Title (en)

NON-INVASIVE DELIVERY OF POLYPEPTIDES THROUGH THE BLOOD-BRAIN BARRIER, AND IN VIVO SELECTION OF ENDOCYTOTIC LIGANDS

Title (de)

NICHTINVASIVE ABGABE VON POLYPEPTIDEN DURCH DIE BLUT-HIRN-SCHRANKE UND IN-VIVO-AUSWAHL VON ENDOZYTOTISCHEN LIGANDEN

Title (fr)

ADMINISTRATION NON INVASIVE DE POLYPEPTIDES A TRAVERS LA BARRIERE HEMATO-ENCEPHALIQUE ET SELECTION IN VIVO DE LIGANDS ENDOCYTOTIQUES

Publication

EP 1503801 A4 20060208 (EN)

Application

EP 03727872 A 20030428

Priority

- AU PS193502 A 20020426
- IB 0302371 W 20030428
- US 18818402 A 20020702

Abstract (en)

[origin: WO03091387A2] A treatment method and genetic vectors are disclosed for non-invasive delivery of polypeptides through the blood brain barrier (BBB), to treat brain or spinal tissue. A genetic vector is used to transfect one or more neurons which "straddle" the BBB, such as sensory neurons, nocioceptive neurons, or lower motor neurons; this is done by administering the vector in a manner that causes it to contact neuronal projections that extend outside the BBB. Once inside a peripheral projection that belongs to a BBB-straddling neuron, the vectors (or some portion thereof) will be transported to the main cell body of the neuron, through a process called retrograde transport. Inside the main cell body, at least one gene carried by the genetic vector will be expressed, to form polypeptides. Some of these polypeptides (which can include leader sequences that will promote anterograde transport and secretion by BBB-straddling neurons) will be transported by the neurons to secretion sites inside the BBB. The polypeptides will be secreted by transfected neurons at locations inside the BBB, and will then contact and exert their effects upon secondary "target" neurons located entirely within the BBB. By using this system, polypeptides that stimulate nerve growth or activity can be used to treat neurodegenerative diseases, impaired limbs in stroke victims, etc., and polypeptides that suppress neuronal activity can be used to treat unwanted excessive neuronal activity, such as neuropathic pain. This approach also provides new methods for delivering endocrine and paracrine polypeptides into the CNS, thereby allowing improved medical and reproductive treatments in humans, and improved ability to modulate growth, maturation, reproduction, or other endocrine-related functions among livestock, endangered species, and other animals.

IPC 1-7

A61K 48/00; C12N 15/12; C12N 15/79; C12N 15/16; C12N 15/18; A61P 11/00; G01N 33/74

IPC 8 full level

C12N 15/09 (2006.01); **A61K 9/127** (2006.01); **A61K 35/76** (2015.01); **A61K 38/00** (2006.01); **A61K 38/22** (2006.01); **A61K 39/395** (2006.01); **A61K 45/00** (2006.01); **A61K 47/46** (2006.01); **A61K 47/48** (2006.01); **A61K 48/00** (2006.01); **A61P 11/00** (2006.01); **A61P 25/00** (2006.01); **C07K 16/00** (2006.01); **C07K 16/28** (2006.01); **C12N 15/12** (2006.01); **C12N 15/16** (2006.01); **C12N 15/18** (2006.01); **C12N 15/861** (2006.01); **C12N 15/867** (2006.01); **C12N 15/869** (2006.01)

CPC (source: EP)

A61K 48/0058 (2013.01); **A61K 48/0075** (2013.01); **A61P 11/00** (2018.01); **A61P 25/00** (2018.01); **C07K 16/005** (2013.01); **C07K 16/2878** (2013.01); **C12N 15/86** (2013.01); A61K 48/00 (2013.01); C07K 2317/21 (2013.01); C07K 2317/622 (2013.01); C12N 2710/10343 (2013.01); C12N 2710/16643 (2013.01); C12N 2740/15043 (2013.01)

Citation (search report)

