Abstract:
A recombinant neurotrophic viral vector is administered to the brain of a subject suffering from a motor neuron disorder, which results in the delivery of the transgene to the brain and the expression of the encoded product in the brain. In one aspect, the invention provides compositions for treating motor neuron disorders, which may include spinal cord injuries and spinal cord disorders. In another aspect, the invention provides techniques for treating the spinal cord, e.g., by administering a recombinant neurotrophic viral vector containing the transgene to the subject's brain.

Inventors/Applicants:  
DODGE, James [US/US]; 1 Gates Circle, Worcester, MA 01603 (US); SHIHABUDDIN, Lamya [US/US]; 1933 Commonwealth Avenue, Brighton, MA 02135 (US); O'RIORDAN, Catherine, R. [US/US]; 17 Wilde Road, Waban, MA 02468 (US).


Published:  
— with international search report  
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments  
— with sequence listing part of description published separately in electronic form and available upon request from the International Bureau

Date of publication of the international search report: 22 May 2008

Title: GENE THERAPY FOR AMYOTROPHIC LATERAL SCLEROSIS AND OTHER SPINAL CORD DISORDERS

Abstract: This disclosure provides methods and compositions for treating disorders or injuries that affect motor function and control in a subject. In one aspect, the invention a transgene product is delivered to a subject's spinal cord by administering a recombinant neurotrophic viral vector containing the transgene to the brain. The viral vector delivers the transgene to a region of the brain which is susceptible to infection by the virus and which expresses the encoded recombinant viral gene product. Also provided are compositions for delivery of a transgene product to a subject's spinal cord by administering a recombinant neurotrophic viral vector containing the transgene to the subject's brain.
INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 07/13391

A  CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C12N 15/00; A01 K 67/027 (2008.01)
USPC - 435/320.1; 800/14

According to International Patent Classification (IPC) or to both national classification and IPC

B  FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC: 435/320.1; 800/14

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Cancer Research. 15 Jan 2001, Vol 61

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST (PGPB, USPT, EPAB, JPAB) amyotrophic lateral sclerosis, ALS, AAV, insulin, growth, factor, vector, transgene, brain, ventricle
esp@cenet: gene, amyotrophic, lateral, Genzyme, insulin growth factor; Google Scholar: transgene, amyotrophic lateral sclerosis, IGF-1,
AAV4, assay, HIV, TAT, IGF-1, ventricle, ALS, transduction

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>X</td>
<td>US 2005/0032219 A1 (AUBOURG et al.) 10 Feb 2005 (10.02.2005); abstract: para [0012], [0016], [0077], [0078], [0083], [0086], [0113], [0146], [0147], [0149], [0196], [0204]</td>
<td>1-6, 8-15, 17-23, 26, 31</td>
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<td>Y</td>
<td>US 2004/0076613 A1 (MAZARAKIS et al.) 22 Apr 2004 (22.04.2004);</td>
<td>7, 16, 24, 29, 30</td>
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<td>X</td>
<td>US 2004/01 10707 A1 (MADEN et al.) 10 Jun 2004 (10.06.2004); para [0007], [0114], [0144]</td>
<td>27 and 28</td>
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</table>

I 1 Further documents are listed in the continuation of Box C.

T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand
the principle or theory underlying the invention

X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive
step when the document is taken alone

Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is
combined with one or more other such documents, such combination being obvious to a person skilled in the art

K" document member of the same patent family

Date of the actual completion of the international search
20 January 2008 (20.01.2008)

Date of mailing of the international search report
10 MAR 2008

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
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Facsimile No 571-273-3201

Authorized officer Lee W. Young
PCT Helpdesk 571-272-4300
PCTOSIP 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2007)
INTERNATIONAL SEARCH REPORT

<table>
<thead>
<tr>
<th>Box No. I</th>
<th>Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>L.J Claims Nos because they relate to subject matter not required to be searched by this Authority, namely</td>
</tr>
<tr>
<td>2</td>
<td>L.J Claims Nos because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically</td>
</tr>
<tr>
<td>3</td>
<td>D Claims Nos because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 64(a)</td>
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<th>Box No. III</th>
<th>Observations where unity of invention is lacking (Continuation of item 3 of first sheet)</th>
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<tr>
<td>This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims</td>
</tr>
<tr>
<td>2</td>
<td>As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees</td>
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<tr>
<td>3</td>
<td>As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos</td>
</tr>
<tr>
<td>4</td>
<td>No required additional search fees were timely paid by the applicant Consequently, this international search report is restricted to the invention first mentioned in the claims, it is covered by claims Nos Claims 1-24 and 26-31</td>
</tr>
</tbody>
</table>

Remark on Protest
- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation
- No protest accompanied the payment of additional search fees
Continuation of Box III: Observations where unity of invention is lacking

Group VI: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to VEGF.

Group VII: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to SMN-1.

Group VIII: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to SMN-2.

Group IX: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to CNTF.

Group X: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to shh.

Group XI: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to EPO.

Group XII: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to LOX.

Group XIII: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to progranulin.

Group XIV: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to prolactin.

Group XV: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to ghrelin.

Group XVI: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to neuroserpin.

Group XVII: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to angiogenin.

Group XVIII: claims 1-3, 5-8, 10-12, 14-17, 19-24 and 26-31, wherein claims 19, 24, 26, 28, 30 and 31 are limited to placenta lactogen.

Group XIX: claims 1, 10 and 31, directed to delivering at least two proteins to a ventricle of the brain. Applicant is invited to make a selection.

The inventions listed as Groups I-XIX do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The technical feature of Groups I-XIX resides in the step of utilizing a transgene product, whereby said transgene is expressed and the expressed protein product is delivered to the spinal cord. However, said common technical feature cannot maintain unity of invention because it is not an improvement over the prior art of Demeneix et al. (US 2005/101552 A1) that teaches administering to a ventricle of the brain a viral vector encoding a protein, having tropism for neurons.

In addition, IGF-1, calbindin D28, paravalbumin, HIF1-alpha, SIRT-2, VEGF, SMN-1, SMN-2, CNTF, shh, EPO, LOX, progranulin, prolactin, ghrelin, neuroserpin, angiogenin and lactogen would be regarded as having the same or corresponding technical feature if they had a common property or activity, and shared a significant structural element that is essential to the common property or activity. There is no teaching as to a common property or a shared significant structural element, and hence, there is no disclosure of the same or corresponding technical feature. None of these technical features are common to the other groups, nor do they correspond to a special technical feature in the other groups. Therefore, unity of invention is lacking.