

PHARMACEUTICAL PATENT ATTORNEYS, LLC

www.LicensingLaw.Net

55 Madison Avenue, 4th floor
Morristown, NJ 07960-7397 USA

Practice limited to Domestic & International
Pharmaceutical Patent law

SELECTED CELL AND GENE THERAPY PATENTS

PHARMACEUTICAL PATENT ATTORNEYS, LLC

+1 (973) 984 6159



US 20170016028A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2017/0016028 A1**
YLA-HERTTUALA et al. (43) **Pub. Date: Jan. 19, 2017**

(54) **PRODUCTION OF LENTIVIRAL VECTORS**

(30) **Foreign Application Priority Data**

(71) Applicant: **FinVector Vision Therapies Ltd.**,
Kuopio (FI)

Feb. 12, 2007 (GB) 07/02695.8

(72) Inventors: **Seppo YLA-HERTTUALA**, Kuopio (FI); **Kari J. AIRENNE**, Kuopio (FI);
Hanna P. LESCH, Kuopio (FI)

Publication Classification

(51) **Int. Cl.**
C12N 15/86 (2006.01)
C12N 7/00 (2006.01)

(73) Assignee: **FinVector Vision Therapies Ltd.**,
Kuopio (FI)

(52) **U.S. Cl.**
CPC **C12N 15/86** (2013.01); **C12N 7/00**
(2013.01); **C12N 2710/14021** (2013.01); **C12N**
2710/14043 (2013.01); **C12N 2740/15043**
(2013.01); **C12N 2740/15051** (2013.01); **A61K**
48/00 (2013.01)

(21) Appl. No.: **15/221,265**

(22) Filed: **Jul. 27, 2016**

Related U.S. Application Data

(60) Division of application No. 14/862,731, filed on Sep. 23, 2015, which is a continuation of application No. 12/522,646, filed on Jul. 9, 2009, filed as application No. PCT/GB2008/000464 on Feb. 12, 2008.

(57) **ABSTRACT**

A high-volume gene therapy vector manufacturing process which produces a recombinant gene therapy vector which is able to transform host cells even when they are not dividing.



US009439977B2

(12) **United States Patent**
Benedict(10) **Patent No.:** **US 9,439,977 B2**(45) **Date of Patent:** **Sep. 13, 2016**(54) **METHODS AND COMPOSITIONS FOR TREATMENT OF INTERFERON-RESISTANT TUMORS**2005/0025742 A1 2/2005 Engler et al.
2005/0287119 A1 12/2005 Benedict
2006/0199782 A1 9/2006 Engler et al.
2007/0249043 A1 10/2007 Mayall(75) Inventor: **William F. Benedict**, The Woodlands, TX (US)

FOREIGN PATENT DOCUMENTS

(73) Assignee: **FKD Therapies Oy**, Kuopio (FI)EP 0331635 A2 8/1989
WO WO 97/05209 A1 2/1997
WO WO 97/25072 A1 7/1997
WO WO 98/17801 A1 4/1998
WO WO 03/053365 A2 7/2003
WO WO 03/053365 A3 7/2003
WO WO 03/073998 A2 9/2003
WO WO 03/073998 A3 9/2003

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 1494 days.

(21) Appl. No.: **12/706,625**

OTHER PUBLICATIONS

(22) Filed: **Feb. 16, 2010**(65) **Prior Publication Data**

US 2010/0266547 A1 Oct. 21, 2010

Related U.S. Application Data

(63) Continuation of application No. 11/009,689, filed on Dec. 10, 2004, now Pat. No. 7,691,822.

(60) Provisional application No. 60/528,525, filed on Dec. 10, 2003.

