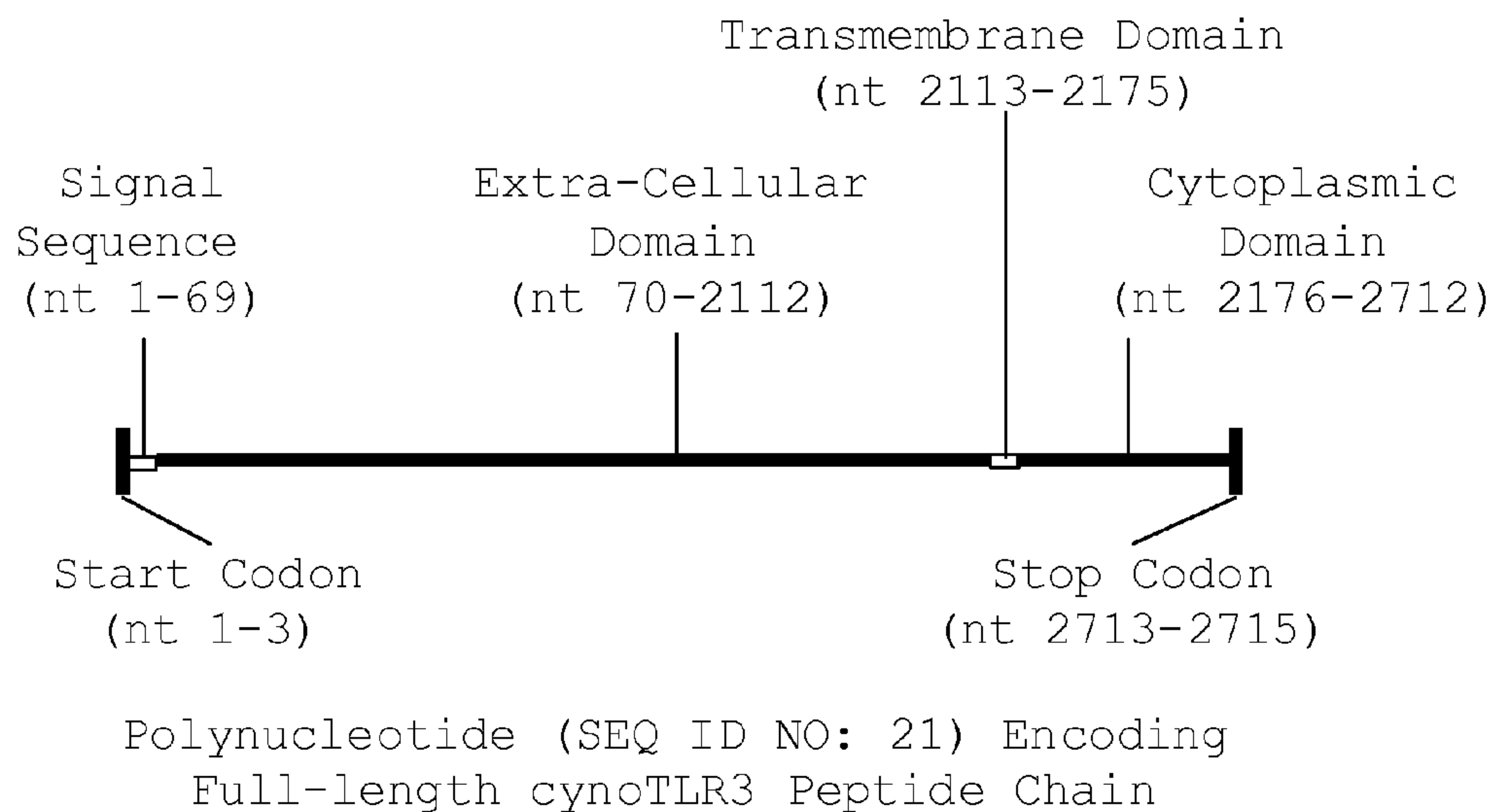




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(57) **Abrégé/Abstract:**

Isolated polynucleotides encoding Cynomolgus monkey Toll-Like Receptor 3 (cynoTLR3), polypeptides obtainable from expression of these polynucleotides, recombinant cells, methods and uses of these are disclosed.

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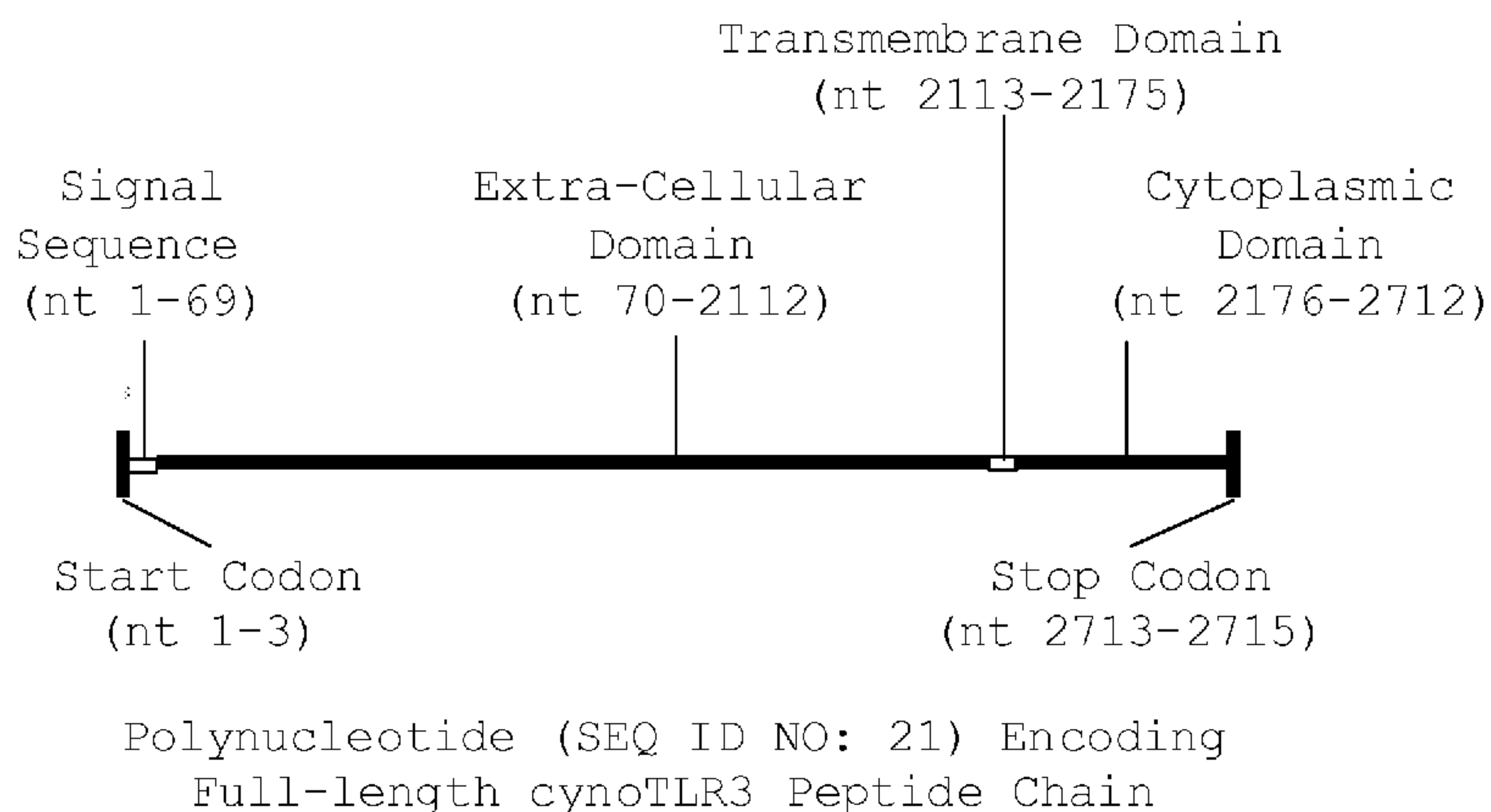
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Fig. 1



(57) **Abstract:** Isolated polynucleotides encoding Cynomolgus monkey Toll-Like Receptor 3 (cynoTLR3), polypeptides obtainable from expression of these polynucleotides, recombinant cells, methods and uses of these are disclosed.



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Cynomolgus Toll-Like Receptor 3**Field of the Invention**

The present invention relates to Cynomolgus monkey Toll-
5 Like Receptor 3 (cynoTLR3) and its uses.

Background of the Invention

Recognition of microbial antigens by the host immune
system is mediated through innate immune receptors, whose
10 activation represents an important step in the initiation of
an inflammatory response. Toll-Like Receptors (TLR) are a
family of innate immune receptors that play a crucial role in
mediating an immune response to foreign antigens. TLR3s are
pathogen associated molecular pattern recognition receptors
15 that recognize double-stranded RNA (dsRNA) as well as the
synthetic dsRNA analog poly-riboinosinic-ribocytidylic acid
(poly(I:C)). See e.g. Alexopoulou et al., 413 Nature 732
(2001)). Moreover, TLR3 has been shown to recognize
endogenous ligands such as mRNA released from necrotic cells
20 suggesting that necrotic cell death at inflammation sites may
contribute to activation of TLR3. See e.g. Kariko et al., 26
J. Biol. Chem. 12542 (2004).

Activation of TLR3s by dsRNA or poly(I:C) ligands
induces secretion of pro-inflammatory cytokines and
25 chemokines and can modulate disease outcomes during
infection-associated inflammation. Importantly, TLR3
activation *in vivo* occurs in the context of viral infection
or necrosis associated with inflammation. See Tabeta et al.,
101 Proc. Natl. Acad. Sci. USA 3516 (2004)); see also Kariko
30 et al., 26 J. Biol. Chem. 12542 (2004). For example, the
human TLR3 peptide chain is expressed in the central nervous
system (CNS), where it is required to control infection by
the HSV-1 virus, which spreads from the epithelium to the
central nervous system via cranial nerves to cause herpes
35 simplex encephalitis in TLR3 deficient patients. See e.g.
Zhang et al., 317 Science 1522 (2007). Furthermore, human

TLR3 peptide chain activation results in inflammatory responses associated with pathological conditions such as, for example, primary biliary cirrhosis of liver tissues. See e.g. Takii et al., 85 Lab. Invest. 836 (2005).

5 Overall, these data demonstrate that activation of TLR3 initiates cascades of phosphorylation and transcriptional activation events that result in the production of numerous inflammatory cytokines that contribute to innate immunity (reviewed by Takeda and Akira, *J. Derm. Sci.* 34:73-82
10 (2004)). Further, these data indicate that sustained TLR3 activation is a critical component in the modulation of infection-associated inflammatory diseases. Published data lend further support to this hypothesis as shown by findings that associate over-production of pro-inflammatory cytokines
15 to systemic inflammatory response syndrome, infection-associated acute cytokine storms (reviewed by Van Amersfoort et al., *Clin. Microbiol. Rev.* 16: 379-414 (2003)) and immune-mediated chronic conditions such as rheumatoid arthritis (reviewed by Miossec et al., *Curr. Opin. Rheumatol.* 16:218-
20 222 (2004)) and inflammatory bowel diseases (reviewed by Ogata and Hibi, *Curr. Pharm. Des.* 9: 1107-1113 (2003)).

Currently, a number of different therapeutic approaches have been taken to target the activity of TLR3s for treatment of different indications. These TLR3 therapeutics include
25 human peptide chain based TLR3 therapeutics, monoclonal antibody antagonists of TLR3, and TLR3 ligand agonists such as dsRNA, poly(I:C) as well as functional analogs of these that target TLR3 activity. The potential indications for monoclonal antibody antagonist based TLR3 therapeutics
30 include inflammatory conditions, sepsis, inflammatory bowel disease, inflammatory pulmonary disease, and autoimmune diseases. The potential indications and uses for TLR3 therapeutics that are agonists include post-viral fatigue syndrome, glioma, prostate cancer, antiviral vaccines,
35 bladder cancer, cervical dysplasia, human papilloma virus

infection, breast cancer, viral infection prevention, tissue regeneration, and avian influenza vaccines.

Extensive safety testing will be required before any TLR3 therapeutic for human use can be brought to the market place. Such safety testing will involve both *in vivo* safety testing in animal models as well as the *in vitro* testing of TLR3 therapeutics. For example, antibody based TLR3 therapeutics may require the generation of surrogate antibodies against a TLR3 peptide chain expressed by a particular model animal as well as significant *in vitro* characterization of such surrogate antibodies. Such surrogate generation and *in vitro* characterization will require the use of TLR3 polynucleotides and peptide chains from a suitable model animal. Importantly, the identification of suitable animal models for such safety testing requires the identification of animal species capable of expressing a TLR3 with high identity and homology to human TLR3 (SEQ ID NO: 13).

Thus, a need exists for the identification of polynucleotides encoding TLR3s and TLR3 peptide chains capable of being expressed in an animal model suitable for the safety testing of TLR3 therapeutics. A need also exists for related methods such as methods of expressing peptide chains and testing the safety of a TLR3 therapeutic in an animal model identified as suitable for safety assessment of TLR3 therapeutics.

