Cytokine antagonists for use in localized clinical disorders are provided for the treatment and prevention of damage to the optic nerve, other cranial nerves, spinal cord, nerve roots, peripheral nerves or muscles caused by any one of the following: a herniated nucleus pulposus, osteoarthritis, other forms of arthritis, disorders of bone, disease, or trauma. The cytokine antagonists are used to treat these disorders by local administration. These cytokine antagonists include antagonists to tumor necrosis factor; interleukin-1; interleukin-6; and interleukin-8.

38 Claims, No Drawings
The present invention relates to specific cytokine antagonists which are provided for the treatment and prevention of damage to the optic nerve, other cranial nerves, brain, spinal cord, nerve roots, peripheral nerves or muscles caused by any one of the following: a herniated nucleus pulposus, osteoarthritis, other forms of arthritis, disorders of bone, disease, or trauma. More particularly, the cytokine antagonists are used in a new treatment of these disorders utilizing localized anatomic administration which causes inhibition of the action of the corresponding pro-inflammatory cytokine in a localized anatomic area of the human body. The administration of these cytokine antagonists is performed by anatomically localized administration which includes, but is not limited to the following routes: perilesional; intraleSIONal; and transconjunctival (for disorders of the optic nerve). Perilesional routes as mentioned above include, but are not limited to, subcutaneous, intramuscular, and epidural routes of administration.

The use of cytokine antagonists to treat localized disorders is discussed in U.S. Pat. Nos. 6,015,557 and 6,177,077 and other pending applications of the applicant. This invention includes further applications of these ideas.

Localized administration, including perilesional or intraleSIONal administration, when compared to systemic administration, carries with it one or more of the following advantages:

1) greater efficacy due to the achievement of higher local concentration;
2) greater efficacy due to the ability of the administered therapeutic molecule to reach the target tissue without degradation caused by hepatic or systemic circulation;
3) more rapid onset of action;
4) longer duration of action; and
5) Potentially fewer side effects, due to lower required dosage.
anti-TNF monoclonal antibody (Knoll Pharmaceuticals) is being developed to treat rheumatoid arthritis and Crohn’s Disease; and Celltech is developing CDP 571 to treat Crohn’s Disease and CDP 870 to treat rheumatoid arthritis.

Members of the interleukin family, including interleukin 1(IL-1), have been demonstrated to be key components of inflammation. Antagonists of these cytokines which are in development include interleukin 1 receptor antagonist (IL-1 RA) (Amgen) and interleukin 1 receptor type II (IL-1R type II) (Immunix). Other interleukin antagonists which are the subject of this patent include antagonists to IL-6 (including monoclonal antibodies directed to IL-6) and antagonists to IL-8 (including monoclonal antibodies directed to IL-8).

Use of these interleukin antagonists can suppress inflammation, which is important to the pathogenesis of a variety of clinical disorders. Localized administration of these cytokine antagonists, either directed against TNF or interleukin, can ameliorate the localized neurologic disorders and inflammatory disorders of muscle which are of consideration in this invention.

DESCRIPTION OF THE PRIOR ART

Pharmacologic chemical substances, compounds and agents which are used for the treatment of neurological disorders, trauma, injuries and compression having various organic structures and metabolic functions have been disclosed in the prior art. For example, U.S. Pat. Nos. 5,756,482 and 5,574,022 to ROBERTS et al disclose methods of attenuating physical damage to the nervous system and to the spinal cord after injury using steroid to hormones or steroid precursors such as pregnenolone, and pregnenolone sulfate in conjunction with a non-steroidal anti-inflammatory substance such as indomethacin. These prior art patents do not teach the use of specific cytokine antagonists for the suppression and inhibition of the action of IL-1 in the human body to treat neurological disease, trauma, injury or compression, as in the present invention.

U.S. Pat. No. 5,863,769 discloses using IL-1 RA for treating various diseases. However, it does not disclose administering cytokine antagonists locally for the treatment of localized neurological or muscular disorders.

U.S. Pat. No. 6,013,253 discloses using interferon and IL-1 RA for treating multiple sclerosis. However, it does not disclose administering cytokine antagonists locally for the treatment of localized neurological or muscular disorders.

