492

BRIGARD& CASTRO
PROPIEDAD INTELECTUAL

CARRERA 7 # 71 – 21 TORRE B – PISO 4
BOGOTÁ – COLOMBIA
TEL: (571) 744 22 00
FAX: (571) 742 22 00 – (571) 3214045
www.bc.com.co



AS. 103.466

Señores
**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO**
**DIVISION DE NUEVAS CREACIONES**
E. S. D.

REF.: Expediente No. 07 034.204 - Solicitud de Patente FASE NACIONAL
Corresp. a la Solicitud Internacional PCT/US2005/034647.
a nombre de: **GENENTECH, INC.**
Titulada: MÉTODO PARA TRATAR VASCULITIS.

JUAN PABLO CADENA SARMIENTO, vecino de Bogotá, portador de la tarjeta profesional No. 57492 del Consejo Superior de la Judicatura, obrando como apoderado de la Sociedad **GENENTECH, INC.**, según lo acreditan el documento de poder presentado en esa División, de acuerdo con el Artículo 44 de la Decisión 486 de la Comisión de la Comunidad Andina, me permito solicitar que se examine si la invención contenida en la solicitud en referencia es patentable.

De acuerdo con lo anterior, me permito anexar el recibo oficial de caja No. 08-44,638 por valor de $420.000.

De la Señora Jefe atentamente,

**JUAN PABLO CADENA SARMIENTO**
C.C. No. 80.410.337 de Usaquén
T.P. No. 57492 del C.S.J.
Cra 7 No. 71-21 Torre B, Piso 4

Bogotá, 08 de agosto de 2008
MEV/CAG/jpg

AS 103466 493

2

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 08 - 44,632
FECHA : JUNIO 5 DE 2008

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

**No. 07-034204- -00003-0000**

Fecha: 2008-08-08 16:17:37 Dep 2020 NUEVACREACION
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 538 PETICION Folios: 2

***** C O N S I G N A C I O N *****

| DEPOSITANTE | TIPO PAGO | BANCO | CUENTA | No. PAGO | FECHA PAG | Vr. PAGO |
|---|---|---|---|---|---|---|
| PRIGARO & CASTRO LTDA | CONSIGNACION | BANCO DE BOGOTA | 062754387 | 3255976 | 04/06/2008 | 83,[illegible],000.00 |

***** C O N C E P T O *****

| CANT. | RENTISTICO | CONCEPTO | | TOTAL CONCEPTO |
|---|---|---|---|---|
| 1 | 50006-01-01 SOLICITUDES | 85 EXAMEN DE PATENTABILIDAD DE INVEN | | 420,000.00 |
| | | TOTAL : | $ | 420,000.00 |

CUATROCIENTOS VEINTE MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

Industria y Comercio
SUPERINTENDENCIA

**DIRECCIÓN DE NUEVAS CREACIONES**

RADICACIÓN EXPEDIENTE No. PCT 07-34204

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCIÓN**

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **589** DE

FECHA **29 DE FEBRERO DE 2008** EL TÉRMINO HÁBIL SEÑALADO POR LA

LEY EXPIRA EL **03 DE JUNIO DE 2008**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI _____ NO ____x____

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 April 2004 (29.04.2004)

PCT

(10) International Publication Number
WO 2004/035607 A2

(51) International Patent Classification[7]: C07K

(21) International Application Number:
PCT/US2003/033057

(22) International Filing Date: 17 October 2003 (17.10.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

| | | |
|---|---|---|
| 60/419,163 | 17 October 2002 (17.10.2002) | US |
| 60/460,028 | 2 April 2003 (02.04.2003) | US |

(71) Applicants *(for all designated States except US)*: **GENMAB A/S** [DK/DK]; Toldbodgade 33, DK-1253 Copenhagen K (DK). **MEDAREX, INC.** [US/US]; 707 State Road, Princeton, NJ 08540 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **TEELING, Jessica** [NL/NL]; Lisdoddelaan 70, NL-1562 SN Krommenie (NL). **RUULS, Sigrid** [NL/NL]; Hessenweg 121B, NL-3731 JG De Bilt (NL). **GLENNIE, Martin** [GB/GB]; 1 Thornhill Road, Southampton SO16 7AU (GB). **VAN DE WINKEL, Jan, G., J.** [NL/NL]; Werlengde Slotlaan 80, NL-3707 CK Zeist (NL). **PARREN, Paul** [NL/NL]; Werdorperwaard 17, NL-3984 PR Odijk (NL). **PETERSEN, Jorgen** [DK/DK]; Solkrogen 6, DK-2960 Rungsted Kyst (DK). **BAADSGAARD, Ole, D., M., Sc.** [DK/SE]; Kyrkogatan 3, S-211 22 Malmo (SE). **HUANG, Haichun** [US/US]; 2425 Sueno Way, Fremont, CA 94539 (US).