(51) **Int. Cl.****C12N 15/11** (2006.01)
A61K 48/00 (2006.01)
A61K 9/00 (2006.01)
A61K 9/127 (2006.01)
A61K 38/21 (2006.01)
C07K 14/56 (2006.01)
C12N 15/86 (2006.01)(52) **U.S. Cl.**CPC **A61K 48/0008** (2013.01); **A61K 9/0034** (2013.01); **A61K 9/1271** (2013.01); **A61K 38/212** (2013.01); **A61K 48/00** (2013.01); **C07K 14/56** (2013.01); **C12N 15/86** (2013.01); **C12N 2710/10343** (2013.01)(58) **Field of Classification Search**CPC C12N 15/11
See application file for complete search history.(56) **References Cited**

(Continued)

U.S. PATENT DOCUMENTS

5,120,316 A 6/1992 Morales et al.
5,552,309 A 9/1996 March
5,602,023 A 2/1997 Csatory
5,789,244 A 8/1998 Heidrun et al.
5,804,566 A 9/1998 Carson et al.
6,066,624 A 5/2000 Woo et al.
6,165,779 A 12/2000 Engler et al.
6,207,454 B1 3/2001 Zsebo et al.
6,210,939 B1 4/2001 Gregory et al.
6,312,681 B1 11/2001 Engler et al.
6,392,069 B2 5/2002 Engler et al.
7,002,027 B1 2/2006 Engler et al.
7,355,056 B2 4/2008 Connor et al.
7,534,769 B2 5/2009 Engler et al.
2002/0111502 A1 8/2002 Engler et al.
2003/0170216 A1 9/2003 Ihnat et al.
2003/0211598 A1 11/2003 Engler et al.
2004/0014709 A1 1/2004 Engler et al.Torti et al. (J. Clin. Oncol. 1988; 6(3):476-83).
Hand et al. (Anticancer Drugs 1993; 4(3):365-8).
Adam, Liana, et al. "Adenoviral Mediated Interferon- α 2b Gene Therapy Suppresses the Pro-Angiogenic Effect of Vascular Endothelial Growth Factor in Superficial Bladder Cancer," The Journal of Urology, 2007, vol. 177, pp. 1900-1906.
Ahmed et al., *Cancer Gene Therapy*, 8(10):788-795 (2001).
Ahmed et al., *Hum. Gene Ther.*, 10:77-78 (1999).
Ahmed et al., *Journal of Interferon and Cytokine Research*, 21(6):399-408 (2001).
Associated Press, "One Way to Kill Cancer: Give a Cold," *The Augusta Chronicle*, May 20, 1997, accessed by PTO at <http://www.cnn.com> on May 22, 1997.
Belldegrun et al., *J. Urol.*, 159:1793-1801 (1998).
Benedict et al., *Molecular Therapy*, 10(3):525-532 (2004).
Chester, J.D. et al., "Adenovirus-mediated gene therapy for bladder cancer: efficient gene delivery to normal and malignant human urothelial cells in vitro and ex vivo," *Gene Therapy*, 2003, vol. 10, pp. 172-179.
Connor et al., *Gene Ther.*, 8:41-48 (2001).
Croyle, M.A. et al., "Development of formulations that enhance physical stability of viral vectors for gene therapy," *Gene Therapy*, 2001, vol. 8, pp. 1281-1290.
Crystal, R.G. et al., "Transfer of Genes to Humans: Early Lessons and Obstacles to Success," *Science*, 1995, vol. 270, pp. 404-410.
Culver, K.W. et al., "Gene Therapy for Cancer," *Trends in Genetics*, May 1994, vol. 10, No. 5, pp. 174-178.
Dalbagni et al., *Urol. Clin. North Am.*, 27(1):137-146 (2000).
Freedmann, T., "Gene Therapy of Cancer Through Restoration of Tumor-Suppressor Functions?" *Cancer*, 1992, vol. 70, pp. 1810-1817.*Primary Examiner* — Jon E Angell(74) *Attorney, Agent, or Firm* — Pharmaceutical Patent Attorneys, LLC(57) **ABSTRACT**

The present invention provides a method for the treatment of interferon resistant tumors through the use of recombinant vectors encoding interferon species. In particular it is noted that interferon species provided by recombinant vectors possesses properties not associated with the recombinantly produced interferon proteins. The present invention further provides compositions useful in the treatment of interferon resistant tumors using recombinant vectors encoding interferons.