PCT Application WO 00/18409 (Apr. 6, 2000) discloses the use of various medications to treat nerve root injury. It does not disclose the methods discussed herein, including localized administration, perilesional administration, or intralesional administration, of the substances discussed herein.

None of the prior art patents disclose or teach the use of localized administration of a cytokine antagonist as in the present invention for suppression and inhibition of the action of a specific cytokine in a human to treat localized neurological or muscular disease, in which the cytokine antagonist provides the patient with a better opportunity to heal, slows disease progression, prevents neurological damage, or otherwise improves the patient’s health.

Accordingly, it is an object of the present invention to provide a cytokine antagonist administered through anatomically localized administration as a new method of pharmacologic treatment of neurological disorders, trauma, injuries and compression affecting the nervous system of the human body; and for treating localized disorders of muscle; such that the use of these cytokine antagonists will result in the amelioration of these conditions.

Another object of the present invention is to provide cytokine antagonists for providing suppression and inhibition of the action of specific cytokines in a human to treat neurological injury, trauma or compression; and localized muscular disorders.

Another object of the present invention is to provide cytokine antagonists that reduce inflammation by inhibiting the action of specific cytokines in the human body for the immediate, short term (acute conditions) and long term (chronic conditions), such that this reduction in inflammation will produce clinical improvement in the patient and will give the patient a better opportunity to heal, slow disease progression, prevent neurological damage, prevent muscular damage, or otherwise improve the patient’s health.

Another object of the present invention is to provide cytokine antagonists, using anatomically localized administration as the preferred form of administration, that offer acute and chronic treatment regimens for neurological conditions caused by neurological trauma, compression, injury and/or disease, such conditions including acute spinal cord injury; herniated nucleus pulposus (herniated disc); other related neurological disorders and diseases; spinal cord compression due to metastatic cancer; Bell’s Palsy; glaucoma and glaucomatous optic nerve degeneration; and muscular disorders.

SUMMARY OF THE INVENTION

The present invention provides a method for inhibiting the action of pro-inflammatory cytokines, including TNF, IL-1, IL-6, and IL-8, for treating neurological, optic nerve (glaucoma), and muscular disorders in a human by administering to the human therapeutically effective doses of a specific cytokine antagonist directed against one of the aforementioned cytokines for reducing the inflammation of neuronal, optic nerve, or muscular tissue of the human and/or preventing immune system damage to neuronal tissue (including spinal cord, nerve root, cranial nerve, or peripheral nerve) or muscular tissue. The preferred forms of administration are localized anatomic administration, including perilesional, intralesional, or transconjunctival (for disorders of the optic nerve) routes. Perilesional routes as mentioned above include, but are not limited to, subcutaneous, intramuscular, and epidural routes of administration.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Anatomically localized administration is a novel new concept for a delivery method for cytokine antagonists. In this invention it is particularly well matched to the localized clinical disorders being considered.

Some of the clinical conditions being considered here lend themselves to intralesional administration. The most common use of this delivery method is for treating muscle spasm caused by sports injuries, exercise, or trauma. Injection directly into the involved muscle using a small gauge needle is the most efficient way to treat these conditions.

For the great majority of the clinical conditions considered herein, however, perilesional administration is the preferred method of delivery. Perilesional is defined by the
Johnson and Johnson; D2E7, a human anti-TNF monoclonal antibody (Knoll Pharmaceuticals, Abbott Laboratories); and CDP 571 (a humanized anti-TNF IgG4 antibody) and CDP 870 (an anti-TNF alpha humanized monoclonal antibody fragment), both from Celltech. IL-1 antagonists which are suitable for these regimens are IL-1RA (interleukin 1 receptor antagonist) from Amgen Corporation.

