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CENTRO DE
INGENIERÍA GENÉTICA
Y BIOTECNOLOGÍA

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EP 1 466 617 B1

(12)

EUROPEAN PATENT SPECIFICATION

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of the grant of the patent:
18.02.2009 Bulletin 2009/08

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(51) Int Cl.:
A61K 38/18^(2006.01) C07K 14/485^(2006.01)

(86) International application number:
PCT/CU2002/000011

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WO 2003/053458 (03.07.2003 Gazette 2003/27)

(54) **USE OF A PHARMACEUTICAL COMPOSITION CONTAINING EPIDERMAL GROWTH FACTOR (EGF) FOR DIABETIC FOOT AMPUTATION PREVENTION**

VERWENDUNG EINER EPIDERMALEN WACHSTUMSFAKTOR (EGF) ENTHALTENDEN
PHARMAZEUTISCHEN ZUSAMMENSETZUNG ZUR VERMEIDUNG EINER FUSSAMPUTATION
BEI DIABETES

UTILISATION D'UNE COMPOSITION PHARMACEUTIQUE CONTENANT LE FACTEUR DE
CROISSANCE EPIDERMIQUE (EGF) POUR LA PREVENTION DE L'AMPUTATION DU PIED
DIABETIQUE

(84) Designated Contracting States:
**AT BE BG CH CY CZ DE DK EE ES FI FR GB GR
IE IT LI LU MC NL PT SE SI SK TR**
Designated Extension States:
AL LT LV MK RO

(30) Priority: **20.12.2001 CU 30801**

(43) Date of publication of application:
13.10.2004 Bulletin 2004/42

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EP 1 466 617 B1



US007465704B2

(12) **United States Patent**
Berlanga Acosta et al.

(10) **Patent No.:** **US 7,465,704 B2**
(45) **Date of Patent:** **Dec. 16, 2008**

(54) **METHODS FOR ENHANCING HEALING OF
DIABETIC FOOT ULCERS BY INJECTING
EPIDERMAL GROWTH FACTOR (EGF)**

(75) Inventors: **Jorge Berlanga Acosta**, Playa, Ciudad de la Habana (CU); **José I Fernández Montequin**, Amargura 318 entre Aguacate y Compostela, Habana Vieja, Ciudad de la Habana (CU); **Calixto Valdés Pérez**, Playa, Ciudad de la Habana (CU); **Neobalis Franco Pérez**, Marianao, Ciudad del al Habana (CU); **Ingrid Rojas Constantin**, Playa, Ciudad de la Habana (CU); **Héctor Santana Milián**, Playa, Ciudad de la Habana (CU); **Larissa Chacón Corvea**, Playa, Ciudad de la Habana (CU); **Gerardo E. Guillén Nieto**, Plaza de la Revolución, Ciudad de la Habana (CU); **Luis Herrera Martínez**, Playa, Ciudad de la Habana (CU); **Leonardo Canan-Haden Frías**, Playa, Ciudad de la Habana (CU); **Haydee Gerónimo Pérez**, Playa, Ciudad de la (CU); **Jorge Sotolongo Pena**, Playa, Ciudad de la (CU)

(73) Assignee: **Centro de Ingeniera Genetica y Biotecnologia**, Ciudad de la Habana (CU)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 237 days.

(21) Appl. No.: **10/499,457**

(22) PCT Filed: **Dec. 4, 2002**

(86) PCT No.: **PCT/CU02/00011**

§ 371 (c)(1),
(2), (4) Date: **Jan. 7, 2005**

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US 2005/0107294 A1 May 19, 2005

(30) **Foreign Application Priority Data**

Dec. 20, 2001 (CU) 0308/01

(51) **Int. Cl.**
A61K 38/18 (2006.01)
C07K 14/485 (2006.01)

(52) **U.S. Cl.** **514/12; 530/399**

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

(56) **References Cited**

U.S. PATENT DOCUMENTS

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Brown G. L. et al., "Enhancement of Epidermal Regeneration by Biosynthetic Epidermal Growth Factor", *The Journal of Experimental Medicine* (1986), 163(5):1319-1324.

Hogge J. et al., "The Potential Benefits of Advanced Therapeutic Modalities in the Treatment of Diabetic Foot Wounds", *J. American Podiatric Med. Assoc.*(2000), 90(2):57-65.

Zhu Xier et al., "Studies on Enhancing the Repair of Gangrenous Skin Diabetic Foot by Epidermal Growth Factor", *5th China-Japan Symposium on Diabetes Mellitus* (1997), 1141:241-243.

English Translation of Zhu et al., "Clinical Studies on Enhancing the Repair of Gangrenous Skin of Diabetic Foot by Epidermal Growth Factor," *Natl. Med. J. China.*, 1996, 76:862.

* cited by examiner

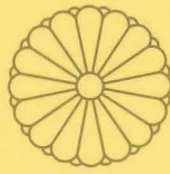
Primary Examiner—Marianne P Allen

(74) *Attorney, Agent, or Firm*—Hoffman & Baron, LLP

(57) **ABSTRACT**

The invention relates to the use of Epidermal Growth Factor (EGF) in a preferably-injectable pharmaceutical composition which is administered by means of infiltration into and around chronic cutaneous ischaemic lesions in order to prevent diabetic foot amputation. Said composition can be administered to recently-created surgical surfaces damaged by the effect of acute reperfusion with oxygenated blood following prolonged ischaemia, thereby preventing further surgical procedures and favouring the preservation of the extremity. The aforementioned composition can be used to improve (i) the cell microenvironment, thereby increasing the reparative and defensive capacity and viability of the tissues and (ii) the cicatrization of cutaneous ischaemic lesions, thereby stimulating cell proliferation. The invention is suitable for use in human, veterinary and experimental medicine, specifically in vascular angiology and surgery, dermatology, burn treatment and reconstructive surgery and geriatric medicine. Said composition can be used for recalcitrant ulcers which are associated with lesions in the macro and/or microvasculature, patients with inadequate lymphatic and/or venous return and ulcers or other lesions which are difficult to cicatrize and/or heal.