Summary

In one aspect, there is provided an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 1.

In one aspect, there is provided an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 2.

In one aspect, there is provided an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 3.

In one aspect, there is provided an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 4.

5 In one aspect, there is provided an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 5.

In one aspect, there is provided a vector comprising an isolated polynucleotide having a sequence selected from the group
10 consisting of a sequence shown in SEQ ID NO: 1, 2, 3, 4, 5, 6, and 7.

In one aspect, there is provided an isolated host cell comprising a vector as disclosed herein.

In one aspect, there is provided an isolated peptide chain
15 comprising a peptide chain having the sequence shown in SEQ ID NO: 8.

In one aspect, there is provided an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 9.

20 In one aspect, there is provided an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 10.

In one aspect, there is provided an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO:
25 11.

In one aspect, there is provided a method for expressing a peptide chain comprising the steps of:

- a) providing a host cell as disclosed herein;
- b) culturing the host cell under conditions sufficient for
30 the expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11; and
- c) confirming expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID
35 NO: 10 or SEQ ID NO: 11.

In one aspect, there is provided a method for expressing a peptide chain comprising the steps of:

a) providing a polynucleotide as disclosed herein capable of being transcribed into an RNA coding for at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11;

b) providing the components of a cell free expression system;

c) initiating cell free expression from the polynucleotide provided; and

d) confirming expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11.

In one aspect, there is provided a method for expressing a peptide chain comprising the steps of:

a) providing an RNA coding for at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11;

b) providing the components of a cell free expression system;

c) initiating cell free expression from the RNA provided; and

d) confirming expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11.

In one aspect, there is provided a peptide chain produced by a method as disclosed herein.

In one aspect, there is provided use of an isolated peptide chain disclosed herein for assessing the safety of a TLR3 therapeutic. In one embodiment, the TLR3 therapeutic is an antibody.

Brief Description of the Drawings

Fig. 1 shows a feature map of the polynucleotide (SEQ ID NO: 21) coding sequence encoding the full-length cynoTLR3 peptide chain.

Fig. 2 shows a feature map of the full-length cynoTLR3 peptide chain (SEQ ID NO: 20).

Detailed Description

One aspect of the invention is an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 1 or a complementary sequence thereof.

Another aspect of the invention is an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 2 or a complementary sequence thereof.

Another aspect of the invention is an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 3 or a complementary sequence thereof.

Another aspect of the invention is an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 4 or a complementary sequence thereof.

Another aspect of the invention is an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 5 or a complementary sequence thereof.

Another aspect of the invention is a vector comprising an isolated polynucleotide having a sequence selected from the group consisting of a sequence shown in SEQ ID NO: 1, 2, 3, 4, 5, 6, and 7.

Another aspect of the invention is an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 8.

Another aspect of the invention is an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 9.

Another aspect of the invention is an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 10.

Another aspect of the invention is an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 11.

Another aspect of the invention is a method for
5 expressing a peptide chain comprising the steps of
providing an RNA coding for at least one polypeptide
comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO:
9, SEQ ID NO: 10 or SEQ ID NO: 11; providing the components
of a cell free expression system; initiating cell free
10 expression from the RNA provided; and confirming expression
of at least one peptide chain comprising the sequence shown
in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO:
11.

Another aspect of the invention is a method for
15 determining if a TLR3 therapeutic causes adverse events
comprising providing a TLR3 therapeutic, a first Cynomolgus
monkey, and a second Cynomolgus monkey; administering the
TLR3 therapeutic to the first Cynomolgus monkey; and
determining whether the first Cynomolgus monkey is
20 presenting a deleterious symptom relative to the second
monkey, where presentation of a deleterious symptom by the
first Cynomolgus monkey shows the TLR3 therapeutic is
unsafe and a lack of presentation of a deleterious symptom
by the first Cynomolgus monkey shows the TLR3 therapeutic
25 is safe.

As used herein and in the claims, the singular forms
"a," "and," and "the" include plural reference unless the
context clearly dictates otherwise. Thus, for example,
reference to "a peptide chain" is a reference to one or
30 more peptide chains and includes equivalents thereof known
to those skilled in the art.

Unless defined otherwise, all technical and scientific
terms used herein have the same meaning as commonly

understood by one of ordinary skill in the art to which an invention belongs. Although any compositions and methods similar or equivalent to those described herein can be used in the practice or testing of the invention, exemplary
5 compositions and methods are described herein.

The present invention provides isolated Cynomolgus monkey (*Macaca fascicularis*) Toll-Like Receptor 3 (cynoTLR3) polynucleotides, vectors comprising these polynucleotides, isolated host cells, peptide chains obtainable from
10 expression of these polynucleotides, methods for expressing the peptide chains of the invention, and uses of these are disclosed.

TLR3s are members of the Toll-like receptor family of pathogen associated molecular pattern (PAMP) recognition
15 receptors. TLR3s are activated by binding of double-stranded RNAs. Double stranded RNAs (dsRNAs) are produced during viral infection, infection by other organisms and by cell injury or necrosis. See e.g. Kariko et al., 279 J. Biol. Chem. 12542 (2004); see also Alexopoulou et al., 413 Nature
20 732 (2001)). Activation of TLR3s in response to the detection of viral infection associated dsRNA or dsRNAs produced by other sources results in activation of NF- κ B to increase production of type I interferons that have antiviral and immune system stimulatory functions. See e.g. Takeda and
25 Akira, 5 Cell. Micro. 143, 144 (2003). The result of TLR3 activation in the context of a viral infection is stimulation of the antiviral defenses of the innate and humoral immune systems. For example, the human TLR3 peptide chain is
30 required to control infection by the HSV-1 virus, which spreads from the epithelium to the central nervous system via cranial nerves to cause herpes simplex encephalitis in TLR3 deficient patients. See e.g. Zhang et al., 317 Science 1522 (2007). In other contexts, however, human TLR3 peptide chain
35 activation results in inflammatory responses associated with pathological conditions such as, for example, primary biliary

cirrhosis of liver tissues. See e.g. *Takii et al.*, 85 Lab. Invest. 836 (2005). Importantly, the full-length cynoTLR3 peptide chain sequence (SEQ ID NO: 10) is 95.7% identical, and 96.8% similar to the well-characterized human TLR3

5 peptide chain (SEQ ID NO: 13).

The compositions and methods of the invention can be used for a variety of specific applications. The polynucleotides and vectors of the invention are useful because they encode Cynomolgus monkey (*Macaca fascicularis*)
10 TLR3 (cynoTLR3) peptide chains and can be used to express these peptide chains. These cynoTLR3 peptide chains are, in turn, useful because they can be used to increase or control antiviral responses after exposure to dsRNA or other TLR3 ligands when they are recombinantly over expressed or
15 introduced by other means into a host animal or tissue.

Peptide chains comprising the extracellular domain of cynoTLR3 can also be used as ligand sink type antagonists that bind available TLR3 ligands or TLR3 associated proteins necessary for TLR3 activation and thus control TLR3 activity.
20 cynoTLR3 peptide chains can also be used to generate therapeutic antibodies for the positive or negative modulation of the activity of cynoTLR3 or TLR3s from other sources. This is desirable because agonist therapeutic antibodies can be used to increase activation of cynoTLR3 or
25 other TLR3s to help control infections while antagonist therapeutic antibodies can be used to decrease activation of cynoTLR3 or other TLR3s to help control pathological conditions associated with TLR3 receptor activation mediated inflammatory responses. cynoTLR3 peptide chains can also be
30 used in *in vitro* or *in vivo* assays to identify other therapeutics such as small molecules capable of modulating the activity of cynoTLR3 or other TLR3s. The methods of expression disclosed are useful because these methods permit the expression of cynoTLR3 peptides. Other methods disclosed
35 are useful because they permit a safety assessment of a TLR3 therapeutic.

The term "polynucleotide" means a molecule comprising a chain of nucleobases covalently linked by a sugar-phosphate backbone or other equivalent covalent chemistry. Double and single stranded DNAs and RNAs are typical examples of
5 polynucleotides.

The term "complementary sequence" means a second isolated polynucleotide sequence that is antiparallel to a first isolated polynucleotide sequence and that comprises nucleobases complementary to the nucleobases in the first
10 polynucleotide sequence. Typically, such "complementary sequences" are capable of forming a double stranded polynucleotide molecule such as double stranded DNA or double stranded RNA when combined under appropriate conditions with the first isolated polynucleotide sequence.

15 The term "vector" means a polynucleotide capable of being duplicated within a biological system or that can be moved between such systems. Vector polynucleotides typically contain elements, such as origins of replication or selection markers, that function to facilitate the duplication or
20 maintenance of these polynucleotides in a biological system. Examples of such biological systems may include cell, virus, animal, plant, and reconstituted biological systems utilizing biological components capable of duplicating a vector. The polynucleotides comprising a vector may be DNA or RNA
25 molecules or hybrids of these.

The term "expression vector" means a vector that can be utilized in a biological system or a reconstituted biological system to direct the translation of a peptide chain encoded by a polynucleotide sequence present in the expression
30 vector.

The term "peptide chain" means a molecule that comprises at least two amino acid residues linked by a peptide bond to form a chain. Large peptide chains of more than 50 amino acids may be referred to as "polypeptides" or "proteins."
35 Small peptide chains of less than 50 amino acids may be referred to as "peptides."

The term "antibody" means immunoglobulin or antibody molecules comprising polyclonal antibodies, monoclonal antibodies including murine, human, humanized and chimeric monoclonal antibodies and antibody fragments, portions, or variants. Antibodies are secreted proteins constitutively expressed and secreted by plasma cells. Antibodies may be of any isotype such as IgG, IgA, or IgM and may comprise antibody fragments such as Fab' fragments. An antibody may also be a bispecific antibody that specifically binds two different peptide chain epitopes.

Antibodies can be produced using plasma cells immortalized by standard methods such as hybridoma generation or by transfection of antibody heavy and/or light chain genes into an immortalized B cell such as a myeloma cell or other cell types, such as Chinese hamster ovary (CHO) cells, plant cells and insect cells.

The term "monoclonal antibody" (mAb) as used herein means an antibody (or antibody fragment) obtained from a population of substantially homogeneous antibodies. Monoclonal antibodies are highly specific, typically being directed against a single antigenic determinant. The modifier "monoclonal" indicates the substantially homogeneous character of the antibody and does not require production of the antibody by any particular method. For example, murine mAbs can be made by the hybridoma method of Kohler *et al.*, 256 Nature 495 (1975). Chimeric mAbs containing a light chain and heavy chain variable region derived from a donor antibody (typically murine) in association with light and heavy chain constant regions derived from an acceptor antibody (typically another mammalian species such as human) can be prepared by the method disclosed in U.S. Pat. No. 4,816,567. Humanized mAbs having CDRs derived from a non-human donor immunoglobulin (typically murine) and the remaining immunoglobulin-derived parts of the molecule being derived from one or more human immunoglobulins, optionally

having altered framework support residues to preserve binding affinity, can be obtained by the techniques disclosed in Queen *et al.*, 86 Proc. Natl. Acad. Sci. (USA) 10029 (1989) and Hodgson *et al.*, 9 Bio/Technology 421 (1991).

- 5 Exemplary human framework sequences useful for humanization are disclosed, *e.g.*, on various publicly available websites and in Kabat *et al.*, *Sequences of Proteins of Immunological Interest*, U.S. Dept. Health (1987).

Fully human mAbs lacking any non-human sequences can be prepared from human immunoglobulin transgenic mice by techniques referenced in, e.g., Lonberg *et al.*, 368 Nature 856 (1994); Fishwild *et al.*, 14 Nature Biotech. 845 (1996) and Mendez *et al.*, 15 Nature Genetics 146 (1997). Human mAbs can also be prepared and optimized from phage display libraries by techniques referenced in, e.g., Knappik *et al.*, 296 J. Mol. Biol. 57 (2000) and Krebs *et al.*, 254 J. Immunol. Meth. 67 (2001).

10 An antibody molecule or preparation "specifically binds" a given antigen when it binds this antigen with higher affinity and in a specific, as opposed to non-specific fashion, relative to a second non-identical antigen. Stated differently, the "specific binding" of an antibody molecule
15 or preparation can be used to distinguish between two different peptide chains.

A "fragment" is a peptide chain having an amino acid sequence that comprises a portion, but not all, of any amino acid sequence of any peptide chain of the invention.

20 Fragments can include, for example, truncated peptide chain having a portion of an amino acid sequence corresponding to a signal peptide, extracellular domain, transmembrane domain, or cytoplasmic domain, or variants thereof, such as a continuous series of residues that includes a heterologous
25 amino- and/or carboxy-terminal amino acid sequence.

Degradation forms of the peptide chains of the invention produced by, or in, a host cell are also included. Other exemplary fragments are characterized by structural or functional attributes such as fragments that comprise alpha-helix or alpha-helix forming regions, beta-sheet or beta-sheet forming regions, turn or turn-forming regions, coil or coil-forming regions, hydrophilic regions, hydrophobic regions, alpha-amphipathic regions, beta-amphipathic regions, flexible regions, surface-forming regions, substrate binding
30 regions, extracellular regions and high antigenic index
35

regions. Importantly, the peptide chains of the invention can be used or provided as fragments.

