Patent Landscape Analyses of Health Innovations

Application to Intellectual Property and Technology-transfer Strategies to Accelerate Global Access

Stanley P. Kowalski
Professor of Law
Director
International Technology Transfer Institute (ITTI)
UNH-Law
Concord, NH USA

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Overview

- **Patent Landscapes: tools and methods**
- **Chagas disease, overview**
- **Chagas disease, vaccines and diagnostics patent landscape analysis**
- **WHO Essential Medicines List Update, overview**
- **WHO Essential Medicines List Update, patent landscape analysis**
- **Patent information and global access to health innovation**

Patent Landscapes: tools and methods

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

LANDSCAPE SEARCH

- Identifies actors in a specific field of technology, countries in which the technology is being patented and important information about market trends.
- Provides a broad overview of a technology or industry over time and location.
- Landscape searches can be especially useful for technology development or technology transfer purposes.
- Patent Landscapes can also identify "patent family" information. Patent family searches are used to find commercial, technical, and strategic potential.

Patent Landscapes: tools and methods

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Why patent landscaping?

- Identify gaps and clusters in technology.
- Assess self-portfolios alongside competition or possible collaborators.
- Develop future R&D and licensing strategies.
- Identify new application areas of existing patents.
- Develop new products and improve existing products.
- Determine commercial value of patents.
- Identify fundamental invention vis-à-vis improvements.
- Monitor patent activity in particular geographic markets.

Patent Landscapes: tools and methods

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Access to information drives innovation: Patent Landscape Information, can inform:

- **Legal/intellectual property management strategies: license-in, cross-license, oppose third-party patents, seek non assert covenant, seek compulsory license**
- **Research and Development strategies: modify product, or invent around**
- **Business strategies: merge and/or acquire, wait and see, abandon project**

As relating to our discussions today, the existence of IPR, whereby patents are licensed with *associated know-how and regulatory data,* may accelerate the introduction of important drugs, diagnostics and vaccines, suggesting an opportunity for access to technology rather than a hindrance.

Modified from: Access to Medicines, Patent Information and Freedom to Operate World Health Organization (WHO) Geneva, February 18, 2011

Patent Landscapes: tools and methods
Patent Families

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

A collection of published patent documents relating to the same invention, or to several inventions sharing a common aspect, that are published at different times in the same country or published in different countries or regions. Each patent document in such a collection is normally based on the data for the application(s) on which the basis for its "priority right" has been claimed.
From WIPO

Patent Landscapes: tools and methods

What is a patent search?

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

- **A patent search identifies relevant categories of patents, and pending patent applications**
- **It can be extended into a search of foreign patents and also non-patent literature.**

Patent Landscapes: tools and methods: Patent Database Platforms

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Patent Landscapes: tools and methods

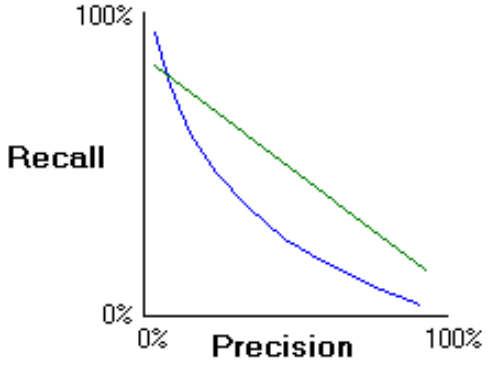
Precision vs. Recall

- When *searching data*, *the set can* be divided into two subsets: relevant and non-relevant data.
- Precision is the fraction of retrieved documents that are relevant
- Recall is the fraction of relevant documents that are successfully retrieved.

As recall ↑ precision ↓

conversely:

As recall ↓ precision ↑



Patent Landscapes: tools and methods

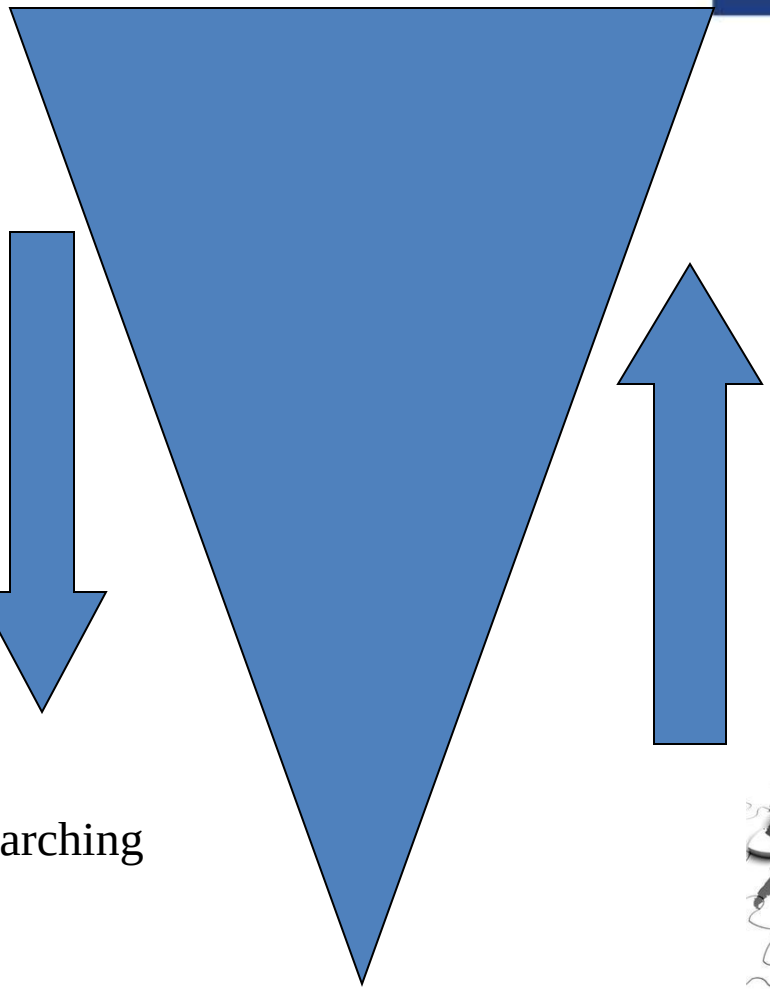
Broaden & narrow search...

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Unrestricted full text

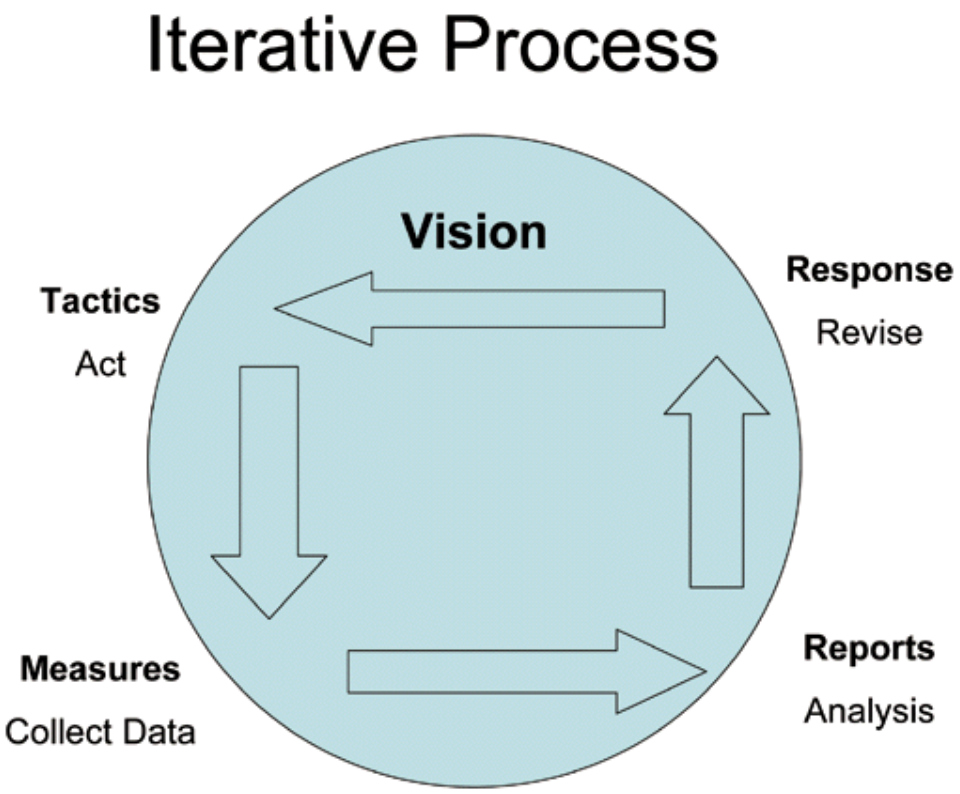
Bibliographic file

- Try different field restrictors:
- Class
- Spec
- Abstract
- Title
- Mix & match with keywords
- Keyword plus Class Hybrid Searching



Patent Landscapes: tools and methods

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



Patent Landscapes: tools and methods
Patent Information Analytics

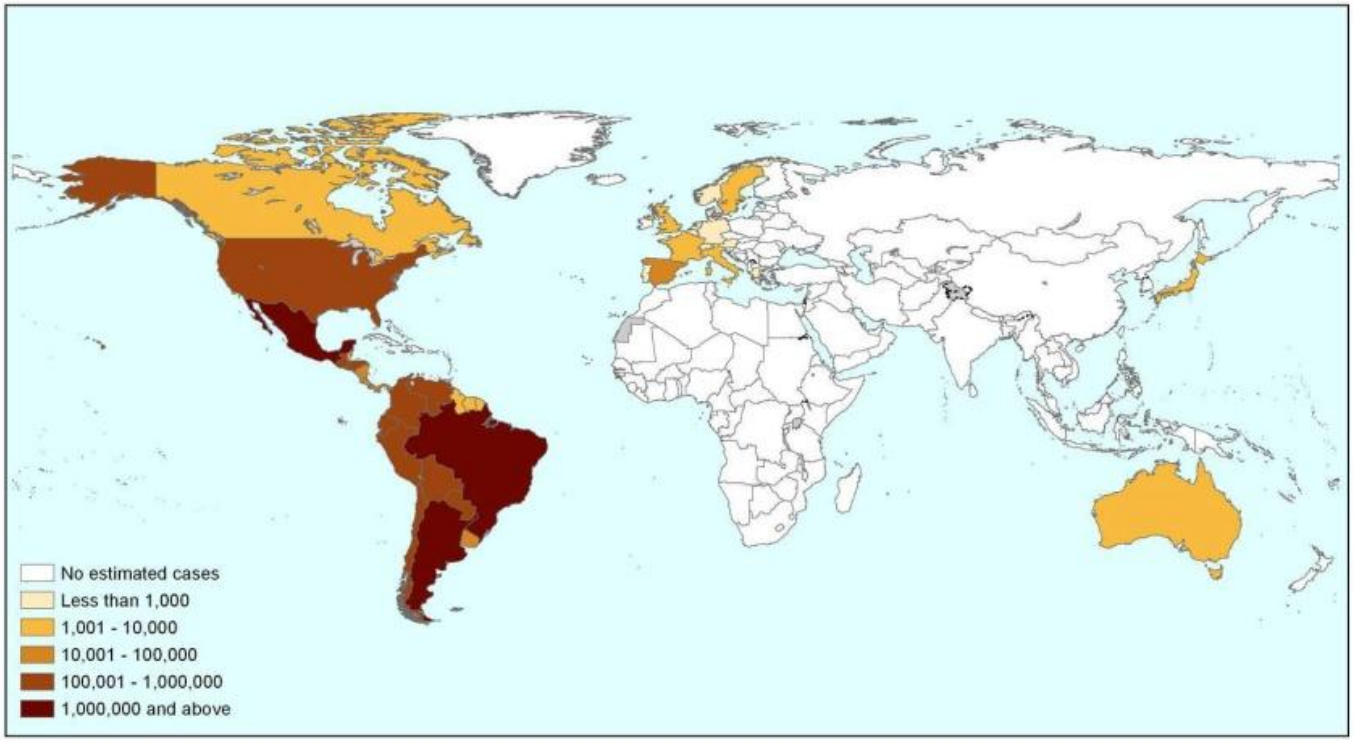
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Chagas Disease Vaccines/Diagnostics:
Global Epidemiology

THE FRANKLIN PIERCE *Center for* INTELLECTUAL PROPERTY
UNIVERSITY *of* NEW HAMPSHIRE SCHOOL *of* LAW

We will update this map regurlarly (version: June 2009)

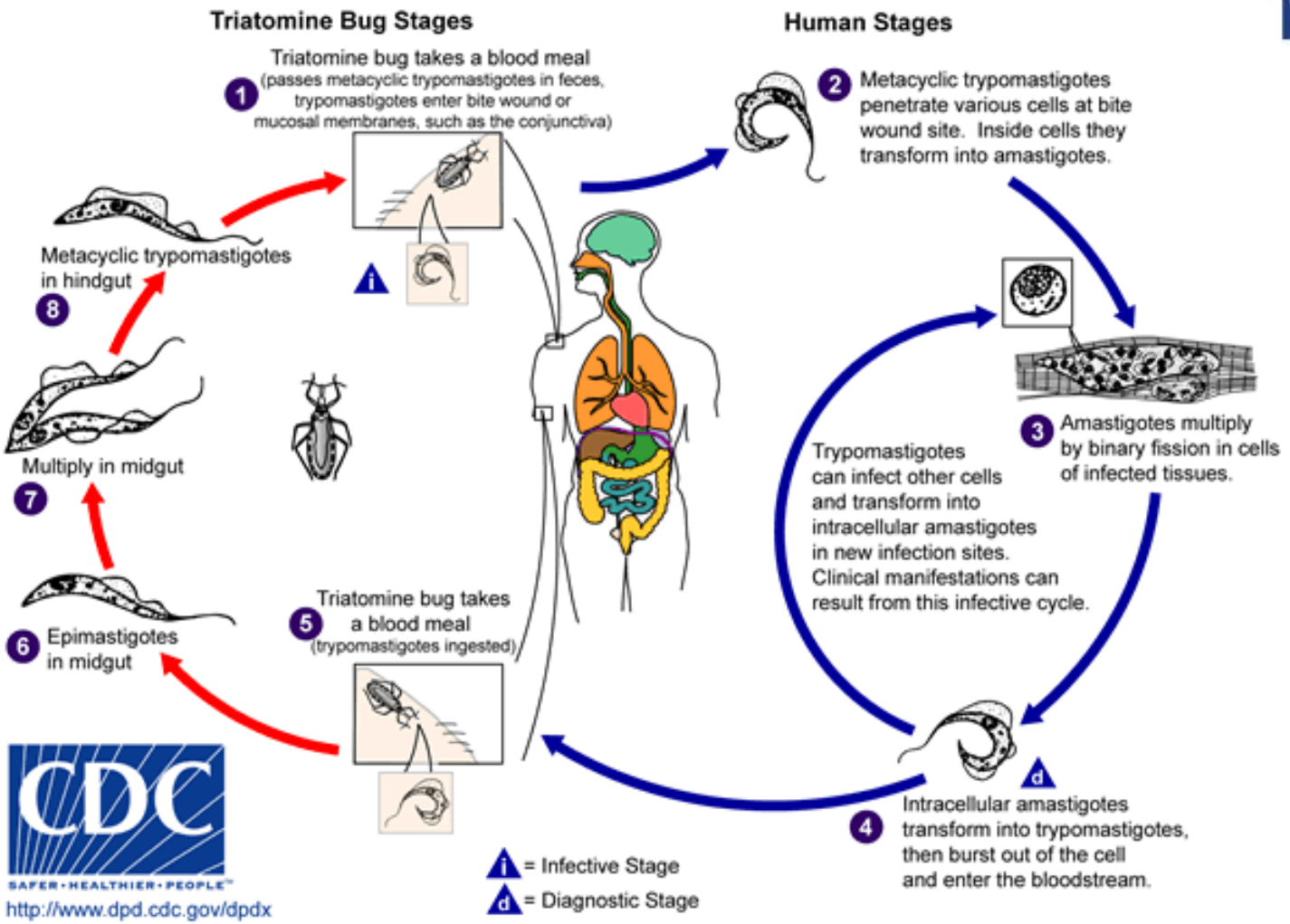
Estimated global population infected by *Trypanosoma cruzi*, 2009



Sources:
1. OPS/HDM/CD/425-06 Estimación cuantitativa de la enfermedad de Chagas en las Américas.
2. Guerri-Guttenberg RA, Grana D.R., Giuseppe Ambrosio, Milei J. Chagasic cardiomyopathy: Europe is not spared! European Heart Journal (2008); 29: 2587-2591.
3. Schmunis. G. A. Epidemiology of Chagas Disease in non-endemic countries: the role of international migration. Mem Inst Oswaldo Cruz, Rio de Janeiro, Vol. 102(Suppl. I): 75-85, 2007.
4. De Ayala A.P, Pérez-Molina J.A, Norman F., and López-Vélez R.Chagasic cardiomyopathy in inmigrants from Latin America to Spain. Emerging Infectious Disease Volume 15, Number 4–April 2009.
5. According to the numbers of inmigrants registered for 2007in the website of the Japanese Ministry of Justice and estimated seroprevalence for non endemic countries according to Paricio-Talayero J.M. Vigilancia epidemiológica de la transmisión vertical de la enfermedad de Chagas en tres maternidades de la Comunidad Valenciana. Enferm Infecc Microbiol Clin 2008;26(10):609-13.