13 Claims, 5 Drawing Sheets



US 20160097060A1

(19) **United States**

(12) **Patent Application Publication**
LESCH et al.

(10) **Pub. No.: US 2016/0097060 A1**

(43) **Pub. Date: Apr. 7, 2016**

(54) **PRODUCTION OF VECTORS FOR
NON-DIVIDING HOST CELLS**

Publication Classification

(71) Applicant: **FinVector Vision Therapies Ltd.**,
Kuopio (FI)

(51) **Int. Cl.**
C12N 15/86 (2006.01)

(72) Inventors: **Hanna P. LESCH**, Kuopio (FI); **Kari J. Airene**, Kuopio (FI); **Seppo Yla-Herttuala**, Kuopio (FI)

(52) **U.S. Cl.**
CPC **C12N 15/86** (2013.01); **C12N 2710/14051** (2013.01); **A61K 48/00** (2013.01)

(73) Assignee: **FinVector Vision Therapies Ltd.**,
Kuopio (FI)

(57) **ABSTRACT**

(21) Appl. No.: **14/862,731**

(22) Filed: **Sep. 23, 2015**

Related U.S. Application Data

(63) Continuation of application No. 12/522,646, filed on Jul. 9, 2009, filed as application No. PCT/GB2008/000464 on Feb. 11, 2008.

A high-volume gene therapy vector manufacturing process, entailing using a recombinant baculovirus to transform a producer cell, which producer cell in turn produces a recombinant gene therapy vector which is able to transform host cells even when they are not dividing.



- (51) International Patent Classification:
C12N 5/00 (2006.01)
- (21) International Application Number:
PCT/US2015/046927
- (22) International Filing Date:
26 August 2015 (26.08.2015)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
GB1417042.7 25 September 2014 (25.09.2014) GB
- (71) Applicant: FINVECTOR VISION THERAPIES OY [FI/FI]; Mocrokatu 1 S, FI-70210 Kuopio (FI).
- (71) Applicant (for US only): PHARMACEUTICAL PATENT ATTORNEYS, LLC [US/US]; 55 Madison Avenue, 4th Floor, Morristown, NJ 07960 (US).
- (72) Inventors: LESCH, Hanna, P.; Mocrokatu 1 S, FI-70210 Kuopio (FI). KARHINEN, Minna; Mocrokatu 1 S, FI-70210 Kuopio (FI). HASSINEN, Minna; Mocrokatu 1 S, FI-70210 Kuopio (FI). SHAW, Robert; Mocrokatu 1 S,

FI-70210 Kuopio (FI). PARKER, Nigel; 38 Oakley Road, Chinnor, Oxfordshire OX39 4TW (GB). YLA-HERTTU-ALA, Seppo; Mocrokatu 1 S, FI-70210 Kuopio (FI).

- (74) Agent: POHL, Mark; Pharmaceutical Patent Attorneys, LLC, 55 Madison Avenue, 4th Floor, Morristown, NJ 07960-7397 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE,

[Continued on next page]

(54) Title: SEEDING AN ADHERENT CELL BIOREACTOR WITH NON-ADHERENT CELLS INCREASES SEEDING DENSITY LIMIT AND REDUCES REQUIRED EXPANSION TIME

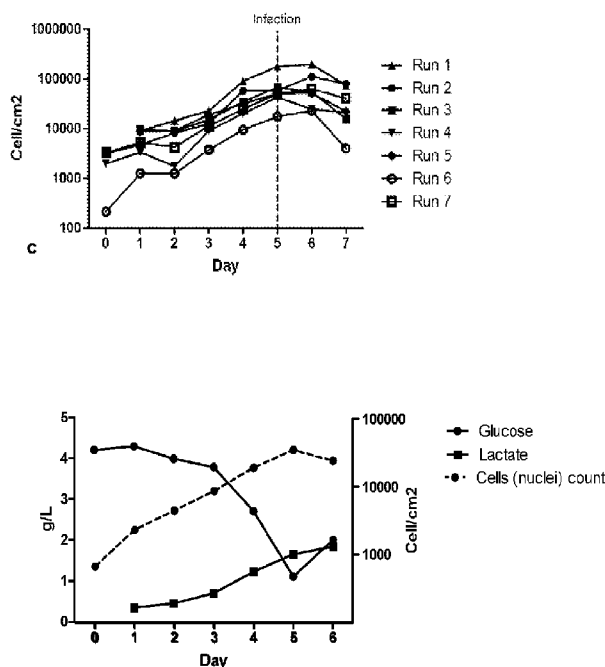


Figure 2.