Trauma, injury, compression and disease can affect individual nerves, nerve roots, the spinal cord, or localized areas of muscle. The disorders which are of most concern and which are included here are the following:

- Spinal Cord Injury
- Spinal Cord Compression
- Herniated Intervertebral Disc (herniated nucleus pulposus)
- Glaucoma
- Bell’s Palsy
- Localized Muscular Disorders, including acute muscle pulls, muscle sprains, muscle tears, and muscle spasm
- Alzheimer’s Disease

Postherpetic Neuralgia

Scientific Background

Antibodies (immunoglobulins) are proteins produced by one class of lymphocytes (B cells) in response to specific exogenous foreign molecules (antigens). Monoclonal antibodies (mAB), identical immunoglobulin copies which recognize a single antigen, are derived from clones (identical copies) of a single B cell. This technology enables large quantities of an immunoglobulin with a specific target to be mass produced.

Monoclonal antibodies with a high affinity for a specific cytokine will tend to reduce the biologic activity of that cytokine. Substances which reduce the biologic effect of a cytokine can be described in any of the following ways: as a cytokine blocker, as a cytokine inhibitor, or as a cytokine antagonist. In this patent, the terms blocker, inhibitor, and antagonist are used interchangeably with respect to cytokines.

Advances in biotechnology have resulted in improved molecules as compared to simply using monoclonal antibodies. One such molecule is CDP 870 which, rather than being a monoclonal antibody, is a new type of molecule, that is an antibody fragment. By removing part of the antibody structure, the function of this molecule is changed so that it acts differently in the human body. Another new type of molecule, distinct from monoclonal antibodies and soluble receptors, is a fusion protein. One such example is etanercept. This molecule has a distinct function which acts differently in the human body than a simple soluble receptor or receptors.

Cytokine antagonists can take several forms. They may be monoclonal antibodies (defined above). They may be a monoclonal antibody fragment. They may take the form of a soluble receptor to that cytokine. Soluble receptors freely circulate in the body. When they encounter their target cytokine they bind to it, effectively inactivating the cytokine, since the cytokine is then no longer able to bind with its biologic target in the body. An even more potent antagonist consists of two soluble receptors fused together to a specific portion of an immunoglobulin molecule (F2 fragment). This produces a dimer composed of two soluble receptors which have a high affinity for the target, and a prolonged half-life. This new molecule is called a fusion protein. An example of this new type of molecule, called a fusion protein, is etanercept (Enbrel®).

TNF, a naturally occurring cytokine, plays a key role in the inflammatory response, in the immune response, and in the response to infection. TNF is formed by the cleavage of a precursor transmembrane protein, forming soluble molecules which aggregate in vivo to form trimolecular complexes. These complexes then bind to receptors found on a
A detailed discussion of each of the clinical conditions follows:

1) Herniated Nucleus Pulposus (Herniated Disc)

Acute low back pain is one of the most common reasons for patients to seek medical care. In the United States over $20 billion is expended annually for the medical treatment of low back pain, and indirect costs, including loss of time from work, are even greater. Sciatica due to a herniated nucleus pulposus is an important cause of acute low back pain. Although many of these patients recover with conservative management, a substantial number need surgery due to persistent severe pain not responding to medical treatment.

Conservative treatment consists of physical measures, the use of analgesics, muscle relaxants, non-steroidal anti-inflammatory drugs, systemic corticosteroids, or epidural steroid injections. Epidural injections of corticosteroids are commonly used for patients not responding to other methods of treatment, but their true benefit has been questioned.

Newer imaging techniques, including computerized axial tomographic (CAT) scans and magnetic resonance imaging (MRI) scans provide non-invasive methods to determine the anatomic extent and location of disc herniation. The medical practitioner can correlate the findings with history and physical examination to thereby more accurately distinguish sciatica due to herniated nucleus pulposus from other causes of low back pain.

The anatomic basis for sciatica has long been established, but the biochemical basis for the nerve root damage which accompanies disc herniation is less understood. Recent medical research has shed new light on this area. It is now known that the nucleus pulposus contains TNF which causes neuronal damage when it comes into contact with the nerve root.

This new data suggests that nerve root damage from disc herniation is not solely due to mechanical compression, as long thought, but rather is primarily due to direct neurotoxicity from the release of TNF from the herniated disc. Concurrent with these new discoveries regarding the pathogenesis of sciatica are the recent availability of new medications which are specific blockers of TNF.

