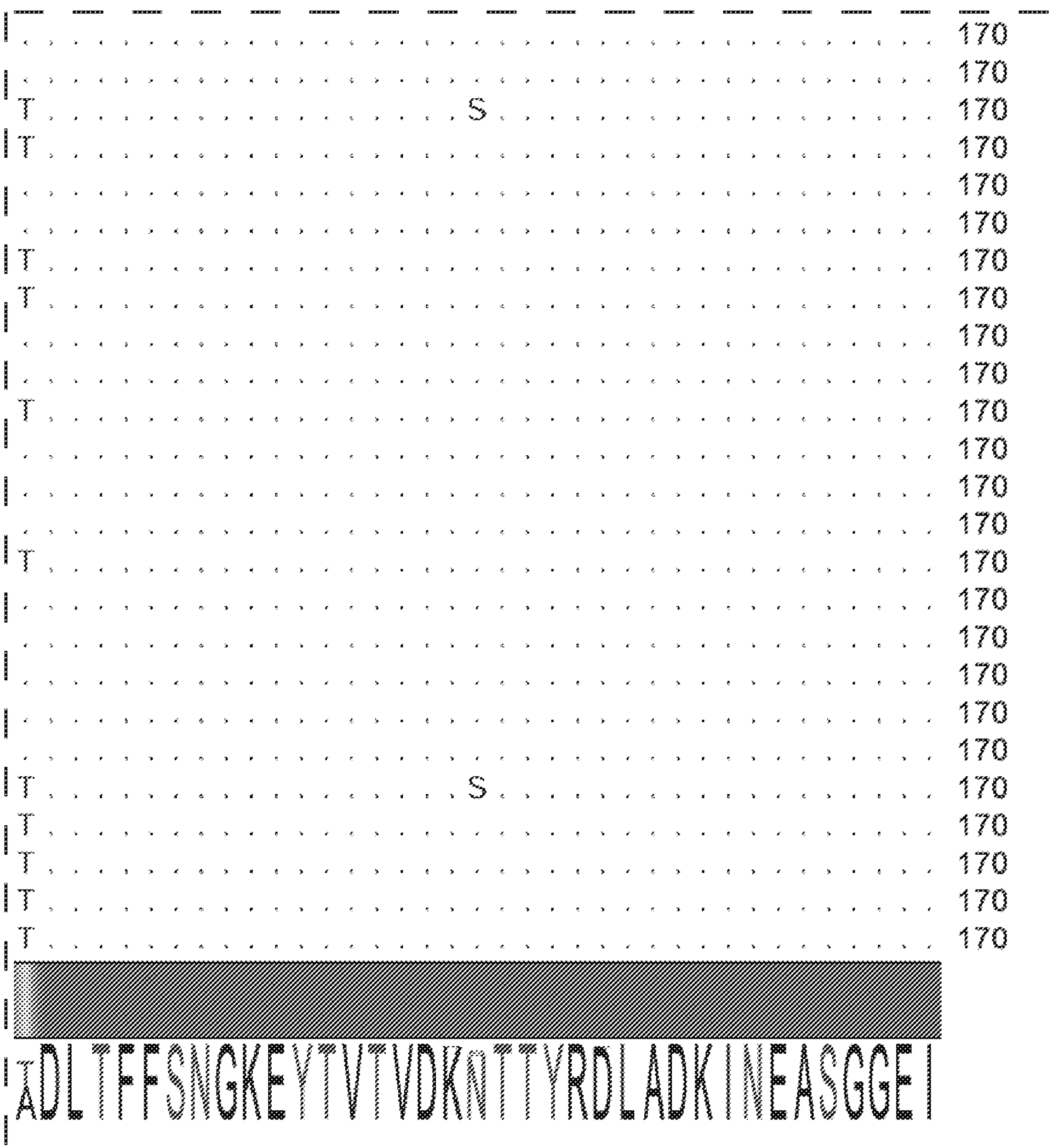


FIG. 12
(Continued)

FIG. 12 (Continued)

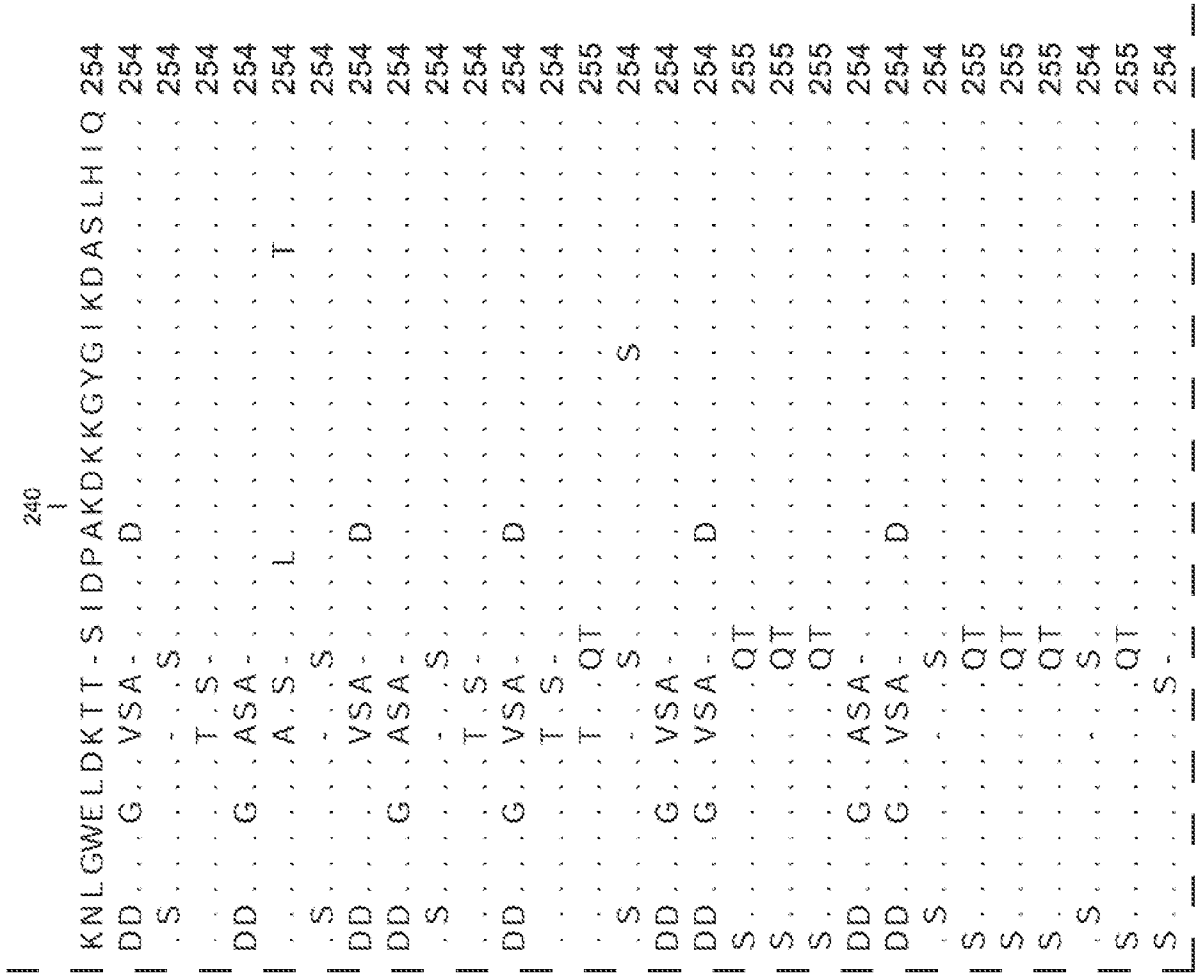


FIG. 12
(Continued)

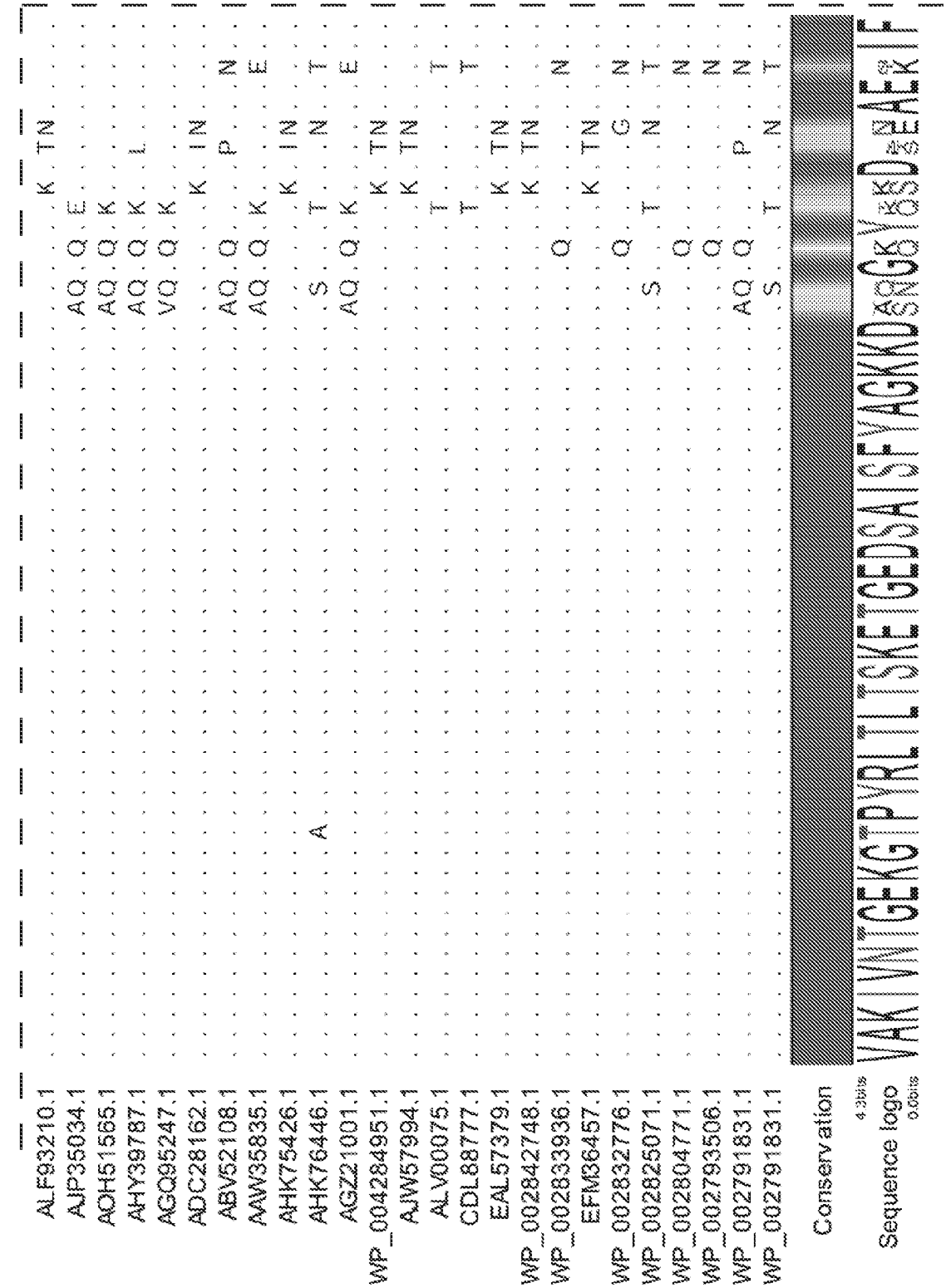


FIG. 12
(Continued)

FIG. 12
(Continued)

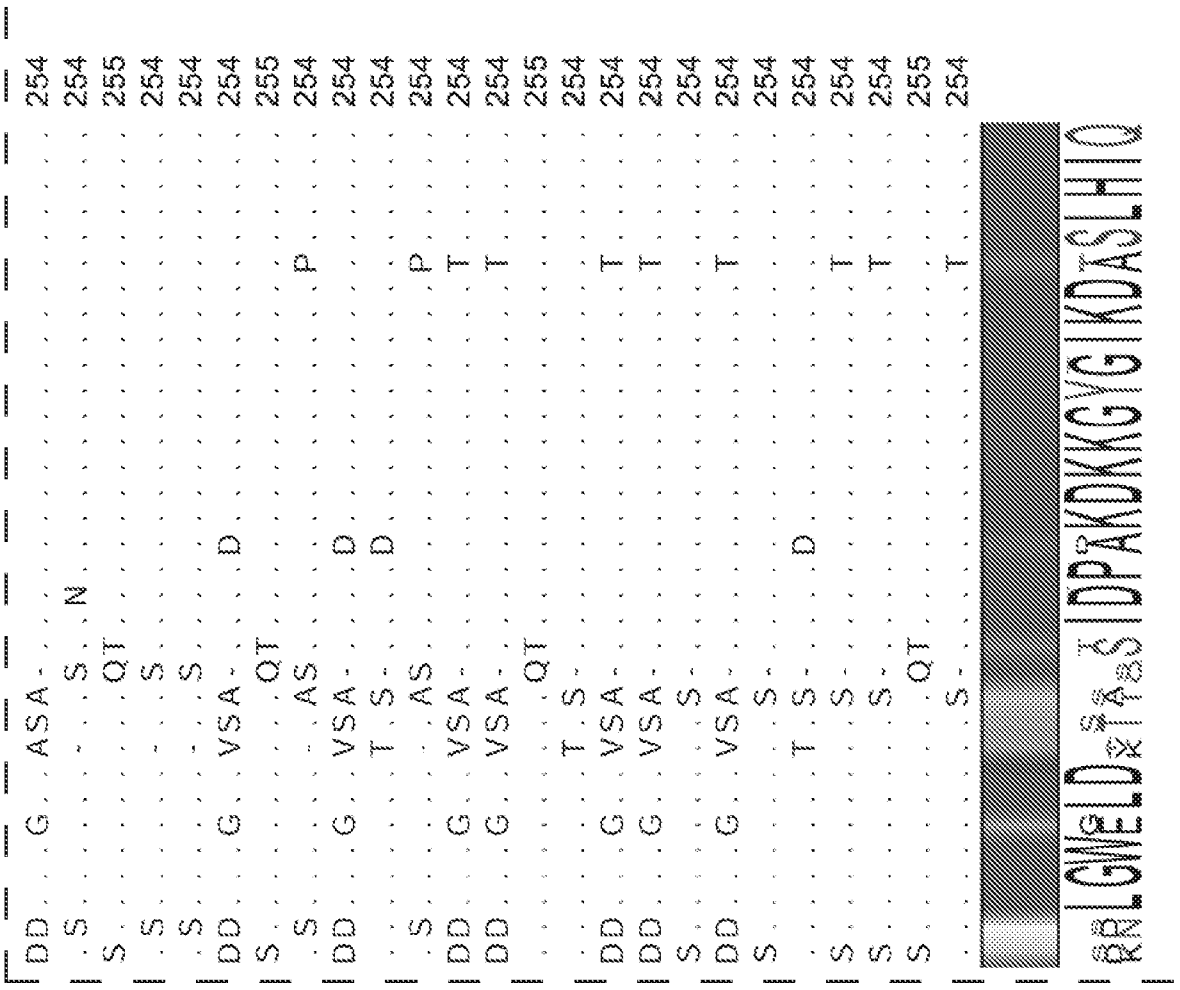


FIG. 12
(Continued)