A "variant peptide chain" is a second peptide chain in which amino acid substitutions, insertions, deletions or
5 combinations thereof have been made relative to a first peptide chain. Naturally occurring, modified or atypical amino acids can be used for substitutions and insertions. The peptide chains described by SEQ ID NO: 8 and SEQ ID NO: 9 are exemplary variant peptide chains relative to the peptide
10 chain having the amino acid sequence shown in SEQ ID NO: 11.

A "variant polynucleotide" is a second polynucleotide in which nucleic acid residue substitutions, insertions, deletions, or combinations thereof have been made relative to a first polynucleotide sequence. Naturally occurring or
15 modified nucleobases can be used for substitutions and deletions. The polynucleotides described by SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, and SEQ ID NO: 5 are exemplary variant polynucleotides relative to the polynucleotide having the amino acid sequence shown in SEQ ID NO: 4.

20 The term "TLR3 therapeutic" means a molecule or preparation that is believed to provide a therapeutic benefit and is believed to provide that therapeutic benefit, in part, through the activity of a TLR3. Such TLR3s may comprise the peptide chains of the invention. Examples of TLR3
25 therapeutics include known TLR3 ligands such as dsRNA or poly(I:C) which bind and activate TLR3s to produce the therapeutic benefits of increased antiviral activity and immune system stimulation.

The term "deleterious symptom" means any symptom
30 presented by an animal that indicates harm to the animal has occurred.

One aspect of the invention is an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 1 or a complementary sequence
35 thereof. The polynucleotide sequence shown in SEQ ID NO: 1

encodes a peptide chain comprising the predicted mature form of the cynoTLR3 extracellular domain.

The polynucleotides of the invention may be produced by chemical synthesis such as solid phase polynucleotide
5 synthesis on an automated polynucleotide synthesizer. Alternatively, the polynucleotides of the invention may be produced by other techniques such a PCR based duplication, vector based duplication, or restriction enzyme based DNA manipulation techniques. Techniques for producing or
10 obtaining polynucleotides of a given known sequence are well known in the art.

The polynucleotides of the invention may also comprise at least one non-coding sequence, such as transcribed but not translated sequences, termination signals, ribosome binding
15 sites, mRNA stabilizing sequences, introns and polyadenylation signals. The polynucleotide sequences may also comprise additional sequences encoding additional amino acids. These additional polynucleotide sequences may, for example, encode a marker or tag sequence such as a hexa-
20 histidine peptide, as described in Gentz *et al.*, 86 Proc. Natl. Acad. Sci. (USA) 821 (1989) or the HA peptide tag as described in Wilson *et al.*, 37 Cell 767 (1984) which facilitate the purification of fused polypeptides.

Another aspect of the invention is an isolated
25 polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 2 or a complementary sequence thereof. The polynucleotide sequence shown in SEQ ID NO: 2 encodes a peptide chain comprising the predicted cynoTLR3 signal peptide without its amino terminal methionine residue,
30 and the extracellular domain.

Another aspect of the invention is an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 3 or a complementary sequence thereof. The polynucleotide sequence shown in SEQ ID NO: 3
35 encodes a peptide chain comprising the predicted mature form of

the cynoTLR3 extracellular domain, the transmembrane domain, and the cytoplasmic domain.

Another aspect of the invention is an isolated polynucleotide comprising a polynucleotide having the
5 sequence shown in SEQ ID NO: 4 or a complementary sequence thereof. The polynucleotide sequence shown in SEQ ID NO: 4 encodes a peptide chain comprising the predicted cynoTLR3 signal peptide without its amino terminal methionine residue, the extracellular domain, the transmembrane domain, and the
10 cytoplasmic domain.

Another aspect of the invention is an isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 5 or a complementary sequence thereof. The polynucleotide sequence shown in SEQ ID NO: 5
15 is a nucleic acid with 5' and 3' sequences flanking an open reading frame encoding a peptide chain comprising full-length cynoTLR3.

Another aspect of the invention is a vector comprising an isolated polynucleotide having a sequence selected from
20 the group consisting of a sequence shown in SEQ ID NO: 1, 2, 3, 4, 5, 6, and 7. The polynucleotide sequence shown in SEQ ID NO: 6 is a polynucleotide (DNA) expression vector designated p4078 that encodes a peptide chain comprising full-length cynoTLR3. The polynucleotide sequence shown in SEQ ID
25 NO: 7 is a polynucleotide (DNA) expression vector designated p4037 that encodes a peptide chain comprising the predicted cynoTLR3 signal sequence with an amino terminal methionine residue, and extracellular domain fused via a flexible glycine and serine link to six amino terminal histidine amino
30 acid residue tags. The polynucleotides shown in SEQ ID NO: 1, 2, 3, 4, and 5 are described above.

The vectors of the invention are useful for maintaining polynucleotides, duplicating polynucleotides, or driving expression of a peptide chain encoded by a vector of the
35 invention in a biological systems--including reconstituted biological systems.

Vectors may be chromosomal-, episomal- and virus-derived such as vectors derived from bacterial plasmids, bacteriophages, transposons, yeast episomes, insertion elements, yeast chromosomal elements, baculoviruses, papova
5 viruses such as SV40, vaccinia viruses, adenoviruses, fowl pox viruses, pseudorabies viruses, picornaviruses and retroviruses and vectors derived from combinations thereof, such as cosmids and phagemids.

The vectors of the invention can be formulated in
10 microparticles, with adjuvants, with lipid, buffer or other excipients as appropriate for a particular application.

In one embodiment of the invention the vector is an expression vector.

Expression vectors typically comprise nucleic acid
15 sequence elements that can control, regulate, cause or permit expression of a peptide chain encoded by such a vector. Such elements may comprise transcriptional enhancer binding sites, RNA polymerase initiation sites, ribosome binding sites, and other sites that facilitate the expression of encoded peptide
20 chains in a given expression system. Such expression systems may be cell based, or cell free systems well known in the art. Nucleic acid sequence elements and parent vector sequences suitable for use in the expression of encoded peptide chains are also well known in the art.

25 Another embodiment of the invention is an isolated host cell comprising a vector of the invention.

An exemplary plasmid derived expression vector useful for expression of the polypeptides of the invention comprises an *E. coli* origin of replication, an aph(3')-1a kanamycin
30 resistance gene, HCMV immediate early promoter with intron A, a synthetic polyA sequence and a bovine growth hormone terminator. Another exemplary plasmid derived expression vector comprises an *E. coli* origin of replication, an ant(4')-1a kanamycin resistance gene, Rous sarcoma virus long
35 terminal repeat sequences, HCMV immediate early promoter and an SV40 late polyA sequence.

Representative host cell examples include Archaea cells; bacterial cells such as *Streptococci*, *Staphylococci*, *Enterococci*, *E. coli*, *Streptomyces*, cyanobacteria, *B. subtilis* and *S. aureus*; fungal cells such as *Kluveromyces*,
5 *Saccharomyces*, Basidiomycete, *Candida albicans* or *Aspergillus*; insect cells such as *Drosophila* S2 and *Spodoptera* Sf9; animal cells such as CHO, COS, HeLa, C127, 3T3, BHK, 293, CV-1, Bowes melanoma and myeloma; and plant cells, such as gymnosperm or angiosperm cells. The host cells in the
10 methods of the invention may be provided as individual cells, or populations of cells. Populations of cells may comprise an isolated or cultured population of cells or cells present in a matrix such as a tissue.

Introduction of a polynucleotide, such as a vector, into
15 a host cell can be effected by methods well known to those skilled in the art from laboratory manuals such as Davis *et al.*, Basic Methods in Molecular Biology, 2nd ed., Appleton & Lange, Norwalk, CT (1994) and Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 3rd ed., Cold Spring Harbor
20 Laboratory Press, Cold Spring Harbor, NY (2001). These methods include calcium phosphate transfection, DEAE-Dextran mediated transfection, microinjection, cationic lipid-mediated transfection, electroporation, transduction, scrape loading, ballistic introduction and infection.

25 Another aspect of the invention is an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 8. SEQ ID NO: 8 is a peptide chain comprising the predicted mature form of the cynoTLR3 extracellular domain.

The peptide chains of the invention may be produced by
30 chemical synthesis, such as solid phase peptide syntheses, on an automated peptide synthesizer. Alternatively, the peptide chains of the invention can be obtained from polynucleotides encoding these peptide chains by the use of cell free expression systems such as reticulocyte lysate based
35 expression systems, wheat germ extract based expression systems, and *Escherichia coli* extract based expression

systems. The peptide chains of the invention can also be obtained by expression and isolation from cells harboring a nucleic acid sequence of the invention by techniques well known in the art, such as recombinant expression of easily
5 isolated affinity labeled peptide chains. Those skilled in the art will recognize other techniques for obtaining the peptide chains of the invention.

The peptide chains of the invention may comprise fusion peptide chains comprising a peptide chain of the invention
10 fused with second peptide chain. Such second peptide chains may be leader or secretory signal sequences, a pre- or pro- or prepro-protein sequence, as well as naturally occurring, or partially synthetic sequences derived in part from a naturally occurring sequence or an entirely synthetic
15 sequence. Secretory signal or leader peptide chain sequences may be selected to direct secretion of the peptide chains of the invention into the lumen of the endoplasmic reticulum or extracellular environment; such peptide chain sequences may be heterologous or endogenous to any peptide chain from a
20 Cynomologus monkey or comprise hybrids of these.

The peptide chains of the invention can also be formulated in a pharmaceutically acceptable carrier or diluent. A variety of aqueous carriers may be employed, e.g., 0.4% saline, 0.3% glycine and the like. These
25 solutions are sterile and generally free of particulate matter. These solutions may be sterilized by conventional, well-known sterilization techniques (e.g., filtration). The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological
30 conditions, such as pH adjusting and buffering agents. The concentration of the peptide chains of the invention in such pharmaceutical formulation can vary widely, *i.e.*, from less than about 0.5%, usually at or at least about 1% to as much as 15 or 20% by weight and will be selected primarily based
35 on fluid volumes, viscosities and other factors, according to the particular mode of administration selected.

The peptide chains and nucleic acids of the invention, can also be provided in the form of a pharmaceutical preparation, such as a vaccine for eliciting an immune response, that can be provided in unit dose forms. The
5 appropriate therapeutically effective dose can be determined readily by those of skill in the art. A determined dose may, if necessary, be repeated at appropriate time intervals selected as appropriate by a physician or other person skilled in the relevant art (e.g. nurse, veterinarian, or
10 veterinary technician) during the treatment period.

The peptide chains of the invention can be lyophilized for storage and reconstituted in a suitable carrier prior to use. This technique has been shown to be effective with conventional protein preparations. Lyophilization and
15 reconstitution techniques are well known in the art.

Another aspect of the invention is an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 9. SEQ ID NO: 9 is a peptide chain comprising the predicted cynoTLR3 signal peptide without its amino terminal
20 methionine residue, and the extracellular domain.

Another aspect of the invention is an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 10. SEQ ID NO: 10 is a peptide chain comprising the predicted mature form of the cynoTLR3 extracellular
25 domain, the transmembrane domain, and the cytoplasmic domain.

Another aspect of the invention is an isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 11. SEQ ID NO: 11 is a peptide chain comprising the predicted cynoTLR3 signal peptide without its amino
30 terminal methionine residue, the extracellular domain, the transmembrane domain, and the cytoplasmic domain.

Another embodiment of the invention is a method for expressing a peptide chain comprising the steps of providing a host cell of the invention; culturing the host cell under
35 conditions sufficient for the expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8,

SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11; and confirming expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11.

5 Host cells can be cultured under any conditions suitable for maintaining or propagating a given type of host cell and sufficient for expressing a peptide chain. Culture conditions, media, and related methods sufficient for the expression of peptide chains are well known in the art. For
10 example, many mammalian cell types can be aerobically cultured at 37°C using appropriately buffered DMEM media while bacterial, yeast and other cell types may be cultured at 37°C under appropriate atmospheric conditions in LB media.

In the methods of the invention the expression of a
15 peptide chain can be confirmed using a variety of different techniques well known in the art. For example, expression of a peptide chain can be confirmed using detection reagents, such as antibodies or receptor ligands, specific for an expressed peptide chain. Antibodies that specifically bind
20 to the cynoTLR3 peptide chains of the invention are one example of such reagents. TLR3 receptor ligands such as dsRNA or poly(I:C) that bind TLR3 are another example of such reagents. Detection reagents may be detectably labeled by conjugation or incorporation of a radiolabel, fluorophore,
25 chromophore or other detectable molecule to, or into, the detection reagent.

Alternatively, the expression of a cynoTLR3 peptide chain of the invention can be confirmed by assaying for a biological activity associated with activation of TLR3s, such
30 as activation of NF- κ B or increased production of type I interferons. Such assays may also utilize reporter gene constructs responsive to TLR3 activation.