Chagas Disease Vaccines/Diagnostics:

Biology



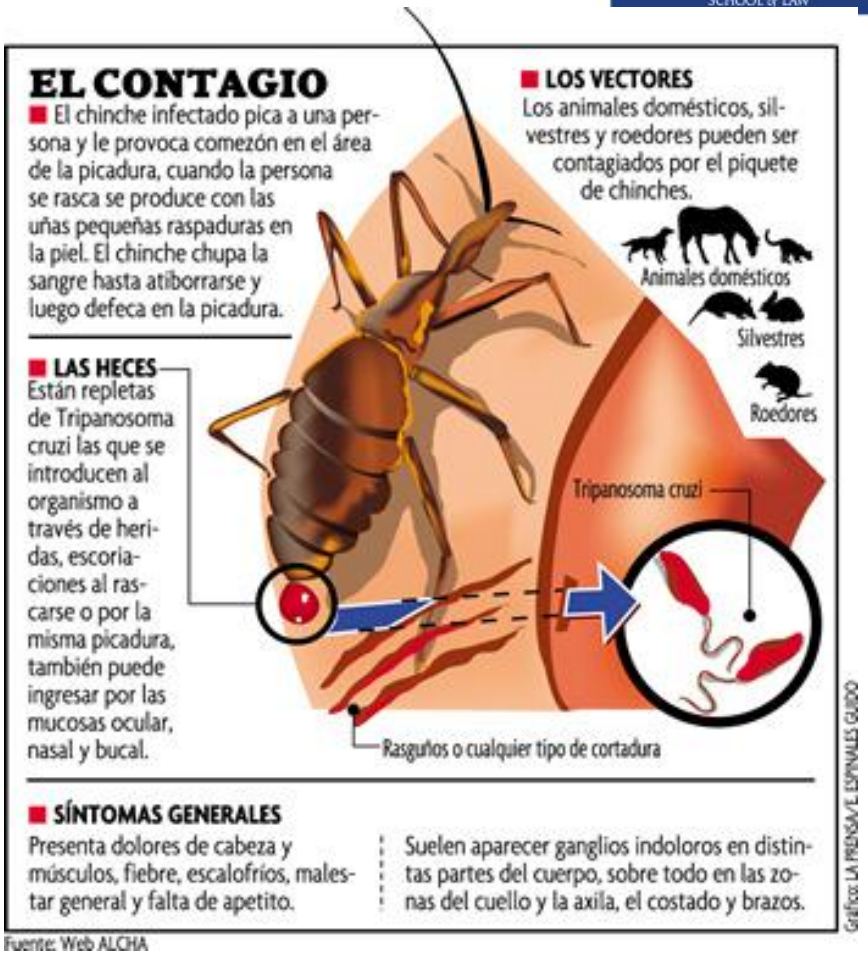
CDC
SAFER·HEALTHIER·PEOPLE™
http://www.dpd.cdc.gov/dpdx

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Chagas Disease Vaccines/Diagnostics:
Vector and Transmission

THE FRANKLIN PIERCE *Center for* INTELLECTUAL PROPERTY
UNIVERSITY *of* NEW HAMPSHIRE SCHOOL *of* LAW

Chagas disease, named after the Brazilian physician Carlos Chagas, who discovered the disease in 1909, is caused by the parasite *Trypanosoma cruzi*, which is transmitted to animals and people by insect vectors (Triatomine bugs) and is found only in the Americas (mainly, in rural areas of Latin America where poverty is widespread). Chagas disease (*T. cruzi* infection) is also referred to as American trypanosomiasis, and is considered one of the Neglected Parasitic Infections, a group of five parasitic diseases that have been targeted by CDC for public health action.

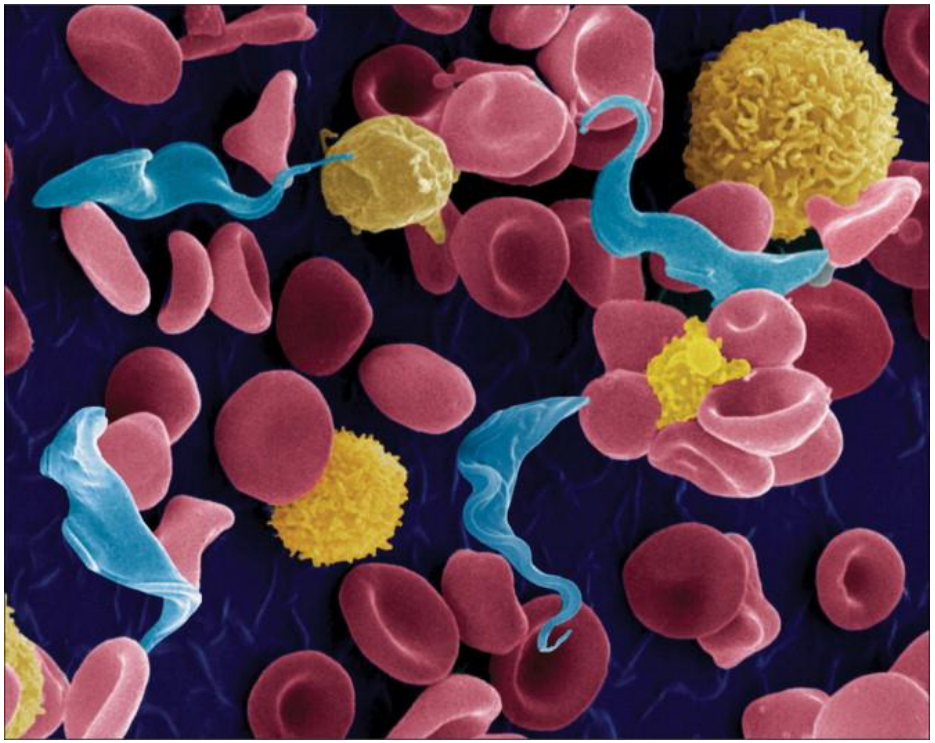


http://ameliecalot.es/2011/02/08/%C2%BFque-es-el-chagas

Chagas Disease Vaccines/Diagnostics:
Parasitic Infectious Agent

THE FRANKLIN PIERCE *Center for* INTELLECTUAL PROPERTY
UNIVERSITY *of* NEW HAMPSHIRE SCHOOL *of* LAW

Inside the host, the trypomastigotes invade cells near the site of inoculation, where they differentiate into intracellular amastigotes. Amastigotes multiply by binary fission and differentiate into trypomastigotes, and then are released into the circulation as bloodstream trypomastigotes. Trypomastigotes infect cells from a variety of tissues and transform into intracellular amastigotes in new infection sites.



Chagas Disease Vaccines/Diagnostics:
Clinical Manifestations

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Acute Chagas disease occurs immediately after infection, may last up to a few weeks or months. There may be fever or swelling around the site of infection; acute infection may result in severe inflammation of the heart muscle or the brain and lining around the brain. Following the acute phase, most infected people enter into a prolonged asymptomatic form of disease (called **"chronic indeterminate")** during which few or no parasites are found in the blood. During this time, most people are unaware of their infection. **An estimated 20 - 30% of infected people will develop debilitating and sometimes life-threatening medical problems over the course of their lives**:

- heart rhythm abnormalities that can cause sudden death;
- a dilated heart that doesn't pump blood well;
- a dilated esophagus or colon, leading to difficulties with eating or passing stool.

Chagas Disease Vaccines/Diagnostics:
Intellectual Property Issues

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
NEW HAMPSHIRE SCHOOL OF LAW

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

(10) **Patent No.: US 6,875,584 B1**
(45) **Date of Patent: Apr. 5, 2005**

(54) **PROPHYLACTIC AND THERAPEUTIC IMMUNIZATION AGAINST PROTOZOAN INFECTION AND DISEASE**

(75) Inventors: **Rick L. Tarleton**, Watkinsville, GA (US); **Nisha Garg**, League City, TX (US)

(73) Assignee: **University of Georgia Research Foundation, Inc.**, Athens, GA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/518,156**

(22) Filed: **Mar. 2, 2000**

Related U.S. Application Data

(60) Provisional application No. 60/122,532, filed on Mar. 2, 1999.

(51) **Int. Cl.**[7] **C12P 21/06**; C12P 15/09

(52) **U.S. Cl.** **435/69.1**; 435/69.2; 435/69.3; 435/69.5; 514/44

(58) **Field of Search** 435/69.1, 69.2, 435/69.3, 69.5; 514/44

Armah et al., "*S*–Myristoylation of a Glycosylphosphatidylinositol–specific Phospholipase C in *Trypanosoma brucei*," *J. Biol. Chem., 274*(9):5931–5938 (Feb. 26, 1999).

Abrahamson, "Cytokines in innate and acquired immunity to *Trypanosoma cruzi* infection," *Braz. J. Med. Biol. Res., 31*(1):117–121 (Jan. 1998).

Alberti et al., "Specific cellular and humoral immune response in Balb/c mice immunised with an expression genomic library of *Trypanosoma cruzi*," *Vaccine, 16*(6):608–612 (Apr. 1998).

Al Qahtani et al., "A 5' untranslated region which directs accurate and robust translation by prokaryotic and mammalian ribosomes," *Nuc. Acids Res., 24*(6):1173–1174 (1996).

Andrerws et al., "Presence of antibodies to the major surface glycoprotein of *Trypanosoma cruzi* amastigotes in sera from chagasic patients," *Am. J. Trop. Med. Hyg., 40*(1):46–49 (1989).

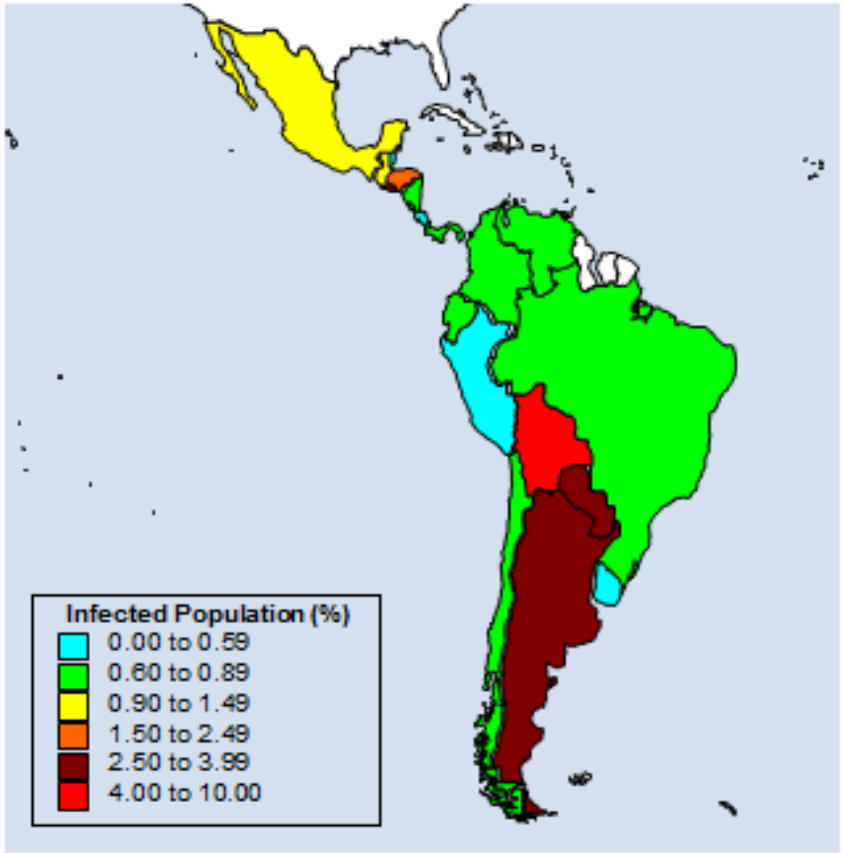
Andrews, "The Acid–Active Hemolysin of *Trypanosoma cruzi*," *Exp. Parasitol., 71*:241–244 (1990).

Barry et al., "Protection against mycoplasma infection using expression–library immunization," *Nature, 377*(6550):632–635 (1995).

Barry et al., "Biological features of genetic immunization," *Vaccine, 15*(8):788–791 (1997).

Prevalence of Chagas' Disease Endemic and Non-Endemic

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



Non-Endemic Populations of Chagas' Disease

Country	Total
United States	>300,000
Europe	68,000 – 123,000
Canada	>5,000
Japan	>3,000
Australia	>1,500

Disease Burden in Disability-Adjusted Life Years (DALYs)

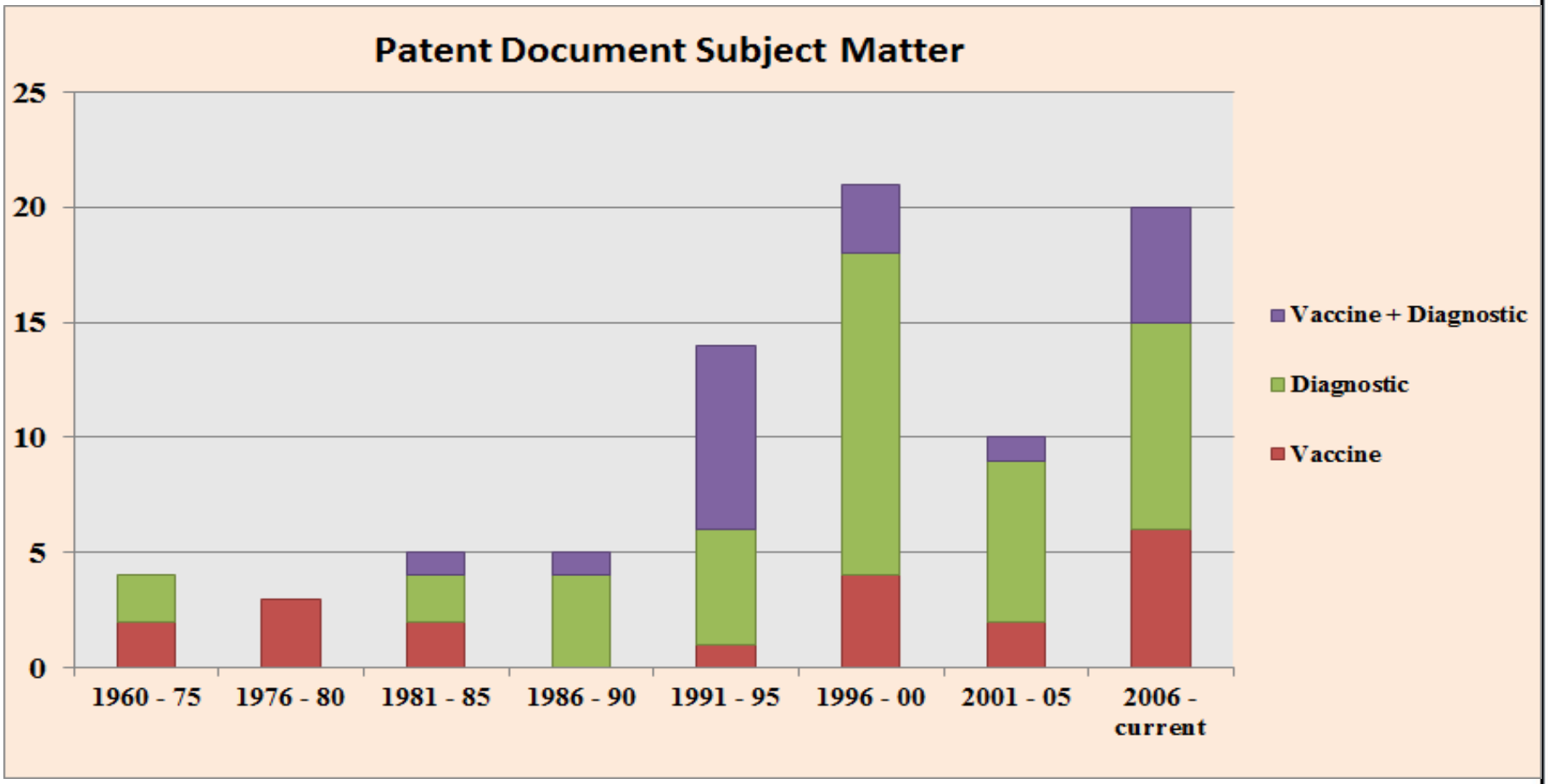
HIV/AIDS	3,200,000
Chagas' Disease	662,000
Malaria	111,000
Dengue/ Dengue Homrrhagic Fever	69,000
Leishmaniasis	44,000
Schistosomiasis	36,000
Lymphatic Filariasis	34,800
Trachoma	23,200
Leprosy	18,000