19 Claims, No Drawings



特 許 証

(CERTIFICATE OF PATENT)

特許第4808378号
(PATENT NUMBER)

発明の名称
(TITLE OF THE INVENTION)

上皮増殖因子 (EGF) を包含する医薬組成物
を用いた、糖尿病における下肢切断の予防方法

特許権者
(PATENTEE)

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タメント デ パテンテス (番地なし)
国籍 キューバ共和国
セントロ デ インヘニエリア ヘネ
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フェルナンデス モンテキン, ホセ
イー.
バルデス ペレス, カリクスト

その他別紙記載

出願番号
(APPLICATION NUMBER)

特願2003-554215

出願日
(FILING DATE)

平成14年12月 4日 (December 4, 2002)

登録日
(REGISTRATION DATE)

平成23年 8月26日 (August 26, 2011)

この発明は、特許するものと確定し、特許原簿に登録されたことを証する。
(THIS IS TO CERTIFY THAT THE PATENT IS REGISTERED ON THE REGISTER OF THE JAPAN PATENT OFFICE.)

平成23年 8月26日 (August 26, 2011)

特許庁長官
(COMMISSIONER, JAPAN PATENT OFFICE)

岩井良行



特 許 証

(CERTIFICATE OF PATENT)

(続葉 1)

特許第4808378号

(PATENT NUMBER)

特願2003-554215

(APPLICATION NUMBER)

発明者
(INVENTOR)

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ッド
サンタナ ミリアン, エクトル
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ギーエン ニエト, ヘラルド エー.
ヘレラ マルティネス, ルイス
カナシーアデン フリアス, レオナル
ド
ヘロニモ ペレス, アイデー
ソトロongo ペニャ, ホルヘ

[以下余白]

证书号第315944号



发明专利证书

发明名称：表皮生长因子在制备预防糖尿病肢端坏疽截肢的注射用药物组合物中的用途

发明人：豪尔赫·贝兰加阿科斯塔
何赛·I·费尔南德斯蒙特金
卡利斯托·巴尔德斯佩雷斯

专利号：ZL 02 8 28268.X

专利申请日：2002 年 12 月 4 日

专利权人：遗传和生物技术工程中心

授权公告日：2007 年 3 月 28 日

本发明经过本局依照中华人民共和国专利法进行审查，决定授予专利权，颁发本证书并在专利登记簿上予以登记。专利权自授权公告之日起生效。

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局长

田力普



证书号第315944号



发明专利证书

发 明 人：内奥巴里斯·弗朗哥佩雷斯
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埃克托尔·桑塔纳米利安
拉里莎·查孔科尔维
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路易斯·埃雷拉马丁内斯
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艾德·赫罗尼莫佩雷斯
豪尔赫·索托隆戈培尼亚

本发明经过本局依照中华人民共和国专利法进行审查，决定授予专利权，颁发本证书并在专利登记簿上予以登记。专利权自授权公告之日起生效。

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局长

田力普



No. 315944

(Emblem)

Patent Office Chop
for Printing Tax

CERTIFICATE OF INVENTION PATENT

Title of Invention :Use of epidermal growth factor in the manufacture of a
pharmaceutical injection composition for preventing diabetic limb
amputation

Inventor(s):BERLANGA ACOSTA, Jorge;FERNANDEZ MONTEQUIN, Jose
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Ingrid;SANTANA MILIAN, Hector;CHACON CORVEA, Larissa;GUILLEN
NIETO, Gerardo E.;HERRERA MARTINEZ, Luis;CANAN-HADEN FRIAS,
Leonardo;GERONIMO PEREZ, Haydee;SOTOLONGO PENA, Jorge;

Patent No.: ZL 02828268.X

Filing Date: December 4, 2002

Patentee(s): CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA;

Issue Date: March 28, 2007

After the examination performed according to the Chinese Patent Law, the patent right is granted. The Certificate of Patent is therefore issued and the status of the patent has been recorded on the Patent Register. The patent right will be effective as of the issue date.

The term of the patent is twenty years, counting from the filing date. The patentee should pay annuities according to the provisions prescribed in the Chinese Patent Law and its Implementing Regulations. Payment of annuities for the patent shall be effected within one month prior to December 4, each year. Failure to pay the annuities would result in the expiration of the patent right at the end of the last annual term.

The Certificate records only the legal status of the patent when it is granted. Items concerning the transfer, pledge, invalidation, termination and restoration of patent right, as well as the change of patentee's name, nationality, address, etc., are to be recorded on the Patent Register.

Director General : Tian, Lipu

(Official chop of the SIPO)
Date: March 28, 2007

РОССИЙСКАЯ ФЕДЕРАЦИЯ



ПАТЕНТ

НА ИЗОБРЕТЕНИЕ

№ 2289424

**ПРИМЕНЕНИЕ ФАРМАЦЕВТИЧЕСКОЙ
КОМПОЗИЦИИ, СОДЕРЖАЩЕЙ ФАКТОР
ЭПИДЕРМАЛЬНОГО РОСТА (EGF), ДЛЯ
ПРЕДОТВРАЩЕНИЯ АМПУТАЦИИ ДИАБЕТИЧЕСКОЙ
КОНЕЧНОСТИ**

Патентообладатель(ли): **СЕНТРО ДЕ ИНЖЕНЬЕРИА ГЕНЕТИКА
И БИОТЕКНОЛОГИА (CU)**

Автор(ы): *см. на обороте*

Заявка № 2004122091

Приоритет изобретения 20 декабря 2001 г.