(57) Abstract: We have found a counter-intuitive way to improve the commercial-scale production of recombinant biological products in adherent-cell bioreactors, which reduces the risk of cell culture contamination, increases total yield and reduces the delay between seeding and harvest, thus minimizing expression product degradation, by inter alia inoculating an adherent culture bioreactor with suspension-adapted producer cells.

WO 2016/048556 A1



US 20160045618A1

(19) **United States**

(12) **Patent Application Publication**
BENEDICT

(10) **Pub. No.: US 2016/0045618 A1**

(43) **Pub. Date: Feb. 18, 2016**

(54) **METHODS AND COMPOSITIONS FOR TREATMENT OF INTERFERON-RESISTANT TUMORS**

(71) Applicant: **FKD Therapies Oy**, Kuopio (FI)

(72) Inventor: **William F. BENEDICT**, The Woodlands, TX (US)

(73) Assignee: **FKD Therapies Oy**, Kuopio (FI)

(21) Appl. No.: **14/924,136**

(22) Filed: **Oct. 27, 2015**

Related U.S. Application Data

(63) Continuation of application No. 12/706,625, filed on Feb. 16, 2010, which is a continuation of application No. 11/009,689, filed on Dec. 10, 2004, now Pat. No. 7,691,822.

(60) Provisional application No. 60/528,525, filed on Dec. 10, 2003.

Publication Classification

(51) **Int. Cl.**
A61K 48/00 (2006.01)
A61K 38/21 (2006.01)
C07K 14/56 (2006.01)

(52) **U.S. Cl.**
CPC *A61K 48/0008* (2013.01); *C07K 14/56* (2013.01); *A61K 38/212* (2013.01)

(57) **ABSTRACT**

The present invention provides a method for the treatment of interferon resistant bladder tumors through the use of a non-replicating agent which induces human cells to express interferon species. In particular it is noted that inducing interferon expression in the patient's body possesses properties not associated with recombinant produced, intravenously-administered interferon proteins. The present invention further provides compositions useful in the treatment of bladder cancer resistant to treatment with intravenous interferon polypeptide, by using a non-replicating agent which induces human cells to express interferon species, e.g., an antigenic, replication-deficient virus optionally carrying an interferon transgene.



(51) International Patent Classification:

A61K 33/24 (2006.01) A61K 35/76 (2006.01)
A61K 31/282 (2006.01)

(21) International Application Number:

PCT/US2014/044809

(22) International Filing Date:

30 June 2014 (30.06.2014)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

13/932,202 1 July 2013 (01.07.2013) US
14/030,399 18 September 2013 (18.09.2013) US

(71) Applicant: FKD HOLDING OY [FI/FI]; Microkatu 1S,
FI-70210 Kuopio (FI).

(71) Applicant (for US only): PHARMACEUTICAL PAT-
ENT ATTORNEYS, LLC [US/US]; 55 Madison Ave.,
4th Floor, Morristown, NJ 07960 (US).

(72) Inventors; and

(71) Applicants : PARKER, Nigel [GB/GB]; 88 Edgware
Way, Edgware, Middlesex HA8 8JS (GB). YLA-
HERTTUALA, Seppo [FI/FI]; Helminauha 18, FI-70840
Kuopio (FI).