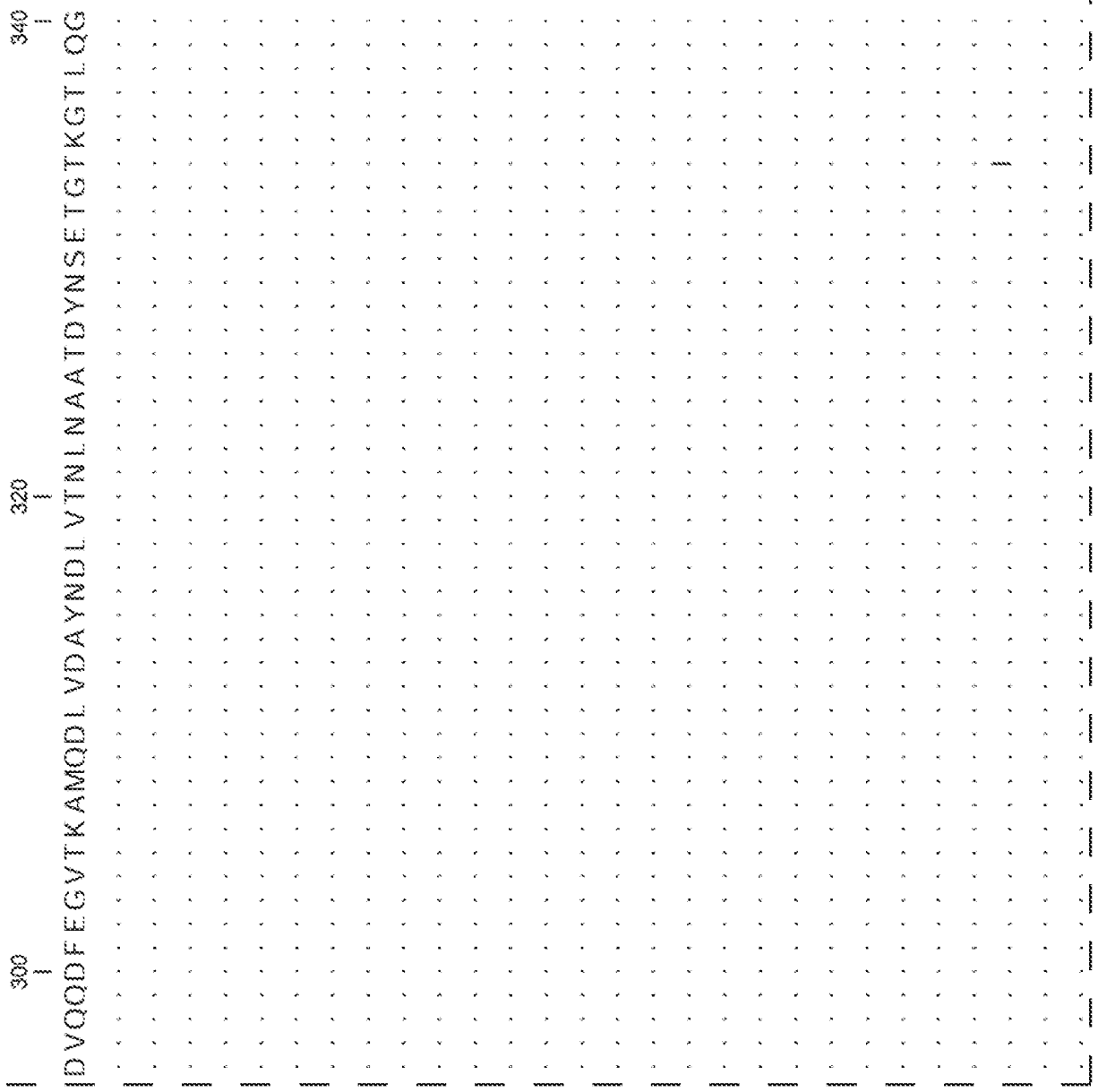


FIG. 12
(Continued)

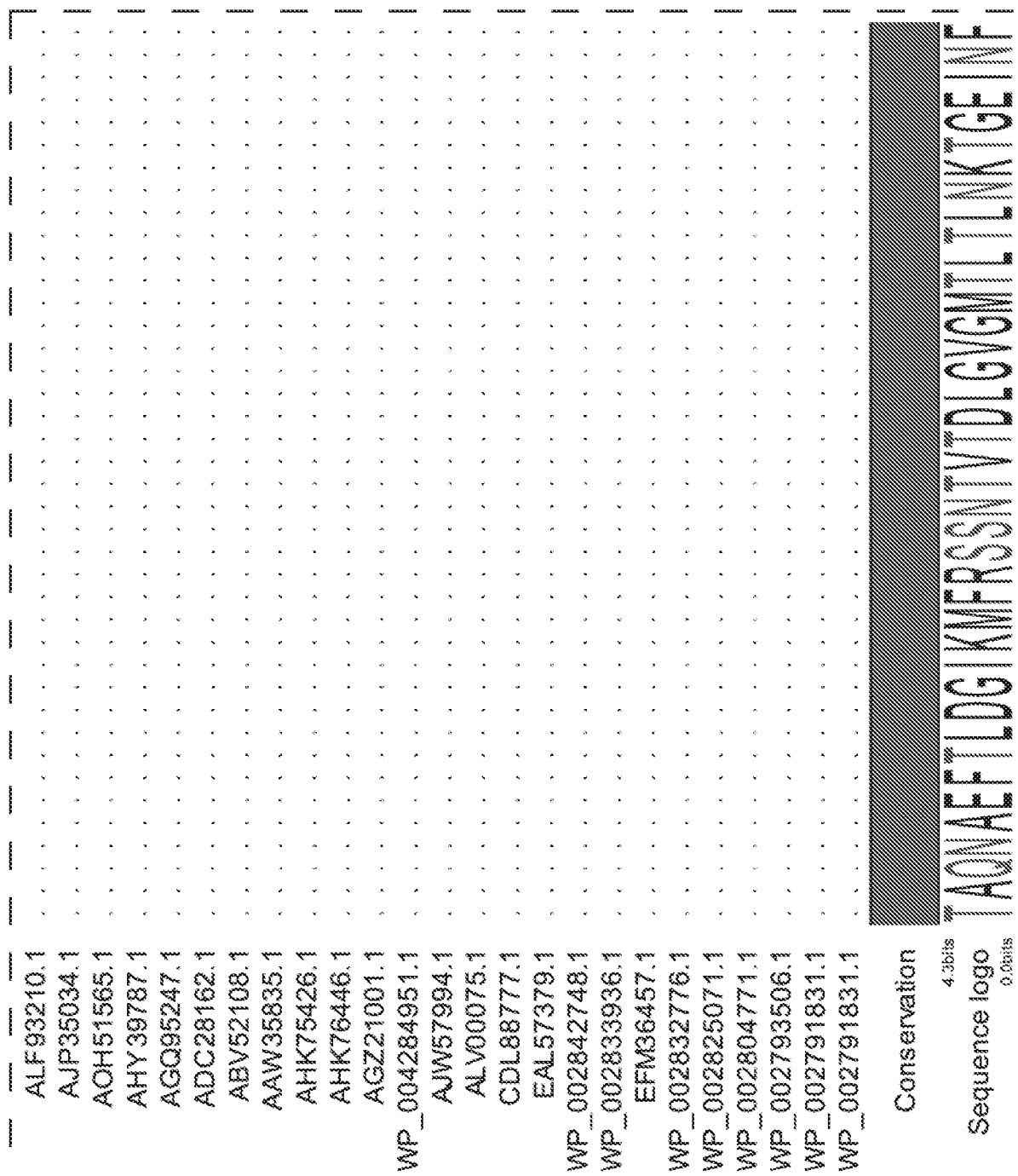
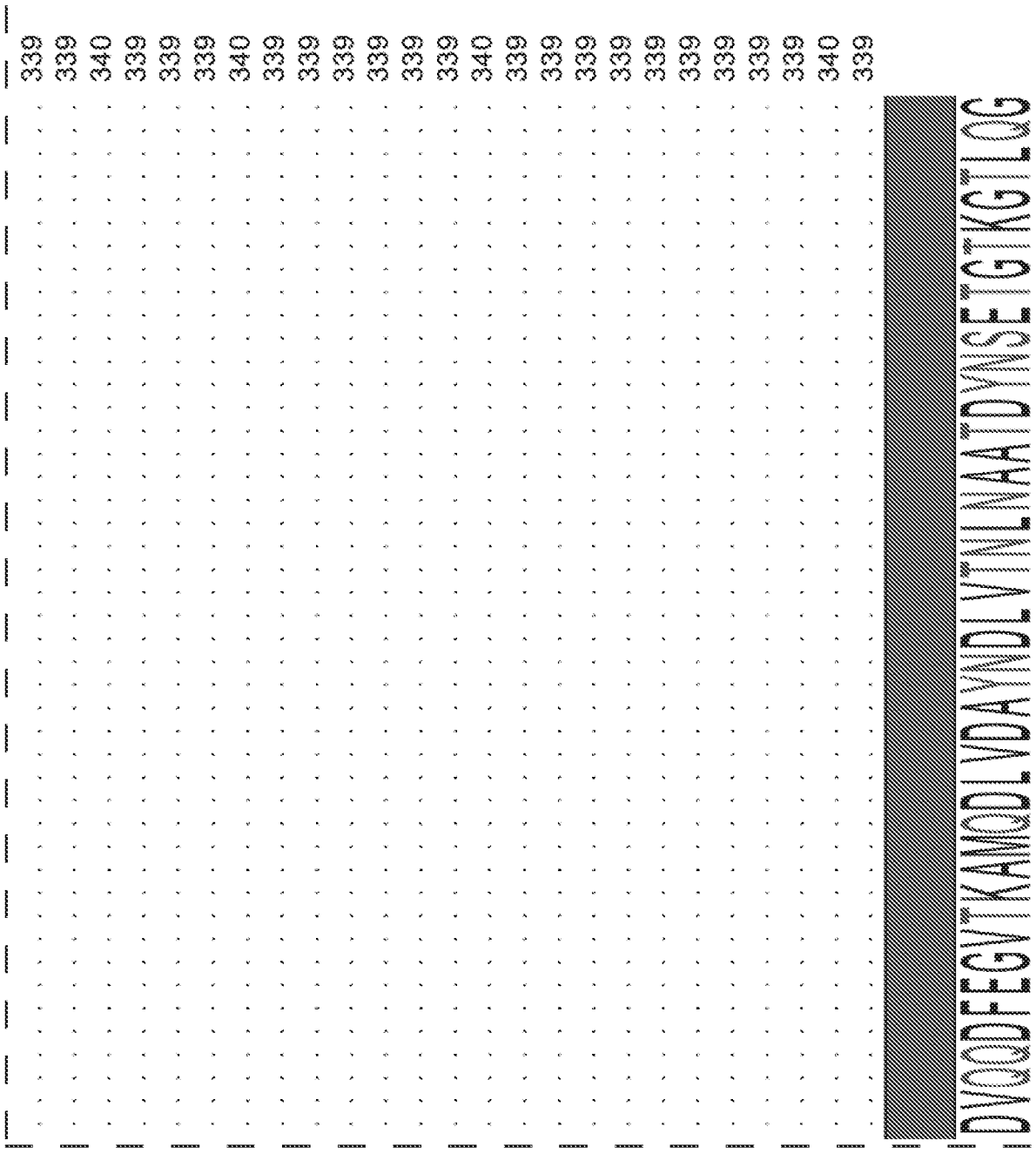


FIG. 12
(Continued)

FIG. 12
(Continued)



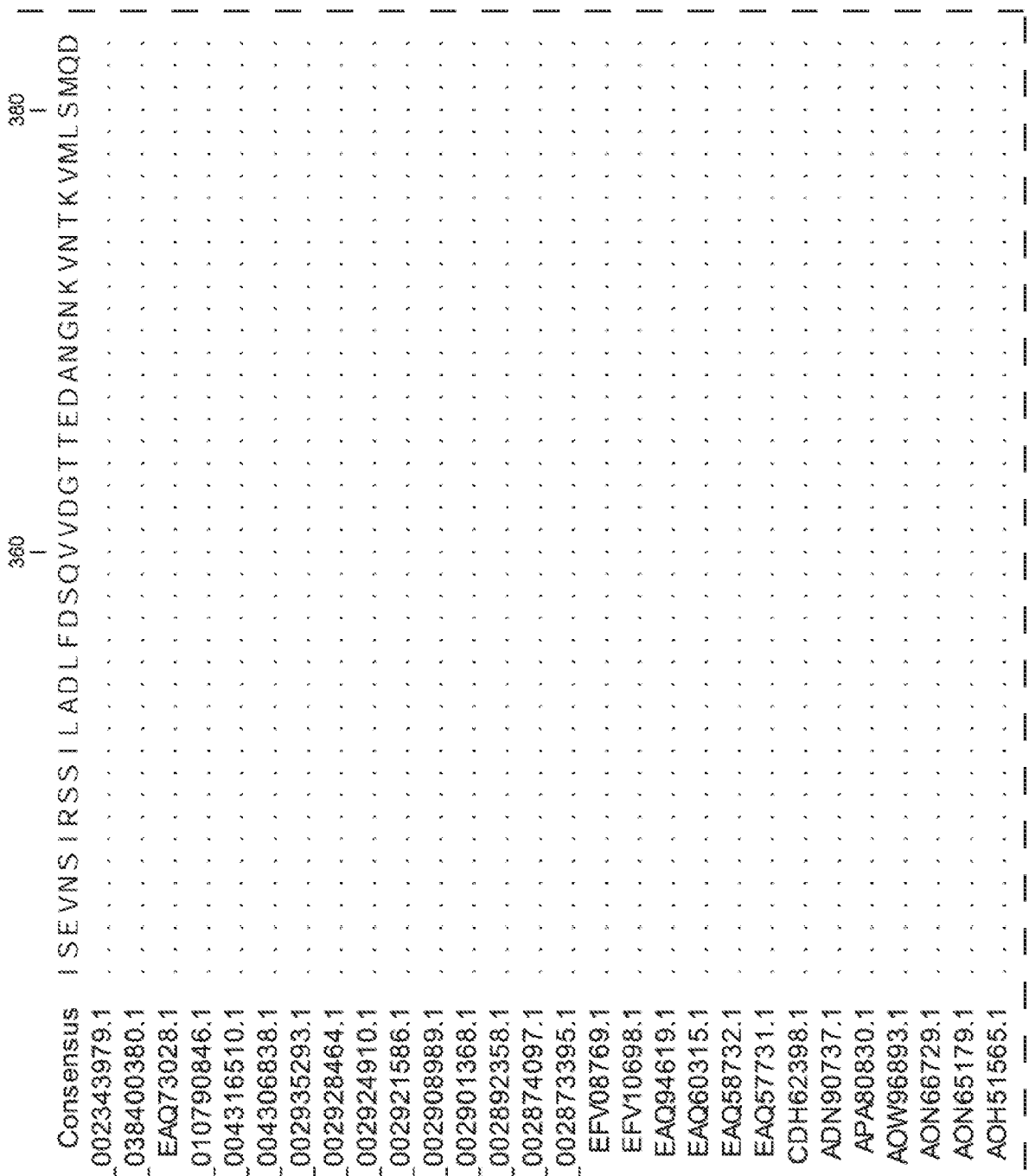


FIG. 12 (Continued)

