

Antibody drugs, especially monoclonal antibodies, have achieved good efficacy in the treatment of various diseases. Preparing safe and effective anti-NGF monoclonal antibodies can provide a new class of analgesic drugs in the treatment of chronic pain and cancer pain different from opiates, non-steroids, *etc.* that are addictive or cause side effects in digestive tract. Currently, Tanezumab, developed by Pfizer Pharmaceuticals Co., Ltd., has shown good analgesic effects in preclinical and clinical studies. However, there is still a lack of other anti-NGF antibodies with higher activity.

SUMMARY

The object of the present disclosure is to overcome the defects of low activity and species differences of antibodies against nerve growth factor in the prior art, and to provide a monoclonal antibody against nerve growth factor with high activity and eliminating species difference, and an encoding gene and use thereof, as well as use thereof in preparing detection kits and various drugs.

In order to achieve the above object of the disclosure, the present disclosure provides a monoclonal antibody that can specifically bind to human nerve growth factor, comprising heavy chains and light chains, the heavy chain comprises a heavy chain constant region and a heavy chain variable region, and the light chain comprises a light chain constant region and a light chain variable region.

In one aspect, the present disclosure refers to a monoclonal antibody against nerve growth factor, comprising heavy chains comprising a heavy chain constant region and a heavy chain variable region, and light chains comprising a light chain constant region and a light chain variable region, wherein the heavy chain variable region comprises three complementarity determining regions HCDR1, HCDR2 and HCDR3, and the light chain variable region comprises three complementarity determining regions LCDR1, LCDR2 and LCDR3; the amino acid sequence of the complementarity determining region HCDR1 is set forth in SEQ ID NO: 5;

the amino acid sequence of the complementarity determining region HCDR2 is set forth in SEQ ID NO: 6;

the amino acid sequence of the complementarity determining region HCDR3 is set forth in SEQ ID NO: 7;

the amino acid sequence of the complementarity determining region LCDR1 is set forth in SEQ ID NO: 8;

the amino acid sequence of the complementarity determining region LCDR2 is set forth in SEQ ID NO: 9; and

the amino acid sequence of the complementarity determining region LCDR3 is set forth in SEQ ID NO: 10.

The variable regions of the light chain and heavy chain determine the binding of the antigen; the variable region of each chain contains three hypervariable regions, called complementarity determining regions (CDRs) (the CDRs of the heavy chain (H) include HCDR1, HCDR2, HCDR3, and the CDRs of the light chain (L) include LCDR1, LCDR2, LCDR3; which were named by Kabat et al., see *Sequences of Proteins of Immunological Interest*, Fifth Edition (1991), Volumes 1-3, NIH Publication 91-3242, Bethesda Md).

In the present disclosure, the heavy chain variable region comprises three complementarity determining regions HCDR1, HCDR2 and HCDR3, and the light

chain variable region comprises three complementarity determining regions LCDR1, LCDR2 and LCDR3;
wherein the amino acid sequence of the complementarity determining region HCDR1 is set forth in SEQ ID NO: 5;
the amino acid sequence of the complementarity determining region HCDR2 is set forth in SEQ ID NO: 6;
the amino acid sequence of the complementarity determining region HCDR3 is set forth in SEQ ID NO: 7;
the amino acid sequence of the complementarity determining region LCDR1 is set forth in SEQ ID NO: 8;
the amino acid sequence of the complementarity determining region LCDR2 is set forth in SEQ ID NO: 9; and
the amino acid sequence of the complementarity determining region LCDR3 is set forth in SEQ ID NO: 10.

In the present disclosure, the amino acid sequences of 6 CDR regions are constructed, and specific modifications are made to improve the antigen-binding activity of antibody variable regions. To accommodate the changes in the CDR regions, the framework regions are also modified. However, it is necessary to ensure that the modifications of these framework regions are still compatible with human germline sequences. Framework modifications will also be analyzed to ensure that these changes have no effect on the binding of the CDR regions to antigens.