*P.J. Hotez, M.E. Bottazzi, C. Franco-Paredes, S.K. Ault, M.R. Periago, PLoS Negl. Trop. Dis. 2(9): e300. doi:10.1371/journal.pntd.0000300

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

What Patent Protection has been Sought?*

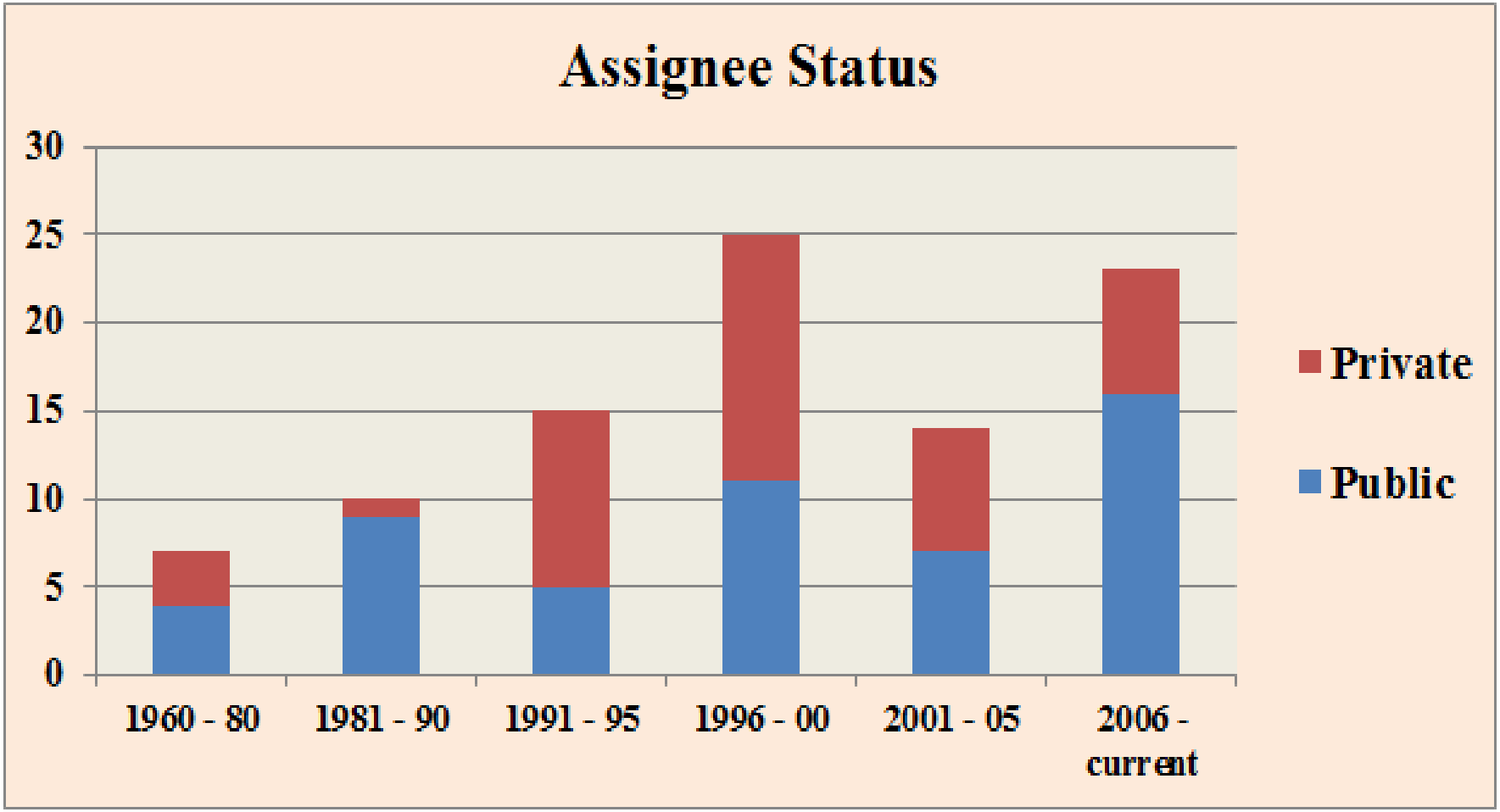
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



*20 Vaccine, 43 Diagnostic, 19 Vaccine +Diagnostic

Who Has Been Seeking Patent Protection?

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



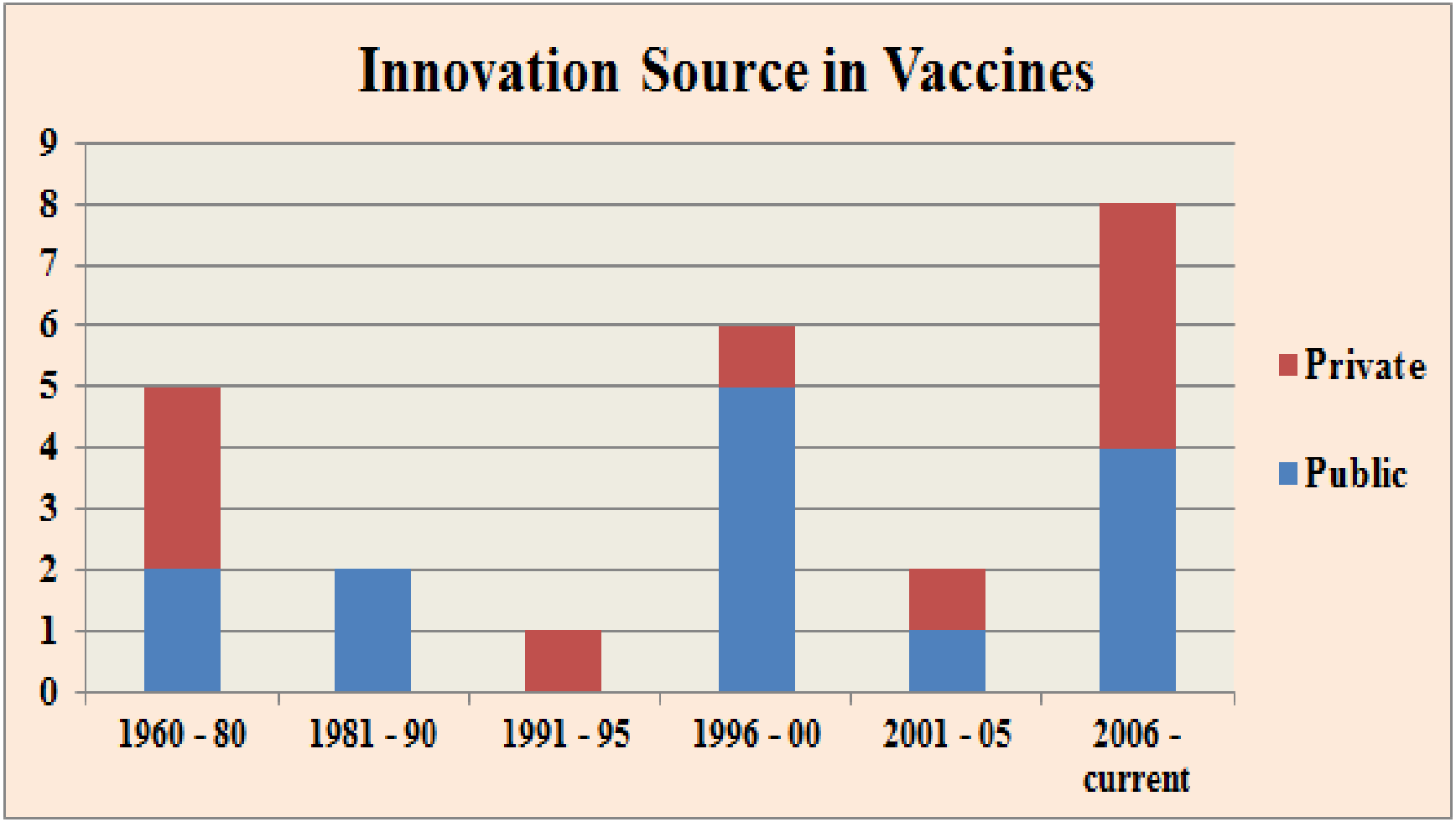
Who Has Been Seeking Patent Protection?

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Top Assignees	Documents
University of Georgia Research Foundation Inc. (US)	5
Abbott Laboratories (US)	4
Universidade Federal de Minas Gerais (BR)	3
Fundacao Oswaldo Cruz (BR)	3
Corixa Corporation (US)	3
Consejo Superior de Investigaciones Cientificas (CSIC) (ES)	3
Nine Assignees	2
Fifty – Four Assignees	1