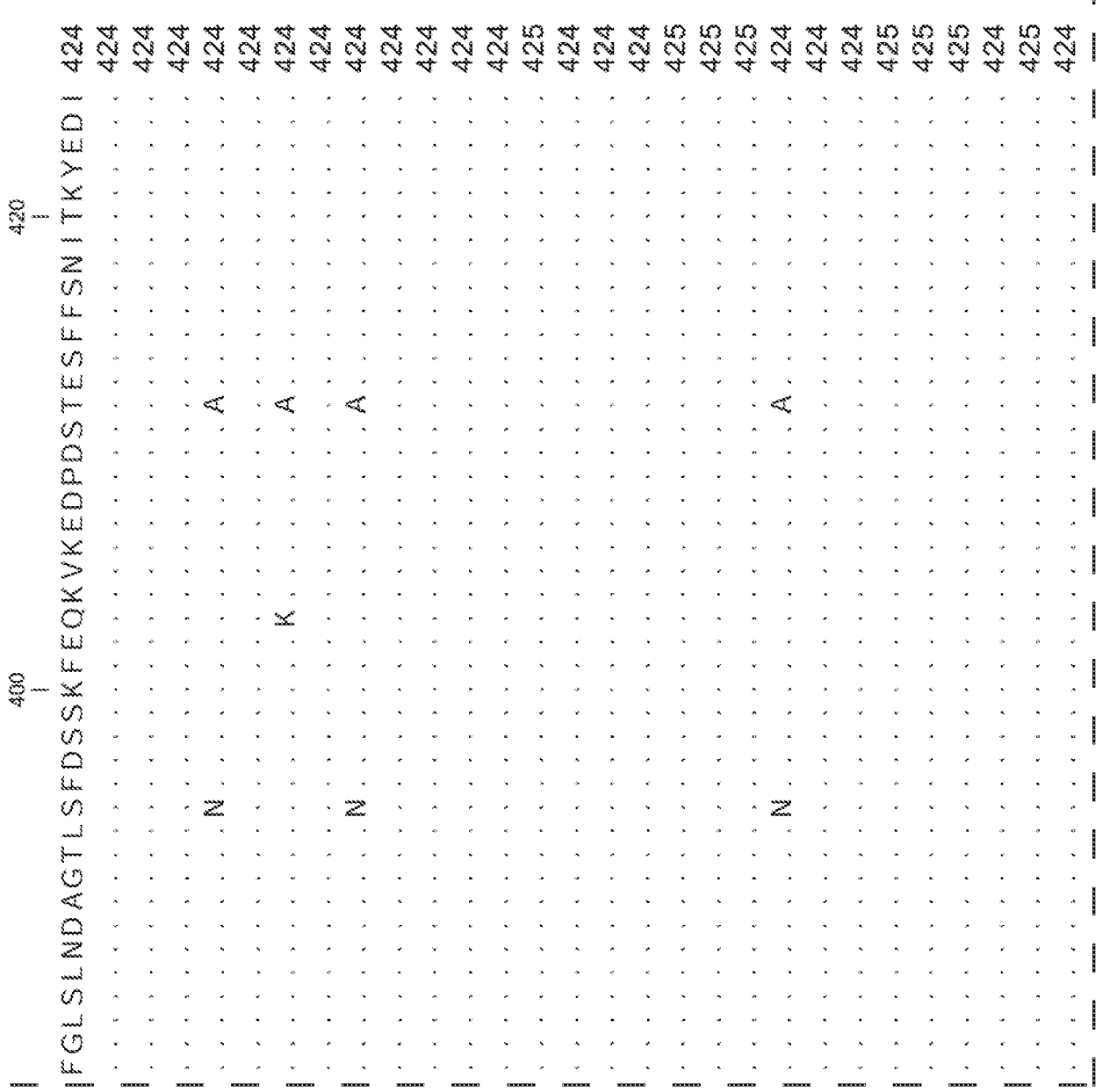


FIG. 12
(Continued)

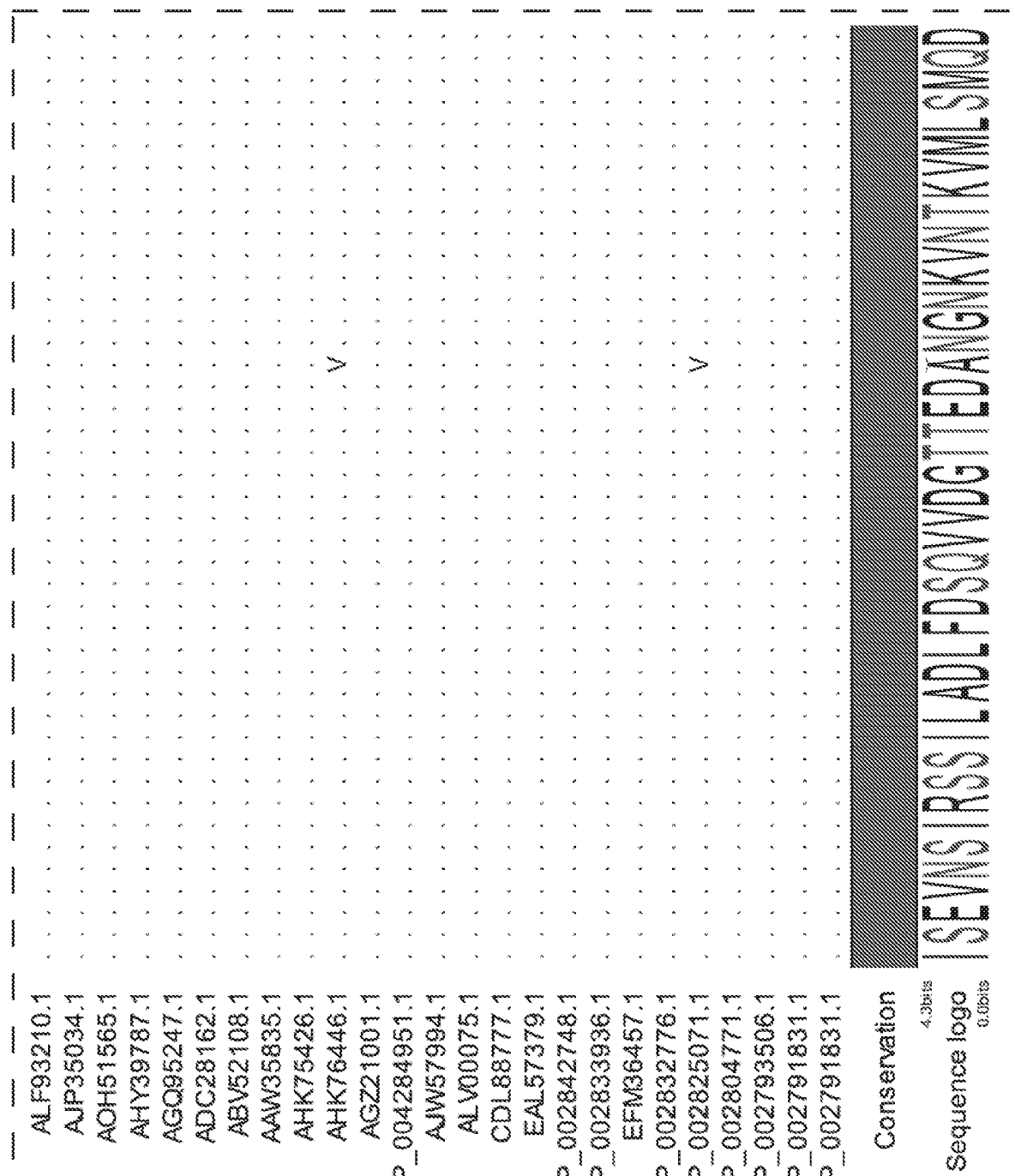
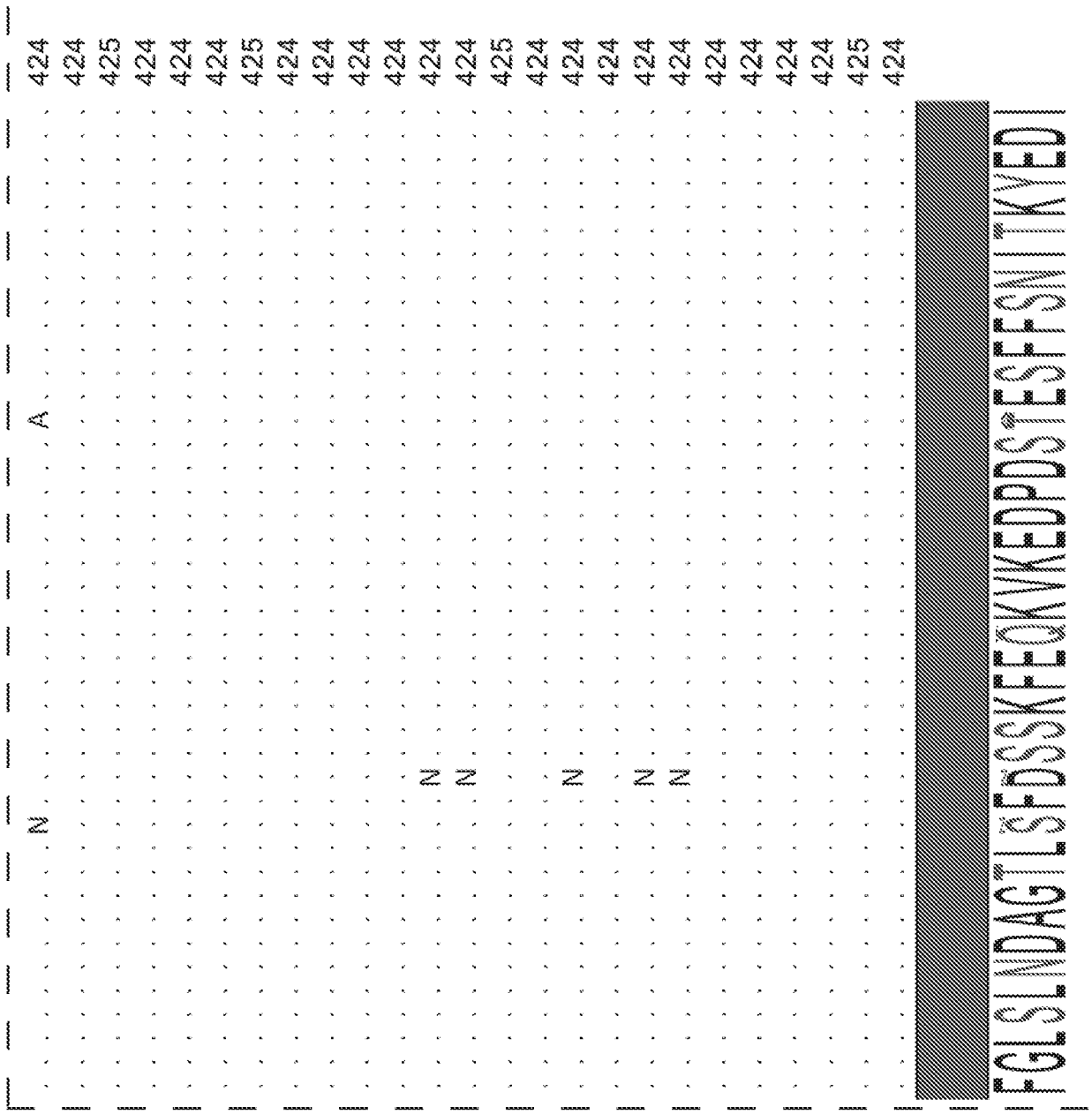


FIG. 12
(Continued)

FIG. 12
(Continued)



```
                            440                 460
                             |                   |
        Consensus NHTGEVIKTGSLSKYLNSNGGNTNGLEFKPGDFTIVFNNQTYDL
    YP_002343979.1 ............................................
    WP_038400380.1 ..........................A.................
       EAQ73028.1 ........Q...NQ..D.S.TGNK..D.................
    WP_010790846.1 .....I....................D.................
    WP_004316510.1 ............................................
    WP_004306838.1 .....................SA...D.................
    WP_002935293.1 ...............................Y............
    WP_002928464.1 .....I....................D.................
    WP_002924910.1 ............................................
    WP_002921586.1 ........Q...NQ..D.S.TGNK..D.................
    WP_002908989.1 ........Q...NQ..D.S.TGNK..D.................
    WP_002901368.1 ........Q...NQ..D.S.TGNK..D.................
    WP_002892358.1 ........Q...NQ..D.S.TGNK..D.................
    WP_002874097.1 ............................................
    WP_002873395.1 ............................................
       EFV08769.1 ............................................
       EFV10698.1 ........Q...NQ..D.S.TGNK..D.................
       EAQ94619.1 ............................................
       EAQ60315.1 ........Q...NQ..D.S.TGNK.......G............
       EAQ58732.1 .....I....N...............D.................
       EAQ57731.1 ............................................
       CDH62398.1 ............................................
       ADN90737.1 ........Q...NQ..D.S.TGNK..D.................
       APA80830.1 ............................................
       AOW96893.1 ........Q...NQ..D.S.TGNK.......G............
       AON66729.1 ............................................
       AON65179.1 ..........................A.................
       AOH51565.1 .......N.........P.------.D.................
```

FIG. 12
(Continued)

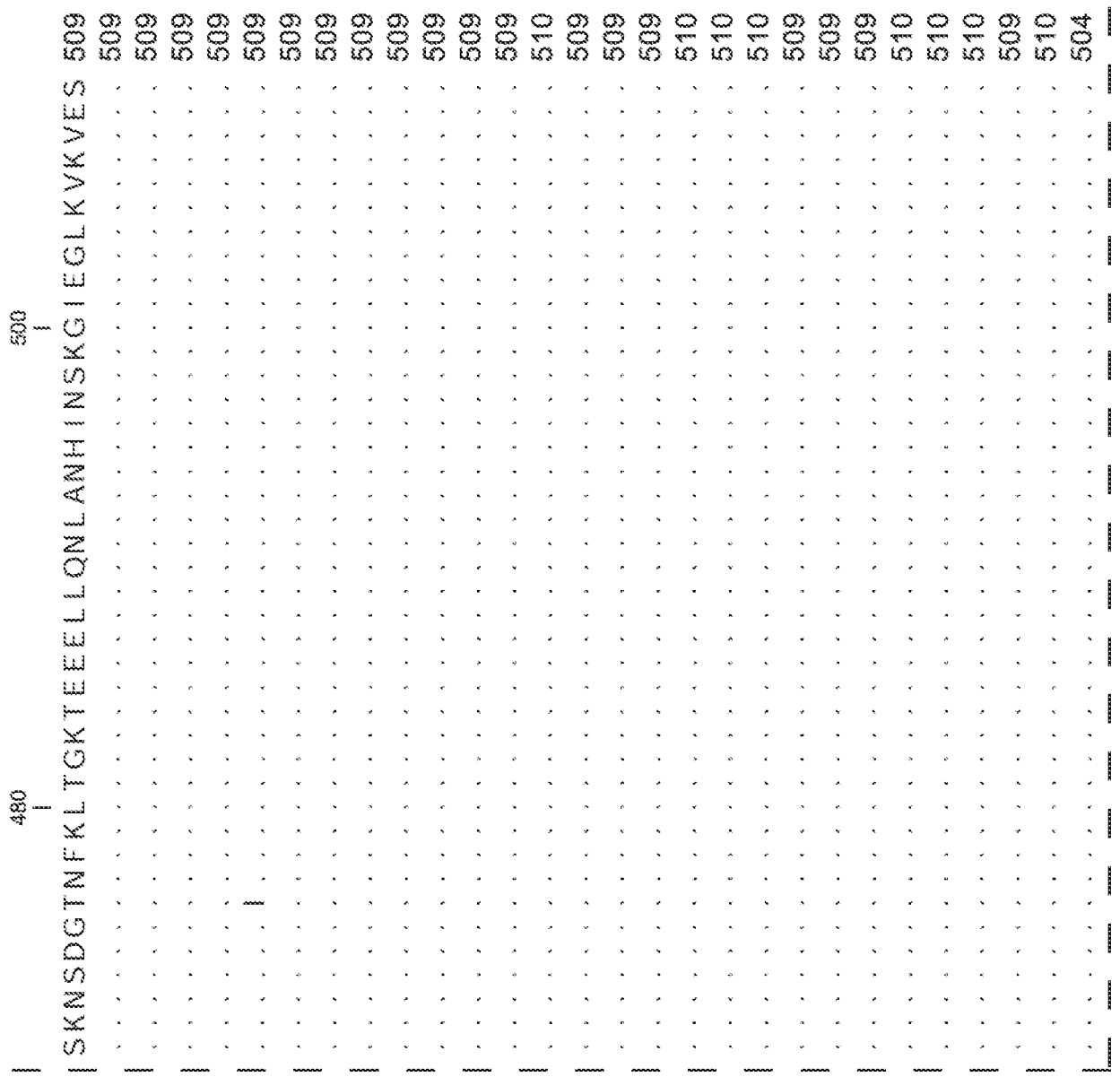


FIG. 12
(Continued)