Through the technical means known to those skilled in the art, for example, through the website of the National Center for Biotechnology Information (NCBI), the complementarity determining regions (CDRs) of the heavy chain variable region and light chain variable region of the monoclonal antibody are analyzed, which are set forth in the above SEQ ID NOs: 5-7 and SEQ ID NOs: 8-10, respectively. In the present disclosure, this monoclonal antibody is named as H26L17.

As a preferred technical scheme of the monoclonal antibody against nerve growth factor of the present disclosure, the amino acid sequence of the heavy chain variable

region is set forth in SEQ ID NO: 2; the amino acid sequence of the light chain variable region is set forth in SEQ ID NO: 4.

As a further preferred technical scheme of the monoclonal antibody against nerve growth factor of the present disclosure, the nucleotide sequence encoding the heavy chain variable region is set forth in SEQ ID NO: 1; the nucleotide sequence encoding the light chain variable region is set forth in SEQ ID NO: 3.

In one example of the monoclonal antibody against nerve growth factor of the present disclosure, the monoclonal antibody against nerve growth factor is selected from a Fab, a Fab', an F(ab')₂, an Fd, an Fv, a dAb, a complementarity determining region fragment, a single chain antibody (*e.g.*, scFv), a humanized antibody, a chimeric antibody, and a diabody.

In one example of the monoclonal antibody against nerve growth factor of the present disclosure, the monoclonal antibody against nerve growth factor binds to NGF protein with an EC₅₀ of less than 100 nM (*e.g.*, less than about 10 nM, 1 nM, 0.9 nM, 0.8 nM, 0.7 nM, 0.6 nM, 0.5 nM, 0.4 nM, 0.3 nM, 0.2 nM, 0.1 nM, or less). Wherein, EC₅₀ can be measured by ELISA sandwich method.

In one example of the monoclonal antibody against nerve growth factor of the present disclosure, the monoclonal antibody against nerve growth factor comprises a non-CDR region, and the non-CDR region is from a species other than murine, for example, from a human antibody.

In order to achieve the above object of the disclosure, the present disclosure also provides a gene encoding the above monoclonal antibody against nerve growth factor.

In another aspect, the present disclosure refers to a nucleotide sequence encoding the monoclonal antibody against nerve growth factor as disclosed herein.

In order to achieve the above object of the disclosure, the present disclosure also provides a vector comprising the nucleotide sequence of the heavy chain variable region and/or the nucleotide sequence of the light chain variable region.

In another aspect, the present disclosure refers to a vector, comprising the nucleotide sequence as disclosed herein.

In order to achieve the above object of the disclosure, the present disclosure also provides a host cell comprising the nucleotide sequence of the heavy chain variable region and/or the nucleotide sequence of the light chain variable region;

or

a vector comprising the nucleotide sequence of the heavy chain variable region and/or the nucleotide sequence of the light chain variable region.

In another aspect, the present disclosure refers to a host cell, comprising the nucleotide sequence as disclosed herein.

In order to achieve the above object of the disclosure, the present disclosure also provides a method for preparing the monoclonal antibody against nerve growth factor, which includes culturing the host cell of the present disclosure under suitable conditions, and isolating the monoclonal antibody against nerve growth factor from the cell culture.

In another aspect, the present disclosure refers to a monoclonal antibody conjugate, comprising the monoclonal antibody against nerve growth factor as disclosed herein and a conjugated portion conjugated thereto, wherein the conjugated portion is a detectable label. Preferably, the conjugated portion is a radioisotope, a luminescent substance, a colored substance or an enzyme.

In another aspect, the present disclosure refers to a kit, comprising the monoclonal antibody against nerve growth factor as disclosed herein and/or the monoclonal antibody conjugate as disclosed herein.

As a preferred technical scheme of the kit of the present disclosure, the kit further comprises a secondary antibody which specifically recognizes the monoclonal antibody against nerve growth factor; in addition, the secondary antibody further comprises a detectable label, such as a radioisotope, a luminescent substance, a colored substance, or an enzyme.

The present disclosure also provides use of the monoclonal antibody against nerve growth factor and/or the monoclonal antibody conjugate in the kit that can detect the presence and/or level of nerve growth factor. The kit is used to detect the presence or level of NGF in a sample.