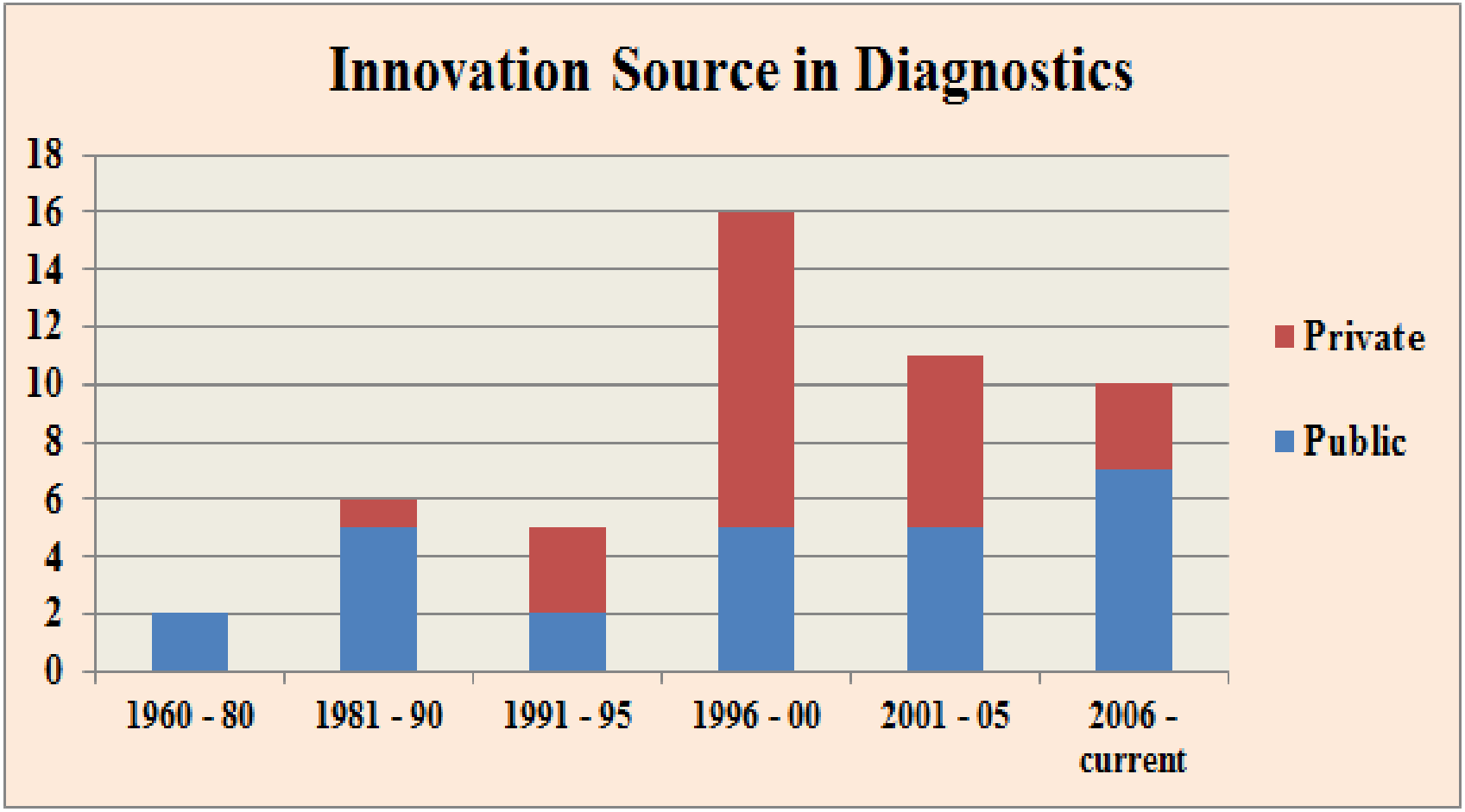
Patent Subject Matter Further Refined

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



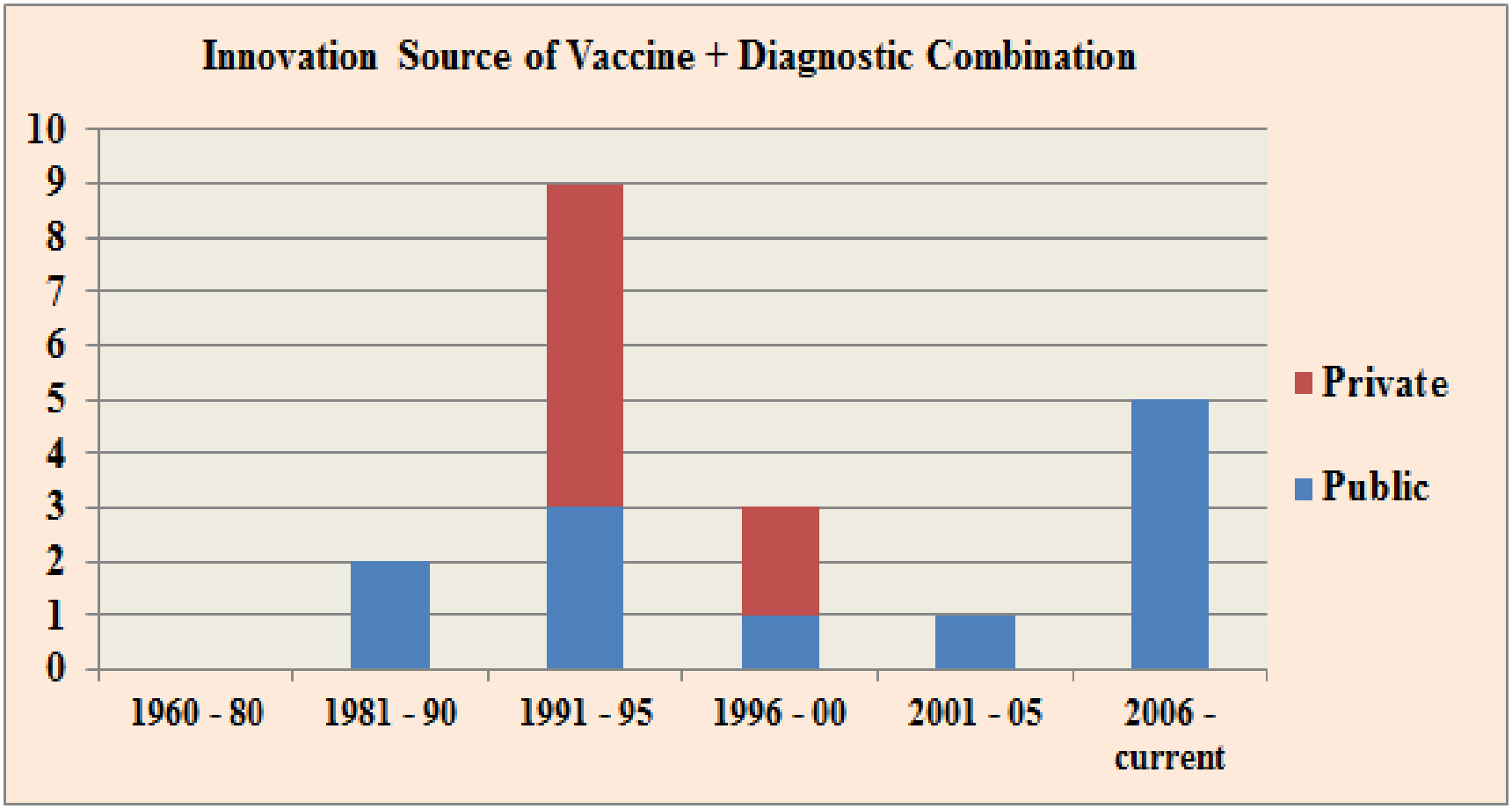
Patent Subject Matter Further Refined

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



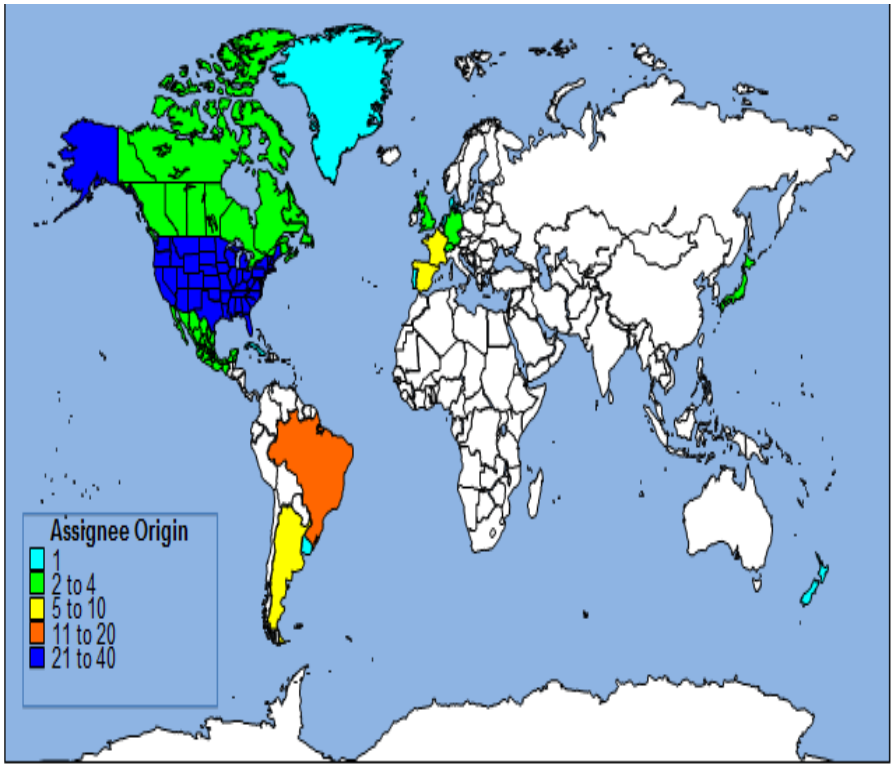
Patent Subject Matter Further Refined

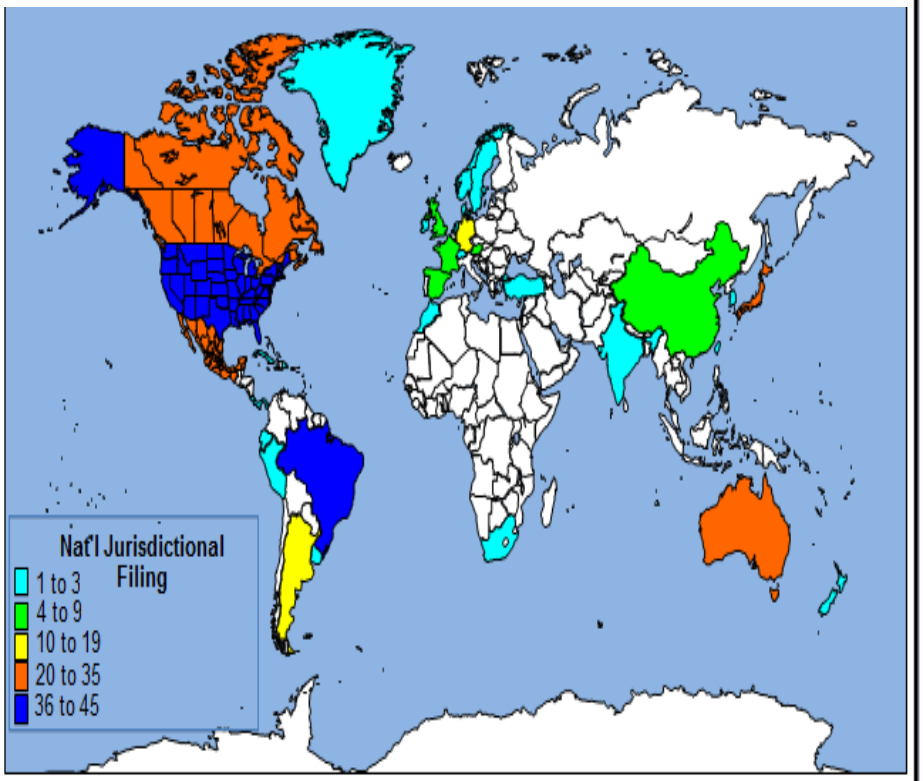
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



The 82 Patent Families

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

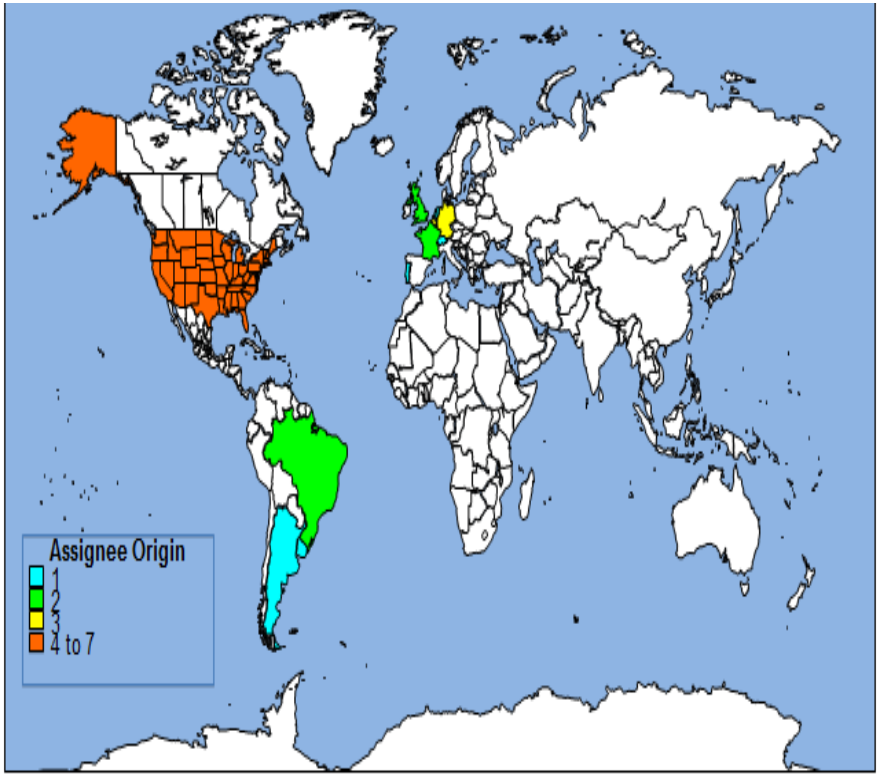


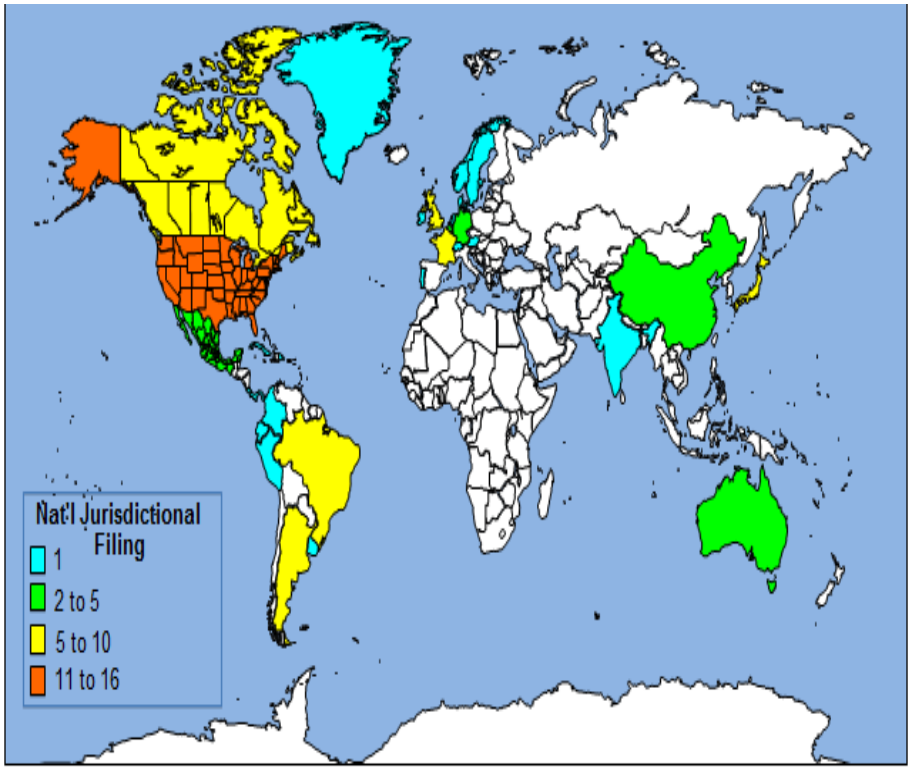


* 45 filed in PCT (WO) and 31 filed in European Union (EP)

Vaccines Only

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

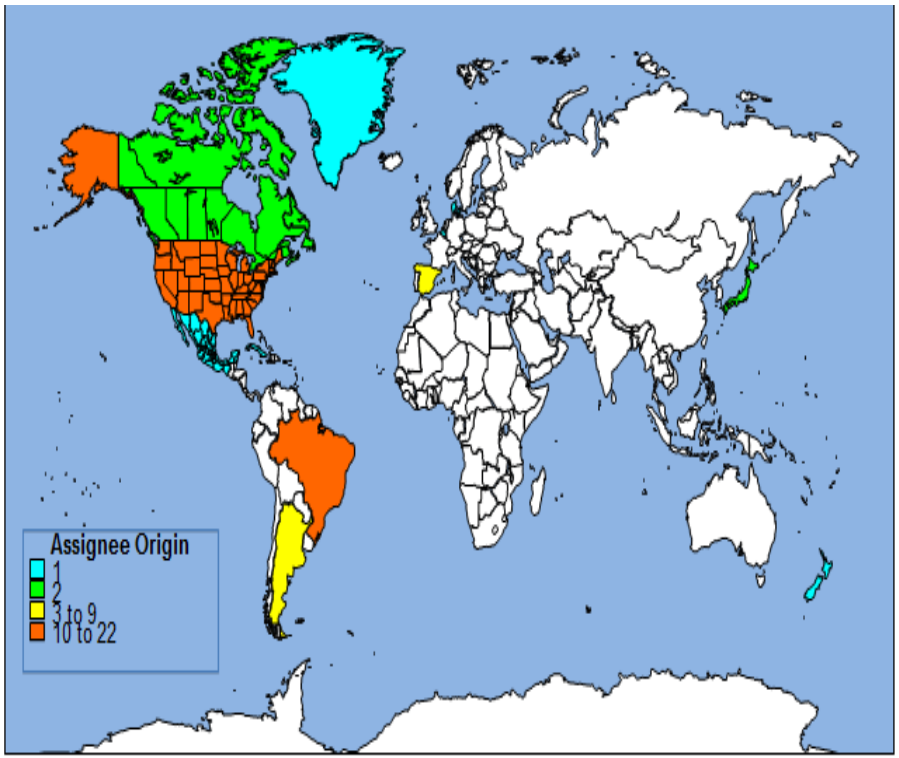


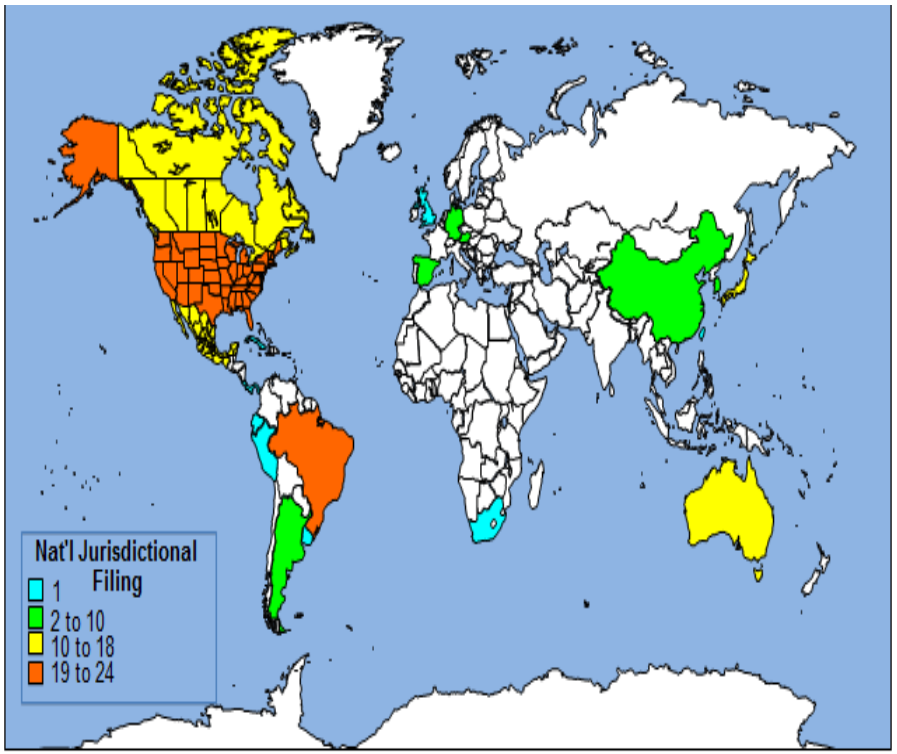


* 10 filed in PCT (WO) and 7 filed in European Union (EP)