Peptide chain expression can also be confirmed by identification of a peptide chain with the physical
35 characteristics of a peptide chain of the invention in a preparation of peptide chains. For example, SDS-PAGE

techniques and other well-known protein characterization techniques utilizing criteria such as, for example, protein molecular weight or isoelectric point can be used to confirm expression of the peptide chains of the invention. Protein
5 purification techniques such as ammonium sulfate or ethanol precipitation, acid extraction, high-performance liquid chromatography, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxyapatite
10 chromatography and lectin chromatography can also be used to confirm expression of a peptide chain of the invention.

Importantly, in the methods of the invention the peptide chain expressed need not be isolated. Consequently, expression of a peptide chain may be confirmed to have
15 occurred on, or in, a cell, or in a mixture of peptide chains for example. Flow cytometry based techniques such as fluorescence activated cell sorting (FACS) may also be used, when appropriate, to confirm expression of a peptide chain by a cell. As discussed above peptide chain expression may be
20 confirmed using any suitable technique known in the art.

Another embodiment of the invention is a method for expressing a peptide chain comprising the steps of providing a polynucleotide of the invention capable of being transcribed into an RNA coding for at least one peptide chain
25 comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11; providing the components of a cell free expression system; initiating cell free expression from the polynucleotide provided; and confirming expression of at least one peptide chain comprising the sequence shown
30 in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11.

Techniques for transcribing a polynucleotide into an RNA, obtaining an RNA coding for a peptide chain, or initiating cell free expression are well known in the art
35 and reagent kits for accomplishing these steps are commercially available from a variety of sources.

In another embodiment of the method of the invention the cell free expression system is selected from the group consisting of a reticulocyte lysate based expression system, a wheat germ extract based expression system, and an
5 *Escherichia coli* extract based expression system.

Another embodiment of the invention is a method for expressing a peptide chain comprising the steps of providing an RNA coding for at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10
10 or SEQ ID NO: 11; providing the components of a cell free expression system; initiating cell free expression from the RNA provided; confirming expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11.

15 In another embodiment of the method of the invention the cell free expression system is selected from the group consisting of a reticulocyte lysate based expression system, a wheat germ extract based expression system, and an *Escherichia coli* extract based expression system.

20 Another embodiment of the invention is a peptide chain produced by the methods of invention. Such peptide chains may comprise post-translational modifications including glycosylation or phosphorylation for example. Such peptide chains may also comprise alternative peptide chain forms such
25 as splice variants, truncated forms, or proteolytically modified forms.

Another embodiment of the invention is an antibody that specifically binds a peptide chain of the invention. The peptide chains of the invention can be used to produce
30 polyclonal or monoclonal antibodies against cynoTLR3. Techniques for making murine, chimeric, humanized and fully human monoclonal antibodies using protein or nucleic acid immunization are routine and well known to those skilled in the art. Additional discussion and description of such
35 techniques can be found above.

Another embodiment of the invention is a monoclonal antibody that specifically binds a peptide chain of the invention.

Another aspect of the invention is a method for
5 determining if a TLR3 therapeutic is safe or unsafe comprising providing a TLR3 therapeutic, a first Cynomolgus monkey, and a second Cynomolgus monkey; administering the TLR3 therapeutic to the first Cynomolgus monkey; and
10 determining whether the first Cynomolgus monkey is presenting a deleterious symptom relative to the second monkey, where presentation of a deleterious symptom by the first Cynomolgus monkey shows the TLR3 therapeutic is unsafe and a lack of presentation of a deleterious symptom by the first Cynomolgus monkey shows the TLR3 therapeutic is safe.

15 In the methods of the invention the first and second Cynomolgus monkey provided should be equivalent with regard to the presentation of deleterious symptoms. Stated differently both animals should be presenting either no deleterious symptoms or the same deleterious symptoms when
20 they are provided.

In the methods of the invention TLR3 therapeutics can be administered by any route appropriate such as parenterally, subcutaneously, intravenously, etc. Examples of TLR3
25 therapeutics suitable for use in the method of the invention include, for example, known TLR3 ligands such as dsRNA or poly(I:C) and peptide chains such as those comprising the TLR3 extracellular domain.

In the methods of the invention the determination of whether the first Cynomolgus monkey is presenting a
30 deleterious symptom relative to the second Cynomolgus monkey is readily accomplished. For example, a person of ordinary skill in the art such as a veterinarian, veterinarian's assistant, animal technician, or research scientist can determine if a symptom presented by an animal is deleterious.
35 Examples of deleterious symptoms include death, coma, seizures, fever, organ failure, tissue abnormalities,

impaired organ function, impaired tissue function, cancers, tumors, ulcers, bleeding, infections and the like.

In one embodiment of the method of the invention the TLR3 therapeutic is an antibody.

5 The present invention will now be described with reference to the following specific, non-limiting examples.

Example 1

Isolation, Cloning and Sequencing of Polynucleotides Encoding 10 Full-Length Cynomolgus Monkey Toll-Like Receptor 3 (cynoTLR3)

RNA was purified from Cynomolgus monkey peripheral blood mononuclear cells (PBMC) using TRIZOL® reagent (Invitrogen, Carlsbad, CA) according to the manufacturer's instructions. Reverse transcription reactions were carried out using
15 SUPERScript II REVERSE TRANSCRIPTASE® kit and were primed using an oligo-dT primer. Primers for initial PCR cloning were designed based on the sequence of the polynucleotide encoding the human TLR3 peptide chain. PCR for the cloning of a polynucleotide (SEQ ID NO: 5) encoding the full-length
20 cynoTLR3 peptide chain (SEQ ID NO: 11) was then performed using the 2535 primer (SEQ ID NO: 14) and 2664 primer (SEQ ID NO: 15). PCR was performed using 100 ng of each primer with 100 ng of cDNA template under the following conditions: 30 cycles of 94°C 30 seconds, 60°C 1 minute, 68°C 1 minute,
25 followed by one cycle of 68°C for 5 minutes. PCR reaction products were analyzed on agarose gels, and revealed a polynucleotide band of approximately 2700 bp corresponding to the PCR cloned polynucleotide was obtained.

Cloned PCR products were purified using QIAQUICK® PCR
30 purification (Qiagen, Valencia, CA). PCR products were cloned into a pCR4 TOPO TA® vector to obtain sequence between the 2535 primer (SEQ ID NO: 14) and 2664 primer (SEQ ID NO: 15) for the approximately 2700 bp PCR product.

Sequence masked by the 2535 primer (SEQ ID NO: 14) and
35 2664 primer (SEQ ID NO: 15) from the approximately 2700 bp

PCR product was cloned via the 5' and 3' RACE (Rapid Amplification of cDNA Ends) methods. This was accomplished by first designing the cynoTL3 cDNA specific 2589 primer (SEQ ID NO: 17), 2590 primer (SEQ ID NO: 18), and 2625 primer (SEQ ID NO: 19) using the cynoTLR3 sequence obtained as described above. 3' primers, placed about 150 to 250bp downstream of the initiation site, was designed to pair with a 5' GENERACER® primer for amplification, cloning and sequencing of the 5' end of the full-length polynucleotide cDNA encoding cynoTLR3. 5' primers, placed about 150 to 250bp upstream of the termination site, was designed to pair with a 3' GENERACER® primer for amplification, cloning and sequencing of the 3' end of the full-length polynucleotide cDNA encoding cynoTLR3. The PCR products obtained from these amplifications were then cloned into pCR4 TOPO TA® vector and 5' untranslated sequence, amino-terminal coding sequence, carboxy-terminal coding sequence, and 3' untranslated sequence were obtained from the polynucleotides. Primers used to obtain additional sequence had the sequences shown in SEQ ID NO: 17, SEQ ID NO: 18, and SEQ ID NO: 19. Multiple sequence alignment of the sequences obtained was then performed and a polynucleotide (SEQ ID NO: 5) comprising 5' untranslated sequence, a coding sequence encoding the full-length cynoTLR peptide chain (SEQ ID NO: 20), and 3' untranslated sequence was obtained.

Sequence analysis was then performed using Vector NTI v9.0.0 software (Invitrogen Corp., Carlsbad, CA). Domains identified in the full-length cynoTLR3 peptide chain are encoded by the cloned polynucleotide (SEQ ID NO: 5) shown in Figure 1 and Figure 2. The amino-terminal methionine is encoded by nucleotide residues 1-3 of SEQ ID NO: 21 and corresponds to amino acid residue 1 of SEQ ID NO: 20. The signal peptide is encoded by nucleotide residues 1-69 of SEQ ID NO: 21 and corresponds to amino acid residues 1-23 of SEQ ID NO: 20. The extracellular domain is encoded by nucleotide residues 70-2112 of SEQ ID NO: 21 and corresponds to amino acid residues 24-704 of SEQ ID NO: 20. The transmembrane

domain is encoded by nucleotide residues 2113-2175 of SEQ ID NO: 21 and corresponds to amino acid residues 705-725 of SEQ ID NO: 20. The cytoplasmic domain is encoded by nucleotide residues 2176-2712 of SEQ ID NO: 21 and corresponds to amino acid residues 726-904 of SEQ ID NO: 20. The stop codon is encoded by nucleotide residues 2713-2715 of SEQ ID NO: 21.

Multiple sequence alignment analyses were performed using the default settings of the CLUSTALW algorithm employed by the AlignX module of the Vector NTI v9.0.0 software. The full-length polynucleotide coding sequence encoding cynoTLR3 (nucleotide residues 1-2712 of SEQ ID NO: 21) was found to be 96.8% identical to the full-length polynucleotide coding sequence (nucleotide residues 1-2715 of SEQ ID NO: 12) encoding the well characterized full-length human TLR3 peptide chain. The full-length cynoTLR3 peptide chain (SEQ ID NO: 20) was found to be 95.7% identical to the well characterized full-length human TLR3 peptide chain (SEQ ID NO: 13). The mature form of the cynoTLR3 extracellular domain peptide chain (SEQ ID NO: 1) was found to be 95.4% identical to the extracellular domain of the human TLR3 peptide chain (amino acid residues 24 to 704 of SEQ ID NO: 13).

The full-length polynucleotide coding sequence encoding cynoTLR3 (nucleotide residues 1-2712 of SEQ ID NO: 21) was found to be 99.3% identical to the full-length polynucleotide coding sequence (nucleotide residues 1-2712 of SEQ ID NO: 22) encoding the rhesus monkey TLR3 peptide chain. The full-length cynoTLR3 peptide chain (SEQ ID NO: 20) was found to be 98.5% identical to the rhesus monkey TLR3 peptide chain (SEQ ID NO: 23). The mature form of the cynoTLR3 extracellular domain peptide chain (SEQ ID NO: 1) was found to be 98.2% identical to the extracellular domain of the human TLR3 peptide chain (amino acid residues 24 to 704 of SEQ ID NO: 23). The cloning of the polynucleotide (SEQ ID NO: 22) encoding rhesus monkey TLR3 was reported by Sanghavi and

Reinhart. See Sanghavi and Reinhart, 175 J. Immunol. 5314 (2005).

Example 2

5 Expression and Purification of a Peptide Chain Comprising the cynoTLR3 Extracellular Domain

A polynucleotide encoding an N-terminal methionine, the cynoTLR3 signal peptide chain, and the cynoTLR3 extracellular domain fused via a flexible glycine and serine link to six
10 amino terminal histidine amino acid residue tags was constructed and cloned into an mammalian expression vector to generate the p4037 expression vector construct (SEQ ID NO: 7). Primer 2523 (SEQ ID NO: 16) was used to facilitate the generation of p4037. HEK293 cells were transiently
15 transfected with p4037 using standard methods. The HEK293 cell line is derived from human embryonic kidney cells. These HEK293 cells were then cultured for six days and the cell culture media was collected. TALON® resin purification to isolate the histidine tagged cynoTLR3 extracellular domain
20 fusion peptide chain encoded by p4037 from the collected media was then conducted as directed by the manufacturer (Clontech Laboratories Inc., Mountain View, CA). The eluate from the TALON® resin was then analyzed by SDS-PAGE conducted on non-reduced samples and samples subjected to reducing
25 conditions. SDS-PAGE was followed by Western blotting. Western blots were probed with a histidine tag specific probe. Western blots analysis of both reduced and non-reduced samples revealed that a apparently monomeric protein with an approximate molecular weight of 98 kDal was expressed
30 and isolated. The calculated molecular weight of the cynoTLR3 histidine tagged cynoTLR3 extracellular domain fusion peptide chain encoded by p4037 was approximately 80 kDal which is smaller than the 98 kDal histidine tagged peptide chain detected in the Western blots. However, the
35 peptide chain encoded by p4037 comprises 15 N-linked glycosylation sites, and it is believed post-translational

glycosylation is largely responsible for the increased molecular weight of the histidine tagged protein expressed.

5 The present invention now being fully described, it will be apparent to one of ordinary skill in the art that many changes and modifications can be made. The scope of the claims may be given the broadest interpretation consistent with the description as a whole.