- [X] GLORIOSO J C ET AL: "Use of HSV vectors to modify the nervous system", CURRENT OPINION IN DRUG DISCOVERY AND DEVELOPMENT, CURRENT DRUGS, LONDON, GB, vol. 5, no. 2, 2002, pages 289 - 295, XP002278729, ISSN: 1367-6733
- [X] WANG S ET AL: "Transgene expression in the brain stem effected by intramuscular injection of polyethylenimine/DNA complexes.", MOLECULAR THERAPY : THE JOURNAL OF THE AMERICAN SOCIETY OF GENE THERAPY. MAY 2001, vol. 3, no. 5 Pt 1, May 2001 (2001-05-01), pages 658 - 664, XP002358454, ISSN: 1525-0016
- [X] YAMAMURA J ET AL: "Long-term gene expression in the anterior horn motor neurons after intramuscular inoculation of a live herpes simplex virus vector", GENE THERAPY, vol. 7, no. 11, June 2000 (2000-06-01), pages 934 - 941, XP002358455, ISSN: 0969-7128
- [X] PALMER J A ET AL: "Development and optimization of herpes simplex virus vectors for multiple long-term delivery to the peripheral nervous system", JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 74, no. 12, June 2000 (2000-06-01), pages 5604 - 5618, XP002164866, ISSN: 0022-538X
- [X] PICKARD GARY E ET AL: "Intravitreal injection of the attenuated pseudorabies virus PRV Bartha results in infection of the hamster suprachiasmatic nucleus only by retrograde transsynaptic transport via autonomic circuits", JOURNAL OF NEUROSCIENCE, vol. 22, no. 7, 1 April 2002 (2002-04-01), pages 2701 - 2710, XP002358460, ISSN: 0270-6474
- [X] MAZARAKIS N D ET AL: "RABIES VIRUS GLYCOPROTEIN PSEUDOTYPING OF LENTIVIRAL VECTORS ENABLES RETROGRADE AXONAL TRANSPORT AND ACCESS TO THE NERVOUS SYSTEM AFTER PERIPHERAL DELIVERY", HUMAN MOLECULAR GENETICS, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 10, no. 19, 15 September 2001 (2001-09-15), pages 2109 - 2121, XP001058914, ISSN: 0964-6906
- [X] SOUDAIS CLAIRE ET AL: "Preferential transduction of neurons by canine adenovirus vectors and their efficient retrograde transport in vivo", FASEB JOURNAL (FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY), BETHESDA, US, vol. 15, no. 12, October 2001 (2001-10-01), pages 2283 - 2285, XP002347771, ISSN: 0892-6638
- [XD] YAN Q ET AL: "Retrograde transport of nerve growth factor (NGF) in motoneurons of developing rats: assessment of potential neurotrophic effects.", NEURON. JUN 1988, vol. 1, no. 4, June 1988 (1988-06-01), pages 335 - 343, XP002358456, ISSN: 0896-6273
- [X] KASSNER P D ET AL: "Genetic selction of phage engineered for receptor-mediated gene transfer to mammalian cells", BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 264, 1999, pages 921 - 928, XP002189963, ISSN: 0006-291X
- [A] KAY M A ET AL: "VIRAL VECTORS FOR GENE THERAPY: THE ART OF TURNING INFECTIOUS AGENTS INTO VEHICLES OF THERAPEUTICS", NATURE MEDICINE, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 7, no. 1, January 2001 (2001-01-01), pages 33 - 40, XP008042487, ISSN: 1078-8956
- [A] BERRY M ET AL: "GENE THERAPY FOR CENTRAL NERVOUS SYSTEM REPAIR", CURRENT OPINION IN MOLECULAR THERAPEUTICS, CURRENT DRUGS, LONDON,, GB, vol. 3, no. 4, August 2001 (2001-08-01), pages 338 - 349, XP009055046, ISSN: 1464-8431

Citation (examination)

- WO 9404695 A1 19940303 - UNIV ROCKEFELLER [US], et al
- See also references of WO 03091387A2

Designated contracting state (EPC)

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LU MC NL PT RO SE SI SK TR

DOCDB simple family (publication)

WO 03091387 A2 20031106; **WO 03091387 A3 20040108**; **WO 03091387 A9 20040226**; CA 2483980 A1 20031106; CA 2483980 C 20130716; EP 1503801 A2 20050209; EP 1503801 A4 20060208; JP 2005535580 A 20051124; JP 2013136586 A 20130711

DOCDB simple family (application)

IB 0302371 W 20030428; CA 2483980 A 20030428; EP 03727872 A 20030428; JP 2003587923 A 20030428; JP 2013010399 A 20130123