Diagnostics

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

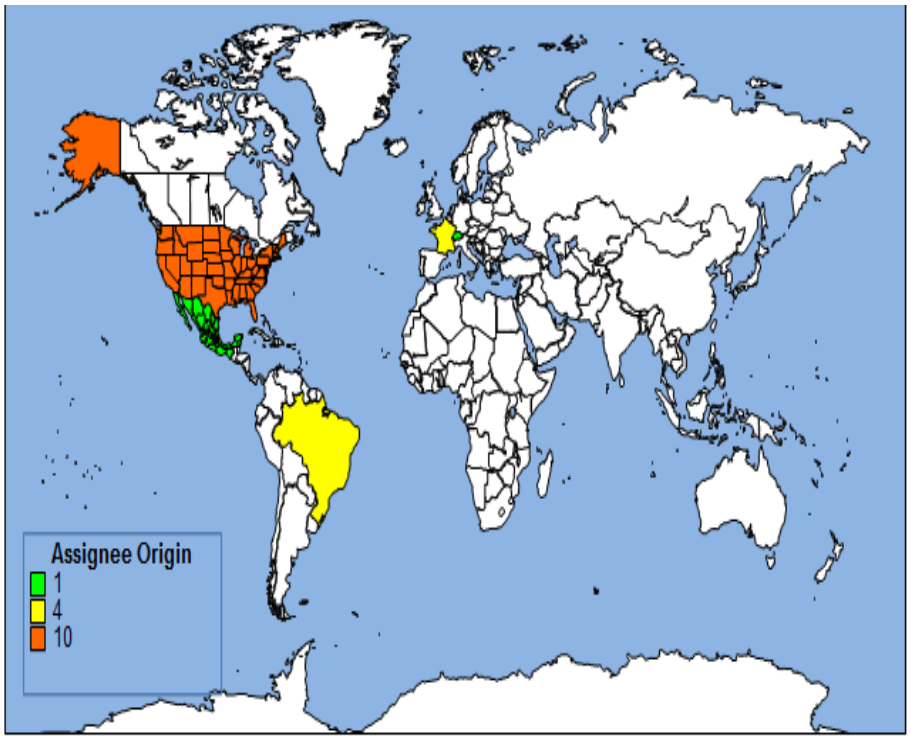


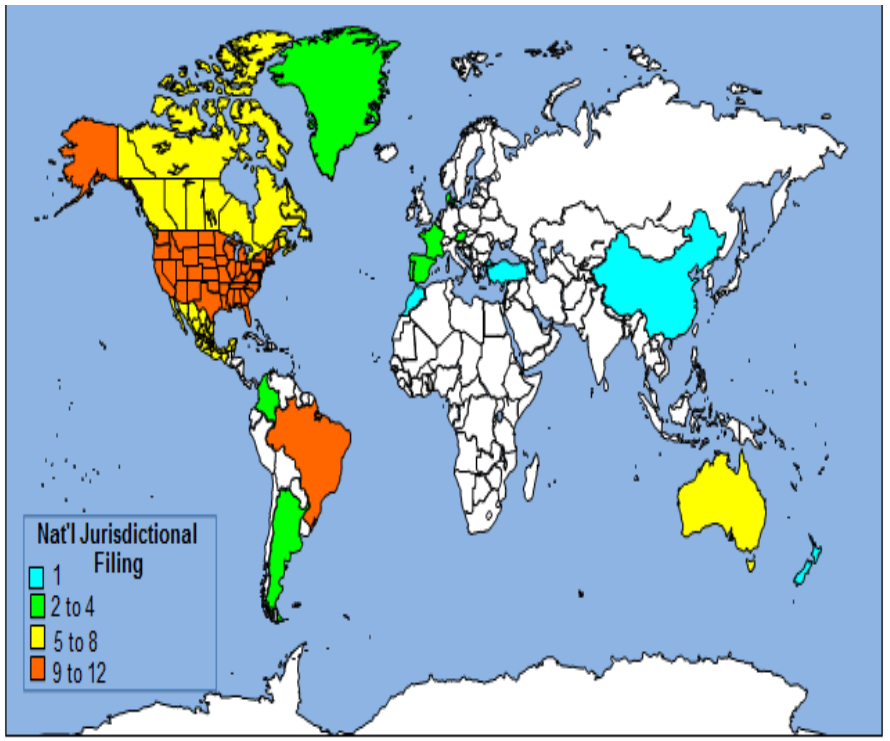


* 23 filed in PCT (WO) and 15 filed in European Union (EP)

Vaccine + Diagnostic Combination Patents

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW





* 12 filed in PCT (WO) and 9 filed in European Union (EP)

Innography Platform Patent Analytics

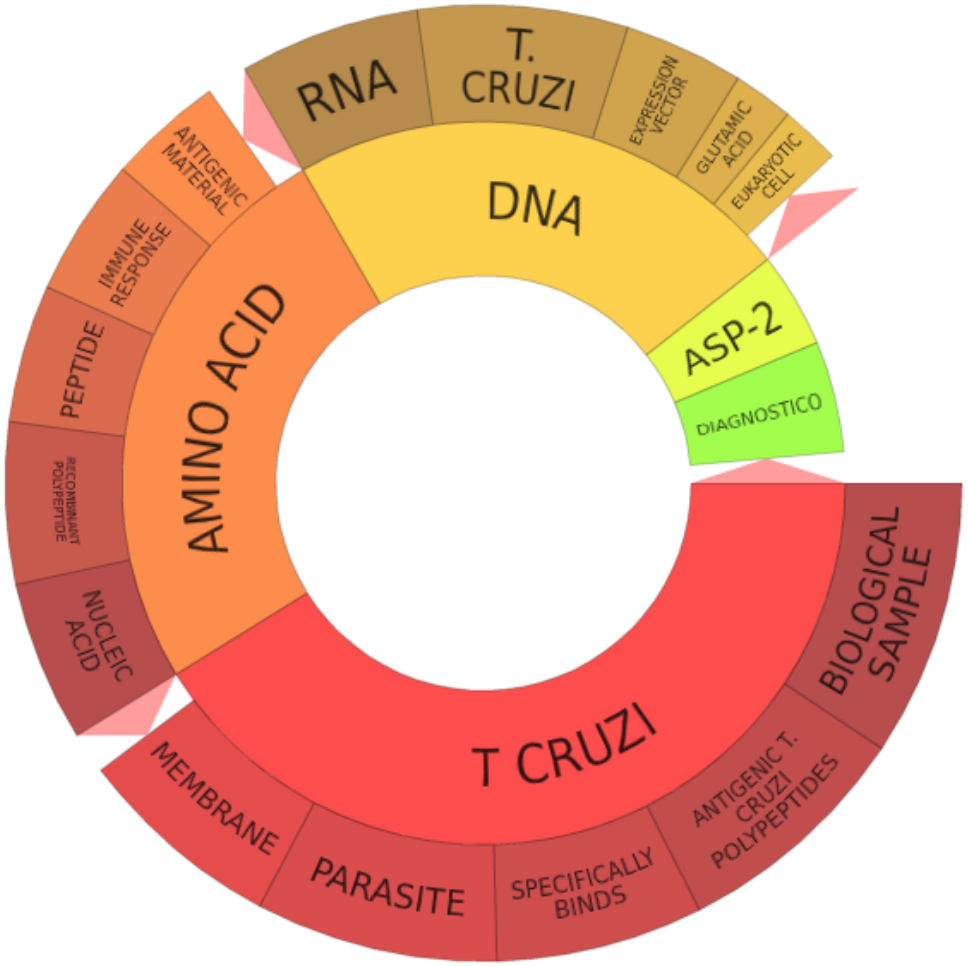
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

INNOGRAPHY

Innography Platform Patent Analytics:

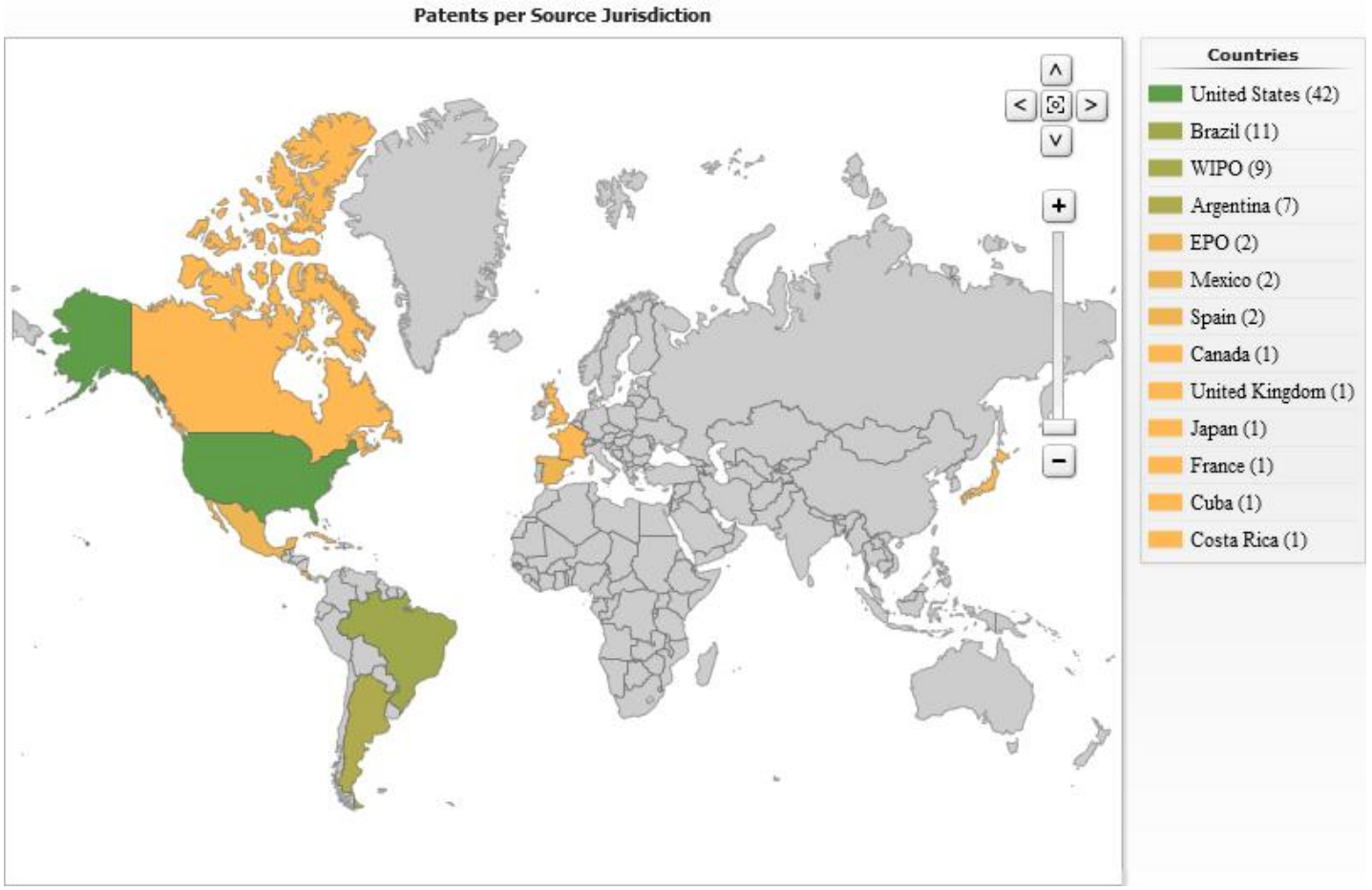
Text Clustering for 82 Patent Families

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



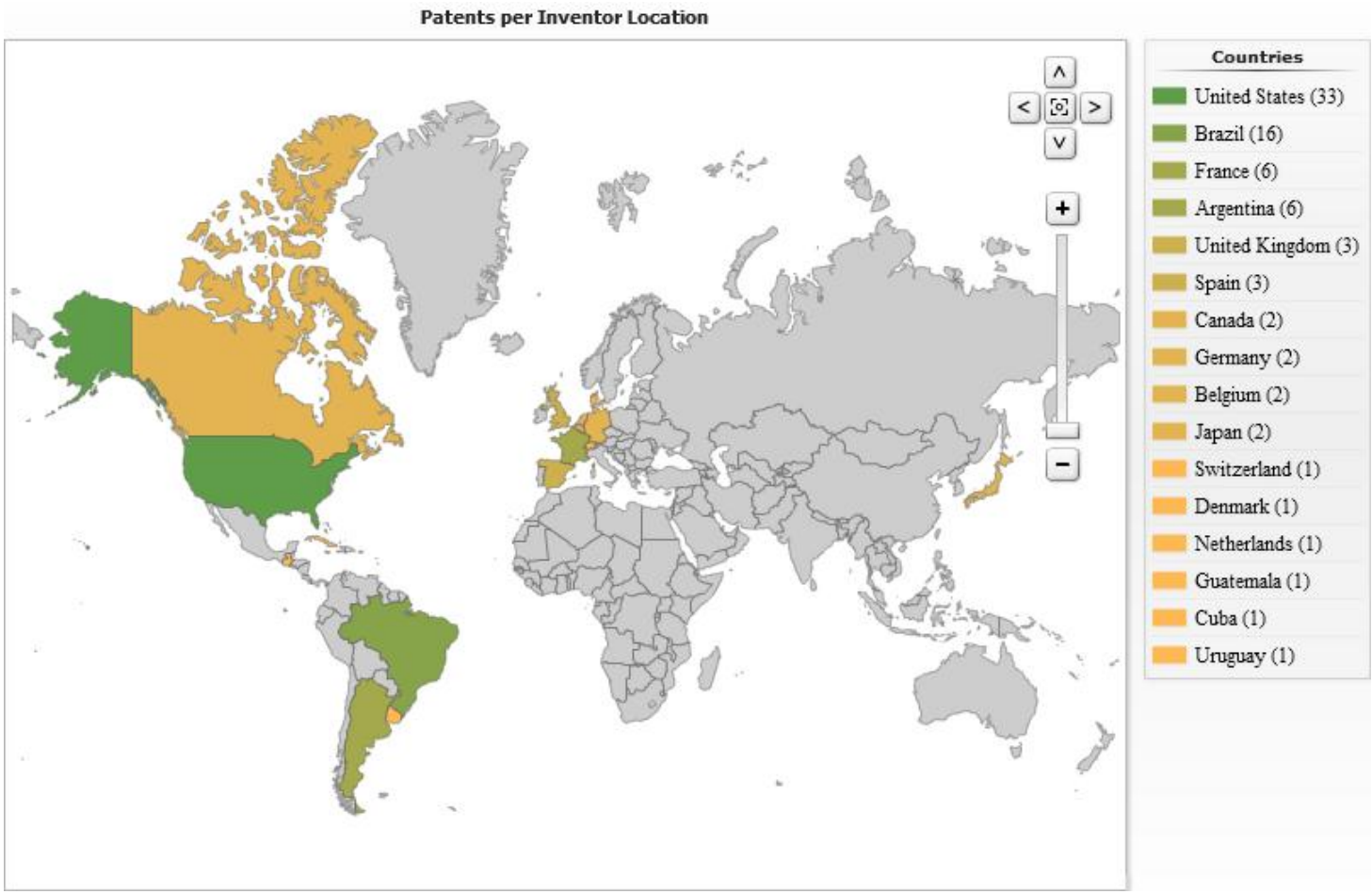
Innography Platform Patent Analytics

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



Innography Platform Patent Analytics

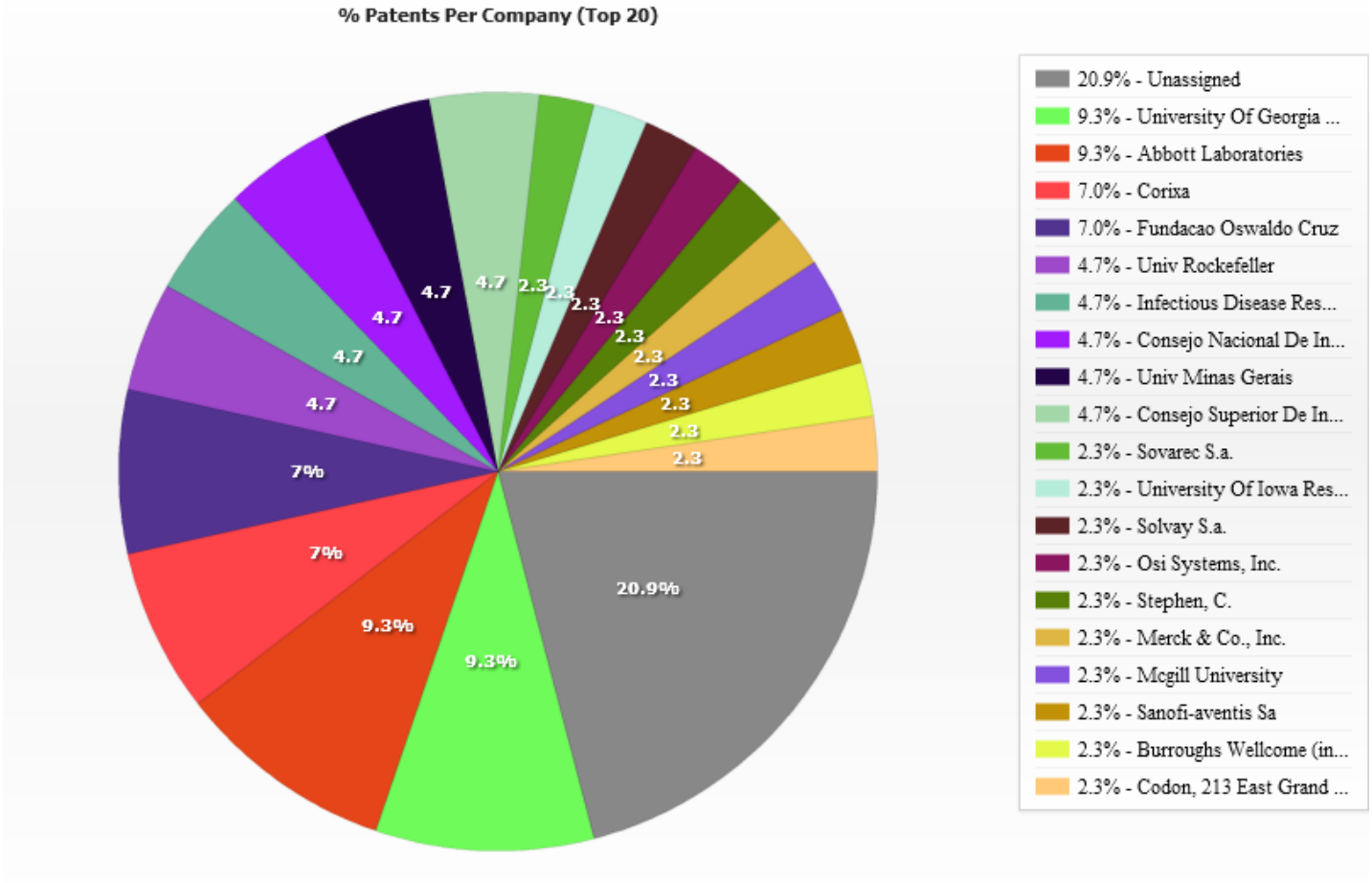
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