SEQUENCE LISTING KEY

SEQ ID NO: 1

Source: *Macaca fascicularis*

Description: Nucleic acid encoding a peptide chain comprising the predicted mature form of the cynoTLR3 extracellular domain.

tccaccaacaaatgcactggttagccaagaagttgctgactgcagccacctgaagttaactcagg
taccgatgatctccccacaaacataacagtgttgaatcttaccataatcaactcagaagatt
accagctgccaattttacaagatatagccaactaactatcttggatgtaggattttaactccatc
tcaaaactggagccagaattgtgccaaaaacttcccatgtttaaagttttgaacctccagcaca
atgagctatctcaactttctgataaaaacttttgccttctgcacgaatttgacggaactccatct
catgtccaactcaatccagaaaattaaaaataatccctttgtaaagcagaagaatttaatcaca
ttagatctgtctcataatggcttgtcatctacaaaattaggaactcagggttcagctggaaaatc
tccaagagcttctattatcaaacaataaaaatccaagcgctaaaaagtgaagaacttggtatcct
tgccaattcatcttttaaaaaagtttagagttgtcatcgaatcaaattaaagagttttctccaggg
tgttttcacgcaattggaagattattgggcctctttctgaacaatgtccagctgggtccccgcc
tcacagagaagctatgtttggaattagcaaacacaaagcgcttcggaatctgtctctgagtaacag
ccagctgtccaccaccagcaatacaactttcttgggactaaagtggacaaacctcactatgctc
gatctttcccacacaaacttaaatgtgattggtaacgattcctttgtttggcttccacatctag
aatatttcttccctggagtataataatatacagcatttgctctctcactctttgcacgggctttt
caatgtgcggtacctgaatttgaaacgggtcttttactaaacaaagtatttcccttgcttcgctc
ccaagattgatgatttttcttttcgggtggctaacatgttttgagcaccttaacatggaagata
atgatatttcaggcataaaaagcaatatgttcacaggattgataaacctgaaatacttaagtct
atccaactcctttacaagtttgcaaaactttgacaaatgaaacatttgatatcacttgctcattct
cccttacacatactcaacctaaccaagaataaaaatctcaaaaatagagagtggtgccttctctt
ggttggggccacctagaagtacttgacttgggccttaatgaaattgggcaagaactcacaggcca
ggaatggagtgggtctagaaaatattttcgaaatctatctttcctacacaaagtacctgcaactg
actaagaactcctttgccttgggtccgaagccttcaacgactgatgctccgaaggggtggccctta
aaaatgtggattgctctccttcaccattccagcctcttggtaacctgaccattctggatctaag
caacaacaacatagccaacataaatgatgacatgttggaaggtcttgagaaactagaaattctg
gatttgcagcataacaacttagcacggctctggaaacacgcaaaccctgggtgggtcctgtttatt
tcctaaaggggtctgtctcacctccacatccttaacttggagtctaattggctttgacgagatccc
agttgaggtcttcaaggatttatctgaactaaagatcattgatttaggattgaataatttaaac
acacttccagcgtctgtctttgataatcaggtgtctctaaagtcattgaaccttcagaagaatc
tcataacatcagttgagaagaaggttttcgggccagctttcaggaacctgagtaacttagatat
gcgctttaatccctttgattgcacatgtgaaagtattgcctgggtttgttaattggattaacaag
accacgccaacatccctgagctgtcaagccactacctttgcaaacactccacccactatcatg
ggttcccagtgagacttttttgatacatcatcctgcaaagacagtgccccctttgaactc

SEQ ID NO: 2

Source: *Macaca fascicularis*

Description: Nucleic acid encoding a peptide chain comprising the predicted cynoTLR3 signal peptide without its amino terminal methionine residue, and the extracellular domain.

tccaccaacaaatgcactgttagccaagaagttgctgactgcagccacctgaagttaactcagg
taccgatgatctccccacaaacataacagtggttgatcttaccataatcaactcagaagatt
accagctgccaattttacaagatatagccaactaactatcttggatgtaggattttaactccatc
tcaaaactggagccagaattgtgccaaaaacttcccatgtttaaagttttgaacctccagcaca
atgagctatctcaactttctgataaaacttttgccttctgcacgaatttgacggaactccatct
catgtccaactcaatccagaaaattaaaaataatccctttgtaaagcagaagaatttaatacaca
ttagatctgtctcataatggcttgtcatctacaaaattaggaactcagggtcagctggaaaatc
tccaagagcttctattatcaaacaataaaaatccaagcgctaaaaagtgagaacttggtatcct
tgccaattcatcttttaaaaaagtttagagttgtcatcgaatcaaattaaagagttttctccaggg
tgttttcacgcaattggaagattattgggcctctttctgaacaatgtccagctgggtccccgcc
tcacagagaagctatgtttggaattagcaaacacaagcggttcggaatctgtctctgagtaacag
ccagctgtccaccaccagcaatacaactttcttgggactaaagtggacaaacctcactatgctc
gatctttcccacacaaacttaaatgtgattggtaacgattcctttgtttggcttccacatctag
aatatttcttccctggagtataataataacagcatttgctctctcactctttgcacgggctttt
caatgtgcggtacctgaatttgaaacgggtcttttactaaacaaagtatcttcccttgcttcgctc
ccaagattgatgatttttcttttcgggtggctaacaatgtttggagcaccttaacatggaagata
atgataatttcaggcataaaaagcaatatgttcacaggattgataaacctgaaatacttaagtct
atccaactcctttacaagtttgcaaaactttgacaaatgaaacatttgatcacttgctcattct
cccttacacatactcaacctaaccaagaataaaaatctcaaaaatagagagtggtgccttctctt
ggttgggccacctagaagtacttgacttgggccttaatgaaattgggcaagaactcacaggcca
ggaatggagtgggtctagaaaatatcttcgaaatctatctttcctacaacaagtacctgcaactg
actaagaactcctttgccttgggtccgaagccttcaacgactgatgctccgaaggggtggccctta
aaaatgtggattgctctccttcaccattccagcctcttggtaacctgaccattctggatctaag
caacaacaacatagccaacataaatgatgacatgttggaaggtcttgagaaactagaaattctg
gatttgcagcataacaacttagcacggctctggaaacacgcaaaccctgggtgggtcctgtttatt
tcctaaaggggtctgtctcacctccacatccttaacttggagtctaattggctttgacgagatccc
agttgaggtcttcaaggatttatctgaactaaagatcattgatttaggattgaataatttaaac
acacttccagcgtctgtctttgataatcagggtgtctctaaagtcattgaaccttcagaagaatc
tcataacatcagttgagaagaaggttttcgggccagctttcaggaacctgagtaacttagatat
gcgctttaatccctttgattgcacatgtgaaagtattgcctgggtttgttaattggattaacaag
accacgccaacatccctgagctgtcaagccactacctttgcaaacctccacccactatcatg
ggttcccagtgagactttttgatacatcatcctgcaaagacagtgccccctttgaactcttttt
catgatcaataccagtatcctgttgatttttatctttgttgacttctcatccactttgagggc
tgaggatattcttttactggaatgtttcagtagatcgagttcttgggtttcaaagaaatagaca
gacagacagaacagtttgaaatgtgcagcatatataattcacgcccataaagataaggattgggt
ctgggaacatttctcttcaatggaaaaggaagaccaatctctcaaattttgtctggaagaaagg
gactttgaggcaggtgtttttgaactggaagcaattgttaacagcatcaaaagaagcagaaaaa
ttatttttattataacacaccatctattaaaagaccattatgcaaaagattcaaggtacatca
tgccgttcaacaagctattgaacaaaatctggattccattatattgattttccttgaggagatt
ccagattataaactgaacctgcactctgtttgcgaagagggaatgtttaaatctcactgcatct
tgaactggccagttcagaaagaacggataggtgcctttcatcataaactgcaagtagcacttgg
atccaaaaactcagtacat

SEQ ID NO: 3

Source: *Macaca fascicularis*

Description: Nucleic acid encoding a peptide chain comprising the predicted mature form of the cynoTLR3 extracellular domain, the transmembrane domain, and the cytoplasmic domain.

tccaccaacaaatgcactgtagccaagaagttgctgactgcagccacctgaagttaactcagg
taccgatgatctccccacaaacataacagtgttgatcttaccataatcaactcagaagatt
accagctgccaattttacaagatatagccaactaactatcttggatgtaggatttaactccatc
tcaaaactggagccagaattgtgccccaaacttcccatgtttaaagttttgaacctccagcaca
atgagctatctcaactttctgataaaacttttgccttctgcacgaatttgacggaactccatct
catgtccaactcaatccagaaaattaaaaataatccctttgtaaagcagaagaatttaatcaca
ttagatctgtctcataatggcttgtcatctacaaaattaggaactcagggtcagctggaaaatc
tccaagagcttctattatcaaacaataaaaatccaagcgctaaaaagtgaagaacttggtatcct
tgccaattcatcttttaaaaaagtttagagttgtcatcgaatcaaattaaagagttttctccaggg
tgttttcacgcaattggaagattattgggcctctttctgaacaatgtccagctgggtccccgcc
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atccaaaaactcagtagat

SEQ ID NO: 4

Source: *Macaca fascicularis*

Description: Nucleic acid encoding a polypeptide comprising the predicted cynoTLR3 signal peptide without an amino terminal methionine residue, the extracellular domain, the transmembrane domain, and the cytoplasmic domain.

agacagactttgccttatacctacttttgggtggggacttttgccctttgggatgctgtgtgcat
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ggatccaaaaactcagtacat

SEQ ID NO: 5

Source: *Macaca fascicularis*

Description: Nucleic acid with 5' and 3' sequences flanking an open reading frame encoding a peptide chain comprising full-length cynoTLR3.

gccacacatttccctgatgaaatgtctggatttggactaaagaaaaaggaatggccagcagtc
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cacataaaaaaaaaaaaaaaaaaaaaaaaaa

SEQ ID NO: 6

Source: *Macaca fascicularis*

Description: Nucleic acid (DNA) expression vector p4078
encoding a peptide chain comprising full-length cynoTLR3.

gttgacattgattattgactagttattaatagtaatcaattacgggggtcattagttcatagccc
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SEQ ID NO: 7

Source: *Macaca fascicularis*

Description: Nucleic acid (DNA) expression vector p4037
encoding a peptide chain comprising the predicted cynoTLR3
signal sequence with an amino terminal methionine residue, and
the extracellular domain fused via a flexible glycine and serine
link to six amino terminal histidine amino acid residue tags.

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agccccccacccctcatcccccttcattgggtcgtcgtcagacagatccagggtctgaaaattcccca
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cctcaagatttgcgctcctgagcctcaagccaggcctcaaattcctcgtccccctttttgctgga
cggtagggatggggattctcgggacccctcctcttctccttcaagggtcaccagacagagatgct
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caaacatgagaattcttgaagacgaaagggcctcgtgatacgcctattttttataggttaatgtc
atgataataatgggttcttagacgtcagggtggcacttttcggggaaatgtgcgcggaaccccta
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gcttcaataatattgaaaaaggaagagtatgagtattcaacatttccgtgtcgcccttattccc
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ctgaagatcagttgggtgcacgagtggttacatcgaactggatctcaacagcggtaagatcct
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ggaggaccgaaggagctaaccgcttttttgcacacatgggggatcatgtaactcgccttgatc
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ggtgaagatcctttttgataatatcatgaccaaatacccttaacgtgagttttcgttccactga
gcgtcagacccccgtagaaaagatcaaaggatcttcttgagatcctttttttctgcgcgtaatct
gctgcttgcaacaacaaaaaaccaccgctaccagcgggtgggtttgtttgcgggatcaagagctacc
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tcctgttaccagtggctgctgccagtggcgataagtcgtgtcttaccgggttggaactcaagacg
atagttaccggataaggcgacgagcgggtcgggctgaacgggggggttcgtgcacacagcccagcttg
gagcgaacgacctacaccgaactgagatacctacagcgtgagctatgagaaagcgccacgcttc
ccgaagggagaaaggcggacaggtatccggtaagcggcaggggtcggaaacaggagagcgcacgag
ggagcttccaggggggaaacgcctgggtatctttatagtcctgtcgggtttcggccacctctgactt
gagcgtcgatttttgtgatgctcgtcaggggggaggagcctatggaaaaacgccagcaacgcgg
cctttttacgggttctggtccttttgctggccttgaagctgtccctgatggctcgtcatctacctg
cctggacagcatggcctgcaacgcgggcatcccgatgccgccggaagcgagaagaatcataatg
gggaaggccatccagcctcgcgtcgcgaacgccagcaagacgtagcccagcgcgtcggccccga
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cgaggtgccgccctgcttcatccccgtggcccggttgcctcgcgtttgctggcggtgtccccggaa
gaaatataatttgcatgtcttttagttctatgatgacacaaaccccgcccagcgtcttgtcattgg
cgaattcgaacacgcagatgcagtcggggcgggcgcggtccgaggtccacttcgcataattaagg
gacgcgtgtggcctcgaacaccgagcgaccctgcagcgacccgcttaacagcgtcaacagcgtg
ccgcagatcccggggggcaatgagatatgaaaaagcctgaactcaccgcgacgtctgtcgagaa
gtttctgatcgaaaagttcgacagcgtctccgacctgatgcagctctcggagggcgagaatct
cgtgctttcagcttcgatgtaggagggcggtggatatgtcctgcgggttaaatagctgcgccgatg
gtttctacaaagatcgttatgtttatcggcactttgcatcggccgcgtcccgattccggaagt
gcttgacattggggaattcagcgagagcctgacctattgcatctcccgcgtgcacaggggtgtc
acgttgcaagacctgcctgaaaccgaactgcccgctgttctgcagccgggtcgcggaggccatgg
atgcgatcgtgcggccgatcttagccagacgagcgggttcggcccatcggaccgcaaggaat
cgggtcaatacactacatggcgtgatttcatatgcgcgattgctgatcccatgtgtatcactgg
caaactgtgatggacgacaccgtcagtcggtccgtcgcgcaggctctcgatgagctgatgcttt
gggcccaggactgccccgaagtccggcacctcgtgcacgcggatttcgggtccaacaatgtcct
gacggacaatggccgcataacagcgggtcattgactggagcgaggcgatgttcggggattcccaa
tacgaggtcgccaacatcttcttctggaggccgtgggttggttgatggagcagcagacgcgt
acttcgagcggaggcatccggagcttgaggatcgccgcgggtccggggcgtatatgctccgc
tggtcttgaccaactctatcagagcttggttgacggcaatttcgatgatgcagcttgggcgag
ggctgatgcgacgcaatcgtccgatccggagccgggactgtcggggcgtacacaaatcgcccgca
gaagcgcggccgtctggaccgatggctgtgtagaagtactcgccgatagtggaaaccgacgcc