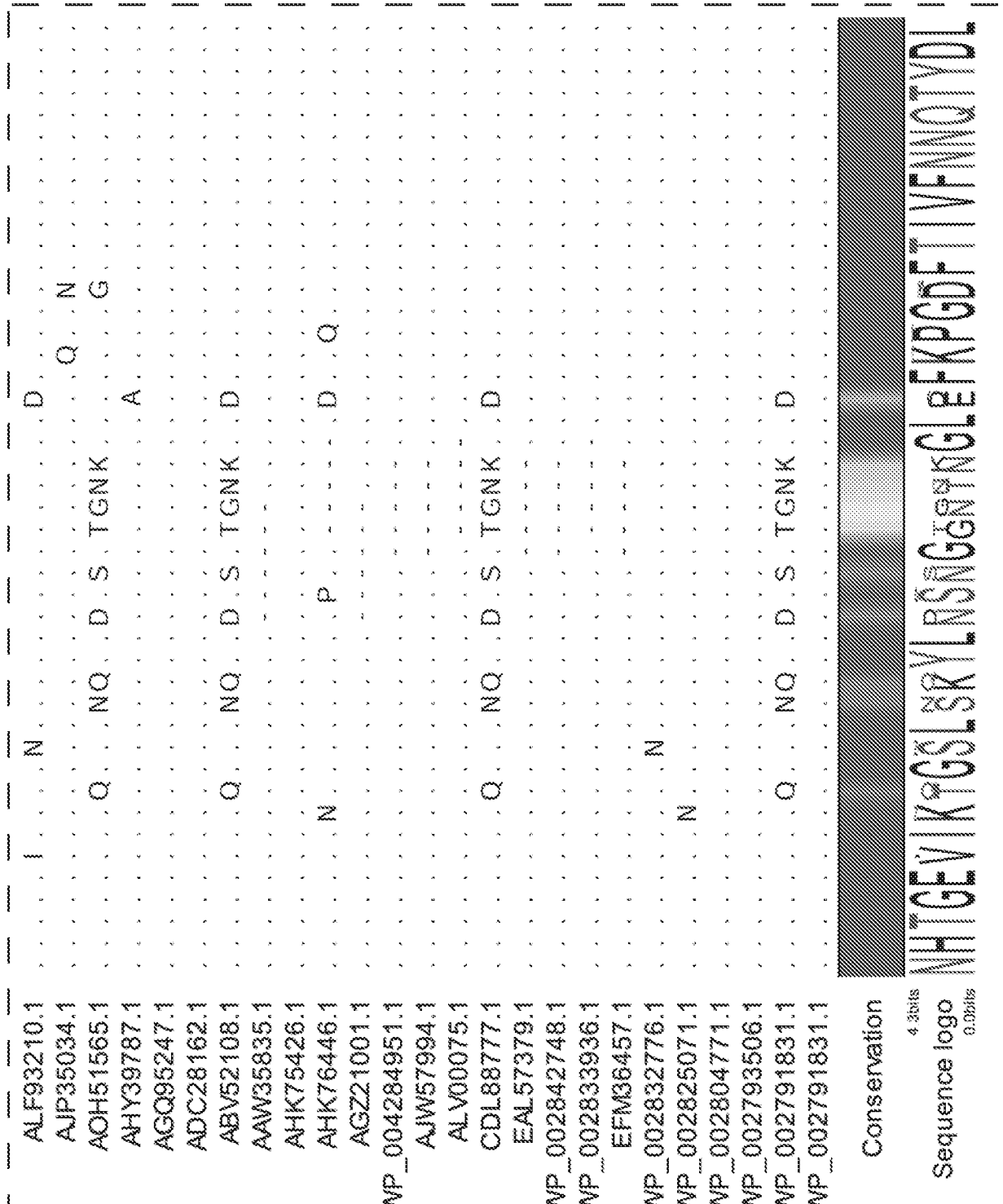


FIG. 12
(Continued)

FIG. 12
(Continued)

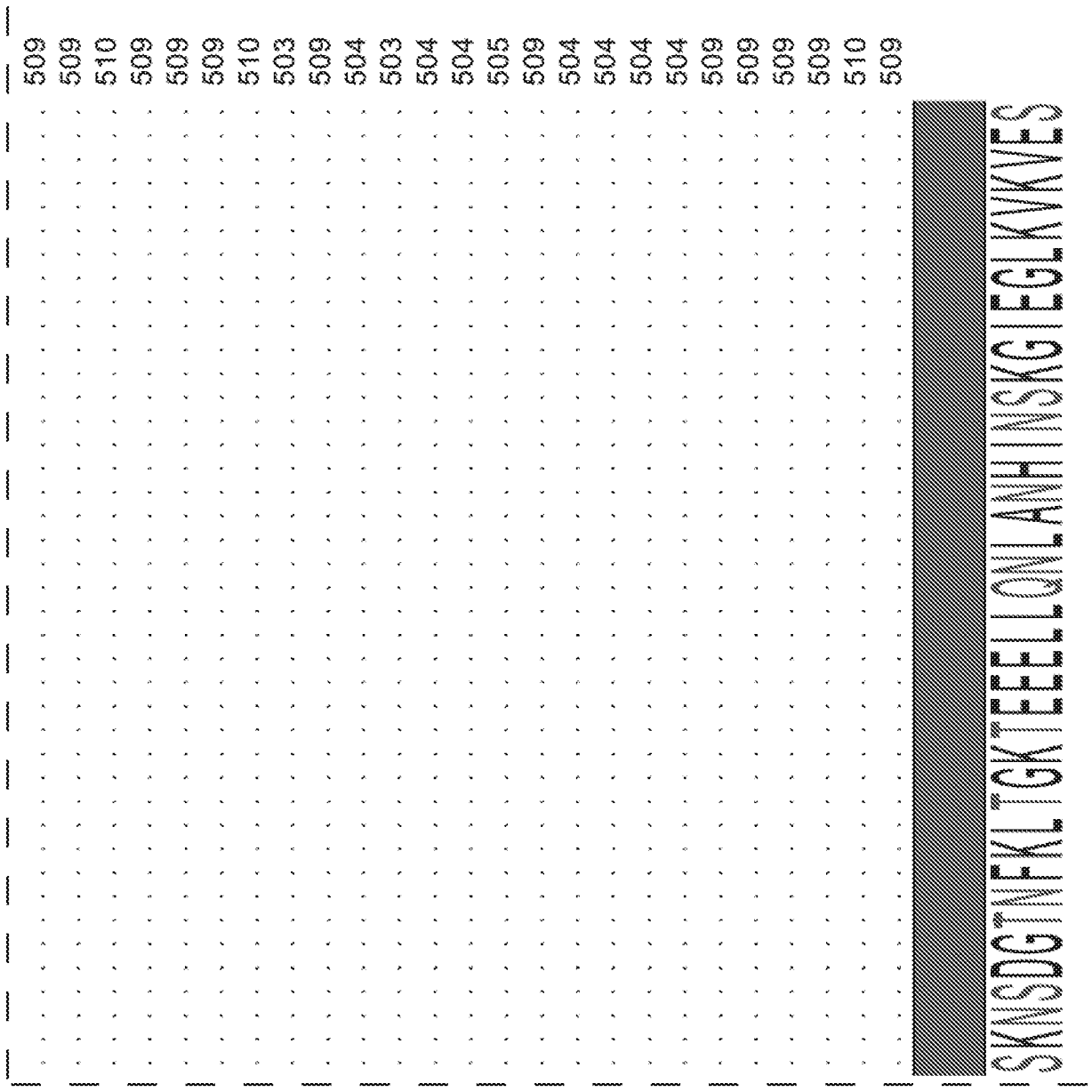


FIG. 12
(Continued)

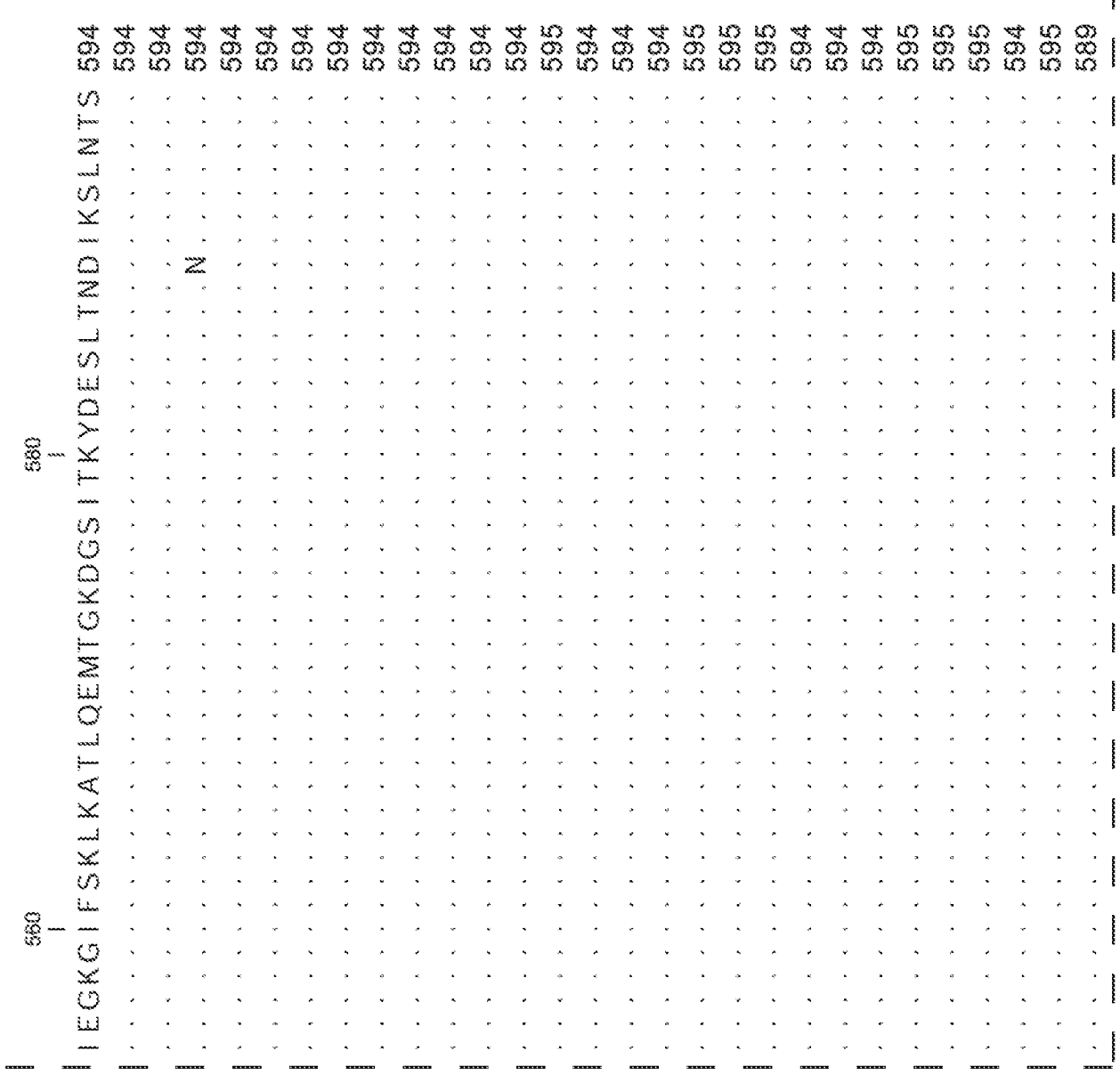


FIG. 12
(Continued)

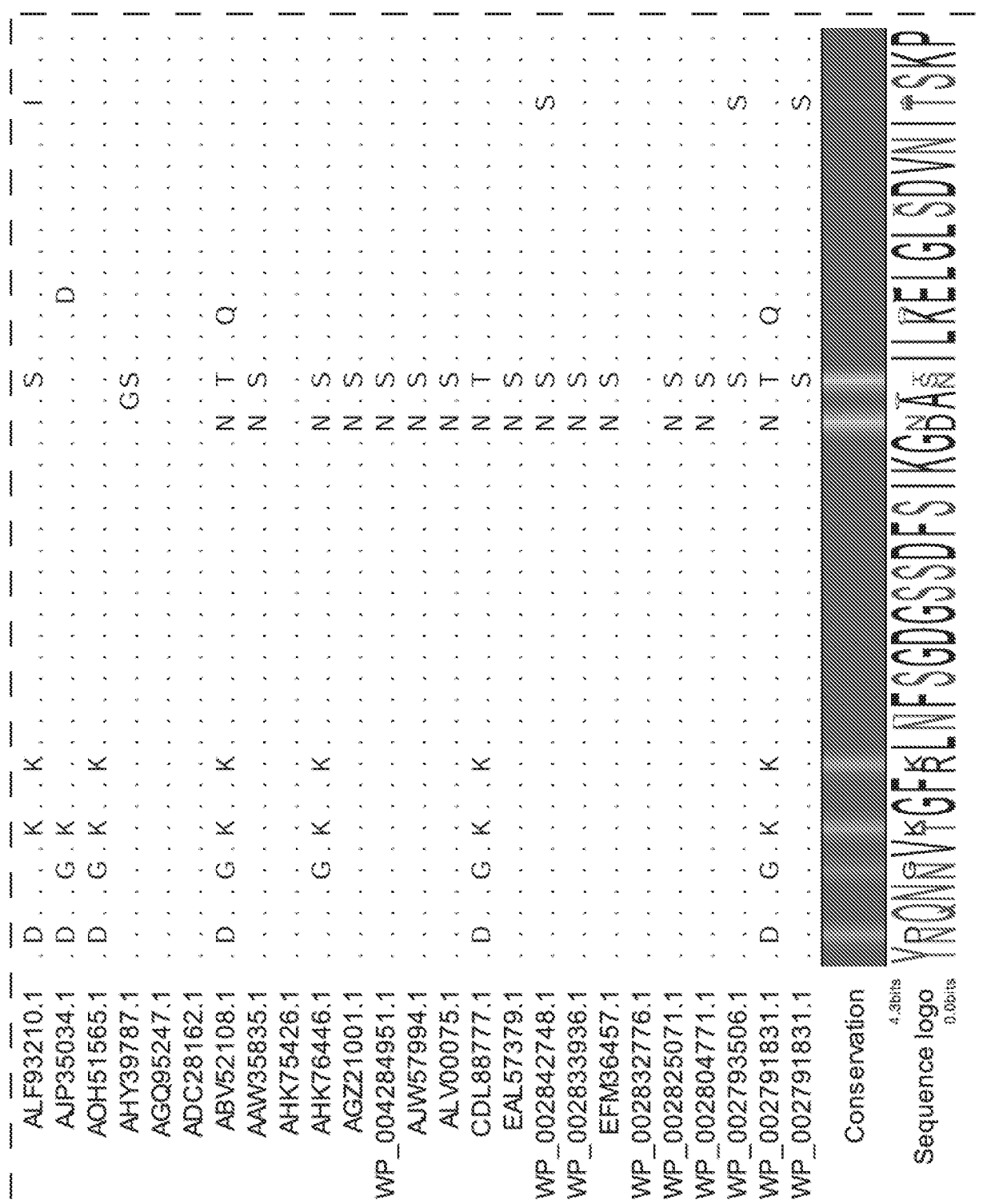


FIG. 12
(Continued)

FIG. 12
(Continued)