Зарегистрировано в Государственном реестре
изобретений Российской Федерации 20 декабря 2006 г.

Срок действия патента истекает 04 декабря 2022 г.

Руководитель Федеральной службы по интеллектуальной
собственности, патентам и товарным знакам



Б.П. Симонов

CERTIFICATE OF GRANT OF PATENT

批予專利證明書

Patents Ordinance (Chapter 514)

專利條例 (第 514 章)

STANDARD PATENT 標準專利

I hereby certify that a standard patent with the following particulars has this day been granted 茲證明下述標準專利在今日批予:

Name and Address of Proprietor 專利所有人姓名或名稱及地址:

CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA

Avenida 31 Entre 158 y 190

Cubanacan, Playa

Ciudad de la Habana 10600

CUBA

遺傳和生物技術工程中心

古巴

Patent No.專利編號 : HK1077740

Application No.申請編號 : 05109793.5

Title of Invention 發明名稱 :

USE OF EPIDERMAL GROWTH FACTOR IN THE MANUFACTURE OF A
PHARMACEUTICAL INJECTION COMPOSITION FOR PREVENTING
DIABETIC LIMB AMPUTATION

表皮生長因子在製備預防糖尿病肢端壞疽截肢的注射用藥物組合物中的用途

Term of Standard Patent 標準專利有效期 :

Twenty years commencing on 04.12.2002

由 04.12.2002 年起計 20 年

Continuation Sheet for the Certificate of Grant of Patent No. 1077740

標準專利號 1077740 的專利批予證明書續頁

Dated this 12th October, 2007

二零零七年十月十二日



Stephen Selby

Registrar of Patents

專利註冊處處長謝肅方

**Patents Registry
Intellectual Property Department
The Hong Kong Special Administrative Region
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REPÚBLICA ARGENTINA
PODER EJECUTIVO NACIONAL
MINISTERIO de ECONOMÍA y PRODUCCIÓN
SECRETARÍA de INDUSTRIA, COMERCIO y de la PEQUEÑA y MEDIANA EMPRESA
INSTITUTO NACIONAL de la PROPIEDAD INDUSTRIAL



TÍTULO DE PATENTE DE INVENCION

AR037824B1

ADMINISTRACION NACIONAL DE PATENTES, CONFORME LO
REGLAMENTADO EN EL EXPEDIENTE RESPECTIVO Y EN VIRTUD DE LO
DECRETADO POR LA LEY 24.481 (T.O.1996), Y SU DECRETO
REGULATORIO (DECRETO 260/96, ANEXO II), EXTIENDE EN
NOMBRE DE LA NACION ARGENTINA EL PRESENTE TITULO A CENTRO
DE INGENIERIA GENETICA Y BIOTECNOLOGIA

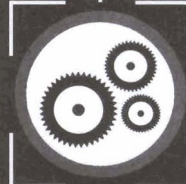
QUE CREDITA LA CONCESION DE PATENTE DE INVENCION
SOLICITADA POR UNA COMPOSICION FARMACEUTICA INYECTABLE PARA EL
TRATAMIENTO DE UNA LESION ISQUEMICA, UNA LESION
NEUROLÓGICA O UNA LESION DEBIDA A LA REPERFUSION EN UN
PACIENTE DIABETICO Y USO DE LA MISMA
CUYA DOCUMENTACION ANEXA ES COPIA FIEL DE LA DEPOSITADA
EN EL INSTITUTO NACIONAL DE LA PROPIEDAD INDUSTRIAL
CONFORME A LO ESTABLECIDO EN EL ART. 35 DE LA LEY 24.481
(DECRETO 260/96 - ANEXO I), EL TERMINO POR EL QUE SE
ACUERDA LA PATENTE ES POR VEINTE AÑOS IMPRORROGABLES
CONTADOS A PARTIR DE LA PRESENTACION DE LA SOLICITUD, POR
LO CUAL EXPIRARA EL DIA:
13 DE DICIEMBRE DE 2022

BUENOS AIRES, 30 DE NOVIEMBRE DE 2010

Dr. EDUARDO ARIAS
COMISARIO
ADMINISTRACION NACIONAL DE PATENTES



INSTITUTO NACIONAL DE LA PROPIEDAD INDUSTRIAL
ARGENTINA



Patentes de Invención
Modelos de Utilidad



Marcas



Modelos y Diseños
Industriales



Transferencia de
Tecnología



Información
Tecnológica

MEMORIA DESCRIPTIVA DE LA PATENTE DE INVENCION



SOBRE

"UNA COMPOSICIÓN FARMACÉUTICA INYECTABLE PARA EL TRATAMIENTO DE UNA LESIÓN ISQUÉMICA, UNA LESIÓN NEUROPÁTICA O UNA LESIÓN DEBIDA A LA REPERFUSIÓN EN UN PACIENTE DIABÉTICO Y USO DE LA MISMA"

SOLICITADA POR:

CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA

CON DOMICILIO EN:

Apartado 6162, Av. 31 e/190 y 158, Cubanacán, la Habana, CU

PRIORIDAD:

Solicitud CU 2001-0308 del 20 de diciembre de 2001

INVENTORES

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CORVEA Larissa; GUILLEN NIETO Gerardo E.; HERRERA MARTINEZ Luis S.;
CANAN-HADEN FRIAS Leonardo; GERONIMO PEREZ Haydee; SOTOLONGO PEÑA Jorge**

POR EL PLAZO DE 20 AÑOS



REPÚBLICA ARGENTINA

(10) PATENTE DE INVENCION

(11) RESOLUCION NUMERO : AR037824B1

(24) FECHA DE RESOLUCION : 30/11/2010

(--) FECHA DE VENCIMIENTO : 13/12/2022

(21) ACTA NUMERO : P20020104843

(22) FECHA DE PRESENTACION : 13/12/2002

(51) INT.CL.7 :A61K 38/18,9/19, 31/7028,31/167, 31/7076, 31/708, 31/455, 31/198, 31/727, 47/30, 47/42, A61P 17/02,

(30) PRIORIDAD CONVENIO DE PARIS

(31) 2001-0308, 20/12/2001, CU

(54) TITULO : UNA COMPOSICION FARMACEUTICA INYECTABLE PARA EL TRATAMIENTO DE UNA LESION ISQUEMICA, UNA LESION NEUROPATICA O UNA LESION DEBIDA A LA REPERFUSION EN UN PACIENTE DIABETICO Y USO DE LA MISMA

(71) TITULAR :

CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA

---- CON RESIDENCIA EN :

APARTADO 6162, AVENIDA 31 E/190 Y 158, CUBANACAN, LA HABANA,
País CU

(74) AGENTE: 895



INSTITUTO NACIONAL DE LA PROPIEDAD INDUSTRIAL
ARGENTINA



Australian Government

IP Australia

LETTERS PATENT

2002361923

STANDARD PATENT

I, Fatima Beattie, the Commissioner of Patents, grant a Standard Patent with the following particulars:

Name and Address of Patentee(s):

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Name of Actual Inventor(s):

Guillen Nieto, Gerardo E.; Berlanga Acosta, Jorge; Santana Millan, Hector; Chacon Corvea, Larissa; Fernandez Montequin, Jose I.; Geronimo Perez, Haydee; Canan-Haden Frias, Leonardo; Valdes Perez, Calixto; Herrera Martinez, Luis; Franco Perez, Neobalis; Rojas Constantin, Ingrid and Sotolongo Pena, Jorge.

Title of Invention:

Use of a pharmaceutical composition containing epidermal growth factor (EGF) for diabetic foot amputation prevention

Term of Letters Patent:

Twenty years from 4 December 2002

Priority Details :

Number
0308/01

Date
20 December 2001

Filed with
CU

Dated this 26th day of May 2006

Fatima Beattie
Commissioner of Patents



PATENTS ACT 1990



Brevet canadien / Canadian Patent

★ Le commissaire aux brevets a reçu une demande de délivrance de brevet visant une invention. Ladite requête satisfait aux exigences de la *Loi sur les brevets*. Le titre et la description de l'invention figurent dans le mémoire descriptif, dont une copie fait partie intégrante du présent document.

Le présent brevet confère à son titulaire et à ses représentants légaux, pour une période expirant vingt ans à compter de la date du dépôt de la demande au Canada, le droit, la faculté et le privilège exclusif de fabriquer, construire, exploiter et vendre à d'autres, pour qu'ils l'exploitent, l'objet de l'invention, sauf jugement en l'espèce rendu par un tribunal compétent, et sous réserve du paiement des taxes périodiques.



★ The Commissioner of Patents has received a petition for the grant of a patent for an invention. The requirements of the *Patent Act* have been complied with. The title and a description of the invention are contained in the specification, a copy of which forms an integral part of this document.

The present patent grants to its owner and to the legal representatives of its owner, for a term which expires twenty years from the filing date of the application in Canada, the exclusive right, privilege and liberty of making, constructing and using the invention and selling it to others to be used, subject to adjudication before any court of competent jurisdiction, and subject to the payment of maintenance fees.

B R E V E T C A N A D I E N

2,470,971

C A N A D I A N P A T E N T

Date à laquelle le brevet a été
accordé et délivré

2011/02/01

Date on which the patent
was granted and issued

Date du dépôt de la demande

2002/12/04

Filing date of the application

Date à laquelle la demande est
devenue accessible au public
pour consultation

2003/07/03

Date on which the application
was made available for
public inspection

Commissaire aux brevets / Commissioner of Patents

Canada



Office de la Propriété
Intellectuelle
du Canada

Un organisme
d'Industrie Canada

Canadian
Intellectual Property
Office

An agency of
Industry Canada

CA 2470971 C 2011/02/01

(11)(21) **2 470 971**

(12) **BREVET CANADIEN
CANADIAN PATENT**

(13) **C**

(86) Date de dépôt PCT/PCT Filing Date: 2002/12/04
(87) Date publication PCT/PCT Publication Date: 2003/07/03
(45) Date de délivrance/Issue Date: 2011/02/01
(85) Entrée phase nationale/National Entry: 2004/06/18
(86) N° demande PCT/PCT Application No.: CU 2002/000011
(87) N° publication PCT/PCT Publication No.: 2003/053458
(30) Priorité/Priority: 2001/12/20 (CU0308/01)

(51) Cl.Int./Int.Cl. *A61K 38/18* (2006.01),
C07K 14/485 (2006.01)

(72) Inventeurs/Inventors:
BERLANGA ACOSTA, JORGE, CU;
FERNANDEZ MONTEQUIN, JOSE I., CU;
VALDES PEREZ, CALIXTO, CU;
FRANCO PEREZ, NEOBALIS, CU;
ROJAS CONSTANTIN, INGRID, CU;
SANTANA MILIAN, HECTOR, CU;
CHACON CORVEA, LARISSA, CU;

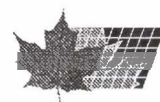
...