cagcactcgtccggatcgggagatgggggaggctaactgaaacacggaaggagacaataaccgga
 aggaacccgcgctatgacggcaataaaaagacagaataaaacgcacgggtggtgggtcgtttgt
 tcataaacgcgggggttcggtcccagggtggaactctgtcgataccccaccgagacccattgg
 ggccaataacgcccgcgttttcttcttttccccaccccccccccaagttcgggtgaaggcccag
 ggctcgcagccaacgtcggggcggcaggccctgccatagccactggccccgtgggttagggacg
 ggggtcccccatggggaatggtttatggttcgtgggggttattattttgggcgttgctggggtc
 aggtccacgactggactgagcagacagacccatgggtttttggatggcctgggcatggaccgcat
 gtactggcgcgacacgaacaccggggtctgtgggtgccaaacacccccgacccccaaaaacca
 ccgcgcggatttctggcgtgccaaagctagtcgaccaatttctcatgtttgacagcttatcatcgc
 agatccgggcaacggttggtgccattgctgcaggcgcagaactggtaggtatggaagatctatac
 attgaatcaatattggcaattagccatattagtcattgggttatatagcataaatcaatattggc
 tattggccattgcatacgttggtatctatatcataatatgtacatttatattgggtcatgtccaa
 tatgaccgcat

SEQ ID NO: 8

Source: *Macaca fascicularis*

Description: Peptide chain comprising the predicted mature form of the cynoTLR3 extracellular domain.

STNKCTVSQEVADCSHLKLTQVPDDLPTNITVLNLTHNQLRRLPAANFTRYSQLTILDVGFNSI
 SKLEPELCQKLPMLKVLNLQHNELSQLSDKTFAFCTNLTELHLMSNSIQKIKNNPFVKQKNLIT
 LDLSHNGLSSTKLGTQVQLENLQELLLSNNKIQALKSEELGILANSSSLKKLELSSNQIKEFSPG
 CFHAIGRLLGLFLNNVQLGPRLTEKLCLELANTSVRNLSLSNSQLSTTSNTTFLGLKWTNLTML
 DLSHNNLNVIIGNDSFVWLPHELYFFLEYNNIQHLLSHSLHGLFNVRYLNLKRSFTKQSI SLASL
 PKIDDFSFRWLTCLHLNMEDNDISGIKSNMFTGLINLKYLSLSNSFTSLQTLTNETFVSLAHS
 PLHILNLTKNKISKIESGAFSWLGHLEVLDLGLNEIGQELTGQEWSGLENIFEIYLSYNKYQL
 TKNSFALVRSLQRLMLRRVALKNVDCSPSPFQPLGNLTILDLSNNNIANINDDMLEGLEKLEIL
 DLQHNNLARLWKHANPGGPVYFLKGLSHLHILNLESNGFDEIPVEVFKDLSELKIIDLGLNNLN
 TLPASVFDNQVSLKSLNLQKNLITSVEKKVFGPAFRNLSNLDMRFPDCTCESIAWVFNWINK
 THANIPELSSHYLCNTPPHYHGFPVRLFDTSCKDSAPFEL

SEQ ID NO: 9

Source: *Macaca fascicularis*

Description: Peptide chain comprising the predicted cynoTLR3 signal peptide without its amino terminal methionine residue, and the extracellular domain.

RQTLPTYTFWWGLLPFGMLCASSTNKCTVSQEVADCSHLKLTQVPDDLPTNITVLNLTHNQLRR
 LPAANFTRYSQLTILDVGFNSISKLEPELCQKLPMLKVLNLQHNELSQLSDKTFAFCTNLTELH
 LMSNSIQKIKNNPFVKQKNLITLDLSHNGLSSTKLGTQVQLENLQELLLSNNKIQALKSEELGI
 LANSSSLKKLELSSNQIKEFSPGCFHAIGRLLGLFLNNVQLGPRLTEKLCLELANTSVRNLSLSN
 SQLSTTSNTTFLGLKWTNLTMLDLSHNNLNVIIGNDSFVWLPHELYFFLEYNNIQHLLSHSLHGL
 FNVRYLNLKRSFTKQSI SLASL PKIDDFSFRWLTCLHLNMEDNDISGIKSNMFTGLINLKYLS
 LSNSFTSLQTLTNETFVSLAHSPLHILNLTKNKISKIESGAFSWLGHLEVLDLGLNEIGQELTG
 QEWSGLENIFEIYLSYNKYQLTKNSFALVRSLQRLMLRRVALKNVDCSPSPFQPLGNLTILDLS
 NNNNIANINDDMLEGLEKLEILDLQHNNLARLWKHANPGGPVYFLKGLSHLHILNLESNGFDEI

PVEVFKDLSELKIIDLGLNNLNTLPASVFDNQVSLKSLNLQKNLITSVEKKVFGPAFRNLSNLD
MRFNPFDCCTCESIAWVFNWINKTHANIPELSSHLYLCNTPPHYHGFPVRLFDTSSCKDSAPFEL

SEQ ID NO: 10

Source: *Macaca fascicularis*

Description: Peptide chain comprising the predicted mature form of the cynoTLR3 extracellular domain, the transmembrane domain, and the cytoplasmic domain.

STNKCTVSQEVADCSHLKLTQVPDDLPTNITVLNLTHNQLRRLPAANFTRYSQLTILDVGFNSI
SKLEPELCQKLPMLKVLNLQHNELSQLSDKTFAFCTNLTELHLSNSIQKIKNNPFVKQKNLIT
LDLSHNGLSSTKLGTVQVQLENLQELLLSNNKIQALKSEELGILANSSSLKKLELSSNQIKEFSPG
CFHAIGRLLGLFLNNVQLGPRLTEKLCLELANTSVRNLSLSNSQLSTTSNTTFLGLKWTNLTML
DLSHNNLNVIGNDSFVWLPHLEYFFLEYNNIQHLLSHSLHGLFNVRYLNLKRSFTKQSSISLASL
PKIDDFSFRWLTCEHLNLMEDNDISGIKSNMFTGLINLKYLSLSNSFTSLQTLTNETFVSLAHS
PLHILNLTKNKISKIESGAFSWLGHLEVLDLGLNEIGQELTGQEWSGLENIFEIYLSYNKYQL
TKNSFALVRSLQRLMLRRVALKNVDCSPSPFQPLGNLTILDLSNNNIANINDDMLEGLEKLEIL
DLQHNNLARLWKHANPGGPVYFLKGLSHLHILNLESNGFDEIPVEVFKDLSELKIIDLGLNNLN
TLPASVFDNQVSLKSLNLQKNLITSVEKKVFGPAFRNLSNLD MRFNPFDCCTCESIAWVFNWINK
THANIPELSSHLYLCNTPPHYHGFPVRLFDTSSCKDSAPFELFFMINTSILLIFIFVLLIHFEG
WRISFYWNVSVHRVLGFKEIDRQTEQFEYAAYIIHAHKDKDWVWEHFSSMEKEDQSLKFCLEER
DFEAGVFELEAIVNSIKRSRKIIIFIITHLLKDPLCKRFKVHHAVQQAIEQNLD SIILIFLEEI
PDYKLNHALCLRRGMFKSHCILNWPVQKERIGAFHHKLQVALGSKNSVH

SEQ ID NO: 11

Source: *Macaca fascicularis*

Description: Peptide chain comprising the predicted cynoTLR3 signal peptide without its amino terminal methionine residue, the extracellular domain, the transmembrane domain, and the cytoplasmic domain.

RQTLPTYTFWWGLLPFGMLCASSTNKCTVSQEVADCSHLKLTQVPDDLPTNITVLNLTHNQLRR
LPAANFTRYSQLTILDVGFNSISKLEPELCQKLPMLKVLNLQHNELSQLSDKTFAFCTNLTELH
LMSNSIQKIKNNPFVKQKNLITLDLSHNGLSSTKLGTVQVQLENLQELLLSNNKIQALKSEELGI
LANSSSLKKLELSSNQIKEFSPGCFHAIGRLLGLFLNNVQLGPRLTEKLCLELANTSVRNLSLSN
SQLSTTSNTTFLGLKWTNLTMLDLSHNNLNVIGNDSFVWLPHLEYFFLEYNNIQHLLSHSLHGL
FNVRYLNLKRSFTKQSSISLASL PKIDDFSFRWLTCEHLNLMEDNDISGIKSNMFTGLINLKYLS
LSNSFTSLQTLTNETFVSLAHSPLHILNLTKNKISKIESGAFSWLGHLEVLDLGLNEIGQELTG
QEWSGLENIFEIYLSYNKYQLTKNSFALVRSLQRLMLRRVALKNVDCSPSPFQPLGNLTILD
SNNNIANINDDMLEGLEKLEILDLQHNNLARLWKHANPGGPVYFLKGLSHLHILNLESNGFDEI
PVEVFKDLSELKIIDLGLNNLNTLPASVFDNQVSLKSLNLQKNLITSVEKKVFGPAFRNLSNLD
MRFNPFDCCTCESIAWVFNWINKTHANIPELSSHLYLCNTPPHYHGFPVRLFDTSSCKDSAPFELF
FMINTSILLIFIFVLLIHFEGWRISFYWNVSVHRVLGFKEIDRQTEQFEYAAYIIHAHKDKDW
VWEHFSSMEKEDQSLKFCLEERDFEAGVFELEAIVNSIKRSRKIIIFIITHLLKDPLCKRFKVH
HAVQQAIEQNLD SIILIFLEEI PDYKLNHALCLRRGMFKSHCILNWPVQKERIGAFHHKLQVAL
GSKNSVH

SEQ ID NO: 12

Source: *Homo sapiens*

Description: Polynucleotide encoding the full-length human TLR3 peptide chain.