Innography Platform Patent Analytics

Collapsed patent family data (82-1 patent families)

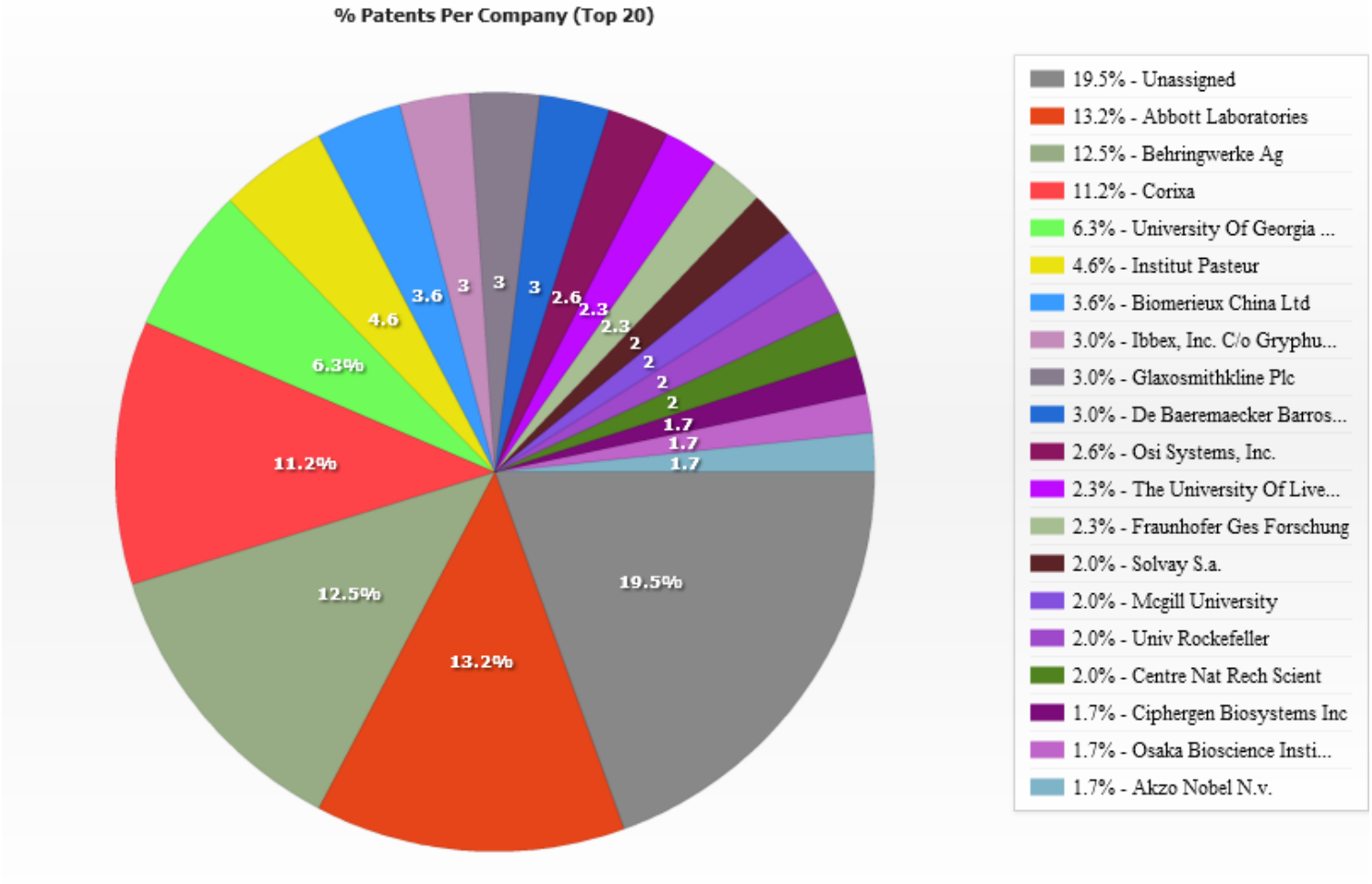
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



Innography Platform Patent Analytics

415 Documents, expanded patent family data

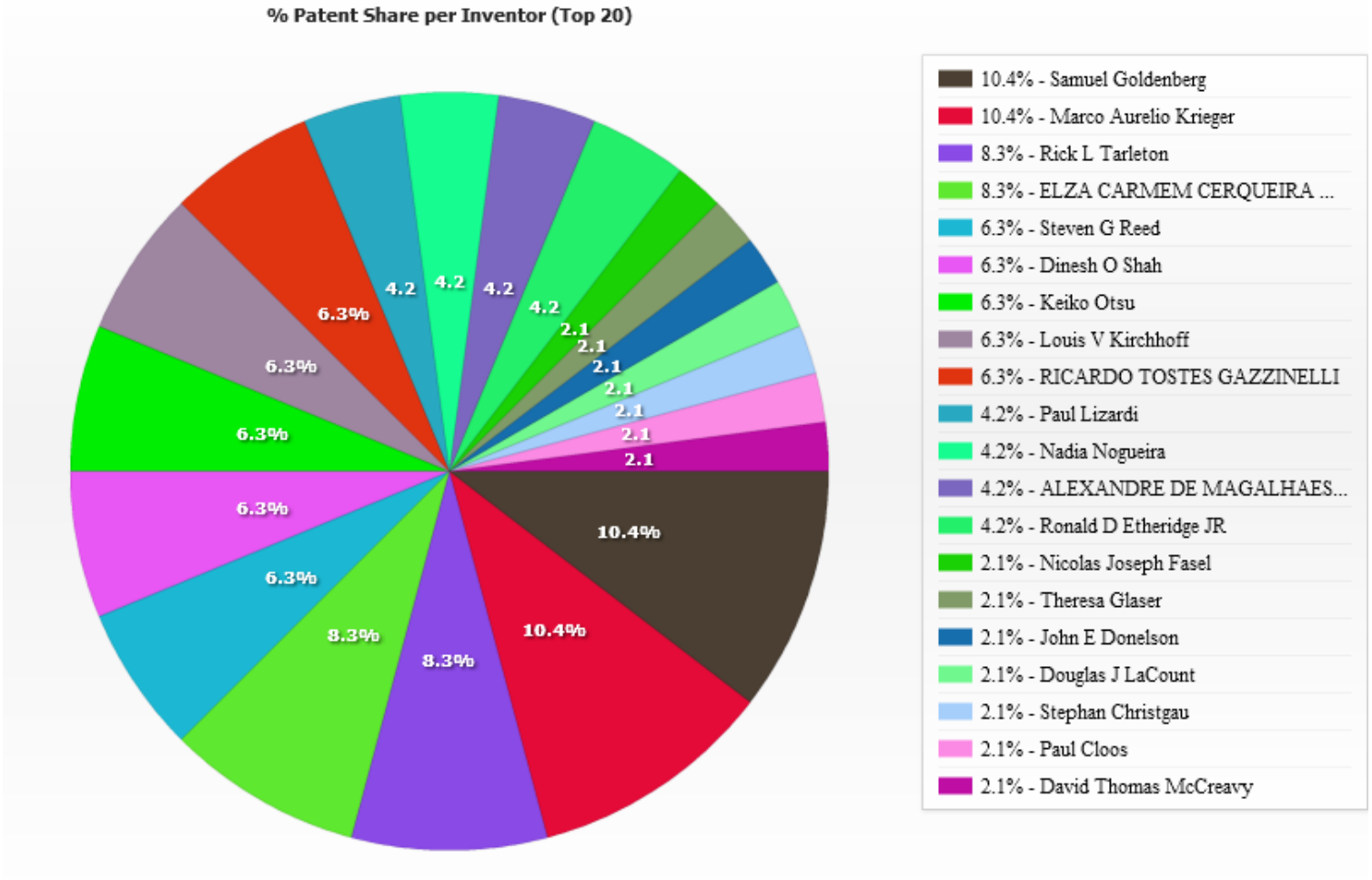
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



Innography Platform Patent Analytics

Inventor, 82-1 patent families (collapsed to one representative document)

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



Sample Vaccine

United States Patent [19]
Hungerer

[11] **4,024,242**
[45] **May 17, 1977**

[54] **SUBSTANCE HAVING IMMUNOLOGICAL ACTIVITY AND PROCESS FOR ITS MANUFACTURE**

[75] Inventor: **Klaus-Dieter Hungerer,** Marburg-Marbach, Germany

[73] Assignee: **Hoechst Aktiengesellschaft,** Frankfurt am Main, Germany

[22] Filed: **June 23, 1975**

[21] Appl. No.: **589,082**

[30] **Foreign Application Priority Data**

June 25, 1974 Germany 2430380

[52] **U.S. Cl.** **424/88;** 195/104
[51] **Int. Cl.²** **A61K 39/00;** C12B 1/00
[58] **Field of Search** 195/104; 424/88

[56] **References Cited**

OTHER PUBLICATIONS

Soltys, Chem. Abst., vol. 67 (1967) p. 62560z.
May & Baker, Chem. Abst., vol. 57 (1962) p. 9825b.

Primary Examiner—Sam Rosen
Attorney, Agent, or Firm—Curtis, Morris & Safford

[57] **ABSTRACT**

Method of chemically attenuating trypanosomes with a phenanthridine compound, such as 3,8-diamino-5-ethyl-6-phenyl phenanthridine, to obtain non-pathogenic organisms with immunological activity; attenuated organisms produced in this way; vaccines containing such attenuated organisms.

11 Claims, No Drawings

0.2μ) resulted in a suspension of 2×10^7 trypanosomes/ml. This suspension was incubated for 24 hours at 28° C in an incubator. After 24 hours, it was centrifuged again at 4500 r.p.m. at 4° C in the Sorvall centrifuge. The supernatent material was eliminated, and the sediment was taken up in 18 ml of medium.

The final concentration of 1×10^8 trypanosomes/ml obtained was, for example, suitable for immunizing mice.

What is claimed is:

1. A process for the manufacture of a substance having immunological activity, which comprises incubating trypanosomes that have been suspended in a monophase, aqueous, liquid culture medium with a phenanthridine derivative until they lose their pathogenicity, and then collecting the trypanosomes thus attenuated.

2. A process as claimed in claim **1,** wherein the phenanthridine derivative used is 3,8-diamino-5-ethyl-6-phenyl-phenanthridinium bromide.

3. A process as claimed in claim **1,** wherein the culture medium is free from proteins.

4. A process as claimed in claim **1,** wherein the composition of trypanosomes in the suspension ranges from 10^3 to 10^8/ml.

5. A process as claimed in claim **1,** wherein the phenanthridine derivative is used in a concentration of 0.5 to 1000γ/ml.

6. A process as claimed in claim **1,** wherein incubation is carried out for 1 to 120 hours at 18° – 37° C.

7. A process as claimed in claim **1,** wherein the concentration of trypanosomes in the suspension ranges from 1×10^7 to to 5×10^7/ml.

8. A process as claimed in claim **1,** wherein the phenanthridine derivatives is used in a concentration of 5 to 100γ/ml.

9. A process as claimed in claim **1,** wherein the incubation is carried out for 20 to 48 hours at 25°–33° C.

10. Chemically attenuated trypanosomes as obtained according to claim **1.**

11. A vaccine effective against the Chagas disease, containing attenuated trypanosomes as claimed in claim **10** as the active ingredient.

* * * * *

Sample Vaccine

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW


US007892555B2

(12) **United States Patent**
Tarleton

(10) **Patent No.: US 7,892,555 B2**
(45) **Date of Patent: Feb. 22, 2011**

(54) **PROPHYLACTIC AND THERAPEUTIC IMMUNIZATION AGAINST PROTOZOAN INFECTION AND DISEASE**

(75) Inventor: **Rick L. Tarleton**, Watkinsville, GA (US)

(73) Assignee: **University of Georgia Research Foundation, Inc.**, Athens, GA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **12/830,063**

(22) Filed: **Jul. 2, 2010**

(65) **Prior Publication Data**

US 2010/0297173 A1 Nov. 25, 2010

Related U.S. Application Data

(60) Continuation of application No. 11/893,951, filed on Aug. 17, 2007, now abandoned, which is a division of application No. 11/015,578, filed on Dec. 17, 2004, now Pat. No. 7,309,784, which is a division of application No. 09/518,156, filed on Mar. 2, 2000, now Pat. No. 6,875,584.

(60) Provisional application No. 60/122,532, filed on Mar. 2, 1999.

(51) **Int. Cl.**
A61K 39/00 (2006.01)
A61K 39/002 (2006.01)
C07K 14/00 (2006.01)

(52) **U.S. Cl.** **424/184.1**; 424/265.1; 424/269.1; 530/350

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

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,304,371	A	4/1994	Reed
5,646,114	A	7/1997	Lambert et al.
6,419,933	B1	7/2002	Reed et al.
6,875,584	B1	4/2005	Tarleton et al.
7,309,784	B2	12/2007	Tarleton et al.
2004/0241729	A1	12/2004	Liew
2005/0158347	A1	7/2005	Tarleton et al.
2005/0244505	A1	11/2005	Higbee et al.
2006/0228300	A1	10/2006	Chang et al.
2007/0178100	A1	8/2007	Tarleton et al.

FOREIGN PATENT DOCUMENTS

WO	WO 2005/111622	A2	11/2005
WO	WO 2005/111622	A3	10/2006

OTHER PUBLICATIONS

Armah et al., "*S*-Myristoylation of a Glycosylphosphatidylinositol-specific Phospholipase C in *Trypanosoma brucei*," *J. Biol. Chem.*, 274(9):5931-5938 (Feb. 26, 1999).

Abrahamsohn, "Cytokines in innate and acquired immunity to *Trypanosoma cruzi* infection," *Braz. J Med. Biol. Res.*, 31(1):117-121 (Jan. 1998).

Alberti et al., "Specific cellular and humoral immune response in Balb/c mice immunised with an expression genomic library of *Trypanosoma cruzi*," *Vaccine*, 16(6):608-612 (Apr. 1998).

Al-Qahtani et al., "A 5' untranslated region which directs accurate and robust translation by prokaryotic and mammalian ribosomes," *Nuc. Acids Res.*, 24(6):1173-1174 (1996).

Andrews et al., "Presence of antibodies to the major surface glycoprotein of *Trypanosoma cruzi* amastigotes in sera from chagasic patients," *Am. J. Trop. Med. Hyg.*, 40(1):46-49 (1989).

Andrews, "The Acid-Active Hemolysin of *Trypanosoma cruzi*," *Exp. Parasitol.*, 71:241-244 (1990).

Barry et al., "Protection against mycoplasma infection using expression-library immunization," *Nature*, 377(6550):632-635 (1995).

Barry et al., "Biological features of genetic immunization," *Vaccine*, 15(8):788-791 (1997).

Basombrio, "*Trypanosoma cruzi*: Partial Prevention of the Natural Infection of Guinea Pigs with a Killed Parasite Vaccine," *Exp. Parasitol.*, 71:1-8 (1990).

Bharadwaj et al., "Induction of Protective Immune Responses by Immunization with Linear Multiepitope Peptides Based on Conserved Sequences from *Plasmodium falciparum* Antigens," *Infect. Immun.*, 66(7):3232-3241 (Jul. 1998).