(74) Agent: POHL, Mark J.; Pharmaceutical Patent Attorneys,
LLC, 55 Madison Ave. 4th Floor, Morristown, New Jersey
07960 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to the identity of the inventor (Rule 4.17(i))
- as to applicant's entitlement to apply for and be granted a
patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the
earlier application (Rule 4.17(iii))

Published:

- with international search report (Art. 21(3))
- with amended claims and statement (Art. 19(1))

(54) Title: TRANSFECTION OF MESOTHELIUM BODY CAVITY LINING WITH GENE AGENTS PRIOR TO CHEMOTHER-
APY TO TREAT CANCER

(57) Abstract: Treating cancer of an organ located in a mesothelium-lined body cavity (i.e., lung, kidney, adrenal gland, ovary, pro-
state, pancreas or bladder cancer) by irrigating the mesothelium-lined body cavity with a solution containing a recombinant viral
gene therapy vector bearing an interferon transgene, optionally administered shortly before administering chemotherapy and / or
COX-2 inhibitor.



WO 2015/002861 A1



US 20140121160A1

(19) **United States**

(12) **Patent Application Publication**
MARTIN et al.

(10) **Pub. No.: US 2014/0121160 A1**

(43) **Pub. Date: May 1, 2014**

(54) **USE OF VEGF IN THE TREATMENT OF
RETARDED FETAL GROWTH IN
PREGNANCY**

Publication Classification

(71) Applicants: **John Francis MARTIN, (US); Charles
Henry RODECK, (US)**

(51) **Int. Cl.**
A61K 48/00 (2006.01)
A61K 38/18 (2006.01)
A61P 15/00 (2006.01)
A61K 38/17 (2006.01)

(72) Inventors: **John Francis MARTIN, (US); Charles
Henry RODECK, (US)**

(52) **U.S. Cl.**
USPC **514/8.1; 514/44 R**

(21) Appl. No.: **13/662,793**

(57) **ABSTRACT**

(22) Filed: **Oct. 29, 2012**

An agonist of the VEGF receptor is useful in the treatment of a disease associated with retarded fetal growth, such as intra-uterine growth retardation. The VEGF agonist may be a VEGF peptide or a gene construct encoding or expressing such a PI-peptide.



US 20140057851A1

(19) **United States**

(12) **Patent Application Publication**
YLA-HERTTUALA

(10) **Pub. No.: US 2014/0057851 A1**

(43) **Pub. Date: Feb. 27, 2014**

(54) **ANTI-ANGIOGENIC GENE THERAPY WITH SOLUBLE VEGF RECEPTORS -1, -2 AND -3 TOGETHER WITH PACLITAXEL PROLONGS SURVIVAL OF MICE WITH HUMAN OVARIAN CARCINOMA**

(52) **U.S. Cl.**
CPC *A61K 38/179* (2013.01); *A61K 31/337* (2013.01)
USPC **514/19.3; 514/44 R**

(71) Applicant: **Seppo YLA-HERTTUALA**, Kuopio (FI)

(57) **ABSTRACT**

(72) Inventor: **Seppo YLA-HERTTUALA**, Kuopio (FI)

(73) Assignee: **WKD Holding Oy**, Kuopio (FI)

(21) Appl. No.: **13/969,763**

(22) Filed: **Aug. 19, 2013**

Related U.S. Application Data

(60) Provisional application No. 61/692,828, filed on Aug. 24, 2012.

Publication Classification

(51) **Int. Cl.**
A61K 38/17 (2006.01)
A61K 31/337 (2006.01)

Anti-angiogenic gene therapy with a combination of soluble Vascular Endothelial Growth Factors (sVEGFR) improves the efficacy of chemotherapy with paclitaxel for reducing ovarian cancer mean tumor volume (in cubic millimetres) as measured using magnetic resonance imaging. The study groups were: AdLacZ control, combination of AdsVEGFR-1, -2 and -3, combination of AdsVEGFR-1, -2, -3 and paclitaxel, bevacizumab monotherapy, paclitaxel monotherapy and carboplatin monotherapy. Effectiveness was assessed by survival time and surrogate measures such as sequential MRI, immunohistochemistry, microvessel density and tumor growth. Antiangiogenic gene therapy combined with paclitaxel significantly prolonged the mean survival compared to the controls and all other treatment groups (p=0.001). Tumors of the mice treated by gene therapy were significantly smaller than in the control group (p=0.021). The mean vascular density and total vascular area were also significantly smaller in the tumors of the gene therapy group (p=0.01).