(73) Propriétaire/Owner:

(54) Titre : UTILISATION D'UNE COMPOSITION PHARMACEUTIQUE CONTENANT LE FACTEUR DE CROISSANCE
EPIDERMIQUE (EGF) POUR LA PREVENTION DE L'AMPUTATION DU PIED DIABETIQUE
(54) Title: USE OF PHARMACEUTICAL COMPOSITION CONTAINING EPIDERMAL GROWTH FACTOR (EGF) FOR
PREVENTING DIABETIC LIMB AMPUTATION

(57) Abrégé/Abstract:

The invention relates to the use of Epidermal Growth Factor (EGF) in a preferably-injectable pharmaceutical composition which is administered by means of infiltration into and around chronic cutaneous ischaemic lesions in order to prevent diabetic foot amputation. Said composition can be administered to recently-created surgical surfaces damaged by the effect of acute reperfusion with oxygenated blood following prolonged ischaemia, thereby preventing further surgical procedures and favouring the preservation of the extremity. The aforementioned composition can be used to improve (i) the cell microenvironment, thereby increasing the reparative and defensive capacity and viability of the tissues and (ii) the cicatrisation of cutaneous ischaemic lesions, hereby stimulating cell proliferation. The invention is suitable for use in human, veterinary and experimental medicine, specifically in vascular angiology and surgery, dermatology, burn treatment and reconstructive surgery and geriatric medicine. Said composition can be used for recalcitrant ulcers which are associated with lesions in the macro and/or microvasculature, patients with inadequate lymphatic and/or venous return and ulcers or other lesions which are difficult to cicatrise and/or heal.





특 허 증

CERTIFICATE OF PATENT

특 허 제 10-0795654 호

(PATENT NUMBER)

출원번호
(APPLICATION NUMBER)

제 2004-7009772 호

출원일
(FILING DATE:YY/MM/DD)

2004년 06월 19일

등록일
(REGISTRATION DATE:YY/MM/DD)

2008년 01월 10일

발명의명칭 (TITLE OF THE INVENTION)

당뇨성 발 절단 예방을 위한 표피성장인자 함유 억제학적조성
물의 용도

특허권자 (PATENTEE)

센트로 데 인제니에리아 제네티카 와이 바이오테크놀로지아

쿠바, 씨. 하바나 10600, 플라야, 쿠바나칸, 아베. 31 엔트레
158와이 190

발명자 (INVENTOR)

등록사항란에 기재

위의 발명은 「특허법」에 의하여 특허등록원부에 등록
되었음을 증명합니다.

(THIS IS TO CERTIFY THAT THE PATENT IS REGISTERED ON THE REGISTER OF THE KOREAN
INTELLECTUAL PROPERTY OFFICE.)

2008년 01월 10일



특 허 청

COMMISSIONER, THE KOREAN INTELLECTUAL PROPERTY OFFICE



LETTERS PATENT**PATENT NO. 795654**

Application No 2004-7009772
Filing Date June 19, 2004
Date of Registration January 10, 2008

Title of Invention Use of a pharmaceutical composition containing epidermal growth factor (EGF) for diabetic foot amputation prevention

Patentee(s) Centro de Ingeniería Genética y Biotecnología

Inventor(s) BERLANGA ACOSTA, Jorge
FERNÁNDEZ MONTEQUÍN, José I.
VALDÈS PÈREZ, Calixto
FRANCO PÈREZ, Neobalis
ROJAS CONSTANTIN, Ingrid
SANTANA MILIÁN, Héctor
CHACÓN CORVEA, Larissa
GUILLÉN NIETO, Gerardo E.
HERRERA MARTÍNEZ, Luis
CANAN-HADEN FRÍAS, Leonardo
GERÓNIMO PÈREZ, Haydee
SOTOLONGO PEÑA, Jorge

This is to certify that the above was registered in the Patent Register in accordance with the Patent Law.

This 10th day of January, 2008

Commissioner of the Korean Intellectual Property Office



REPÚBLICA DE CUBA

La Directora de la Oficina Cubana de la Propiedad Industrial
en uso de sus facultades y de acuerdo con lo establecido
en las disposiciones legales vigentes,
concede el presente:



CERTIFICADO DE AUTOR DE INVENCION

(72) Autor (es) o coautor (es):

JORGE BERLANGA ACOSTA
JOSÉ I. FERNÁNDEZ MONTEQUÍN
CALIXTO VALDÉS PÉREZ
NEOBALIS FRANCO PÉREZ
INGRID ROJAS CONSTATIN
HÉCTOR SANTANA MILIÁN

LARISSA CHACÓN CORVEA
GERARDO E GUILLÉN NIETO
LUIS HERRERA MARTÍNEZ
LEONARDO CANAN-HADEN FRÍAS
HAYDEE GERÓNIMO PÉREZ
JORGE SOTOLONGO PEÑA

(71) Solicitante (es):


CENTRO DE INGENIERÍA GENÉTICA Y BIOTECNOLOGÍA, con domicilio legal en
Ave. 31 entre 158 y 190, Cubanacán, Código Postal 12100, Playa, Ciudad de La Habana,
República de Cuba.