In accordance with the present invention, localized administration of a cytokine antagonist in this setting includes both of the following routes: 1) epidural; or 2) parenteral injection, to an area anatomically adjacent to the disc herniation. Parentreral injection in this setting includes intramuscular injection or subcutaneous injection. Subcutaneous injection is the simplest and safest method.

Experimental Results

Case 1: Etanercept for the Treatment of Acute Lumbar Radiculopathy

A 44 year old man presented with a three week history of lower back pain which had begun after an episode of heavy lifting. At the onset the pain was present in the lower lumbar area with radiation down the right leg in a sciatic distribution. Three weeks of rest and treatment with oral NSAIDS failed to result in improvement. Examination revealed the patient to be in acute discomfort. Etanercept 25 mg was administered subcutaneously at the level of the L4-5 interspace, 1.5 cm lateral to the midline, at a depth of 0.5 inch. After an interval of 10 minutes the patient experienced dramatic pain relief. The patient was then able to walk normally, and resumed normal activities. The pain has not recurred for one year.

Case 2: Perilesional Etanercept for the Treatment of Acute Lumbar Radiculopathy Caused by a Herniated Nucleus Pulposus

A 34 y.o. Caucasian male presented with a three week history of acute and severe low back pain radiating into the right lower leg, worsened by movement or by sneezing. The pain was exacerbated by right leg paresthesias, and numbness in an S1 distribution. Symptoms had persisted despite two courses of oral methylprednisolone. MRI scan demonstrated a herniated nucleus pulposus at the L5-S1 level, with a protruding disc segment causing compression of the right S1 nerve root. Etanercept was administered in a dose of 25 mg subcutaneously to the lumbar area, at the same level as the disc herniation. It was delivered on the ipsilateral side, approximately 1.5 cm lateral to the spinous process, and injected with a 27 gauge needle at a depth of 0.5 inch. Pain relief was dramatic and rapid, with onset beginning within 10 minutes of administration. Other neurologic symptoms, such as paresthesia, anesthesia, and muscular weakness, also responded dramatically.

Other cytokine antagonists considered here can be used in the same fashion. This particularly includes the TNF antagonists, including infliximab, CDP 870, CDP 571, and D2E7. Although all of these agents were originally designed for systemic administration they can all be administered perilesionally as described above.

2) Acute Spinal Cord Injury

About 10,000 new cases occur per year in the U.S., with a current population of over 200,000 patients with residual neurologic damage, many of whom are paralyzed (quadruplegia or paraplegia). Current treatment for the acute injury is inadequate. In the early 1990’s it was shown that early (within 8 hours of injury) treatment with high doses of steroids (methyl prednisolone) was beneficial for some of these patients. Surgical stabilization and spinal decompression is often necessary because of excessive swelling (edema) which can itself cause further severe injury to the cord due to further compression of the cord against its bony spinal canal. The etiology of most of these cases are motor vehicle accidents, with the remainder being sports injuries, falls, and other accidents. The window of opportunity for treatment is small, since massive swelling can occur within minutes.

The emergent use of a cytokine antagonist, delivered by an anatomically localized administration, will ameliorate neurologic damage caused by acute spinal cord injury. In this setting localized injection can include intrathecal administration, epidural administration, or parenteral injection, either intramuscular or subcutaneous, to an area in close anatomic proximity to the area of spinal cord injury. Anatomically localized injection may be used in conjunction
with systemic administration for severe injury. This invention is designed to include the use of cytokine antagonists in the field by paramedical personnel for victims of trauma, such as automobile and motorcycle accidents. It is envisioned that the paramedics will administer a cytokine antagonist, such as etanercept to the victim with known or suspected cord trauma even before they are moved out of the vehicle. This will allow the cytokine antagonist to rapidly act as an anti-inflammatory and neuroprotective agent, helping to ameliorate edema and thereby prevent further neurologic injury.

2) Spinal Cord Compression Due to Metastatic Cancer
Cord compression due to metastatic cancer is a catastrophic event leading to rapid paralysis if not quickly diagnosed and treated. It is most common with cancers of the breast, colon, lung and prostate, but can be a complication of metastatic disease from a wide variety of malignancies, including melanoma and multiple myeloma. Current treatment regimens include high dose steroids, emergency radiation treatment, and/or emergent surgical decompression. Paralysis can occur within hours, so treatment must be initiated within this time period to avoid permanent spinal cord injury.