In another aspect, the present disclosure refers to use of the monoclonal antibody against nerve growth factor as disclosed herein and/or the monoclonal antibody conjugate as disclosed herein in preparing a kit for detecting the presence and/or level of nerve growth factor.

The present disclosure also provides a drug comprising the monoclonal antibody against nerve growth factor and/or the monoclonal antibody conjugate; optionally, it further comprises pharmaceutically acceptable carriers and/or excipients.

In another aspect, the present disclosure refers to a drug, comprising the monoclonal antibody against nerve growth factor as disclosed herein and/or the monoclonal antibody conjugate as disclosed herein as an active ingredient, and a pharmaceutically acceptable carrier or excipient.

The above drug specifically binds to nerve growth factor and can be used to inhibit nerve growth factor-mediated biological effects, such as the proliferation of TF-1 cells;

and/or

to treat or prevent neuropathic pain, chronic pain, and inflammatory pain.

In another aspect, the present disclosure refers to use of the monoclonal antibody against nerve growth factor as disclosed herein and/or the monoclonal antibody conjugate as disclosed herein in the manufacture of a medicament for:

specifically binding to nerve growth factor;

inhibiting the proliferation of nerve growth factor-dependent TF-1 cells;

and/or

treating or preventing at least one of neuropathic pain, chronic pain, and inflammatory pain.

The present disclosure, through *in vivo* experiments, has found that the monoclonal antibody against nerve growth factor of the present disclosure can improve the change of walking behavior of the affected limb and the condition of weight loss of the animal in the knee arthritis pain model of Lenti-IL-1 β -NIH/3T3 mice.

In the present disclosure, unless otherwise defined, the scientific and technical terms used herein have the meanings generally understood by those skilled in the art. In addition, the laboratory operations of cell culture, molecular genetics, nucleic acid chemistry and immunology used in the present disclosure are the routine operations widely used in the corresponding fields. Meanwhile, in order to better understand the present disclosure, the definitions and explanations of the relevant terms are provided below.

As used in the present disclosure, the term "antibody" refers to an immunoglobulin molecule that generally consists of two pairs of polypeptide chains (each pair with one "light" (L) chain and one "heavy" (H) chain). Antibody light chains are classified as κ and λ light chains. Heavy chains are classified as μ , δ , γ , α , or ϵ . And isotypes of antibodies are defined as IgM, IgD, IgG, IgA, and IgE, respectively. In light chains and heavy chains, the variable region and constant region are linked by a "J" region of about 12 or more amino acids, and the heavy chain also comprises a "D" region of about 3 or more amino acids. Each heavy chain consists of a heavy chain variable region (V_H) and a heavy chain constant region (C_H). The heavy chain constant region consists of three domains (C_{H1} , C_{H2} and C_{H3}). Each light chain consists of a light chain variable region (V_L) and a light chain constant region (C_L). The light chain constant region consists of one domain C_L . The constant region of the antibody can mediate the binding of immunoglobulins to host tissues or factors, including the

binding of various cells (*e.g.*, effector cells) of the immune system and the first component (C1q) of classical complement system. The V_H and V_L regions can be further subdivided into highly variable regions (called complementarity determining regions (CDRs)), and between which conservative regions called framework regions (FRs) are distributed. Each V_H and V_L consists of 3 CDRs and 4 FRs arranged from amino terminal to carboxyl terminal in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions (V_H and V_L) of each heavy chain/light chain pair form antibody binding sites, respectively. The assignment of amino acids to each region or domain follows the definition of Kabat *Sequences of Proteins of Immunological Interest* (National Institutes of Health, Bethesda, Md. (1987 and 1991)), or Chothia & Lesk (1987) *J. Mol. Biol.* 196:901-917; Chothia *et al.* (1989) *Nature* 342:878-883. The term "antibody" is not limited by any specific method for producing antibody. For example, the antibody includes, in particular, a recombinant antibody, a monoclonal antibody and a polyclonal antibody. Antibodies can be different isotypes of antibodies, such as antibodies IgG (*e.g.*, subtype IgG1, IgG2, IgG3 or IgG4), IgA1, IgA2, IgD, IgE or IgM.