Biebinger et al., "A Plasmid Shuttle Vector Bearing an rRNA Promoter is Extrachromosomally Maintained in *Crithidia fasciculata*," *Exp. Parasitol.*, 83(2):252-258 (1996).

Bliss et al., "IL-12, as an Adjuvant, Promotes a T Helper 1 Cell, but Does Not Suppress a T Helper 2 Cell Recall Response," *J. Immunol.*, 156:(3):887-894 (1996).

Brener, "Why Vaccines do not work in Chagas Disease," *Parasitol. Today*, 2(7):196-197 (1986).

Carpenter et al., "Linearized free maxicircle DNA in *Crithidia fasciculata* is a product of topoisomerase II-mediated cleavage," *Mol. Biochem. Parasitol.*, 76:115-123 (1996).

Chow et al., "Development of Th1 and Th2 Populations and the Nature of Immune Responses to Hepatitis B Virus DNA Vaccines Can Be Modulated by Codelivery of Various Cytokine Genes," *J. Immunol.*, 160(3):1320-1329 (Feb. 1, 1998).

Clayton et al., "Protein Trafficking in Kinetoplastid Protozoa," *Microbiol. Rev.*, 59(3):325-344 (1995).

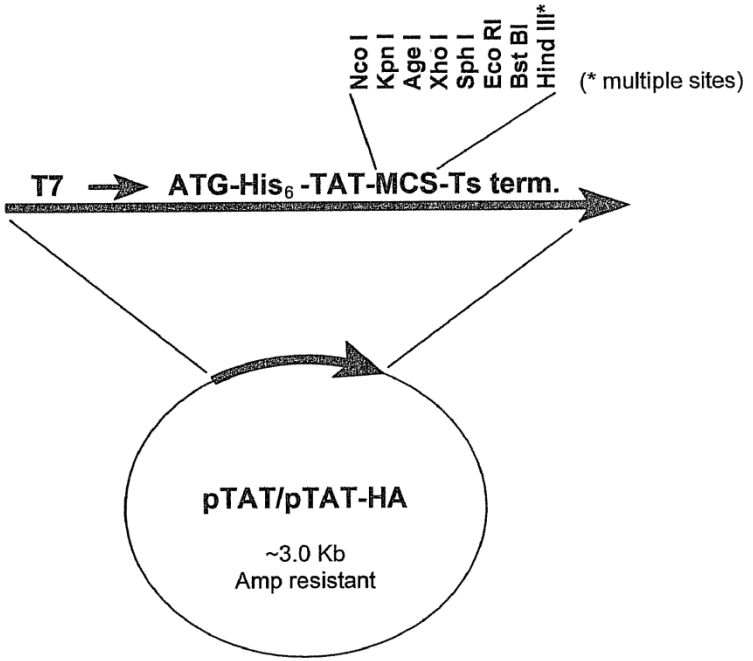
(Continued)

Primary Examiner—Mark Navarro
(74) *Attorney, Agent, or Firm*—Mueting Raasch & Gebhardt, P.A.

(57) **ABSTRACT**

Polypeptide and polynucleotide vaccines effective to treat or prevent infection of a mammal, such as a dog, a cat, or a human, by a protozoan. Methods of treatment and prevention are also provided, including therapeutic administration of the vaccine to an infected mammal to prevent progression of infection to a chronic debilitating disease state. Preferred embodiments of the polynucleotide vaccine contain nucleotide coding regions that encode polypeptides that are surface-associated or secreted by *T. cruzi*. Optionally the efficacy of the polynucleotide vaccine is increased by inclusion of a nucleotide coding region encoding a cytokine. Preferred embodiments of the polypeptide vaccine include immunogenic peptides that contain membrane transducing sequences that allow the polypeptides to translocate across a mammalian cell membrane.

13 Claims, 21 Drawing Sheets



Sample Diagnostic

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

US007888135B2

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

(10) **Patent No.: US 7,888,135 B2**
(45) **Date of Patent: Feb. 15, 2011**

(54) **DIAGNOSTIC ASSAY FOR *TRYPANOSOMA CRUZI* INFECTION**

(75) Inventors: **Rick L. Tarleton**, Watkinsville, GA (US); **Ronald D. Etheridge, Jr.**, Athens, GA (US)

(73) Assignee: **University of Georgia Research Foundation, Inc.**, Athens, GA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 554 days.

(21) Appl. No.: **11/587,283**

(22) PCT Filed: **Apr. 22, 2005**

(86) PCT No.: **PCT/US2005/013777**

§ 371 (c)(1),
(2), (4) Date: **Aug. 2, 2007**

(87) PCT Pub. No.: **WO2005/111622**

PCT Pub. Date: **Nov. 24, 2005**

(65) **Prior Publication Data**

US 2008/0019995 A1 Jan. 24, 2008

Related U.S. Application Data

(60) Provisional application No. 60/564,804, filed on Apr. 23, 2004, provisional application No. 60/623,299, filed on Oct. 29, 2004.

(51) **Int. Cl.**
G01N 33/53 (2006.01)

(52) **U.S. Cl.** **436/518**; 436/523

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

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,232,844	A	8/1993	Horowitz et al.
5,756,662	A	5/1998	Reed
6,368,827	B1	4/2002	Tarleton et al.
6,403,103	B1	6/2002	Paranhos-Baccala et al.
6,419,933	B1	7/2002	Reed et al.
6,875,584	B1	4/2005	Tarleton et al.
2004/0241729	A1	12/2004	Liew
2005/0158347	A1	7/2005	Tarleton et al.
2005/0244505	A1	11/2005	Higbee et al.
2006/0228300	A1	10/2006	Chang et al.

FOREIGN PATENT DOCUMENTS

WO WO 2005/111622 A2 11/2005

OTHER PUBLICATIONS

Luhrs et al. (Vaccine, 21:3058-3069, 2003).*
Mezzasoma et al. (Clin. Chem., 48:121-130, Jan. 2002).*
He et al. (Clin. Diag. Lab. Immunol., 7:899-903, 2000).*
Atwood et al., "The *Trypanosoma cruzi* proteome," *Science*, 2005, 309(5733):473-476.
Bio-Plex System and Suspension Array Technology. Bio-Rad Laboratories. Available online [retrieved Apr. 18, 2005]. Retrieved from the Internet: <http://www.biorad.com/B2B/BioRad/product/br_category.jsp?BV_SessionID=@@@@0429302147.1179497201@@@@&BV_EngineID=ccchaddkmhhmfjkcfngcfkmdhkkdflm.0&categoryPath=%2fCatalogs%2fLife+Science+Research%2fMultiplex+Suspension+Array+System%2fBio-Plex+System+and+Suspension+Array+Technology&catLevel=4&divName=Corporate&loggedIn=false&lang=English&country=HQ&catOID-24083&isPA=false&serviceLevel=Lit+Request>; 5 pgs.
Bio-Plex Workstation and Software. Bio-Rad Laboratories. Available online [retrieved Apr. 18, 2005]. Retrieved from the Internet: <http://www.biorad.com/B2B/BioRad/product/br_category.jsp?BV_SessionID=@@@@0429302147.1179497201@@@@&BV_EngineID=ccchaddlunfihmfjkcfngcflcmdhkkdflm.0&divName=Life+Science+Research&categoryPath=%2fCatalogs%2fLife+Science+Research%2fMultiplex+Suspension+Array+System%2fBio-Plex+Workstation+and+Software&loggedIn=false&lang=English &catLevel=4&country=HQ&catOID=-24084&isPA=false&serviceLevel=Lit+Request>; 3 pgs.
da Silveira et al., "Chagas disease: recombinant *Trypanosoma cruzi* antigens for serological diagnosis," 2001, *Trends Parasitol.*, 17(6):286-291.
Dias et al., "The Evolution of Chagas Disease (American Trypanosomiasis) Control after 90 Years since Carlos Chagas Discovery," 1999, *Mem. Inst. Oswaldo Cruz*, 94:Supp1.1:103-121.
Donnelly et al., "DNA Vaccines," *Ann.Rev.Immunol.* 15:617-648, 1997.
Endresz et al., "Induction of human cytomegalovirus (HCMV)-glycoprotein B (gB)pspecific neutralizing antibody and phosphoprotein 65 (pp65)-specific cytotoxic T lymphocyte responses by naked DNA immunization," 1999, *Vaccine*, 17:50-58.
Etheridge and Tarleton "What is wrong with this test: A high throughput screening of *Trypanosoma cruzi* antigens for seroligical diagnosis." Poster. Woods Hole ImmunoParasitology Conference: Woods Hole, MA. Apr. 25-28, 2004. 1 page; Abstract printed in meeting program.
Ferreira et al., "Enzyme-Linked Immunosorbent Assay for Serological Diagnosis of Chagas' Disease Employing a *Trypanosoma cruzi* Recombinant Antigen that Consists of Four Different Peptides," 2001, *J. Clin.Micro.*, 39(12):4390-4395.
Fifis et al., "Size-Dependent Immunogenicity: Therapeutic and Protective Properties of Nano-Vaccines against Tumors," 2004, *J. Immunol.*, 173:3148-3154.
Fifis et al., "Short peptide sequences containing MHC Class I and/or Class II epitopes linked to nano-beads induce strong immunity and inhibition of growth of antigen-specific tumor challenge in mice," 2004, *Vaccine*, 23:258-266.

(Continued)

Primary Examiner—N. M Minnifield
Assistant Examiner—Brian J Gangle
(74) *Attorney, Agent, or Firm*—Mueting Raasch & Gebhardt, P.A.

(57) **ABSTRACT**

A sensitive, multicomponent diagnostic test for infection with *T. cruzi*, the causative agent of Chagas disease, including methods of making and methods of use. Also provided is a method for screening *T. cruzi* polypeptides to identify antigenic polypeptides for inclusion as components of the diagnostic test, as well as compositions containing antigenic *T. cruzi* polypeptides.

10 Claims, 9 Drawing Sheets

Fig. 1A

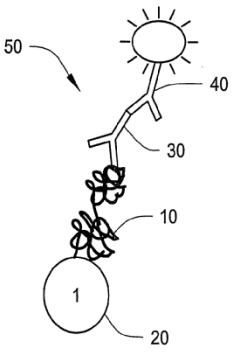


Fig. 1B

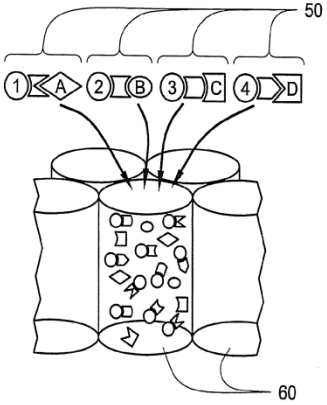
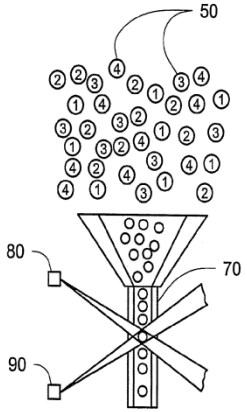


Fig. 1C



Sample Diagnostic

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

United States Patent [19]
Hanson

[11] **3,993,743**
[45] **Nov. 23, 1976**

[54] **METHOD FOR DIAGNOSIS OF CHAGAS' DISEASE**

[75] Inventor: **William L. Hanson,** Bishop, Ga.

[73] Assignee: **Research Corporation,** New York, N.Y.

[22] Filed: **Feb. 7, 1975**

[21] Appl. No.: **547,956**

Related U.S. Application Data

[62] Division of Ser. No. 386,285, Aug. 7, 1973, Pat. No. 3,911,097.

[52] **U.S. Cl.** **424/12;** 424/85; 424/88

[51] **Int. Cl.²** **G01N 31/02;** G01N 33/16; A61K 39/00

[58] **Field of Search** 424/12, 85, 88

[56] **References Cited**

OTHER PUBLICATIONS

Bergendi, Chem. Abs., vol. 74, 1971 p. 175, No. 11475n.

Capron, Chem. Abs., vol. 71, 1969 p. 186, No. 79194p.

Primary Examiner—Albert T. Meyers
Assistant Examiner—A. P. Fagelson
Attorney, Agent, or Firm—James C. Haight

[57] **ABSTRACT**

A process for diagnosing Chagas' disease in a living mammal susceptible to infection by *Trypanosoma cruzi* which comprises reacting in vitro an antibody-containing blood sample from said mammal in an immunoprecipitin test with an immunologically effective amount of a purified water-soluble antigen extract obtained from essentially only the trypomastigote and amastigote growth stages of the protozoa *Trypanosoma cruzi*, and diagnosing the presence of Chagas' disease from the formation of precipitin bands at an antigen-antibody interface.

5 Claims, No Drawings

What is claimed is:

1. A process for diagnosing Chagas' disease in a living mammal susceptible to infection by *Trypanosoma cruzi* which comprises:

a. reacting in vitro an antibody-containing blood sample from said mammal in an immunoprecipitin test with an immunologically effective amount of a purified water-soluble antigen preparation capable of forming a precipitated antigen-antibody complex in an immunoprecipitin reaction when contacted with antibodies associated with chronic Chagas' disease, said antigen preparation comprising an immunoprecipitatingly effective concentration and amount of water-soluble cellular antigens released by disruption of cells from essentially only the trypomastigote and amastigote growth stages of the protozoa *Trypanosoma cruzi* and being substantially free from serum protein antibodies, from antigens associated with the epimastigote growth stage of said protozoa and from water-insoluble cellular material; and

b. diagnosing the presence of Chagas' disease from the formation of precipitin bands at an antigen-antibody interface.

2. The process of claim **1** wherein said immunoprecipitin test is a cross-over electrophoresis test.

3. The process of claim **2** wherein said test is an immuno-osmoelectrophoresis test.

4. The process of claim **1** wherein 60–80% of said antigen preparation is obtained from the trypomastigote growth stage of said protozoa.

5. The process of claim **4** wherein said antigen preparation is in the form of an aqueous balanced salt solution containing 0.1–10 mg. protein per ml.

* * * * *

Sample Combination

US 20110165597A1

(19) **United States**

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

(10) **Pub. No.: US 2011/0165597 A1**

(43) **Pub. Date: Jul. 7, 2011**

(54) **METHOD FOR THE SCREENING OF CONSERVED SECRETED PROTEINS**

(75) Inventors: **Rosa Milagros Corrales**, Montpellier (FR); **Francoise Mathieu-Daude**, Saint Clement De Riviere (FR); **Denis Sereno**, Poussan (FR)

(73) Assignee: **INSTITUT DE RECHERCHE POUR LE DEVELOPPEMENT (I.R.D.)**, MARSEILLE CEDEX 02 (FR)

(21) Appl. No.: **13/002,446**

(22) PCT Filed: **Jul. 3, 2009**

(86) PCT No.: **PCT/EP2009/058443**

§ 371 (c)(1),
(2), (4) Date: **Mar. 24, 2011**

(30) **Foreign Application Priority Data**

Jul. 4, 2008 (FR) 08290657.9

Publication Classification

(51) **Int. Cl.**
G01N 33/53 (2006.01)

(52) **U.S. Cl.** **435/7.24**; 436/501; 435/7.2

(57) **ABSTRACT**

Conserved polypeptides from protozoan parasitic species which are secreted through the endoplasmic reticulum/Golgi dependent secretory pathway, their identification and their use.