The emergent use of a cytokine antagonist, delivered by anatomically localized administration, will ameliorate neurologic damage in this clinical setting.

4) Bell’s Palsy
Bell’s palsy is characterized by the sudden onset of hemifacial paralysis, caused by acute mononeuropathy of the seventh cranial nerve, the facial nerve. It can follow viral infection, vaccination, or may be idiopathic. The mainstay of treatment in the past has been large doses of corticosteroids. Current treatment regimens include high dose steroids, emergency radiation treatment, and/or emergent surgical decompression. Paralysis can occur within hours, so treatment must be initiated within this time period to avoid permanent spinal cord injury.

The emergent use of a cytokine antagonist, delivered by anatomically localized administration, will ameliorate neurologic damage in this clinical setting.

5) Glaucoma
A central feature of glaucoma is pathology of the optic nerve. This is thought to be a key to the pathogenesis of this disorder. Overproduction of inflammatory cytokines, particularly TNF, are centrally involved. In accordance with the present invention, localized administration of a cytokine antagonist by the use of eye drops delivered by the transconjunctival route will ameliorate this condition.

6) Localized Muscular Disorders
Inflammation of muscle, caused by trauma, tear, sprain, strain, injury or disease is the result of the release of pro-inflammatory cytokines, particularly TNF. Local administration of a cytokine antagonist results in rapid clinical improvement.

For example, for acute muscle spasm etanercept may be administrated into the involved muscle (intralesionally) at a dose of 25 mg, with or without a concurrent dose of local anesthetic, such as Marcaine®.

7) Carpal Tunnel Syndrome
Carpal tunnel syndrome involves compression of the median nerve at the wrist, causing pain and neurologic symptoms in the hand. It is a common condition, being aggravated by repetitive stress injury (RSI) in the workplace (such as typists and writers, manual laborers, etc.), and is also a complication of rheumatoid arthritis (RA). Use of TNF blockade for carpal tunnel syndrome in patients with established RA would likely be covered by the existing arthritis medication for treating RA. But most patients with carpal tunnel syndrome do not have RA; they either have idiopathic CTS or CTS caused by RSI. CTS is a major cause of disability and responds poorly to current treatment regimens, which include NSAIDS, wrist splinting, and injection of steroids.

In accordance with the present invention, local administration of a cytokine antagonist is used to treat this condition. Administration is perilesional by subcutaneous administration in the area immediately overlying the affected median nerve.

8) Alzheimer’s Disease
Alzheimer’s Disease is a common form of progressive dementia, of unknown cause and without an effective cure. It is characterized by neurofibrillary tangles and plaques on pathologic examination brain tissue.

Dosages and Routes of Administration
The dosage of a cytokine antagonist used for intralesional or perilesional administration will in general be within one order of magnitude of the dosage used as a single dose for systemic administration. For example, if the usual dose when administered systemically is 100 mg, then the dose used for intralesional therapy will usually be between 10 mg and 100 mg. One exception to this rule is the dose for administration into an anatomically confined structure. In this case, if the structure is small, the dose will need to be reduced accordingly.

For the treatment of acute or severe conditions, the dose will generally be adjusted upward. In the above example the dose selected would therefore be 100 mg, rather than 10 mg, if the condition were acute and/or severe.

Localized perilesional injection can allow the use of subcutaneous, hemorrhagic necrosis, and neuronal loss in the dorsal root ganglion; demyelination, Wallerian degeneration, and sclerosis of peripheral nerves; acute degeneration of the dorsal horn of the spinal cord, and rarely, unilateral segmental myelitis and leptomeningitis.

For treating the above diseases with the above mentioned TNF antagonists, these TNF antagonists may be administered by the following routes:

The above TNF antagonists may be administered subcutaneously in the human and the dosage level is in the range of 1 mg to 300 mg per dose, with dosage intervals varying from 1 day to 1 month.

The above TNF antagonists may be administered intra-muscularly in the human and the dosage level is in the range of 1 mg to 200 mg per dose, with dosage intervals varying from 1 day to 1 month.