(74) Agents: **DECONTI, Giulio, A.** et al.; Lahive & Cockfield, LLP, 28 State Street, Boston, MA 02109 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**
— *without international search report and to be republished upon receipt of that report*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

WO 2004/035607 A2

(54) Title: HUMAN MONOCLONAL ANTIBODIES AGAINST CD20

(57) Abstract: Isolated human monoclonal antibodies which bind to and inhibit human CD20, and related antibody-based compositions and molecules, are disclosed. The human antibodies can be produced by a transfectoma or in a non-human transgenic animal, *e.g.*, a transgenic mouse, capable of producing multiple isotypes of human monoclonal antibodies by undergoing V-D-J recombination and isotype switching. Also disclosed are pharmaceutical compositions comprising the human antibodies, non-human transgenic animals and hybridomas which produce the human antibodies, and therapeutic and diagnostic methods for using the human antibodies.

ARTHRITIS & RHEUMATISM
Vol. 44, No. 12, December 2001, pp 2836–2840

Published by Wiley-Liss, Inc.

# Response of Wegener's Granulomatosis to Anti-CD20 Chimeric Monoclonal Antibody Therapy

Ulrich Specks, Fernando C. Fervenza, Thomas J. McDonald, and Marie C. E. Hogan

**We report on the successful, compassionate use of the anti-CD20 chimeric monoclonal antibody rituximab in a patient with chronic, relapsing cytoplasmic antineutrophil cytoplasmic antibody (cANCA)–associated Wegener's granulomatosis (WG). The patient initially responded to treatment with glucocorticoids and cyclophosphamide. However, bone marrow toxicity during cyclophosphamide treatment of a relapse precluded its further use. Azathioprine and mycophenolate mofetil treatment had failed to maintain remission of the WG, and methotrexate was contraindicated. Because the patient's 5-year course was characterized by close correlation of cANCA levels with disease activity, selective elimination of cANCA was deemed a treatment option for his latest relapse. He was given 4 infusions of 375 mg/m$^2$ of rituximab and high-dose glucocorticoids. Complete remission was associated with the disappearance of B lymphocytes and cANCA. Glucocorticoid treatment was then discontinued. After 11 months, the cANCA recurred, and rituximab therapy was repeated, without glucocorticoids. At 8 months after the second course of rituximab (18 months after the first course), the patient's WG has remained in complete remission. Elimination of B cells by rituximab therapy may prove to be an effective and safe new treatment modality for ANCA-associated vasculitis and possibly other autoimmune diseases. This modality warrants closer examination in a carefully conducted clinical trial.**

Wegener's granulomatosis (WG) is a systemic autoimmune disorder of unknown etiology. Untreated, the disease usually progresses from a limited necrotizing granulomatous process to a generalized phase characterized by complications of small vessel vasculitis (1). Therapy with glucocorticoids and cytotoxic agents has substantially improved the prognosis, but significant side effects frequently preclude their continued or repeated use (1). WG is part of a spectrum of small vessel vasculitides associated with antineutrophil cytoplasmic autoantibodies (ANCA). ANCA that, on ethanol-fixed neutrophil cytospin preparations, cause a characteristic cytoplasmic immunofluorescence staining pattern (cANCA) directed against proteinase 3 (PR3) have become a widely accepted tool in the diagnosis of WG (2). Based on a large body of clinical and experimental data, a significant pathogenic role of ANCA has been proposed (3).

Plasma cells are the principle cellular source of ANCA. Mature antibody-secreting plasma cells presumably are terminally differentiated cells with a life span of 1–2 weeks. Each plasma cell is the clonal progeny of antigen-specific B lymphocytes. Rituximab is a humanized monoclonal antibody directed against the B cell–restricted differentiation antigen CD20 that has been used successfully in the treatment of B cell lymphomas (4). Four weekly infusions of 375 mg/m$^2$ of rituximab effectively deplete B cells and are associated with few side effects (5). Therefore, rituximab represents an attractive new drug for the treatment of autoimmune diseases with pathogenic autoantibodies.

We present the case of a patient with chronic, relapsing PR3 ANCA–associated WG in whom the use of cyclophosphamide was contraindicated and other immunosuppressive agents failed to control disease activity. The patient was treated successfully with rituximab on a compassionate-use basis under the hypothesis that elimination of pathogenic PR3 ANCA would allow the induction and maintenance of a lasting remission during and after tapering of glucocorticoids.

Supported by funds from the Mayo Foundation.

Ulrich Specks, MD, Fernando C. Fervenza, MD, PhD, Thomas J. McDonald, MD, Marie C. E. Hogan, MD: Mayo Clinic and Foundation, Rochester, Minnesota.

Address correspondence and reprint requests to Ulrich Specks, MD, Division of Pulmonary and Critical Care Medicine, Mayo Clinic and Foundation, 200 First Street, SW, Rochester, MN 55905. E-mail: specks.ulrich@mayo.edu.

Submitted for publication December 15, 2000; accepted in revised form July 6, 2001.