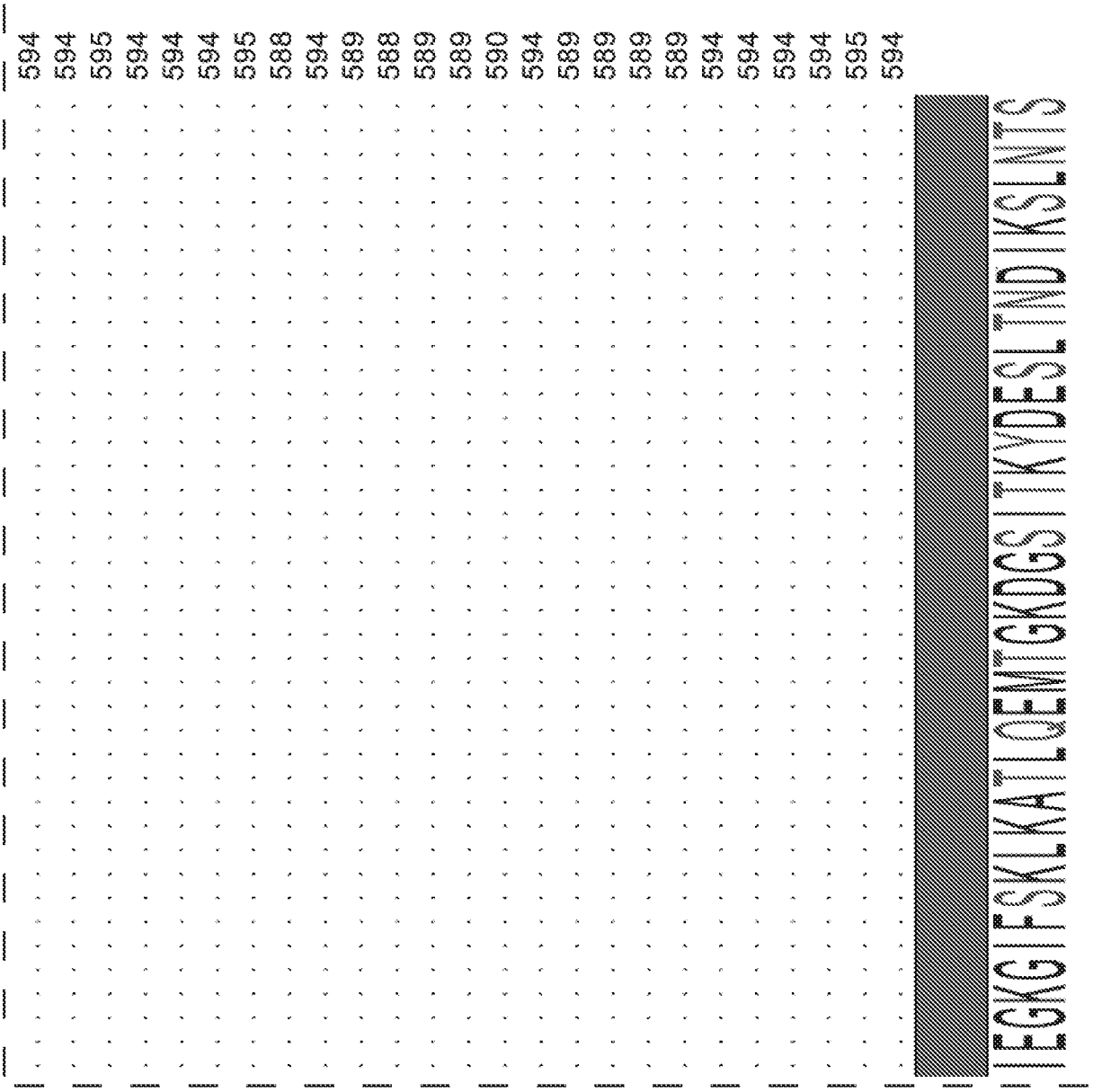


FIG. 12
(Continued)

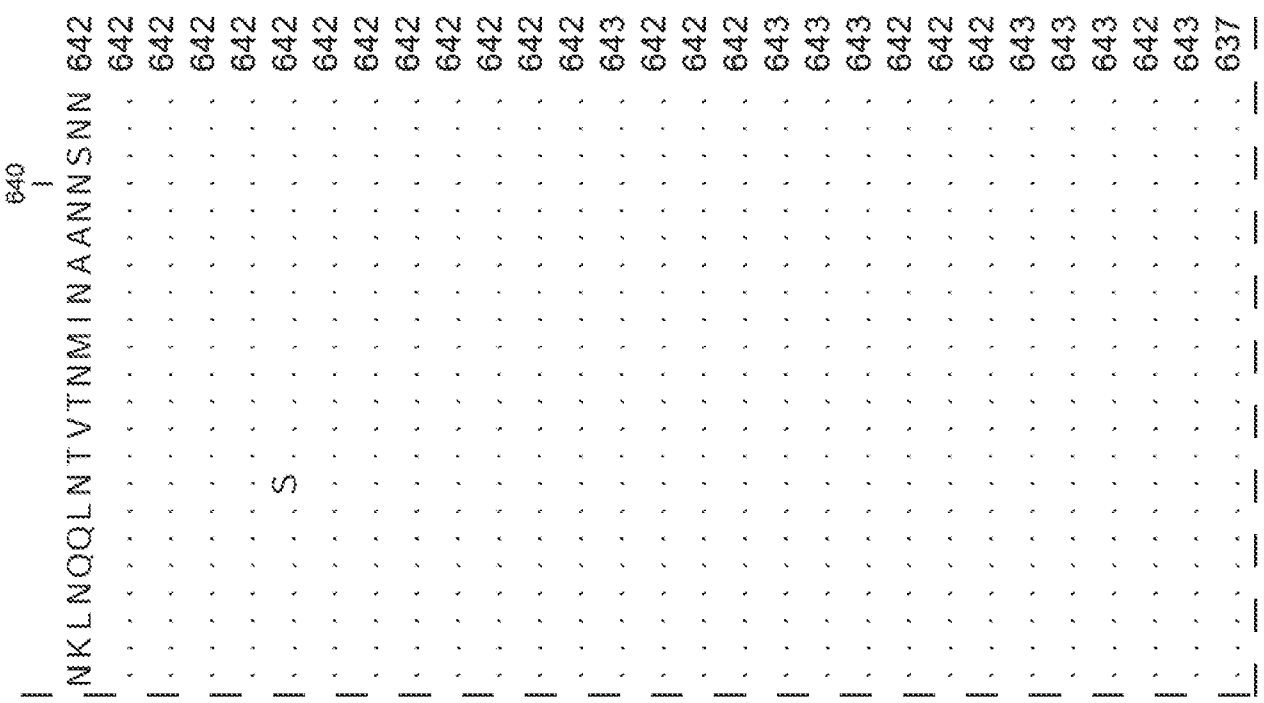


FIG. 12
(Continued)

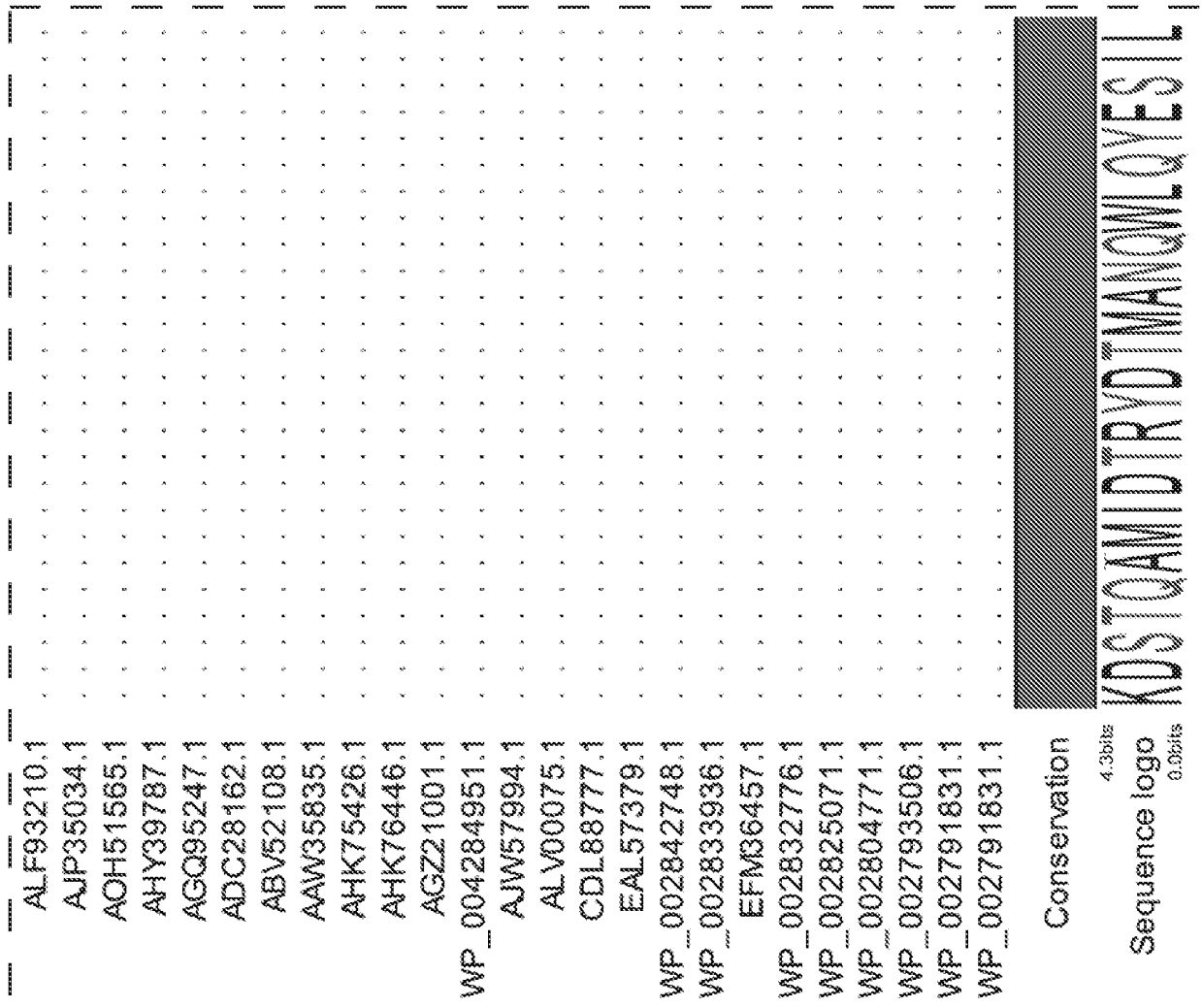
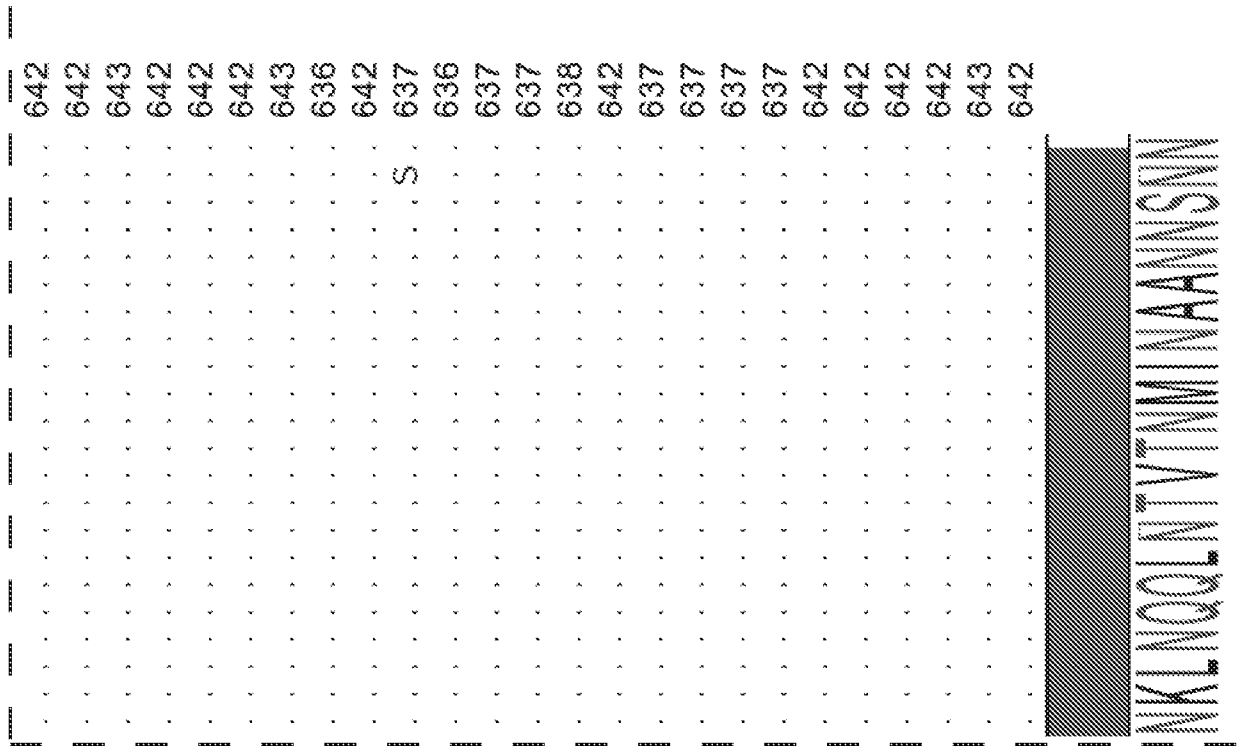


FIG. 12
(Continued)

FIG. 12
(Continued)



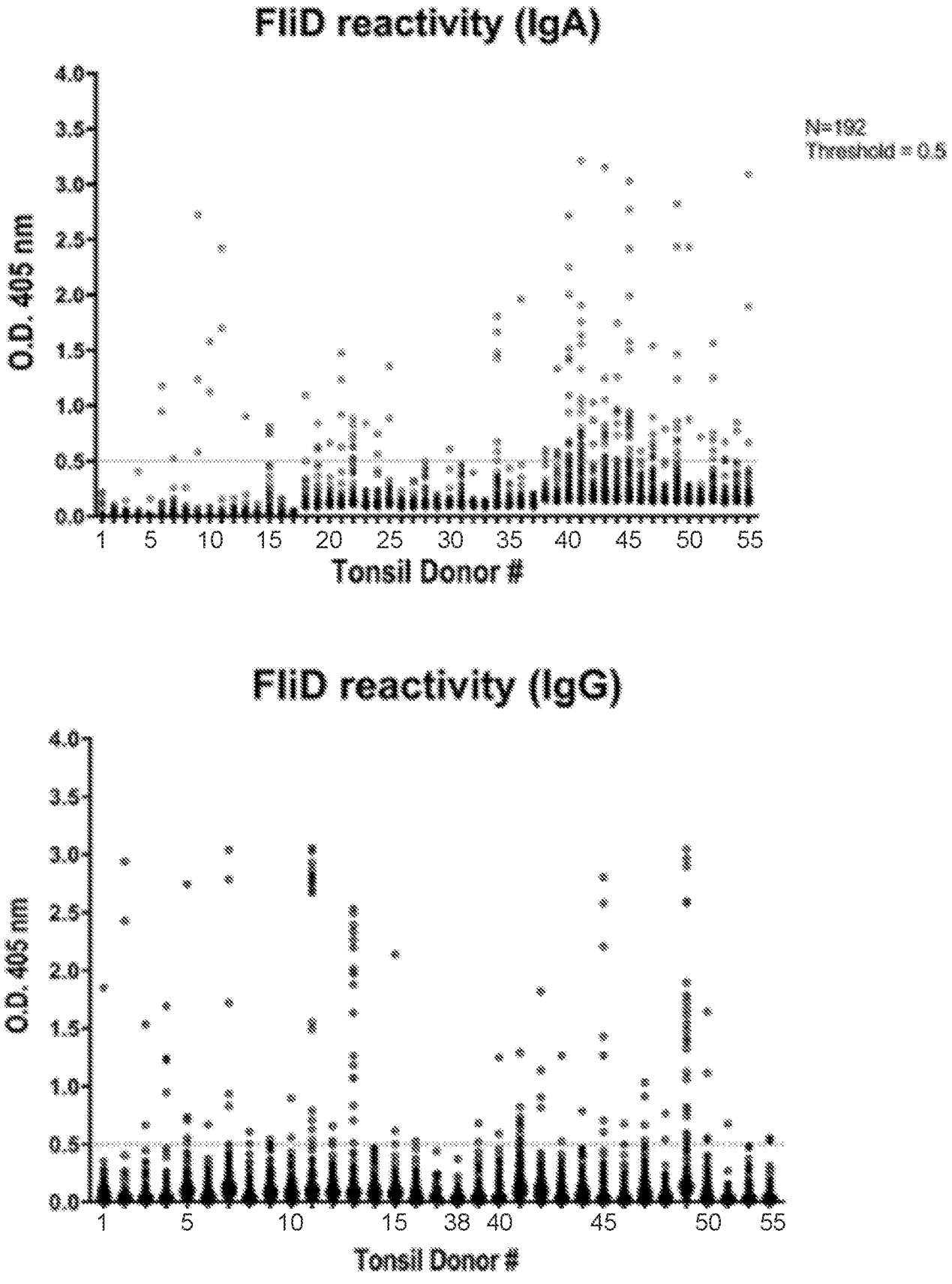

FliD reactivity (IgA)
N=192
Threshold = 0.5
O.D. 405 nm
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1 5 10 15 20 25 30 35 40 45 50 55
Tonsil Donor #
FliD reactivity (IgG)
O.D. 405 nm
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1 5 10 15 38 40 45 50 55
Tonsil Donor #