As used in the present disclosure, the term "antigen binding fragment" of an antibody refers to the polypeptide comprising the fragment of a full-length antibody, which maintains the ability to specifically bind to the same antigen to which the full-length antibody binds, and/or competing with the full-length antibody for the specific binding to antigen, which is also known as the "antigen binding portion". See generally, *Fundamental Immunology*, Ch. 7 (Paul, W., ed., 2nd edition, Raven Press, N.Y. (1989), which is incorporated herein by reference in its entirety for all purposes. Antigen binding fragments of the antibody can be produced by recombinant DNA technology or by enzymatic or chemical cleavage of intact antibodies. In some cases, the antigen binding fragment includes a Fab, a Fab', an F(ab')₂, an Fd, an Fv, a dAb, a complementarity determining region (CDR) fragment, a single chain antibody fragment (*e.g.*, scFv), a chimeric antibody, a diabody and a polypeptide comprising at

least a portion of the antibody sufficient to impart specific antigen binding ability to a polypeptide.

As used in the present disclosure, the term "Fd fragment" refers to an antibody fragment consisting of V_H and C_{H1} domains; the term "Fv fragment" refers to an antibody fragment consisting of the V_L and V_H domains of a single arm of an antibody; the term "dAb fragment" refers to an antibody fragment consisting of a V_H domain (Ward *et al.*, *Nature* 341:544-546 (1989)); the term "Fab fragment" refers to an antibody fragment consisting of V_L, V_H, C_L, and C_{H1} domains; and the term "F(ab')₂ fragment" refers to an antibody fragment comprising two Fab fragments linked by the disulfide bridge on a hinge region.

In some cases, the antigen binding fragment of the antibody is a single chain antibody (*e.g.*, scFv) in which the V_L and V_H domains are paired to form a monovalent molecule via a linker that enables them to produce a single polypeptide chain (see, *e.g.*, Bird *et al.*, *Science* 242:423-426 (1988) and Huston *et al.*, *Proc. Natl. Acad. Sci. USA* 85:5879-5883 (1988)). Such scFv molecules have a general structure:

NH₂-V_L-linker-V_H-COOH or NH₂-V_H-linker-V_L-COOH. An appropriate prior art linker consists of a repeating GGGGS amino acid sequence or a variant thereof. For example, a linker having the amino acid sequence (GGGGS)₄ can be used, but variants thereof can also be used (Holliger *et al.* (1993), *Proc. Natl. Acad. Sci. USA* 90: 6444-6448). Other linkers that can be used in the present disclosure are described by Alfthan *et al.* (1995), *Protein Eng.* 8:725-731, Choi *et al.* (2001), *Eur. J. Immunol.* 31: 94-106, Hu *et al.* (1996), *Cancer Res.* 56:3055-3061, Kipriyanov *et al.* (1999), *J. Mol. Biol.* 293:41-56 and Roovers *et al.* (2001), *Cancer Immunol.*

In some cases, the antigen binding fragment of the antibody is a diabody, that is, a bivalent antibody, in which the V_H and V_L domains are expressed on a single polypeptide chain. However, the linker used is too short to allow the pairing of the two domains on one chain, thereby the domains are forced to pair with the complementary domains on another chain and two antigen binding sites are generated

(see, *e.g.*, Holliger P. *et al.*, *Proc. Natl. Acad. Sci. USA* 90:6444-6448 (1993), and Poljak R. J. *et al.*, *Structure* 2: 1121-1123 (1994)).

Antigen binding fragments of antibodies can be obtained from given antibodies by using conventional techniques known to those skilled in the art (*e.g.*, recombinant DNA technology or enzymatic or chemical cleavage), and the antigen binding fragments of the antibodies are screened for specificity in the same way as for intact antibodies.

In the present disclosure, unless otherwise clearly defined in the context, when referring to the term "antibody", it includes not only intact antibodies but also antigen binding fragments of antibodies.

As used in the present disclosure, the terms "McAb" and "monoclonal antibody" refer to an antibody or a fragment of an antibody that is derived from a group of highly homologous antibodies, *i.e.*, from a group of identical antibody molecules, except for natural mutations that may occur spontaneously. The monoclonal antibody has a high specificity for a single epitope on an antigen. The polyclonal antibody, relative to the monoclonal antibody, generally comprises at least two or more different antibodies which generally recognize different epitopes on an antigen. Monoclonal antibodies can generally be obtained by hybridoma technology first reported by Kohler *et al.* (*Nature*, 256:495, 1975), but can also be obtained by recombinant DNA technology (for example, see U.S.P 4,816,567).