The above TNF antagonists may be administered epidurally in the human and the dosage level is in the range of 1 mg to 300 mg per dose, with dosage intervals varying from 1 day to 2 months.

The above TNF antagonists may be administered transconjunctivally in the human and the dosage level is in the range of 0.1 mg to 5 mg per dose, with dosage intervals varying from TD to once per month.
Interleukin antagonists are administered in a therapeutically effective dose. Dosage interval varies from once per day to once per month for the subcutaneous, intramuscular, and epidural routes; and from TID to once per month for the transconjunctival route.

ADVANTAGES OF THE PRESENT INVENTION

Accordingly, an advantage of the present invention is that it provides for the localized administration of cytokine antagonists as a new pharmacologic treatment of localized disorders of components of the neurological system, optic nerve, or muscles; such that the use of these cytokine antagonists will result in the amelioration of these conditions.

Another advantage of the present invention is that it provides for cytokine antagonists by anatomically localized administration, which, when compared to systemic administration, produces one or more of the following: greater efficacy; more rapid onset; longer duration of action; or fewer side effects.

Another advantage of the present invention is that it provides for cytokine antagonists for providing suppression and inhibition of the action of cytokines in a human to treat localized neurological injury, trauma, disease, or compression; glaucoma; and muscular diseases.

Another advantage of the present invention is that it provides for cytokine antagonists that reduce inflammation by inhibiting the action of cytokines in the human body for the immediate, short term (acute conditions) and long term (chronic conditions), such that this reduction in inflammation will produce clinical improvement in the patient and will give the patient a better opportunity to heal, slow disease progression, prevent neurological damage, prevent optic nerve and muscular damage, or otherwise improves the patient’s health.

Another advantage of the present invention is that it provides for cytokine antagonists, using localized administration, including perilesional or intralesional administration, as the preferred form of administration, for the treatment of localized neurological injury, trauma, disease, or compression; glaucoma; and muscular diseases.

A latitude of modification, change, and substitution is intended in the foregoing disclosure, and in some instances, some features of the invention will be employed without a corresponding use of other features. Accordingly, it is appropriate that the appended claims be construed broadly and in a manner consistent with the spirit and scope of the invention herein.

What is claimed is:

1. A method for inhibiting the action of TNF for treating neurological conditions in a human by administering a TNF antagonist for reducing the inflammation of neuronal tissue of said human, or for modulating the immune response affecting neuronal tissue of said human, comprising the steps of:
   a) administering a therapeutically effective dosage level to said human of said TNF antagonist selected from the group consisting of a fusion protein identified as etanercept, infliximab, CDP571 (a humanized monoclonal anti-TNF-alpha IgG4 antibody), CDP 870 (a humanized monoclonal anti-TNF-alpha antibody fragment) and D2E7 (a human anti-TNF mAb) for reducing the inflammation of neuronal tissue of said human, or for modulating the immune response affecting neuronal tissue of said human; and
   b) administering said dose either intrasessionally or perilesionally.

2. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said dosage level is for treating Alzheimer’s Disease.

3. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said TNF antagonist is performed through any of the following routes: subcutaneous, intrathecal, intramuscular, intranasal, transepidermal, parenteral, transconjunctival, or epidural.

4. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said dosage level is for treating nerve root injury caused by a herniated nucleus pulposus.

5. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said dosage level is for treating Bell’s Palsy.

6. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said dosage level is for treating Carpal Tunnel Syndrome.

7. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said dosage level is for treating acute spinal cord injury.

8. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said dosage level is for treating spinal cord compression.

9. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said dosage level is for treating spinal stenosis.

10. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said dosage level is for treating localized disorders of muscle, including muscle spasm, muscle tear, muscle injury, muscle strain, or muscle sprain.

11. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said dosage level is for treating glaucoma.

12. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said TNF antagonist is performed subcutaneously in said human wherein said dosage level is in the range of 1 mg to 25 mg per dose.

13. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said TNF antagonist in the form of etanercept is performed intramuscularly in said human wherein said dosage level is in the range of 1 mg to 25 mg.

14. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said TNF antagonist in the form of etanercept is performed subcutaneously in said human wherein said dosage level is in the range of 1 mg to 100 mg.

15. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said TNF antagonist in the form of etanercept is performed intramuscularly in said human wherein said dosage level is in the range of 1 mg to 100 mg.

16. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said TNF antagonist in the form of D2E7 is performed subcutaneously in said human wherein said dosage level is in the range of 10 mg to 25 mg.

17. A method for inhibiting the action of TNF in accordance with claim 1, wherein the step of administering said TNF antagonist in the form of D2E7 is performed subcutaneously in said human wherein said dosage level is in the range of 10 mg to 40 mg.

18. A method for inhibiting the action of TNF for treating or preventing nerve root injury in a human by administering...
a TNF antagonist for reducing the inflammation of neuronal tissue of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said nerve root of said human, comprising the steps of:

a) administering a therapeutically effective dosage level to said human of etanercept, for reducing the inflammation of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said human; and

b) administering said dose either intraperitoneally or peri-lesionally.

19. A method for inhibiting the action of TNF for treating or preventing nerve root injury in a human by administering a TNF antagonist for reducing the inflammation of neuronal tissue of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said nerve root of said human, comprising the steps of:

a) administering a therapeutically effective dosage level to said human of etanercept, for reducing the inflammation of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said human; and

b) administering said dose subcutaneously to the area anatomically adjacent to the site of disc herniation.

20. A method for inhibiting the action of TNF in accordance with claim 19, wherein the step of administering said dosage level is for treating nerve root injury due to a herniated nucleus pulposus, wherein the dosage level is between 1 mg and 100 mg.

21. A method for inhibiting the action of TNF for treating or preventing nerve root injury in a human by administering a TNF antagonist for reducing the inflammation of neuronal tissue of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said nerve root of said human, comprising the steps of:

a) administering a therapeutically effective dosage level to said human of etanercept, for reducing the inflammation of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said human; and

b) administering said dose either intraperitoneally or peri-lesionally.

22. A method for inhibiting the action of TNF for treating glaucoma in a human by administering a TNF antagonist for reducing the inflammation of the optic nerve or retina of said human, or for modulating the immune response affecting the optic nerve or retina of said human, comprising the steps of:

a) administering a therapeutically effective dosage level to said human of etanercept, for reducing the inflammation of said nerve root of said human, or for modulating the immune response affecting the optic nerve or retina of said human; and

b) administering said dose either intraperitoneally or peri-lesionally.

23. A method for inhibiting the action of TNF in accordance with claim 22, wherein the step of administering said TNF antagonist is performed through any of the following routes: subcutaneous, intranasal, transdermal, parenteral, or transconjunctival.

24. A method for inhibiting the action of interleukin (IL) for treating neurological disorders in a human by administering an IL Blocker for reducing the inflammation of neuronal tissue of said human, or for modulating the immune response affecting neuronal tissue of said human, comprising the steps of:

a) administering a therapeutically effective dosage level to said human of said IL Blocker for reducing the inflammation of neuronal tissue of said human, or for modulating the immune response affecting neuronal tissue of said human; and

b) administering said dose either intraperitoneally or peri-lesionally.

25. A method for inhibiting the action of IL in accordance with claim 24, wherein said IL Blocker is selected from the group consisting of IL-1 RA, IL-1R type II, a monoclonal antibody to IL-1, soluble receptors to IL-1, soluble receptors to IL-1 fused to an Fc immunoglobulin fragment, a monoclonal antibody to IL-6, and a monoclonal antibody to IL-8.

26. A method for inhibiting the action of IL in accordance with claim 25, wherein the step of administering said IL Blocker is performed through local subcutaneous administration for treating nerve root injury caused by intervertebral disc herniation.

27. A method for inhibiting the action of IL in accordance with claim 25, wherein the step of administering said IL Blocker is performed through local subcutaneous administration for treating Bell’s Palsy.

28. A method for inhibiting the action of IL in accordance with claim 25, wherein the step of administering said IL Blocker is performed through the transconjunctival route via eye drops for treating glaucoma.

29. A method for inhibiting the action of IL in accordance with claim 25, wherein the step of administering said IL Blocker is performed through the transconjunctival route via eye drops for treating glaucoma.