US 20140017202A1

(19) **United States**

(12) **Patent Application Publication**
PARKER et al.

(10) **Pub. No.: US 2014/0017202 A1**

(43) **Pub. Date: Jan. 16, 2014**

(54) **TRANSFECTION OF MESOTHELIUM BODY CAVITY LINING WITH GENE AGENTS FOLLOWED BY CHEMOTHRAPY TO TREAT CANCER OF ORGANS IN THE BODY CAVITY**

(71) Applicants: **Nigel PARKER**, Edgware (GB); **Seppo YLA-HERTTUALA**, Kuopio (FI)

(72) Inventors: **Nigel PARKER**, Edgware (GB); **Seppo YLA-HERTTUALA**, Kuopio (FI)

(73) Assignee: **WKD HOLDING OY**, Kuopio (FI)

(21) Appl. No.: **13/932,202**

(22) Filed: **Jul. 1, 2013**

Related U.S. Application Data

(60) Provisional application No. 61/670,330, filed on Jul. 11, 2012.

Publication Classification

(51) **Int. Cl.**
A61K 35/76 (2006.01)
A61K 31/415 (2006.01)
A61K 31/519 (2006.01)
A61K 31/7068 (2006.01)
A61K 33/24 (2006.01)
A61K 31/282 (2006.01)

(52) **U.S. Cl.**
 CPC *A61K 35/761* (2013.01); *A61K 33/24* (2013.01); *A61K 31/282* (2013.01); *A61K 31/519* (2013.01); *A61K 31/7068* (2013.01); *A61K 31/415* (2013.01)
 USPC **424/93.2**

(57) **ABSTRACT**

Treating cancer of a organ located in a mesothelium-lined body cavity (i.e., lung, kidney, adrenal gland, ovary, prostate, pancreas or bladder cancer) by irrigating the mesothelium-lined body cavity with a solution containing a recombinant viral gene therapy vector bearing an interferon transgene, optionally administered shortly before administering chemotherapy and/or COX-2 inhibitor.



US 20140017204A1

(19) **United States**

(12) **Patent Application Publication**
PARKER et al.

(10) **Pub. No.: US 2014/0017204 A1**

(43) **Pub. Date: Jan. 16, 2014**

(54) **TRANSFECTION OF MESOTHELIUM BODY CAVITY LINING WITH GENE AGENTS FOLLOWED BY CHEMOTHRAPY TO TREAT CANCER OF ORGANS IN THE BODY CAVITY**

(71) Applicants: **Nigel PARKER**, Edgware (GB); **Seppo YLA-HERTTUALA**, Kuopio (FI)

(72) Inventors: **Nigel PARKER**, Edgware (GB); **Seppo YLA-HERTTUALA**, Kuopio (FI)

(73) Assignee: **WKD Holding Oy**, Kuopio (FI)

(21) Appl. No.: **14/030,399**

(22) Filed: **Sep. 18, 2013**

Related U.S. Application Data

(63) Continuation of application No. 13/932,202, filed on Jul. 1, 2013.

(60) Provisional application No. 61/670,330, filed on Jul. 11, 2012.

Publication Classification

(51) **Int. Cl.**

A61K 38/21 (2006.01)
A61K 31/555 (2006.01)
A61K 45/06 (2006.01)
A61K 39/395 (2006.01)
A61K 31/337 (2006.01)
A61K 31/415 (2006.01)

(52) **U.S. Cl.**

CPC *A61K 38/212* (2013.01); *A61K 31/337* (2013.01); *A61K 31/415* (2013.01); *A61K 45/06* (2013.01); *A61K 39/395* (2013.01); *A61K 31/555* (2013.01)
USPC **424/93.2**

(57)

ABSTRACT

Treating cancer of a organ located in a mesothelium-lined body cavity (i.e., lung, kidney, adrenal gland, ovary, prostate, pancreas or bladder cancer) by irrigating the mesothelium-lined body cavity with a solution containing a recombinant viral gene therapy vector bearing an interferon transgene, optionally administered shortly before administering chemotherapy and/or COX-2 inhibitor.