As used in the present disclosure, the term "humanized antibody" refers to an antibody or antibody fragment obtained when all or a part of CDR regions of a human immunoglobulin (receptor antibody) are replaced by the CDR regions of a non-human antibody (donor antibody), wherein the donor antibody may be a non-human (*e.g.*, mouse, rat or rabbit) antibody having expected specificity, affinity or reactivity. In addition, some amino acid residues in the framework regions (FRs) of the receptor antibody can also be replaced by the amino acid residues of corresponding non-human antibodies or by the amino acid residues of other antibodies to further improve or optimize the performance of the antibody. For more

details on humanized antibodies, see, for example, Jones *et al.*, Nature, 321:522 525 (1986); Reichmann *et al.*, Nature, 332:323 329 (1988); Presta, Curr. Op Struct. Biol., 2:593 596 (1992); and Clark, Immunol. Today 21: 397 402 (2000).

As used in the present disclosure, the term "epitope" refers to a site on the antigen that an immunoglobulin or antibody specifically binds to. "Epitope" is also called in the art as an "antigenic determinant". The epitope or antigenic determinant generally consists of chemically active surface groups of a molecule such as amino acids or carbohydrates or sugar side chains, and usually has specific three-dimensional structural characteristics and specific charge characteristics. For example, the epitope generally includes at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 consecutive or non-consecutive amino acids in a unique spatial conformation, which can be "linear" or "conformational". See, for example, Epitope Mapping Protocols in Methods in Molecular Biology, Vol. 66, G. E. Morris, Ed. (1996). In a linear epitope, all interacting points between a protein and an interacting molecule (*e.g.*, an antibody) exist linearly along the primary amino acid sequence of the protein. In a conformational epitope, the interacting points exist across the protein amino acid residues that are separated from each other.

As used in the present disclosure, the term "isolated" refers to "obtained by artificial means from natural state". If a certain "isolated" substance or component appears in nature, it may be due to the change in its natural environment, or it is isolated from the natural environment, or both. For example, a certain non-isolated polynucleotide or polypeptide naturally exists in a certain living animal, and the same polynucleotide or polypeptide with a high purity isolated from such a natural state is called an isolated polynucleotide or polypeptide. The term "isolated" does not exclude the existence of artificial or synthetic substances or other impurities that do not affect the activity of the substance.

As used in the present disclosure, the term "*E. coli* expression system" refers to an expression system consisting of *E. coli* (strain) and a vector, wherein the *E. coli*

(strain) is derived from a commercially available strain, such as but not limited to GI698, ER2566, BL21 (DE3), B834 (DE3), and BLR (DE3).

As used in the present disclosure, the term "vector" refers to a nucleic acid vehicle into which a polynucleotide can be inserted. When the vector allows for the expression of the protein encoded by the inserted polynucleotide, the vector is called an expression vector. The vector can be introduced into a host cell by transformation, transduction, or transfection so that the genetic substance elements carried by the vector can be expressed in the host cell. Vectors are well known to those skilled in the art, including, but not limited to: plasmids; phagemids; cosmids; artificial chromosomes, such as yeast artificial chromosomes (YAC), bacterial artificial chromosomes (BAC) or P1-derived artificial chromosomes (PAC); phages such as lambda phages or M13 phages, and animal viruses, *etc.* Animal viruses that can be used as vectors include, but are not limited to, retroviruses (including lentiviruses), adenoviruses, adeno-associated viruses, herpes viruses (such as herpes simplex virus), poxviruses, baculoviruses, papillomaviruses, and papovaviruses (such as SV40). A vector can contain a variety of elements that control expression, including, but not limited to, promoter sequences, transcription initiation sequences, enhancer sequences, selection elements, and reporter genes. In addition, the vector may further contain a replication initiation site.