(11) Certificado Nro. : **23043**

Concedido por Resolución No. 405/2005

(54) Título: **COMPOSICIÓN FARMACÉUTICA QUE CONTIENE FACTOR DE
CRECIMIENTO EPIDÉRMICO (FCE) PARA LA PREVENCIÓN DE LA
AMPUTACIÓN DEL PIE DIABÉTICO**

Dado en La Habana, a 22 de marzo de 2005.


Ing. María de los Angeles Sánchez Torres
Directora
Oficina Cubana de la Propiedad Industrial

क्रमांक : 022 3068
Sl. No. :



सत्यमेव जयते



INTELLECTUAL
PROPERTY INDIA
PATENTS | DESIGNS | TRADE MARKS
GEOGRAPHICAL INDICATIONS



भारत सरकार
GOVERNMENT OF INDIA
पेटेंट कार्यालय
THE PATENT OFFICE
पेटेंट प्रमाणपत्र
Patent Certificate
(Rule 74 of Patents Rules)

Patent No. : 208341
Application No. : 295/MUMNP/2004
Date of Filing : 04/12/2002
Patentee : CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA.

It is hereby certified that a patent has been granted to the patentee for an invention entitled **PHARMACEUTICAL COMPOSITION CONTAINING EPIDERMAL GROWTH FACTOR (EGF) FOR PREVENTING DIABETIC LIMB AMPUTATION** as disclosed in the above mentioned application for the term of 20 years from the 4 day of **DECEMBER 2002**, in accordance with the provisions of the Patents Act, 1970.

Date of Grant: 23/07/2007


Controller of Patents

Note.-The fees for renewal of this patent, if it is to be maintained, will fall / has fallen due on 4 day of DECEMBER 2004 and on the same day in every year thereafter.



**REPUBLIK INDONESIA
DEPARTEMEN HUKUM DAN HAK ASASI MANUSIA**

SERTIFIKAT PATEN

Menteri Hukum dan Hak Asasi Manusia atas nama Negara Republik Indonesia berdasarkan Undang-Undang Nomor 14 Tahun 2001 tentang Paten, memberikan Paten dengan Nomor Paten: **ID 0 022 098** kepada :

Nama dan Alamat Pemegang Paten : **CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA
Ave. 31 entre 158 y 190, Cubanacan, Playa,
Ciudad de La Habana 10600,
CUBA**

untuk Invensi dengan :

Judul : **PENGUNAAN KOMPOSISI FARMASI YANG MENGANDUNG
FAKTOR PERTUMBUHAN EPIDERMIS (EGF) UNTUK
MENCEGAH AMPUTASI KAKI PENDERITA PENYAKIT
DIABETES**

Inventor : **BERLANGA ACOSTA, Jorge; FERNANDEZ MONTEQUIN, Jose, I.;
VALDEZ PEREZ, Calixto; FRANCO PEREZ, Neobalis;
ROJAS CONSTANTIN, Ingrid; SANTANA MILIAN, Hector;
CHACON CORVEA, Larissa; GUILLEN NIETO, Gerardo, E.;
HERRERA MARTINEZ, Luis; CANAN-HADEN FRIAS, Leonardo;
GERONIMO PEREZ, Haydee; SOTOLONGO PENA, Jorge**

Nomor Permohonan : **W00200401547**

Tanggal Penerimaan : **4 Desember 2002**

Tanggal Pemberian : **9 Oktober 2008**

Perlindungan Paten untuk invensi tersebut diberikan untuk selama 20 tahun terhitung sejak tanggal Penerimaan.

Sertifikat Paten ini dilampiri dengan deskripsi, klaim, abstrak dan gambar (jika ada) dari invensi yang merupakan bagian yang tidak terpisahkan dari sertifikat ini.

Jakarta, 05 Pebruari 2009

a.n. MENTERI HUKUM DAN HAK ASASI MANUSIA
Direktur Jenderal Hak Kekayaan Intelektual
u.b.

Direktur Paten

RAZILU
NIP. 040060484



MALAYSIA



CERTIFICATE OF GRANT OF A PATENT

In accordance with Section 31 (2) of the Patents Act 1983 a patent for an invention having grant number MY - 139214 - A has been granted to CENTRO DE INGENIERÍA GENÉTICA Y BIOTECNOLOGÍA in respect of an invention having the following particulars :

TITLE : USE OF PHARMACEUTICAL COMPOSITION CONTAINING
EPIDERMAL GROWTH FACTOR (EGF) FOR PREVENTING
DIABETIC LIMB AMPUTATION

FILING DATE : 18 DECEMBER 2002

PRIORITY DATE : 20 DECEMBER 2001

NAME OF INVENTOR : 1) BERLANGA ACOSTA, JORGE
2) FERNANDEZ MONTEQUÍN, JOSÉ I.
3) VALDÉS PÉREZ, CALIXTO
4) FRANCO PÉREZ, NEOBALIS
5) ROJAS CONSTANTIN, INGRID
6) SANTANA MILIÁN, HÉCTOR
7) CHACÓN CORVEA, LARISSA
8) GUILLÉN NIETO, GERARDO E.
9) HERRERA MARTÍNEZ, LUIS S.
10) CANAN-HADEN FRÍAS, LEONARDO
11) GERÓNIMO PÉREZ, HAYDEE
12) SOTOLONGO PEÑA, JORGE

PATENT OWNER : CENTRO DE INGENIERÍA GENÉTICA Y BIOTECNOLOGÍA
AVE. 31 ENTRE 158 Y 190
CUBANACAN, PLAYA
CIUDAD DE LA HABANA 10600
CUBA