FIG. 13

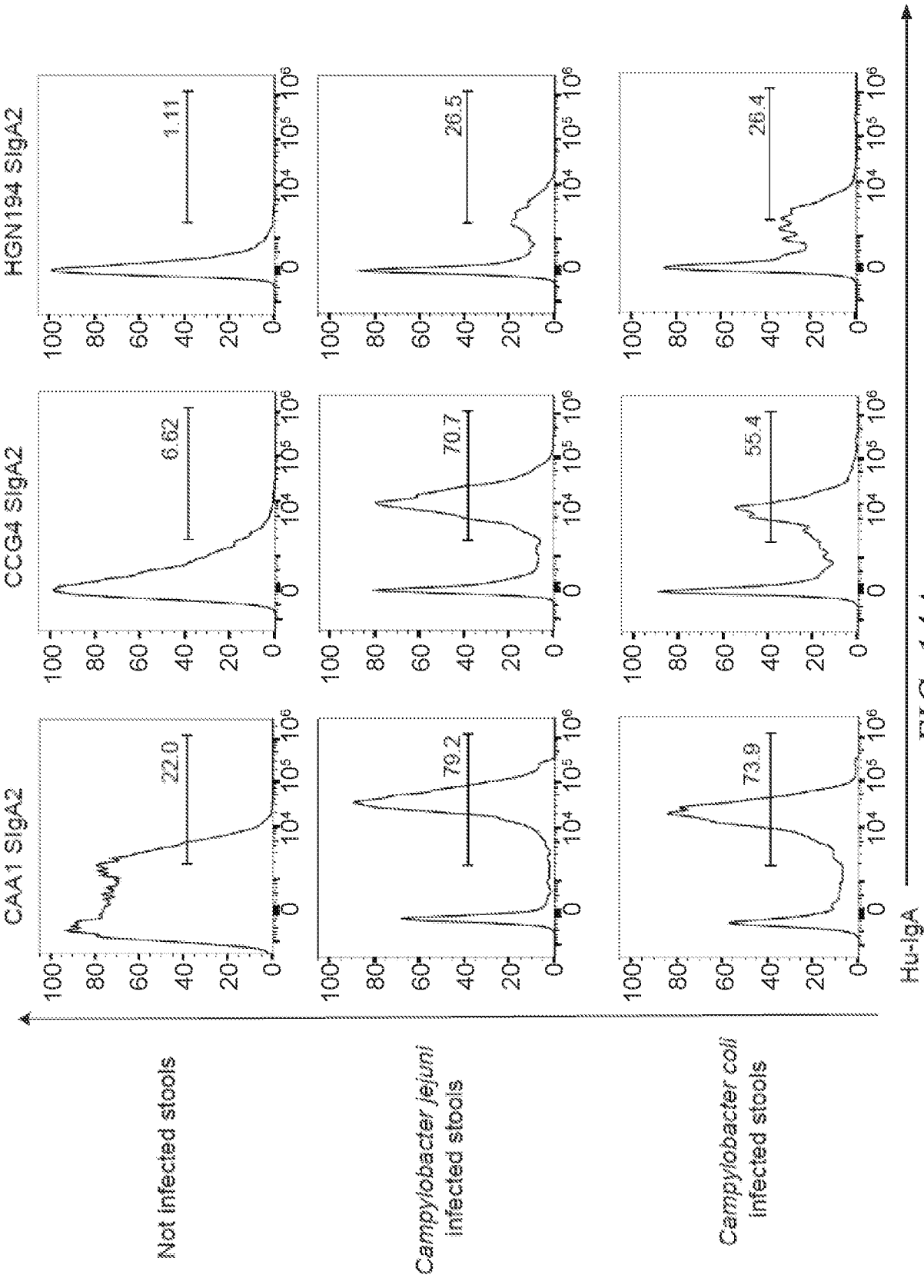

CAA1 SIgA2
CCG4 SIgA2
HGN194 SIgA2
22.0
6.62
1.11
79.2
70.7
26.5
73.9
55.4
26.4
Not infected stools
Campylobacter jejuni infected stools
Campylobacter coli infected stools
Hu-IgA

FIG. 14A

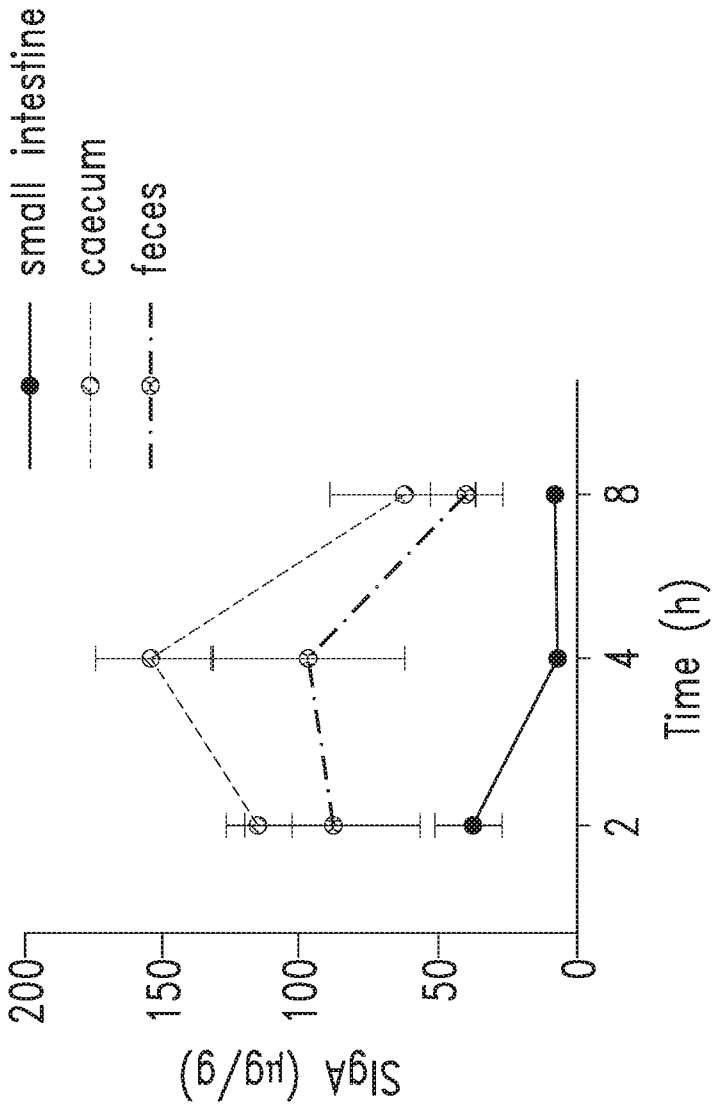

small intestine
caecum
feces
SIgA (µg/g)
200
150
100
50
0
2
4
8
Time (h)

FIG. 14B

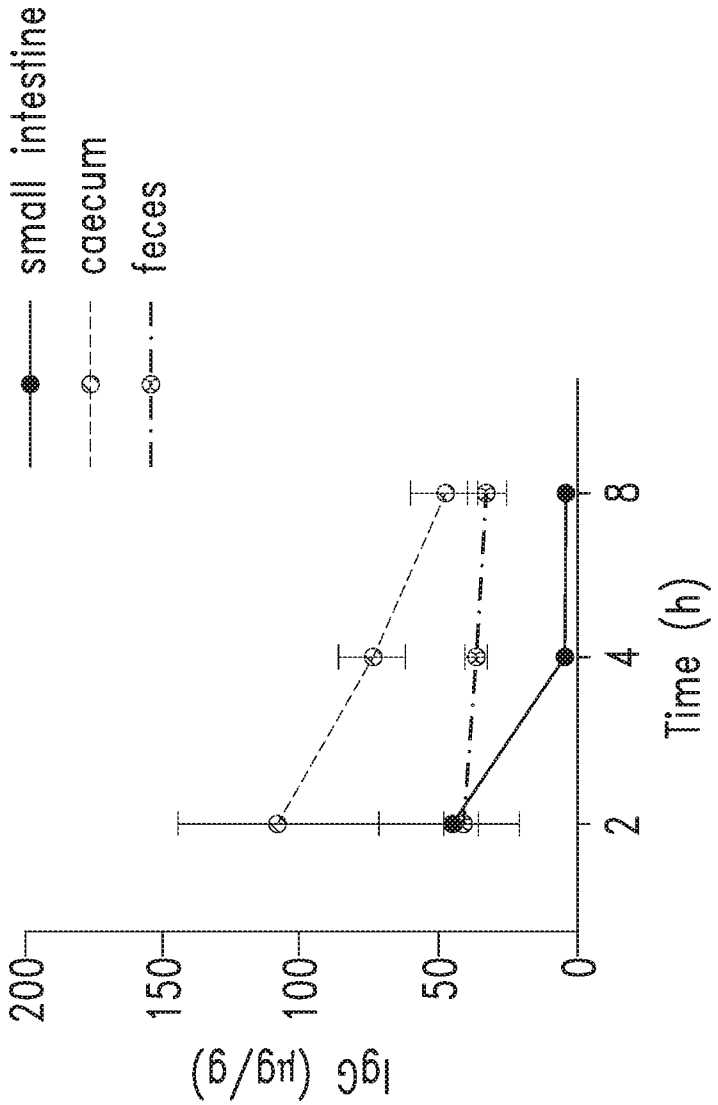

small intestine
caecum
feces
200
150
100
50
0
2
4
8
Time (h)
log (μg/g)