atgagacagactttgccttgtatctacttttgggggggccttttgcctttgggatgctgtgtg
catcctccaccaccaagtgcactgtagccatgaagttgctgactgcagccacctgaagttgac
tcaggtacccgatgatctaccacaaacataacagtgttgaaaccttaccataatcaactcaga
agattaccagccgccaacttcacaaggtatagccagctaactagcttggatgtaggatttaaca
ccatctcaaaactggagccagaattgtgccagaaacttcccatgttaaaagttttgaacctcca
gcacaatgagctatctcaactttctgataaaacctttgccttctgcacgaatttgactgaactc
catctcatgtccaactcaatccagaaaattaaaaataatccctttgtcaagcagaagaatttaa
tcacattagatctgtctcataatggcttgtcatctacaaaattaggaactcaggttcagctgga
aatctccaagagcttctattatcaaacaataaaattcaagcgtaaaaagtgaagaactggat
atctttgccaattcatcttttaaaaaaattagagttgtcatcgaatcaaattaaagagttttctc
caggggtgttttcacgcaattggaagattatttggcctctttctgaacaatgtccagctgggtcc
cagccttacagagaagctatgtttggaattagcaaacacaagcattcggaatctgtctctgagt
aacagccagctgtccaccaccagcaatacaactttcttgggactaaagtggacaaatctcacta
tgctcgatctttcctacaacaacttaaatgtgggttggtaacgattcctttgcttggcttccaca
actagaatatttcttcctagagtataataataacagcatttgttttctcactctttgcacggg
cttttcaatgtgaggtacctgaatttgaaacgggtcttttactaaacaaagtatttcccttgct
cactccccaagattgatgatttttcttttcagtggctaaaatgtttggagcaccttaacatgga
agataatgatattccaggcataaaaagcaatatgttcacaggattgataaacctgaaatactta
agtctatccaactcctttacaagtttgcgaaactttgacaaatgaaacatttgtatcacttgctc
attctcccttacacatactcaacctaaccaagaataaaatctcaaaaatagagagtgatgcttt
ctcttgggttgggccacctagaagtacttgacctgggccttaatgaaattgggcaagaactcaca
ggccaggaatggagaggtctagaaaatattttcgaaatctatctttcctacaacaagtacctgc
agctgactaggaactcctttgccttgggtcccaagccttcaacgactgatgctccgaagggtggc
ccttaaaaatgtggatagctctccttcaccattccagcctcttcgtaacttgaccattctggat
ctaagcaacaacaacatagccaacataaatgatgacatgttggaggggtcttgagaaactagaaa
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atcccagttgaggtcttcaaggattttatttgaactaaagatcatcgatttaggattgaataatt
taaacacacttccagcatctgtctttaataatcaggtgtctctaaagtcattgaaccttcagaa
gaatctcataacatccgttgagaagaaggttttcggggccagcttttcaggaacctgactgagtta
gatatgcgctttaatccctttgattgcacgtgtgaaagtattgcctgggtttgttaattggatta
acgagaccataccaacatccctgagctgtcaagccactacctttgcaacactccacctcacta
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tttttcatgatcaataccagtatcctgttgattttttatctttattgtacttctcatccactttg
agggctggaggatatctttttatttggaaatgtttcagtacatcgagttcttgggtttcaaagaaat
agacagacagacagaacagtttgaatatgcagcatatataattcatgcctataaagataaggat
tgggtctgggaacattttctcttcaatggaaaaggaagaccaatctctcaaattttgtctggaag
aaagggactttgagggcgggtgtttttgaactagaagcaattgttaacagcatcaaaagaagcag
aaaaattatttttgttataacacaccatctattaaaagacccattatgcaaaagattcaaggta
catcatgcagttcaacaagctattgaacaaaatctggattccattatattgggttttccttgagg
agattccagattataaactgaacctgcactctgtttgcgaagaggaatgttttaaattctcactg
catcttgaactggccagttcagaaagaacggataggtgcctttcgtcataaattgcaagtagca
cttggatccaaaaactctgtacat

SEQ ID NO: 13

Source: *Homo sapiens*

Description: Peptide chain comprising full-length human TLR3 peptide chain.

MRQTLPCIYFWGGLLPFGMLCASSTTKCTVSHEVADCSHLKLTQVPDDLPTNITVLNLTHNQLR
RLPAANFTRYSQLTSLDVGFNTISKLEPELCQKLPMLKVLNLQHNELSQLSDKTFAFCTNLTEL
HLMSNSIQKIKNNPFVKQKNLITLDLSHNGLSSTKLGTQVQLENLQELLSNNKIQALKSEELD
IFANSSLKKLELSSNQIKEFSPGCFHAIGRLFGLFLNNVQLGPSLTEKLCLELANTSIRNLSLS
NSQLSTTSNTTFLGLKWTNLTMLDLSYNNLNVVGNDFAWLPQLEYFFLEYNNIQHLFSLSLHG
LFNVRYLNLKRSFTKQSI SLASLPKIDDFSQWLKCLEHLNMEDNDIPGIKSNMFTGLINLKYL
SLSNSFTSLRTLNETFVSLAHSPLHILNLTKNKISKIESDAFSWLGHLVLDLGLNEIGQELT
GQEWRGLENIFEIYLSYNKYQLLTRNSFALVPSLQRLMLRRVALKNVDSSPSPFQPLRNLTILD
LSNNNIANINDDMLEGLEKLEILDQLQHNNLARLWKHANPGGPFIYFLKGLSHLHILNLESNGFDE
IPVEVFKDLFELKIIDLGLNNLNTLPASVFNNQVSLKSLNLQKNLITSVEKKVFGPAFRNLTEL
DMRFNPFDCCTCESIAWFVNWINETHTNIPELSSHLYLCNTPPHYHGFPVRLFDTSSCKDSAPFEL
FFMINTSILLIFIFIVLLIHFEGWRISFYWNVSVHRVLGFKEIDRQTEQFEYAAYIIHAYKDKD
WVWEHFSSMEKEDQSLKFCLEERDFEAGVFELEAIVNSIKRSRKIIFVITHHLLKDPLCKRFKV
HHAQQQAIEQNLD SIILVFLEEIPDYKLNHALCLRRGMFKSHCILNWPVQKERIGAFRHKLQVA
LGSKNSVH

SEQ ID NO: 14

Source: Artificial

Description: Chemically synthesized polynucleotide primer for PCR amplification of polynucleotides encoding cynoTLR3 peptide chains.

cccaagcttgccaccatgagacagactttgccttgtatctac

SEQ ID NO: 15

Source: Artificial

Description: Chemically synthesized polynucleotide primer for PCR amplification of polynucleotides encoding cynoTLR3 peptide chains.

cccctcgagttaatgtacagagtttttggatccaagtgct

SEQ ID NO: 16

Source: Artificial

Description: Chemically synthesized polynucleotide primer for PCR amplification of polynucleotides encoding cynoTLR3 peptide chains.

catggatccttcaaagggggcactgtctttgc

SEQ ID NO: 17

Source: Artificial

Description: Chemically synthesized polynucleotide primer for PCR amplification of polynucleotides encoding cynoTLR3 peptide chains.

cactgttatgtttgtggggagatcatcgg

SEQ ID NO: 18

Source: Artificial

Description: Chemically synthesized polynucleotide primer for PCR amplification of polynucleotides encoding cynoTLR3 peptide chains.

atcctacatccaagatagtttagttggctat

SEQ ID NO: 19

Source: Artificial

Description: Chemically synthesized polynucleotide primer for PCR amplification of polynucleotides encoding cynoTLR3 peptide chains.

caaggtacatcatgccgttcaac

SEQ ID NO: 20

Source: *Macaca fascicularis*

Description: Peptide chain comprising the full-length cynoTLR3 peptide chain. This peptide chain comprises the predicted cynoTLR3 signal peptide with its amino terminal methionine residue, the extracellular domain, the transmembrane domain, and the cytoplasmic domain.

MRQTLPTYFYFWGLLPFGMLCASSTNKCTVSQEVADCSHLKLTQVPDDLPTNITVLNLTHNQLR
RLPAANFTRYSQLTILDVGFNSISKLEPELCQKLPMLKVLNLQHNELSQLSDKTFAFCTNLTEL
HLMSNSIQKIKNNPFVKQKNLITLDLSHNGLSSTKLGTQVQLENLQELLSNNKIQALKSEELG
ILANSSLKKLELSSNQIKEFSPGCFHAIGRLLGLFLNNVQLGPRLTEKLCLELANTSVRNLSLS
NSQLSTTSNTTFLGLKWTNLTMLDLSHNNLNINIGNDSFVWLPHLEYFFLEYNNIQHLLSHSLHG
LFNVRYLNLKRSFTKQSIISLASLPKIDDFSFRWLTCLHLNMEDNDISGIKSNMFTGLINLKYL
SLSNSFTSLQTLTNETFVSLAHSPLHILNLTKNKISKIESGAFSWLGHLEVLDLGLNEIGQELT
GQEWSGLENIFEIYLSYNKYLQLTKNSFALVRSLQRLMLRRVALKNVDCSPSPFQPLGNLTILD
LSNNNIANINDDMLEGLEKLEILDQLHNNLARLWKHANPGGPVYFLKGLSHLHILNLESNGFDE
IPVEVFKDLSELKIIDLGLNNLNTLPASVFDNQVSLKSLNLQKNLITSVEKKVFGPAFRNLSNL
DMRFNPFDCCTCESIAWFVNWINKTHANIPELSSHLYCNTPPHYHGFPVRLFDTSSCKDSAPFEL
FFMINTSILLIFIFVLLIHFEGWRISFYWNVSVHRVLGFKEIDRQTEQFEYAAYIIHAHKDKD
WVWEHFSSMEKEDQSLKFCLEERDFEAGVFELEAIVNSIKRSRKIIFIITHHLLKDPLCKRFKV
HHAVQQAIEQNLDISIILIFLEEIPDYKLNHALCLRRGMFKSHCILNWPVQKERIGAFHHKLQVA
LGSKNVH

SEQ ID NO: 21

Source: *Macaca fascicularis*

Description: Polynucleotide encoding a peptide chain comprising the full-length cynoTLR3 peptide chain. This peptide chain comprises the predicted cynoTLR3 signal peptide with its amino terminal methionine residue, the extracellular domain, the transmembrane domain, the cytoplasmic domain. The stop codon is also included in the polynucleotide sequence.

atgagacagactttgccttatacctacttttgggtggggacttttgccttttgggatgctgtgtg
catcctccaccaacaaatgcactgtagccaagaagttgctgactgcagccacctgaagttaac
tcaggtacccgatgatctccccacaaacataacagtgttgaaatcttaccataatcaactcaga
agattaccagctgccaattttacaagatatagccaactaactatcttggatgtaggatttaact
ccatctcaaaactggagccagaattgtgccaaaaacttcccatgtttaaagttttgaacctcca
gcacaatgagctatctcaactttctgataaaaacttttgccttctgcacgaatttgacggaactc
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tgggtctgggaacatttctcttcaatggaaaaggaagaccaatctctcaaattttgtctggaag
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catcatgccgttcaacaagctattgaacaaaatctggattccattatattgattttccttgagg
agattccagattataaactgaacctgcactctgtttgcgaagaggaatgttttaaactctcactg

catcttgaactggccagttcagaaagaacggataggtgcctttcatcataaactgcaagtagca
cttggatccaaaaactcagtacattaa

SEQ ID NO: 22

Source: *Macaca mulatta*

Description: Polynucleotide encoding the full-length rhesus monkey TLR3 peptide chain.

atgagacagactttgccttatacctacttttgggtggggacttttgcctttgggatgctgtgtg
catcctccaccaacaaatgcactgtagccaagaagttgctgactgcagccacctgaagttaac
tcaggtacccgatgatctccccacaaacataacagtgttgaaatcttaccataatcaactcaga
agattaccagctgccaatttttacaagatatagccaactaactatcttggatgtaggatttaact
ccatctcaaaaccggagccagaattgtgccaaaaacttcccatgtttaaagttttgaacctcca
gcacaatgagctatctcaactttccgataaaaacttttgccttctgcatgaatttgacggaactc
cattccctgtcccactcaatccagaaaaattaaaaataatccctttgtcaagcagaagaatttaa
tcacattagatctgtctcataatggccttgctcatctataaaaattaggaactcaggttcagatgga
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gatatgcgctttaatccctttgattgcacatgtgaaagtattgcctgggtttgttaattggatta
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catcatgccgttcaacaagctattgaacaaaatctggattccattatattgattttccttgagg
agattccagattataaactgaacctgcactctgtttgcgaagaggaatgtttaaatctcactg

catcttgaactggccagttcagaaagaacggataggtgcctttcatcataaactgcaagtagca
cttggatccaaaaactcagtacat

SEQ ID NO: 23

Source: *Macaca mulatta*

Description: Peptide chain comprising full-length rhesus monkey
TLR3 peptide chain.

MRQTLPTYFYFWWGLLPFGMLCASSTNKCTVSQEVADCSHLKLTQVPDDLPTNITVLNLTHNQLR
RLPAANFTRYSQLTILDVGFNSISKPEPELCQKLPMKVLNLQHNELSQLSDKTFAFCMNLTEL
HSLSHSIQKIKNNPFVKQKNLITLDLSHNGLSSIKLGTQVQMENLQELLSNNKIQALKSEELG
ILANSSLKKLELSSNQIKEFSPGCFHAIGRSLGLFLNNVQLGPRLTEKLCLELANTSVRNLSLS
NSQLSTTSNTTFLGLKWTNLTMLDLSHNNLNVVGNDSEAWLPQLEYFFLEYNNIQHLLSHSLHG
LFNVRYLNLKRSFTKQSIISLASLPKIDDFSFRWLTCLHLNMEDNDISGIKSNMFTGLINLKYL
SLSNSFTSLQTLTNETFVSLAHSPLHILNLTKNKISKIESGAFSWLGHLEVLDLGLNEIGQELT
GQEWSGLENIFEIYLSYNKYLQLTKNSFALVRSLQRLMLRRVALKNVDCSPSPFQPLGNLTILD
LSNNNIANINDDMLEGLEKLEILDQLHNNLARLWKHANPGGPVYFLKGLSHLHILNLESNGFDE
IPVEVFKDLSELKIIDLGLNNLNTLPASVFDNQVSLKSLNLQKNLITSVEKKVFGPAFRNLSNL
DMRFNPFDCCTCESIAWFVNWISKTHANIPELSSHLYCNTPPHYHGFVRLFDTSSCKDSAPFEL
FFIINTSILLICIFVLLIHFEQWRISFYWNVSVHRVLGFKEIDRQTEQFEYAAYIIHAHKDKD
WVWEHFSSMEKEDQSLKFCLEERDFEAGVFELEAIVNSIKRSRKIIIFIITHHLLKDPLCKRFKV
HHAVQQAIEQNLDSEIILIFLEEIPDYKLNHALCLRRGMFKSHCILNWPVQKERIGAFHHKLQVA
LGSKNVSVH

Claims

1. An isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 1.

2. An isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 2.

3. An isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 3.

4. An isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 4.

5. An isolated polynucleotide comprising a polynucleotide having the sequence shown in SEQ ID NO: 5.

6. A vector comprising an isolated polynucleotide having a sequence selected from the group consisting of a sequence shown in SEQ ID NO: 1, 2, 3, 4, 5, 6, and 7.