US008334271B2

(12) **United States Patent**
Martin et al.

(10) **Patent No.:** **US 8,334,271 B2**

(45) **Date of Patent:** **Dec. 18, 2012**

(54) **USE OF VEGF IN THE TREATMENT OF
RETARDED FETAL GROWTH IN
PREGNANCY**

FOREIGN PATENT DOCUMENTS

WO WO 2006/034507 A 3/2006

OTHER PUBLICATIONS

(75) Inventors: **John Francis Martin**, London (GB);
Charles Henry Rodeck, London (GB)

Vandenbosche et al (American Family Physician, Oct. 15, 1998, p. 1-8.*

(73) Assignee: **Ark Therapeutics, Ltd.**, London (GB)

Simmons 2001, Diabetes, 50:2279-2286.*

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 239 days.

Abstracts-Friday, *Journal of the Society for Gynecologic Investigation*, Feb. 2006, pp. 228A, vol. 13, No. 2.

(21) Appl. No.: **12/522,640**

Barry et al., "The pregnant sheep as a model for human pregnancy," *Theriogenology*, Nov. 5, 2007, pp. 55-67, vol. 69, No. 1.

(22) PCT Filed: **Feb. 22, 2008**

Boulanger et al., "Avances recentes dans la comprehension de la physiopathologie de la preeclampsia et consequences therapeutiques potentielles," *Nephrologie & Therapeutique*, Nov. 26, 2007, pp. 437-448, vol. 3, No. 7, English Abstract.

(86) PCT No.: **PCT/GB2008/000613**

§ 371 (c)(1),
(2), (4) Date: **Sep. 11, 2009**

Brownbill, P., et al., "Vasoactive and permeability effects of vascular endothelial growth factor-165 in the term in vitro dually perfused human placental lobule," *Endocrinology*, Oct. 2007, pp. 4734-4744, vol. 148, No. 10.

(87) PCT Pub. No.: **WO2008/104747**

PCT Pub. Date: **Sep. 4, 2008**

Karkkainen, Marika J., et al., "Vascular endothelial growth factor receptors in the regulation of angiogenesis and lymphangiogenesis," *Oncogene*, Nov. 20, 2000, pp. 5598-5608, vol. 19, No. 49.

(65) **Prior Publication Data**

US 2010/0249015 A1 Sep. 30, 2010

Maynard, Sharon E., et al., "Excess placental soluble fms-like tyrosine kinase 1 (sFlt1) may contribute to endothelial dysfunction hypertension, and proteinuria in preeclampsia" *Journal of Clinical Investigation*, Mar. 2003, pp. 649-658, vol. 111, No. 5.

(30) **Foreign Application Priority Data**

Feb. 26, 2007 (GB) 0703683.3

Szukiewicz, Dariusz et al., "Isolated placental vessel response to vascular endothelial growth factor and placenta growth factor in normal and growth-restricted pregnancy" *Gynecologic and Obstetric Investigation*, Dec. 9, 2004, pp. 102-107, vol. 59, No. 2.

* cited by examiner

(51) **Int. Cl.**

A61K 48/00 (2006.01)
C07H 21/04 (2006.01)
C12N 15/00 (2006.01)

Primary Examiner — Valarie Bertoglio

(74) *Attorney, Agent, or Firm* — Pharmaceutical Patent Attorneys, LLC

(52) **U.S. Cl.** **514/44 R**; 536/23.1; 435/455

(58) **Field of Classification Search** 514/44 R
See application file for complete search history.

(57) **ABSTRACT**

An agonist of the VEGF receptor is useful in the treatment of a disease associated with retarded fetal growth, such as intra-uterine growth retardation. The VEGF agonist may be a VEGF peptide or a gene construct encoding or expressing such a peptide.