As used in the present disclosure, the term "host cell" refers to cells that can be used to introduce vectors, including, but not limited to, prokaryotic cells such as *E. coli* or *bacillus subtilis*, fungal cells such as yeast cells or aspergillus, insect cells such as S2 drosophila cells or Sf9, or animal cells such as fibroblast, CHO cells, COS cells, NSO cells, HeLa cells, BHK cells, HEK 293 cells, or human cells.

As used in the present disclosure, the term "specifically bind" refers to a non-random binding reaction between two molecules, such as a reaction between an antibody and an antigen it targets. In some examples, an antibody that specifically binds to an antigen (or an antibody that is specific for an antigen) refers to that the antibody binds

to the antigen with an affinity (K_D) of less than about 10^{-5} M, such as less than about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M, 10^{-10} M, or less.

As used in the present disclosure, the term " K_D " refers to a dissociation equilibrium constant for a specific antibody-antigen interaction, which is used to describe the binding affinity between the antibody and the antigen. The smaller the equilibrium dissociation constant, the tighter the antibody-antigen binding, and the higher the affinity between the antibody and the antigen. Generally, antibodies bind to antigens (*e.g.*, L1 protein) with a dissociation equilibrium constant (K_D) of less than about 10^{-5} M, such as less than about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M, 10^{-10} M, or less, for example, as determined in a BIACORE instrument using surface plasmon resonance (SPR).

As used in the present disclosure, the terms "monoclonal antibody" and "McAb" have the same meaning and can be used interchangeably; the terms "polyclonal antibody" and "PcAb" have the same meaning and can be used interchangeably; the terms "polypeptide" and "protein" have the same meaning and can be used interchangeably. And in the present disclosure, amino acids are generally represented by single-letter or three-letter abbreviations known in the art. For example, alanine can be represented by A or Ala.

As used in the present disclosure, the term "effective amount" refers to an amount sufficient to obtain or at least partially obtain a desired effect. For example, a prophylactically effective amount refers to an amount sufficient to prevent, stop, or delay the onset of diseases; a therapeutically effective amount refers to an amount sufficient to cure or at least partially stop a disease and complications thereof in patients suffering from the disease. It is well within the ability of those skilled in the art to determine such an effective amount. For example, the amount effective for therapeutic use will depend on the severity of the disease to be treated, the overall state of the immune system of the patient, the general condition of the patient such as age, weight and sex, the manner of drug administration, and other treatments administered concurrently, *etc.*

Compared with the prior art, the present disclosure has the following advantages:
The monoclonal antibody against nerve growth factor of the present disclosure can specifically bind to nerve growth factor and has the advantages of high activity and the like, and can be used to detect the presence and/or level of nerve growth factor, as well as to prepare a drug for antagonizing nerve growth factor, and to prepare a drug for treating or preventing neuropathic pain, chronic pain, and inflammatory pain, thus having good application prospects and market value.

BRIEF DESCRIPTION OF DRAWINGS

Figure 1 shows the SDS-PAGE analysis results of the monoclonal antibody H26L17 against nerve growth factor of the present invention. The samples of the four lanes from left to right and respective loading amounts thereof are: antibody in non-reduced protein electrophoresis loading buffer, 1 μ g; antibody in reduced protein electrophoresis loading buffer, 1 μ g; protein molecular weight marker (Marker), 5 μ L; bovine serum albumin (BSA), 1 μ g.

Figure 2 shows the analysis results of the binding activity of H26L17 and Tanezumab to the antigen human β -NGF.

Figure 3 shows the standard curve results for the analysis of H26L17 and Tanezumab inhibition on TF-1 cell proliferation by the CCK-8 method.

Figure 4 shows the cell quantity after 72 h of inhibition of NGF-induced TF-1 cell proliferation by the monoclonal antibody H26L17 against nerve growth factor of the present invention.

Figure 5 shows the OD value of each group in measuring the inhibition of TF-1 cell proliferation by H26L17 and Tanezumab by the CCK-8 method.

Figure 6 shows the fitting curve of H26L17 inhibiting NGF-induced TF-1 cell proliferation. Taking the logarithm of antibody concentration (nM) as the x-axis and the OD 450nm value as the y-axis, dose-effect curve fitting was performed to compare the EC₅₀ of different antibodies.