30. A method for inhibiting the action of TNF for treating or preventing nerve root injury in a human by administering a TNF antagonist for reducing the inflammation of neuronal tissue of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said nerve root of said human, comprising the steps of:

a) administering a therapeutically effective dosage level to said human of said TNF antagonist selected from the group consisting of etanercept, infliximab, CDP571 (a humanized monoclonal anti-TNF-alpha IgG4 antibody), CDP 870 (a humanized monoclonal anti-TNF-alpha antibody fragment) and D2E7 (a human anti-TNF mAb), for reducing the inflammation of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said human; and

b) administering said dose perilesionally by subcutaneous administration in the lumbar area (for lumbar or sacral nerve roots) or in the cervical area (for cervical nerve roots).

31. A method for inhibiting the action of TNF for treating or preventing nerve root injury in a human by administering a TNF antagonist for reducing the inflammation of neuronal tissue of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said nerve root of said human, comprising the steps of:

a) administering a therapeutically effective dosage level to said human of said TNF antagonist selected from the group consisting of etanercept, infliximab, CDP571 (a humanized monoclonal anti-TNF-alpha IgG4 antibody), CDP 870 (a humanized monoclonal anti-TNF-alpha antibody fragment) and D2E7 (a human anti-TNF mAb), for reducing the inflammation of the optic nerve or retina of said human, or for modulating the immune response affecting the optic nerve or retina of said human; and

b) administering said dose perilesionally by subcutaneous administration in the lumbar area (for lumbar or sacral nerve roots) or in the cervical area (for cervical nerve roots).
32. A method for inhibiting the action of TNF for treating or preventing nerve root injury in a human by administering a TNF antagonist for reducing the inflammation of neuronal tissue of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said nerve root of said human, comprising the steps of:
   a) administering a therapeutically effective dosage level to said human of infliximab, for reducing the inflammation of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said human; and
   b) administering said dose perilesionally by subcutaneous administration in the lumbar area (for lumbar or sacral nerve roots) or in the cervical area (for cervical nerve roots).

33. A method for inhibiting the action of TNF for treating or preventing nerve root injury in a human by administering a TNF antagonist for reducing the inflammation of neuronal tissue of said nerve root of said human, or for modulating the immune response to affecting neuronal tissue of said nerve root of said human, comprising the steps of:
   a) administering a therapeutically effective dosage level to said human of CDP 870, for reducing the inflammation of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said human; and
   b) administering said dose perilesionally by subcutaneous administration in the lumbar area (for lumbar or sacral nerve roots) or in the cervical area (for cervical nerve roots).

34. A method for inhibiting the action of TNF for treating or preventing nerve root injury in a human by administering a TNF antagonist for reducing the inflammation of neuronal tissue of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said nerve root of said human, comprising the steps of:
   a) administering a therapeutically effective dosage level to said human of CDP 571, for reducing the inflammation of said nerve root of said human, or for modulating the immune response affecting neuronal tissue of said human; and
   b) administering said dose perilesionally by subcutaneous administration in the lumbar area (for lumbar or sacral nerve roots) or in the cervical area (for cervical nerve roots).

35. A method for inhibiting the action of TNF for treating neurological conditions in a human by administering a TNF antagonist for reducing the inflammation of neuronal tissue of said human, or for modulating the immune response affecting neuronal tissue of said human, comprising the steps of:
   a) administering a therapeutically effective dosage level to said human of CDP 870, for reducing the inflammation of neuronal tissue of said human, or for modulating the immune response affecting neuronal tissue of said human; and
   b) administering said dose perilesionally by subcutaneous administration in the lumbar area (for lumbar or sacral nerve roots) or in the cervical area (for cervical nerve roots).

36. A method for inhibiting the action of TNF in accordance with claim 35, wherein the step of administering said dosage level is for treating Alzheimer's Disease.

37. A method for inhibiting the action of TNF in accordance with claim 35, wherein the step of administering said dosage level is for treating glaucoma.

38. A method for inhibiting the action of TNF in accordance with claim 35, wherein the step of administering said dosage level is for treating Postherpetic Neuralgia.