7. The vector of claim 6 that is an expression vector.

8. An isolated host cell comprising the vector of claim 6.

9. An isolated host cell comprising the vector of claim 7.

10. An isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 8.

11. An isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 9.

12. An isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 10.

13. An isolated peptide chain comprising a peptide chain having the sequence shown in SEQ ID NO: 11.

14. A method for expressing a peptide chain comprising the steps of:

a) providing a host cell of claim 9;

b) culturing the host cell under conditions sufficient for the expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11; and

c) confirming expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11.

15. A method for expressing a peptide chain comprising the steps of:

a) providing a polynucleotide having a sequence shown in SEQ ID NO: 1, 2, 3, 4, 5, 6, or 7 capable of being transcribed into an RNA coding for at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11;

b) providing the components of a cell free expression system;

c) initiating cell free expression from the polynucleotide provided; and

d) confirming expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11.

16. The method of claim 15 wherein the cell free expression system is selected from the group consisting of a reticulocyte lystate based expression system, a wheat germ extract based expression system, and an *Escherichia coli* extract based expression system.

17. A method for expressing a peptide chain comprising the steps of:

a) providing an RNA coding for at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11;

b) providing the components of a cell free expression system;

c) initiating cell free expression from the RNA provided; and

d) confirming expression of at least one peptide chain comprising the sequence shown in SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11.

18. The method of claim 17 wherein the cell free expression system is selected from the group consisting of a reticulocyte lystate based expression system, a wheat germ extract based expression system, and an *Escherichia coli* extract based expression system.

19. A peptide chain produced by the method of claim 14.

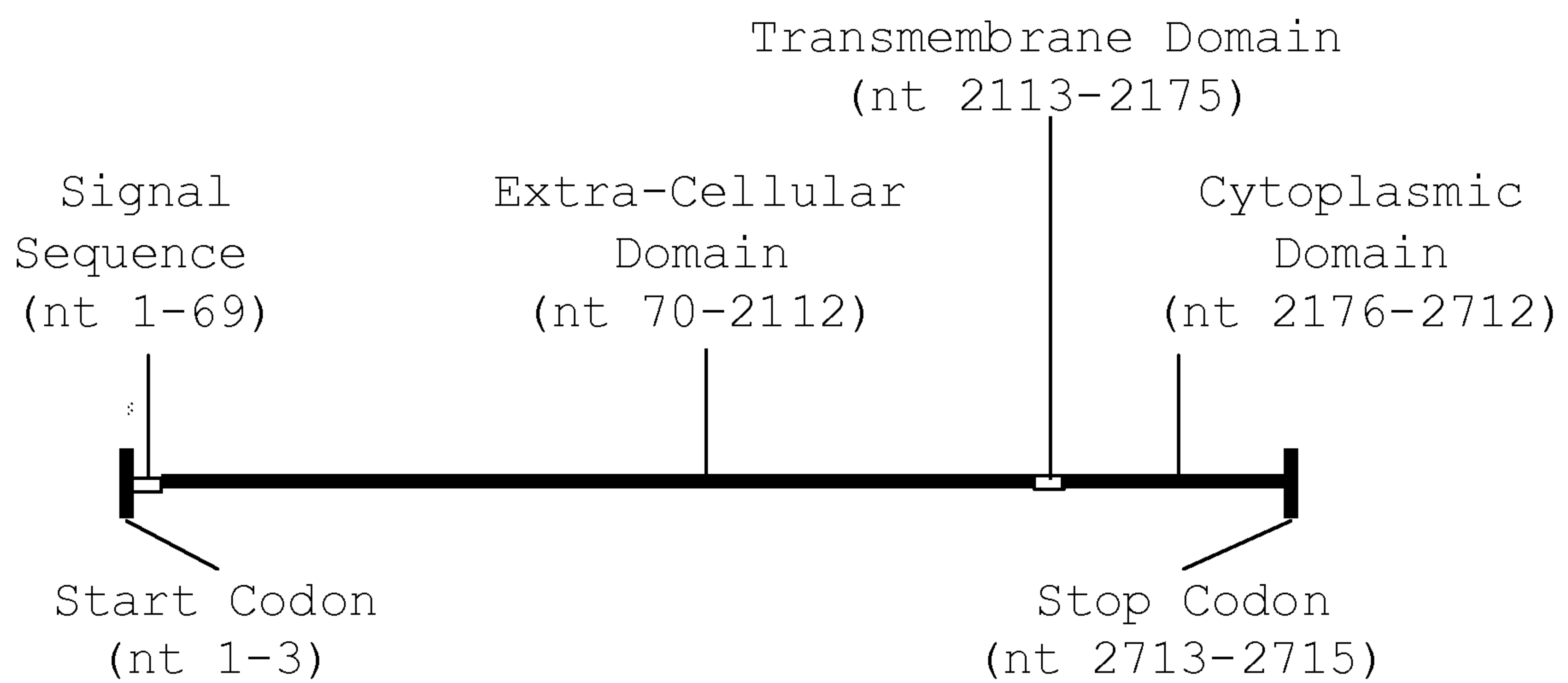
20. A peptide chain produced by the method of claim 15.

21. A peptide chain produced by the method of claim 17.

22. Use of an isolated peptide chain of any one of claims 10 to 13 for assessing the safety of a TLR3 therapeutic.

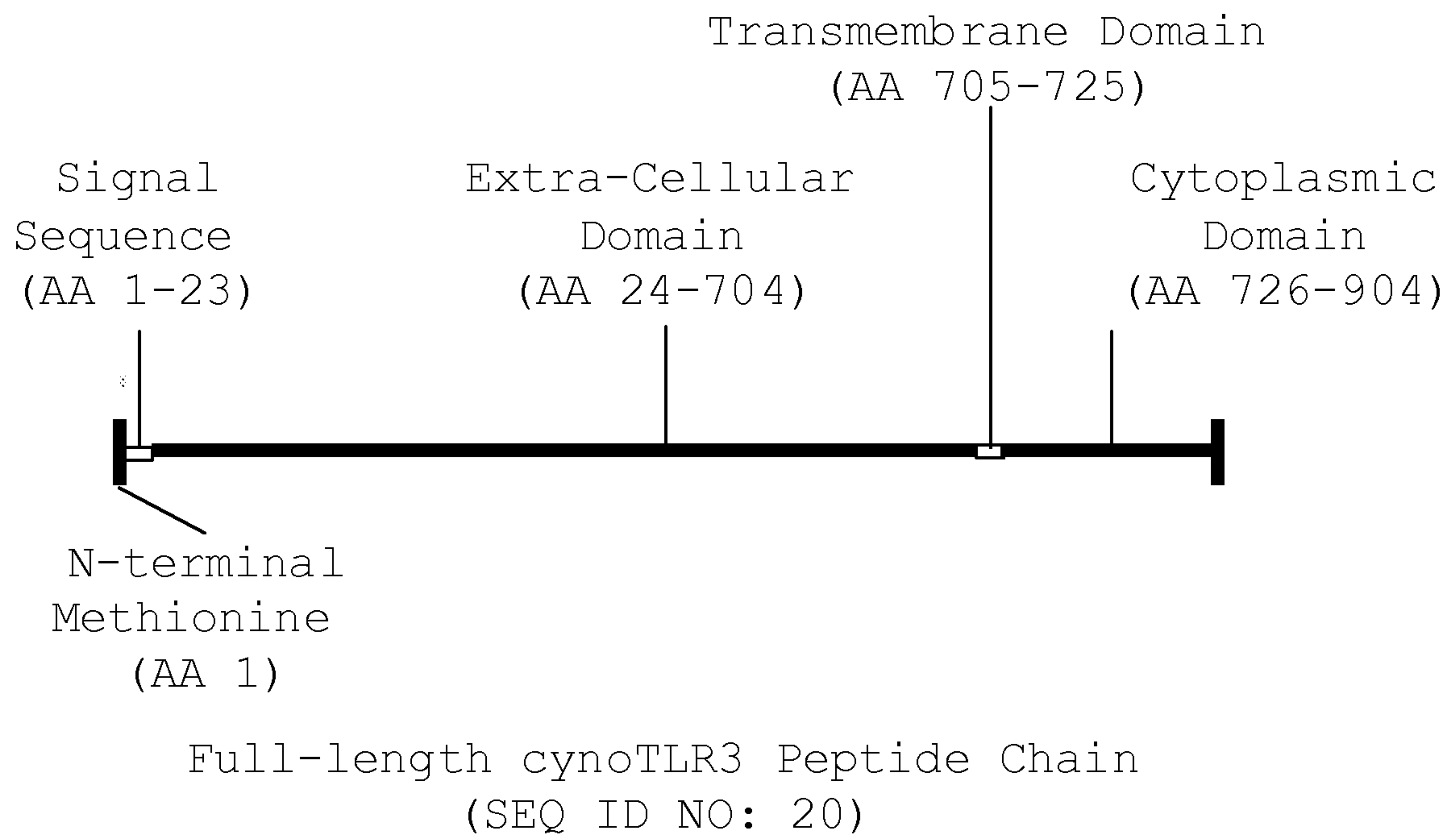
23. The use of claim 22 wherein the TLR3 therapeutic is an antibody.

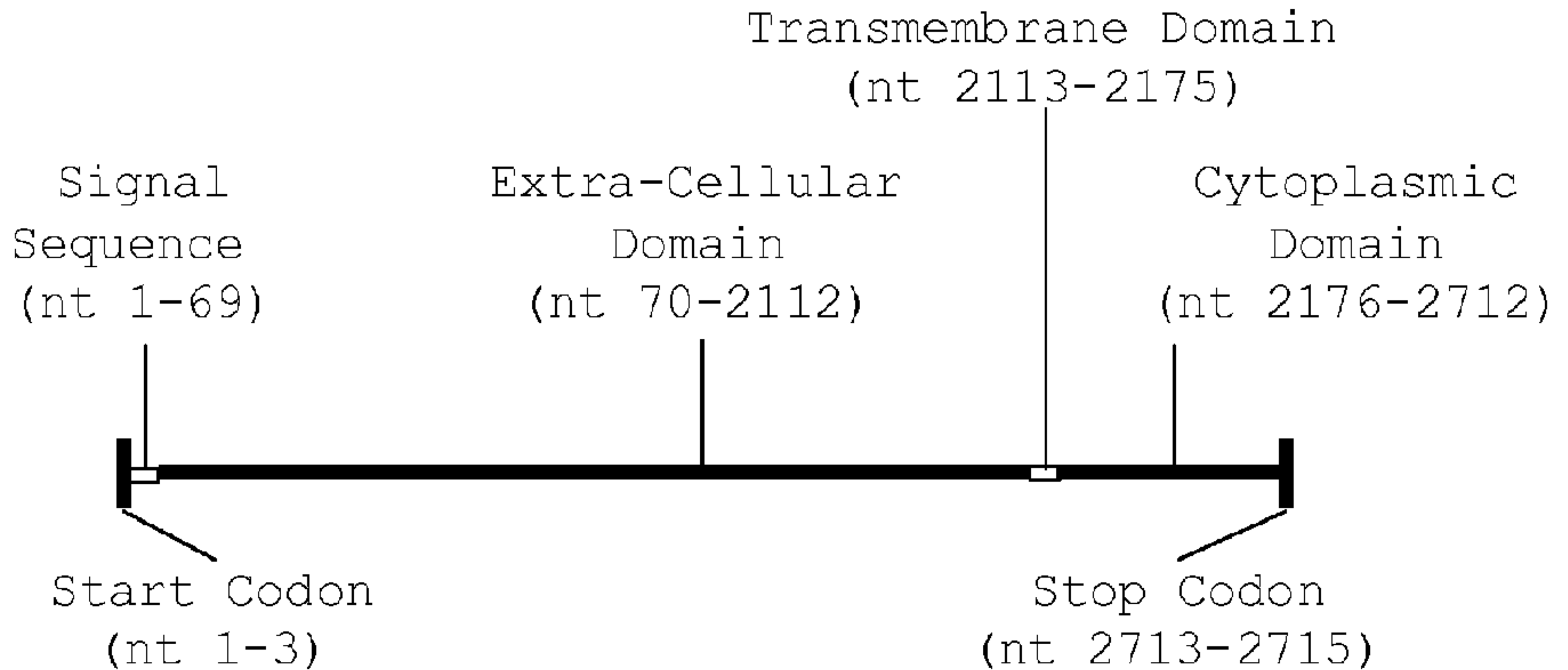
Fig. 1



Polynucleotide (SEQ ID NO: 21) Encoding
Full-length cynoTLR3 Peptide Chain

Fig. 2





Polynucleotide (SEQ ID NO: 21) Encoding
Full-length cynoTLR3 Peptide Chain