DATE OF GRANT : 28 AUGUST 2009

Dated this 28 day of AUGUST 2009

(SHAMSIAH BINTI KAMARUDDIN)
for Registrar of Patents
MALAYSIA



TÍTULO DE PATENTE NO. **260823**

Titular(es):	CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA	
Domicilio(s):	Avenida 31 entre 158 y 190, Cubanacán, Playa, Ciudad de La Habana, 10600, CUBA	
Denominación:	USO DE UNA COMPOSICION FARMACEUTICA QUE CONTIENE FACTOR DE CRECIMIENTO EPIDERMICO (EGF) PARA PREVENCION DE AMPUTACION DEL PIE DIABETICO	
Clasificación:	Int.Cl.8: A61K9/08; A61K9/14; A61K9/19	
Inventor(es):	JORGE BERLANGA ACOSTA; JOSÉ I. FERNÁNDEZ MONTEQUÍN; CALIXTO VALDÉS PÉREZ; NEOBALIS FRANCO PÉREZ; INGRID ROJAS CONSTANTIN; HÉCTOR SANTANA MILIÁN; LARISSA CHACÓN CORVEA; GERARDO E. GUILLÉN NIETO; LUIS HERRERA MARTÍNEZ; LEONARDO CANAN-HADEN FRÍAS; HAYDEE GERÓNIMO PÉREZ; JORGE SOTOLONGO PEÑA	
SOLICITUD		
Número:	Fecha de presentación internacional:	
PA/a/2004/005831	04 de Diciembre de 2002	
PRIORIDAD		
País:	Fecha:	Número:
CU	20 de diciembre de 2001	2001/0308
ESTA PATENTE CONCEDE A SU TITULAR EL DERECHO EXCLUSIVO DE EXPLOTACIÓN DEL INVENTO RECLAMADO EN EL CAPÍTULO REIVINDICATORIO Y TIENE UNA VIGENCIA IMPRORROGABLE DE VEINTE AÑOS CONTADOS A PARTIR DE LA FECHA DE PRESENTACIÓN INTERNACIONAL DE LA SOLICITUD, QUE ESTARÁ SUJETA AL PAGO DE LA TARIFA CORRESPONDIENTE.		

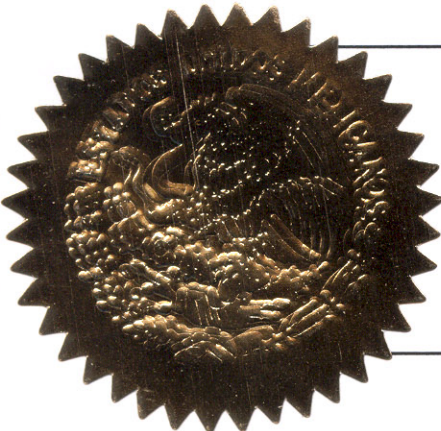
Fecha de expedición: 25 de septiembre de 2008

EL DIRECTOR DIVISIONAL DE PATENTES

QUÍM. FABIÁN R. SALAZAR GARCÍA



MX/2008/94534



THE REGISTRY OF PATENTS
SINGAPORE

THE PATENTS ACT
(CHAPTER 221)

CERTIFICATE OF GRANT OF PATENT

In accordance with section 35 of the Patents Act, it is hereby certified that a patent having the P-No. 105304 [WO 03/053458] has been granted in respect of an invention having the following particulars:

Title : USE OF A PHARMACEUTICAL COMPOSITION
CONTAINING EPIDERMAL GROWTH FACTOR
(EGF) FOR DIABETIC FOOT AMPUTATION
PREVENTION

Application Number : 200403700-8

Date of Filing : 04 December 2002



Priority Data : 20 December 2001 - PATENT APPLICATION NO.
0308/01 (CUBA)

Name of Inventor(s) : BERLANGA ACOSTA, JORGE; FERNANDEZ
MONTEQUIN, JOSÉ I.; VALDES PEREZ, CALIXTO;
FRANCO PEREZ, NEOBALIS; ROJAS CONSTANTIN,
INGRID; SANTANA MILIAN, HÉCTOR; CHACON
CORVEA, LARISSA; GUILLEN NIETO, GERARDO E.;
HERRERA MARTINEZ, LUIS; CANAN-HADEN
FRIAS, LEONARDO; GERONIMO PEREZ, HAYDEE;
SOTOLONGO PEÑA, JORGE

Name(s)
and Address(es) of
Proprietor(s) of Patent : CENTRO DE INGENIERIA GENETICA Y
BIOTECNOLOGIA
DEPARTAMENTO DE PATENTES
AVE. 31 ENTRE 158 Y 190, CUBANACAN
PLAYA, CIUDAD DE LA HABANA 10600
CUBA

Date of Grant : 31 March 2005

Dated this 31st day of March 2005.



Liew Woon Yin (Ms)
Registrar of Patents,
Singapore.

REPUBLIC OF SOUTH AFRICA



REPUBLIEK VAN SUID AFRIKA

PATENTS ACT, 1978

CERTIFICATE

In accordance with section 44 (1) of the Patents Act, No. 57 of 1978, it is hereby certified that

Centro de Ingenieria Genetica Y Biotecnologia

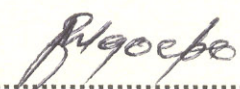
has been granted a patent in respect of an invention described and claimed in complete specification deposited at the Patent Office under the number

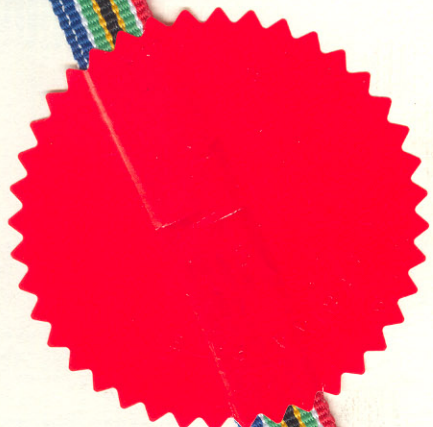
2004/5612

A copy of the complete specification is annexed, together with the relevant Form P2.