Figure 7 shows the effect of H26L17 on the walking behavior of the affected limb caused by pain in the knee arthritis pain model of Lenti-IL-1 β -NIH/3T3 mice.

CLAIMS

1. A monoclonal antibody against nerve growth factor, comprising heavy chains comprising a heavy chain constant region and a heavy chain variable region, and light chains comprising a light chain constant region and a light chain variable region, wherein the heavy chain variable region comprises three complementarity determining regions HCDR1, HCDR2 and HCDR3, and the light chain variable region comprises three complementarity determining regions LCDR1, LCDR2 and LCDR3;

the amino acid sequence of the complementarity determining region HCDR1 is set forth in SEQ ID NO: 5;

the amino acid sequence of the complementarity determining region HCDR2 is set forth in SEQ ID NO: 6;

the amino acid sequence of the complementarity determining region HCDR3 is set forth in SEQ ID NO: 7;

the amino acid sequence of the complementarity determining region LCDR1 is set forth in SEQ ID NO: 8;

the amino acid sequence of the complementarity determining region LCDR2 is set forth in SEQ ID NO: 9; and

the amino acid sequence of the complementarity determining region LCDR3 is set forth in SEQ ID NO: 10.

2. The monoclonal antibody against nerve growth factor according to claim 1, wherein the amino acid sequence of the heavy chain variable region is set forth in SEQ ID NO: 2; the amino acid sequence of the light chain variable region is set forth in SEQ ID NO: 4.

3. The monoclonal antibody against nerve growth factor according to claim 1, wherein the monoclonal antibody against nerve growth factor is selected from a Fab, a Fab', an F(ab')₂, an Fd, an Fv, a dAb, a complementarity determining region

fragment, a single chain antibody, a humanized antibody, a chimeric antibody, and a diabody.

4. The monoclonal antibody against nerve growth factor according to claim 1, wherein the monoclonal antibody against nerve growth factor binds to NGF protein with an EC₅₀ of less than 100 nM.

5. A nucleotide sequence encoding the monoclonal antibody against nerve growth factor according to claims 1 or 2.

6. The nucleotide sequence according to claim 5, wherein the nucleotide sequence encoding the heavy chain variable region is set forth in SEQ ID NO: 1; and the nucleotide sequence encoding the light chain variable region is set forth in SEQ ID NO: 3.

7. A vector, comprising the nucleotide sequence according to claims 5 or 6.

8. A host cell, comprising the nucleotide sequence according to claims 5, 6, or 7.

9. A monoclonal antibody conjugate, comprising the monoclonal antibody against nerve growth factor according to claims 1 or 2, and a conjugated portion conjugated thereto, wherein the conjugated portion is a detectable label.

10. A kit, comprising the monoclonal antibody against nerve growth factor according to claims 1 or 2 and/or the monoclonal antibody conjugate according to claim 9.

11. The kit according to claim 10, further comprising a secondary antibody specifically recognizing the monoclonal antibody against nerve growth factor according to claims 1 or 2.

12. Use of the monoclonal antibody against nerve growth factor according to claims 1 or 2 and/or the monoclonal antibody conjugate according to claim 9 in preparing a kit for detecting the presence and/or level of nerve growth factor.

13. Use of the monoclonal antibody against nerve growth factor according to claims 1 or 2 and/or the monoclonal antibody conjugate according to claim 9 in the manufacture of a medicament for:

specifically binding to nerve growth factor;

inhibiting the proliferation of nerve growth factor-dependent TF-1 cells;
and/or
treating or preventing at least one of neuropathic pain, chronic pain, and
inflammatory pain.

14. A drug, comprising the monoclonal antibody against nerve growth factor
according to claims 1 or 2 and/or the monoclonal antibody conjugate according to
claim 9 as an active ingredient, and a pharmaceutically acceptable carrier or
excipient.

15. The drug according to claim 14, wherein the drug specifically binds to nerve
growth factor to inhibit nerve growth factor-dependent proliferation of TF-1 cells,
and/or
to treat or prevent at least one of neuropathic pain, chronic pain, and inflammatory
pain.