FIG. 14C

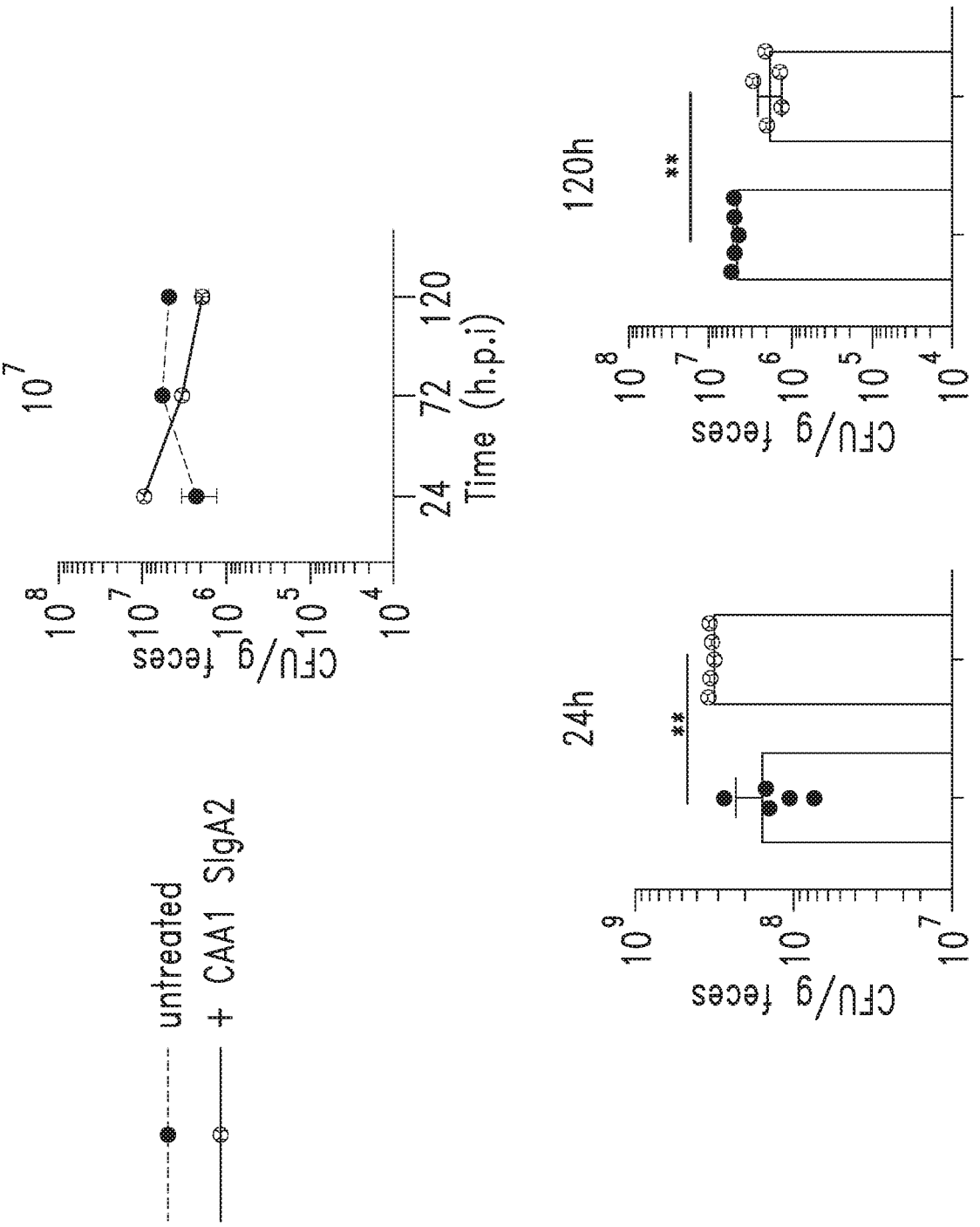


FIG. 15A

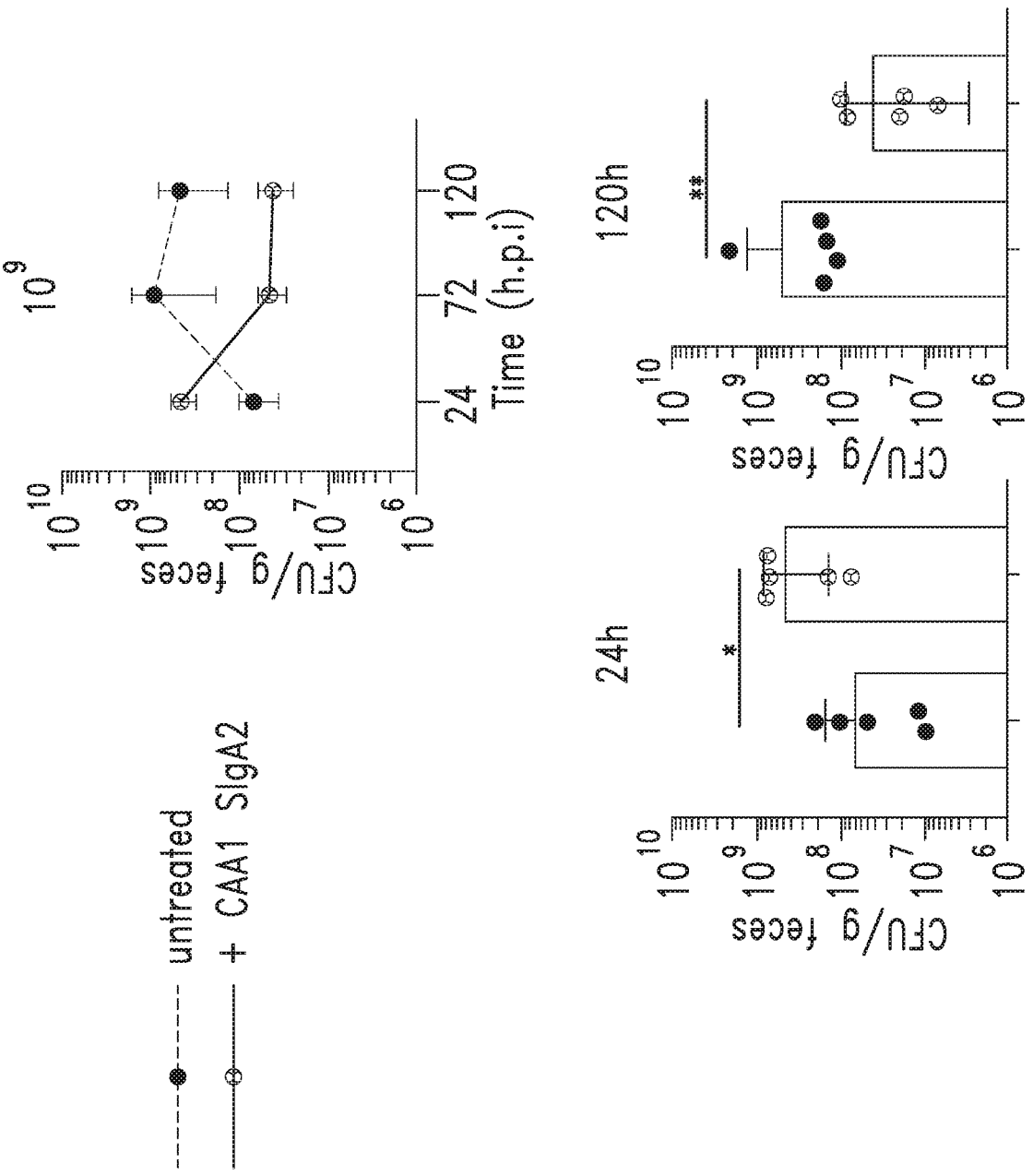


FIG. 15B

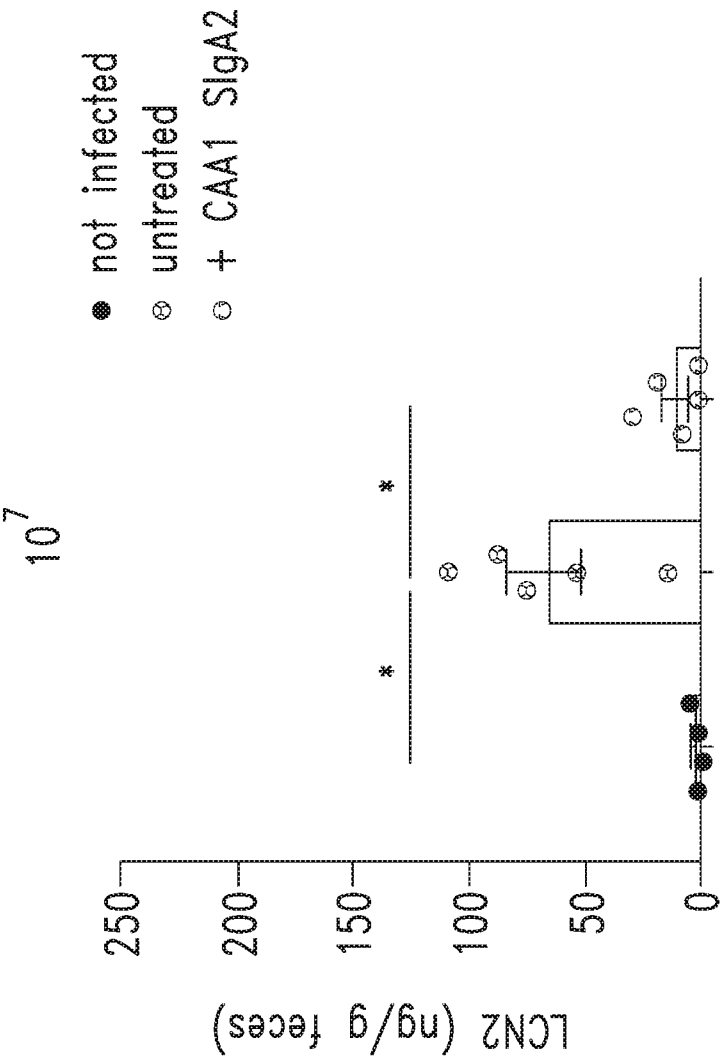

not infected
untreated
+ CAA1 SIgA2
10^7
LCN2 (ng/g feces)
250
200
150
100
50
0
*
*

FIG. 15C

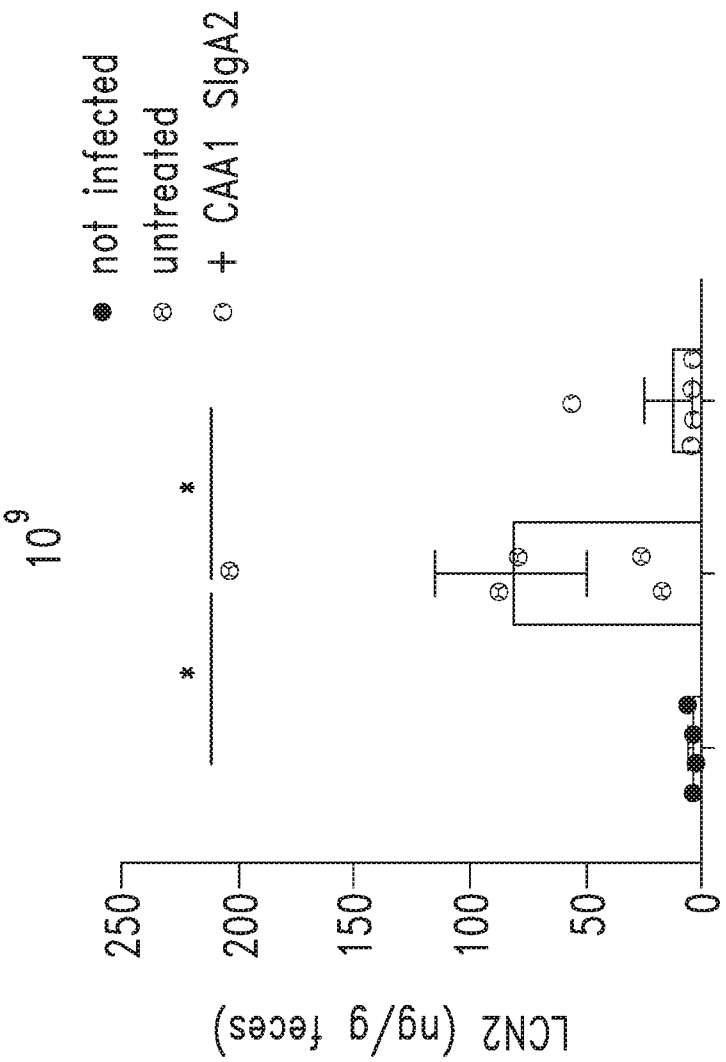

not infected
untreated
+ CAA1 SIgA2
10^9
LCN2 (ng/g feces)
250
200
150
100
50
0
bdl

FIG. 15D

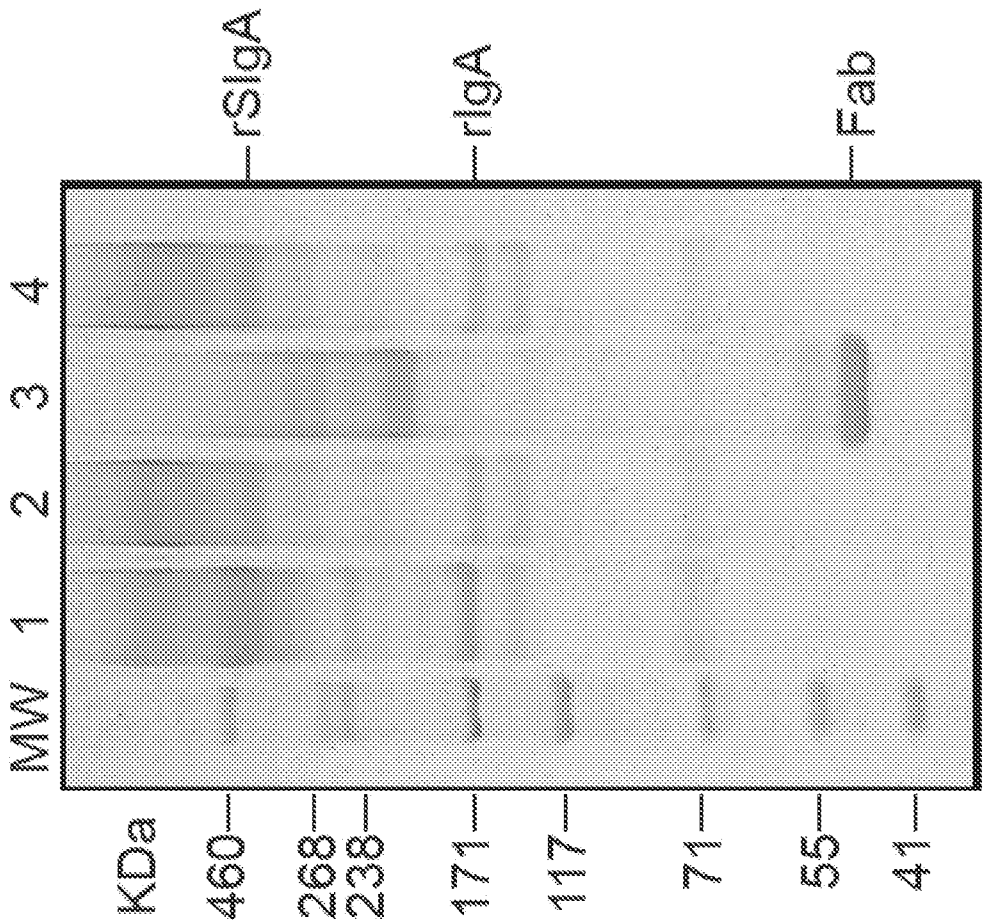


FIG. 16A

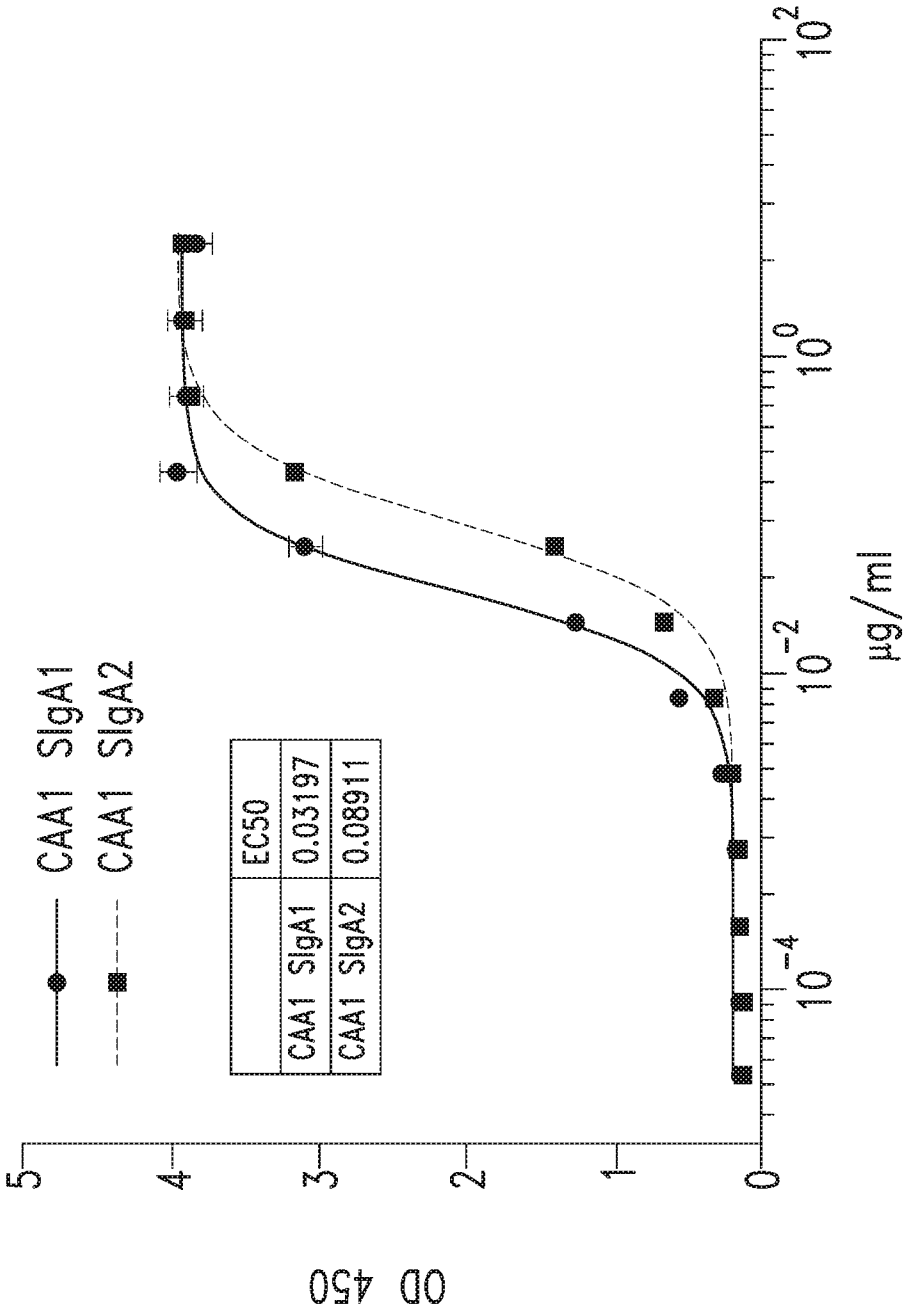

OD 450
0
1
2
3
4
5
10^{-4}
10^{-2}
10^{0}
10^{2}
µg/ml
CAA1 SIgA1
CAA1 SIgA2
EC50
CAA1 SIgA1 0.03197
CAA1 SIgA2 0.08911