In testimony thereof, the seal of the Patent Office has been affixed at Pretoria with effect

from the **25th** day of **May 2005**


.....
Registrar of Patents



REPUBLIC OF SOUTH AFRICA

REGISTER OF PATENTS

PATENTS ACT, 1978

OFFICIAL APPLICATION NO.		LODGING DATE: PROVISIONAL		ACCEPTANCE DATE	
22	01	. 20 04 / 56 12		22	47
INTERNATIONAL CLASSIFICATION		LODGING DATE: COMPLETE		GRANTED DATE	
A61K C07K		14 July 2004		25-5-05	

FULL NAME(S) OF APPLICANT(S)/PATENTEE(S)

71

Centro de Ingenieria Genetica Y Biotecnologia

APPLICANTS SUBSTITUTED:		DATE REGISTERED	
71			
ASSIGNEE(S)		DATE REGISTERED	
71			

FULL NAME(S) OF INVENTOR(S)

72

BERLANGA ACOSTA, Jorge
 VALDES PEREZ, Calixto
 ROJAS CONSTANTIN, Ingrid
 CHACON CORVEA, Larissa
 HERRERA MARTINEZ, Luis
 GERONIMO PEREZ, Haydee

FERNANDEZ MONTEQUIN, José I.
 FRANCO PEREZ, Neobalis
 SANTANA MILIAN, Héctor
 GUILLEN NIETO, Gerardo E.
 CANAN-HADEN FRIAS, Leonardo
 SOTOLONGO PEÑA, Jorge

PRIORITY CLAIMED BY PCT INTERNATIONAL APPLICATION PCT/CU02/00011 FILED 4 December 2002 (WO 03/053458)		COUNTRY		NUMBER		DATE	
N.B. Use International Abbreviation for country (See Schedule 4)		33	CU	31	0308/01	32	20 December 2001

TITLE OF INVENTION

54

Use of a pharmaceutical composition containing epidermal growth factor (EGF)
 for diabetic foot amputation prevention

ADDRESS OF APPLICANT(S)/PATENTEE(S)

Departamento de Patentes, Ave. 31 entre 158 y 190, Cubanacan, Playa, Ciudad de
 La Habana 10600, Cuba

ADDRESS FOR SERVICE		A & A REF:	
74	ADAMS & ADAMS, Pretoria	150641	
PATENT OF ADDITION TO NO.		DATE OF ANY CHANGE	
61			
FRESH APPLICATION BASED ON		DATE OF ANY CHANGE	



(19) **UA** (11) **80 813** (13) **C2**
(51)МПК

МИНИСТЕРСТВО ОБРАЗОВАНИЯ И НАУКИ
УКРАИНЫ

ГОСУДАРСТВЕННЫЙ ДЕПАРТАМЕНТ
ИНТЕЛЛЕКТУАЛЬНОЙ СОБСТВЕННОСТИ

(12) ОПИСАНИЕ ИЗОБРЕТЕНИЯ К ПАТЕНТУ УКРАИНЫ

(21), (22) Заявка: 20040705897, 04.12.2002

(24) Дата начала действия патента: 12.11.2007

(30) Приоритет: 20.12.2001 CU 0308/01

(46) Дата публикации: 12.11.2007A61K 38/18
20060101CFI20070706RMUA C07K
14/485 20060101ALI20070706BNUA
A61K 9/08
20060101CLI20070706RMUA A61P
9/10 20060101ALI20070115RMUA
A61P 17/02
20060101ALI20070115RMUA

(86) Заявка РСТ:
РСТ/CU02/00011, 20021204

(72) Изобретатель:

Берланга Акоста Хорхе, CU,
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Франко Перес Необалис, CU,
Рохас Константин Ингрид, CU,
Сантана Милиан Эктор, CU,
Чакон Корвеа Ларисса, CU,
Гильен Нето Жерардо Энрике, CU,
Эррера Мартинес Луис, CU,
Канан-Аден Фриас Леонардо, CU,
Херонимо-Перес Айде, CU,
Сотолонго Пенья Хорхе, CU

(73) Патентовладелец:

ЦЕНТРО ДЕ ИНЖЕНЕРИЯ ГЕНЕТИКА И
БИОТЕХНОЛОГИА, CU

(54) СПОСОБ ЛЕЧЕНИЯ ПОРАЖЕНИЙ СТОПЫ У ПАЦИЕНТА-ДИАБЕТИКА ФАРМАЦЕВТИЧЕСКОЙ
КОМПОЗИЦИЕЙ, СОДЕРЖАЩЕЙ ЭПИДЕРМАЛЬНЫЙ ФАКТОР РОСТА

(57) Реферат:

Изобретение относится к медицине, в частности к способу лечения ишемического, невропатического или реперфузионного поражения у пациента-диабетика, который включает местную инфильтрацию фармацевтической композиции, которая содержит эпидермальный фактор роста (EGF), в ткань в разных точках инфильтрации, к самому поражению

и вокруг него.

Официальный бюлетьн "Промышленная собственность". Книга 1 "Изобретения, полезные модели, топографии интегральных микросхем", 2007, N 18, 12.11.2007. Государственный департамент интеллектуальной собственности Министерства образования и науки Украины.