(56) **References Cited**

U.S. PATENT DOCUMENTS

7,030,083 B2 4/2006 Schreiner et al.
2004/0126828 A1 7/2004 Karumanchi et al.

3 Claims, No Drawings



US008188039B2

(12) **United States Patent**
Toivanen et al.

(10) **Patent No.:** **US 8,188,039 B2**
(45) **Date of Patent:** **May 29, 2012**

(54) **VEGF-D MUTANTS AND THEIR USE**

(75) Inventors: **Pyry Toivanen**, Kuopio (FI); **Kari Juhani Airene**, Kuopio (FI); **Seppo Yla-Herttuala**, Kuopio (FI)

(73) Assignee: **Ark Therapeutics Group, plc**, London (GB)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 124 days.

(21) Appl. No.: **12/599,294**

(22) PCT Filed: **Jun. 2, 2008**

(86) PCT No.: **PCT/GB2008/001873**

§ 371 (c)(1),

(2), (4) Date: **Aug. 20, 2010**

(87) PCT Pub. No.: **WO2008/146023**

PCT Pub. Date: **Dec. 4, 2008**

(65) **Prior Publication Data**

US 2011/0144013 A1 Jun. 16, 2011

(30) **Foreign Application Priority Data**

May 31, 2007 (GB) 0710457.3

(51) **Int. Cl.**

A61K 388/18 (2006.01)

C07K 14/475 (2006.01)

C12N 15/18 (2006.01)

(52) **U.S. Cl.** **514/8.1; 435/69.1; 536/23.5; 530/399**

(58) **Field of Classification Search** None
See application file for complete search history.

(56) **References Cited**

PUBLICATIONS

Achen, M. G. et al. "Vascular endothelial growth factor D (VEGF-D) is a ligand for the tyrosine VEGF receptor 2 (FLK1) receptor 3

(FLT4)" *Proceedings of the National Academy of Sciences of USA, National Academy of Science*, Washington DC, 1998, pp. 548-553, vol. 95, No. 2.

Claffey, K. P. et al. "Structural Requirements for dimerization, glycosylation, secretion, and biological function of VPF/VEGF" *Biochimica et biophysica acta. Biomembranes*, Amsterdam, NL, 1995, pp. 1-09, vol. 1246.

Kirkin, V. et al. "Characterization of indolinones which preferentially inhibit VEGF-C and VEGF-D induced activation of VEGF-3 rather than VEGFR-2" *European Journal of Biochemistry, Berlin*, 2001, pp. 5530-5540, vol. 268.

McCull, B. K. et al. "Proprotein convertases promote processing of VEGF-D a critical step for binding the angiogenic receptor VEGFR-2" *The FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology*, 2007, pp. 1088-1098, vol. 21, No. 4.

Rissanen, T. T. et al. "VEGF-D is the strongest angiogenic and lymphangiogenic effector among VEGFs delivered into skeletal muscle via adenoviruses" *Circulation Research*, 2003, pp. 1098-1106, vol. 92, No. 10.

Roy of al, "Biology of vascular endothelial growth factors" *FEBS Letters, Elsevier, Amsterdam, NL*, pp. 2879-2887, vol. 580, No. 12.

Stacker, S. et al. "Biosynthesis of vascular endothelial growth factor-D involves generates non-covalent homodimers" *Journal of Biological Chemistry, American Society of Biochemical Biologists, Birmingham*, 1999, pp. 32127-32136, vol. 274 No. 45.

Walsh, T. P. et al. "Computer modelling of the receptor-binding domains of VEGF and PIGF" *Protein Engineering, Oxford University Press, Surrey*, 1997, pp. 389-398, vol. 10, No. 4.

Primary Examiner — Christine J Saoud

(74) *Attorney, Agent, or Firm* — Pharmaceutical Patent Attorneys, LLC

(57) **ABSTRACT**

The present invention is a VEGF-D protein, containing one or more amino acid mutations at the dimer interface, and their use in therapy, particularly in the promotion of angiogenesis.

8 Claims, 2 Drawing Sheets