FIG. 16B

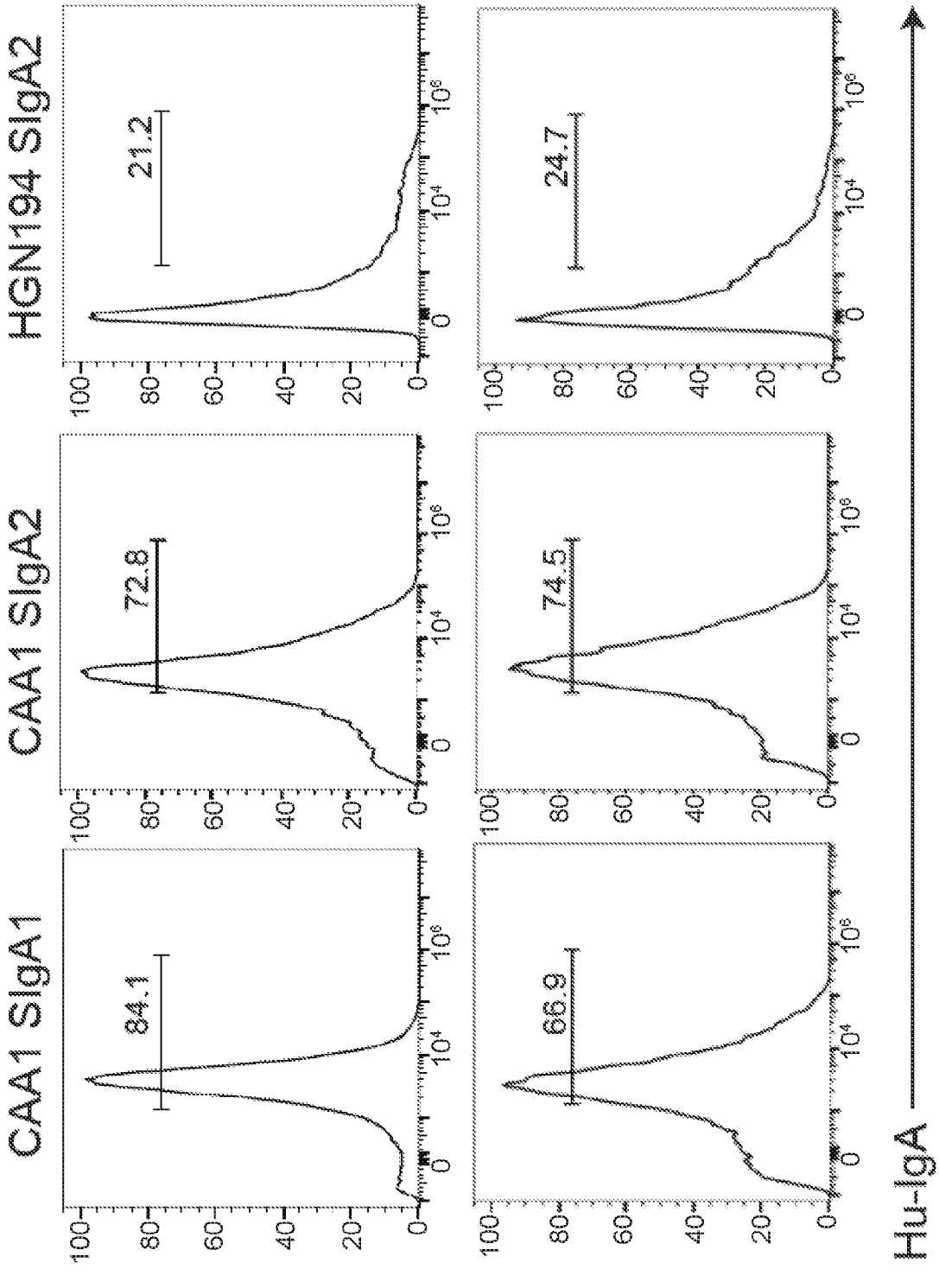

CAA1 SIgA1
CAA1 SIgA2
HGN194 SIgA2
84.1
72.8
21.2
66.9
74.5
24.7
C. jejuni
C. coli
Hu-IgA
0
20
40
60
80
100
10^4
10^6

FIG. 16C

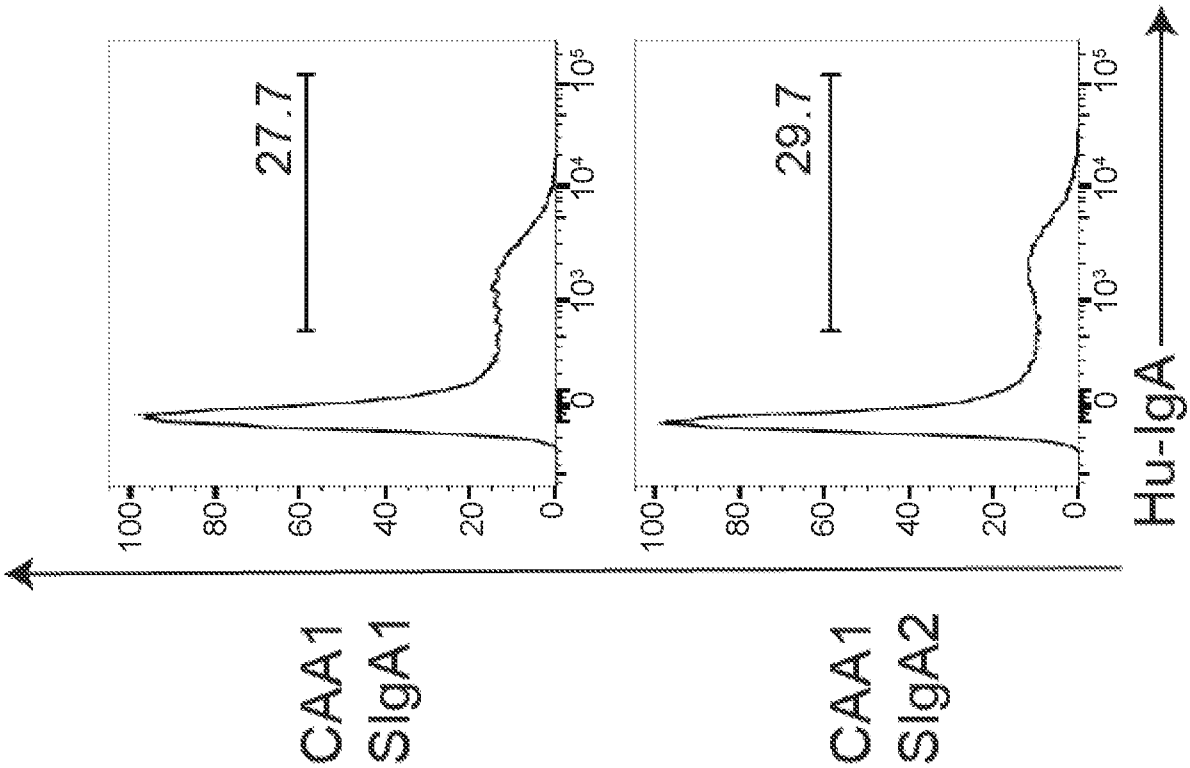

CAA1
SIgA1
27.7
CAA1
SIgA2
29.7
100
80
60
40
20
0
0
10^3
10^4
10^5
Hu-IgA

FIG. 16D

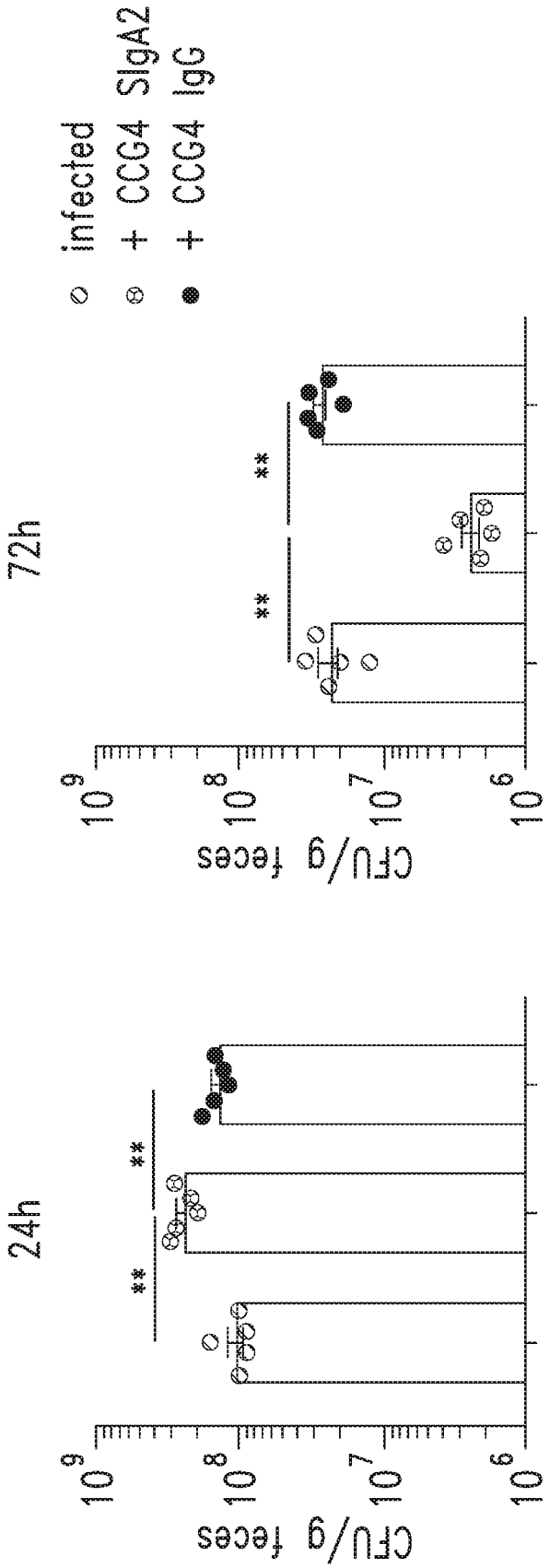

infected
+ CCG4 SIgA2
+ CCG4 IgG
72h
24h
CFU/g feces
10^9
10^8
10^7
10^6
**
**
**
**

FIG. 17A

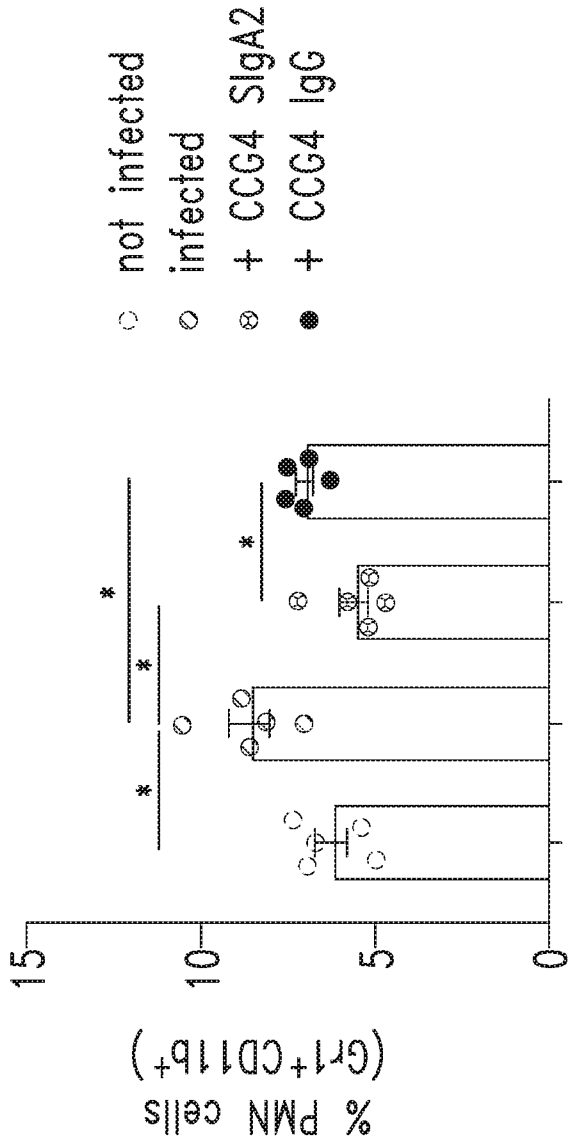

not infected
infected
+ CCG4 SIgA2
+ CCG4 IgG
% PMN cells
(Gr1+CD11b+)
15
10
5
0
*
*
*
*

FIG. 17B

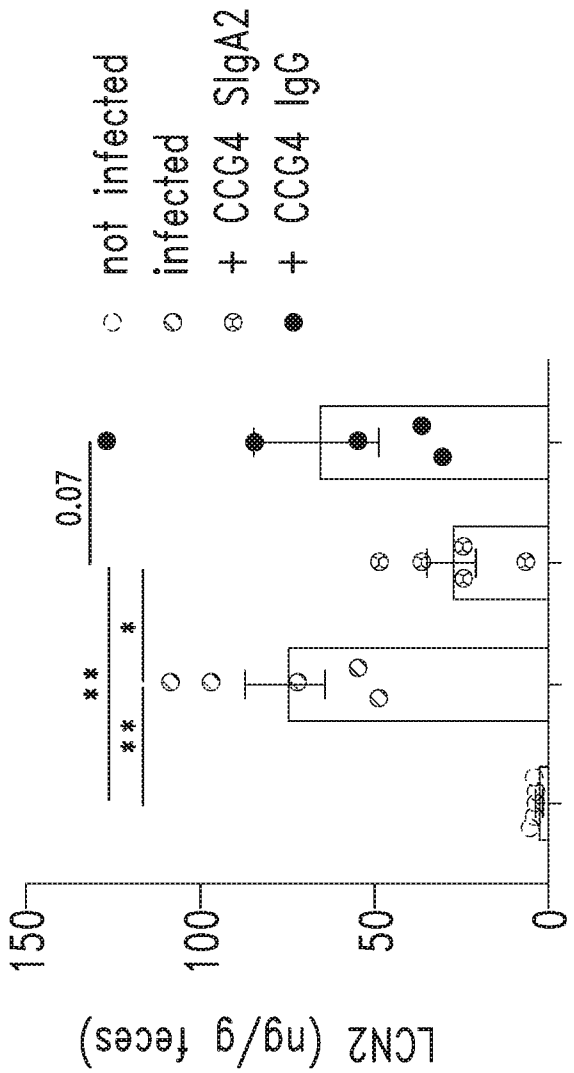

not infected
infected
+ CCG4 SIgA2
+ CCG4 IgG
0.07
**
**
*
150
100
50
0
LCN2 (ng/g feces)

FIG. 17C

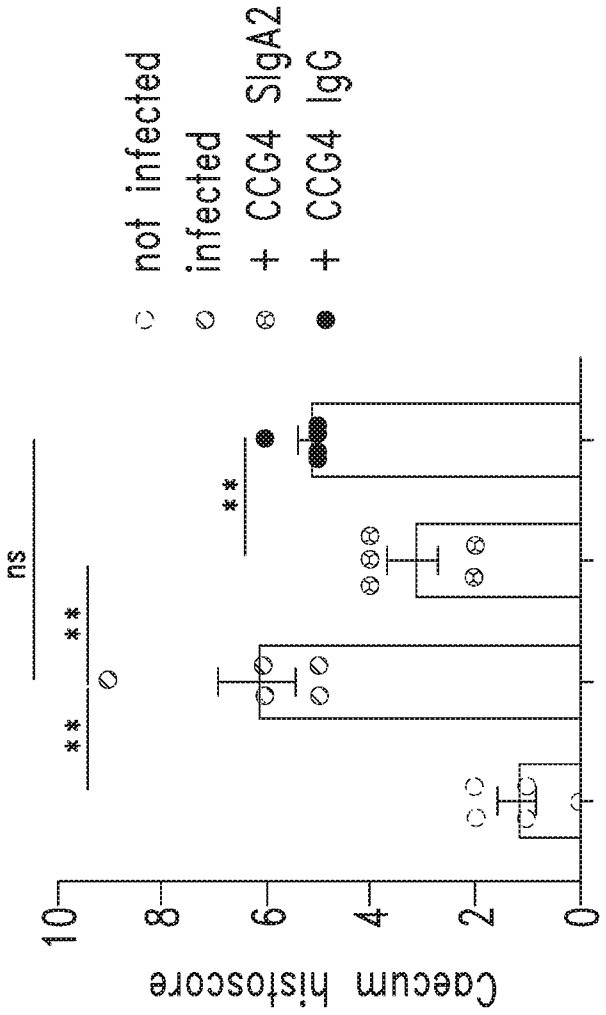

not infected
infected
+ CCG4 SIgA2
+ CCG4 IgG
Caecum histoscore
0
2
4
6
8
10
ns
**
**
**

FIG. 17D