***T. cruzi* genes selected by *in silico* analysis**

T. cruzi GeneDB Accession No.	Orthologous Accession N°			P value		Signal Peptide Sequence
	L. major	*L. infantum*	*T. brucei*	SPP	CSP	
Tc00.1047053506417.30 SEQ ID NO 1	LmjF22.0225 SEQ ID NO 3	LinJ23.0260 SEQ ID NO 5	Tb927.8.2180 SEQ ID NO 7	0.937	0.917	MLSLAEVCLCCPAVRGV SEQ ID NO 111
Tc00.1047053506155.99 SEQ ID NO 103	LmjF36.5220 SEQ ID NO105	LinJ36.5780 SEQ ID NO 107	Tb11.01.2470 SEQ ID NO 109	0.984	0.962	MRWIFLLLAVLSVLKPTDAT SEQ ID NO 112
Tc00.1047053506467.29 SEQ ID NO 9	LmjF26.2000 SEQ ID NO 11	LinJ26.1970 SEQ ID NO 13	Tb09.160.1070 SEQ ID NO 15	0.811	0.7711	MLVLNGISEEQKKLAVVGAAAAFFSSAVTAA SEQ ID NO 113
Tc00.1047053511901.30 SEQ ID NO 17	LmjF24.2160 SEQ ID NO 19	LinJ24.1550 SEQ ID NO 21	Tb927.8.6080 SEQ ID NO 23	0.989	0.898	MFPAQEFLRYSMKSLLLASSLAVAAGWAY SEQ ID NO 114
Tc00.1047053511871.30 SEQ ID NO25	LmjF25.1010 SEQ ID NO 27	LinJ25.1040 SEQ ID NO 29	Tb927.3.950 SEQ ID NO 31	0.979	0.958	MRRTLFCLSTLVKIGRGA SEQ ID NO 115
Tc00.1047053505789.10 SEQ ID NO 93	LmjF19.0540 SEQ ID NO 172 LmjF19.0570 SEQ ID NO 95	LinJ19.0410 SEQ ID NO 97	Tb927.8.6700 SEQ ID NO 99 Tb11.39.0005 SEQ ID NO 101	1.000	0.768	MPSGKATALAAATLLALLVVAPAVASAQ SEQ ID NO 116
Tc00.1047053509669.70 SEQ ID NO 33	LmjF29.1600 SEQ ID NO 35	LinJ29.1910 SEQ ID NO 37	Tb927.3.4190 SEQ ID NO 39	0.999	0.980	MRTSSAVSFFLLAVAAVLFSPFVADAF SEQ ID NO 117
Tc00.1047053507765.20 SEQ ID NO 41	LmjF11.0720 SEQ ID NO 43	LinJ11.0730 SEQ ID NO 45	Tb11.02.4400 SEQ ID NO 47	0.993	0.986	MSAKASRRCNRLIVLFSSINGVTAW SEQ ID NO 118
Tc00.1047053510101.470 SEQ ID NO 49	LmjF11.0720 SEQ ID NO 51	LinJ11.0730 SEQ ID NO 53	Tb11.02.4400 SEQ ID NO 55	0.931	0.919	MSVKASRRCNRLIVLFSSINDVTAW SEQ ID NO 119
Tc00.1047053510443.30 SEQ ID NO 57	LmjF30.3150 SEQ ID NO 59	LinJ30.4200 SEQ ID NO 61	Tb927.6.4500 SEQ ID NO 61	0.903	0.838	MIHTARKKQFGLSALALFVLLLFLLVCITLGL SEQ ID NO 120
Tc00.1047053509799.50 SEQ ID NO 65	LmjF36.5570 SEQ ID NO 67	LinJ36.6060 SEQ ID NO 69	Tb10.6k15.1130 SEQ ID NO 71	0.981	0.931	MKQKMRRKFCDVLFPLLLVFLLTTMEPVTAE SEQ ID NO 121
Tc00.1047053509835.30 SEQ ID NO 73	LmjF19.0540 SEQ ID NO 172 LmjF19.0570 SEQ ID NO 75	LinJ19.0410 SEQ ID NO 77	Tb927.8.6700 SEQ ID NO 79 Tb11.39.0005 SEQ ID NO 81	0.866	0.803	MYSCLSLRLLVGGGMGFASRRRAAMVLSLLVFLLVVPCGVFSQ SEQ ID NO 122
Tc00.1047053509999.10 SEQ ID NO 85	LmjF29.1200 SEQ ID NO 87	LinJ29.1440 SEQ ID NO 89	Tb927.3.3820 SEQ ID NO 91	1.000	0.952	MYVVLFFVLLLSVLGVDAE SEQ ID NO 123

Sample Combination

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW


US007780969B2

(12) **United States Patent**
Tarleton

(10) **Patent No.: US 7,780,969 B2**
(45) **Date of Patent: Aug. 24, 2010**

(54) ***TRYPANOSOMA CRUZI* PROTEOME COMPOSITIONS AND METHODS**

(75) Inventor: **Rick L. Tarleton**, Watkinsville, GA (US)

(73) Assignee: **University of Georgia Research Foundation, Inc.**, Athens, GA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **11/486,710**

(22) Filed: **Jul. 14, 2006**

(65) **Prior Publication Data**

US 2007/0178100 A1 Aug. 2, 2007

Related U.S. Application Data

(60) Provisional application No. 60/699,736, filed on Jul. 15, 2005.

(51) **Int. Cl.**
A61K 39/00 (2006.01)

(52) **U.S. Cl.** **424/269.1**; 424/184.1; 424/191.1; 424/265.1; 435/243; 435/258.1; 530/350; 536/23.1; 536/23.7

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

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,341,761	A	7/1982	Ganfield et al.	
4,399,121	A	8/1983	Albarella et al.	
4,427,783	A	1/1984	Newman et al.	
4,444,887	A	4/1984	Hoffmann	
4,452,570	A	6/1984	Fujisaki et al.	
4,466,917	A	8/1984	Nussenzweig et al.	
4,472,500	A	9/1984	Milstein et al.	
4,491,632	A	1/1985	Wands et al.	
4,493,890	A	1/1985	Morris	
4,816,567	A	3/1989	Cabilly et al.	
6,368,827	B1	4/2002	Tarleton et al.	
6,419,933	B1	7/2002	Reed et al.	
6,833,262	B1	12/2004	Travis et al.	
6,875,584	B1	4/2005	Tarleton et al.	
2002/0182223	A1 *	12/2002	LaCount et al.	424/191.1
2004/0241729	A1	12/2004	Liew	
2005/0158347	A1	7/2005	Tarleton et al.	
2005/0244505	A1	11/2005	Higbee et al.	
2006/0228300	A1	10/2006	Chang et al.	

FOREIGN PATENT DOCUMENTS

WO	2005/111622	A2	11/2005

OTHER PUBLICATIONS

Allaoui et al. Molecular Microbiology 1999 vol. 32 p. 1273-1286.*
Yang et al. Science 1996 vol. 272 p. 1353-1356.*
Zou et al. Journal of Biological Chemistry, 2002 vol. 277 p. 31062-31071.*
Caler et al. The EMBO journal. 1998 vol. 17 p. 4975-4986.*
Bork Peter. 2000 Genome Research p. 398-400.*
Ellis, R.W. (Chapter 29 of "Vaccines" [Plotkin, S.A. et al. (Eds) published by W. B. Saunders Company (Philadelphia) in 1988.*
Oplinger, Anne. NIH Record. vol. LVII No. 9 May 6, 2005.*
El- Sayed et al, Jul. 15, 2005 vol. 39 p. 409-415.*
Williams, Philip Lee. University of Georgia Press Release. Jul. 14, 2005.*
Kolker et al. Nucleic Acid Research, 2004, vol. 32. No. 8 2353-23610.*
Tarleton et al. PLOS medicine. Dec. 2007, vol. 4 issue 12 p. 1852-1857.*
Definition of Vaccine in: The Dictionary of Immunology, Herberts et al eds, Academic Press, 1995.*
Martin et al. PloS Pathog 2(8):e77, p. 731-740.*
Ouaissi et al (Experimental Parasitology 81, 453-461, 1995).*
Coughlin et al. Journal of Biological Chemistry Vo. 275, No. 16, p. 12051-12060 (2000).*
U.S. Appl. No. 11/587,283, filed Oct. 23, 2006, Tarleton et al.
Agüero et al., "TcruziDB: an integrated, post-genomices community resource for *Trypanosoma cruzi*," *Nucleic Acids Research*, 2006; 34(Database issue):D428- D431; doi:10.1093/nar/gkj108.
Akopyants et al., "A survey of the *Leishmania major* Friedlin strain V1 genome by shotgun sequencing: a resource for DNA microarrays and expression profiling," *Mol. Biochem Parasitol*, 2001; 113:337-340.
Almeida et al., "Expression profiling of the *Leishmania* life cycle: cDNA arrays indentify developmentally regulated genes present but not annotated in the genome," *Mol Biochem Parasitol*, 2004; 136:87-100.
Atwood III, et al., "The *Trypanosoma cruzi* Proteome," *Science*, Jul. 15, 2005; 309:473-476 (*available on-line* Jul. 14, 2005), with on-line supporting data (14 pgs).
Atwood et al., "The *Trypanosoma cruzi* Proteome," TriTryp Genomes Meeting. Sep. 13-16, 2004. Seattle, Washington. Abstracts Cover Page, with Abstract p. 6.4.
Berman et al., "Uptake, Distribution, and Oxidation of Fatty Acids by *Leishmania* mexicana Amastigotes," *J. Parasitol*, 1987; 73:555-560.
Berriman et al., "The Genome of the African Trypanosome *Trypanosoma Brucei*," *Science*, Jul. 15, 2005; 309(5733):416-422 (*available on-line* Jul. 14, 2005), with on-line supporting data (61 pgs).
Bringaud et al., "A New, Expressed Multigene Family Containing a Hot Spot for Insertion of Retroelements Is Associated with Polymorphic Subtelomeric Regions of *Trypanosoma brucei*," *Eukaryot Cell*, 2002; 1:137-151.
Clayton, "Life without transcriptional control? From fly to man and back again," *Embo J*, 2002; 21,1881-1888.
Cohen et al., "Modeling Household Transmission of American Trypanosomiasis," *Science*, 2001; 293(5530):694-698.
DGPI, Kronegg, 1999; http://129.194.185.165/dgpi/ 2 pages.
Diehl et al., "Analysis of stage-specific gene expression in the bloodstream and the procyclic form of *Trypanosoma brucei* using a genomic DNA-microarray," *Mol Biochem Parasitol*, 2002; 123:115-123.

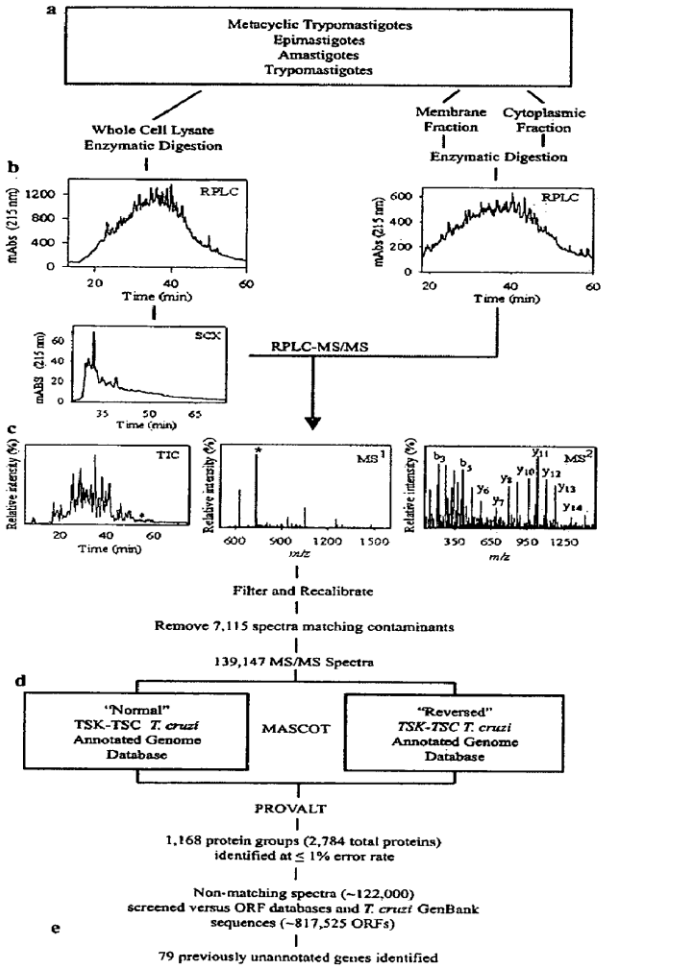
(Continued)

Primary Examiner—Robert Mondesi
Assistant Examiner—Oluwatosin Ogunbiyi
(74) *Attorney, Agent, or Firm*—Mueting Raasch & Gebhardt, P.A.

(57) **ABSTRACT**

Molecular targets are identified in *T. cruzi* suitable for use in diagnosis of Chagas disease, drug development, and vaccines, including live vaccines.

17 Claims, 32 Drawing Sheets
(2 of 32 Drawing Sheet(s) Filed in Color)



The WHO List of Essential Medicines, Updated Patent Landscape (Reader's Digest Version)

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

The WHO List of Essential Medicines, Updated Patent Landscape (Reader's Digest Version)

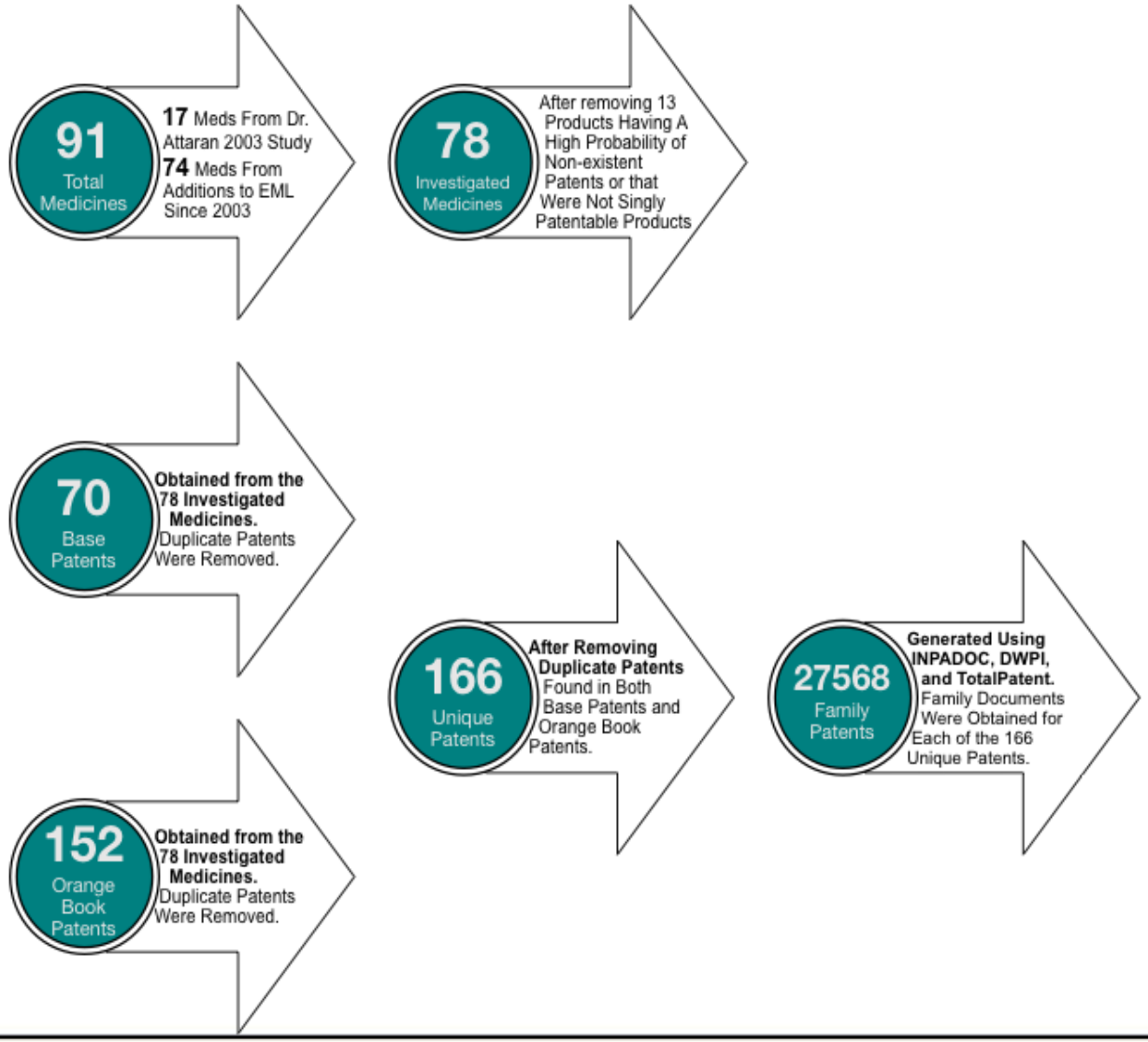
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

The objectives for this project were:

- To develop a robust methodology to assess the patent status of medicines on the WHO Model List of Essential Medicines,
- To place in the public domain a detailed report on the present (2010) patent status of medicines that were on patent in 2003 and those medicines added to the Model List since 2003 by country and level of development, and
- To analyze the patent status of these Essential Medicines by the development status of countries.

The WHO List of Essential Medicines, Updated Patent Landscape (Reader's Digest Version)

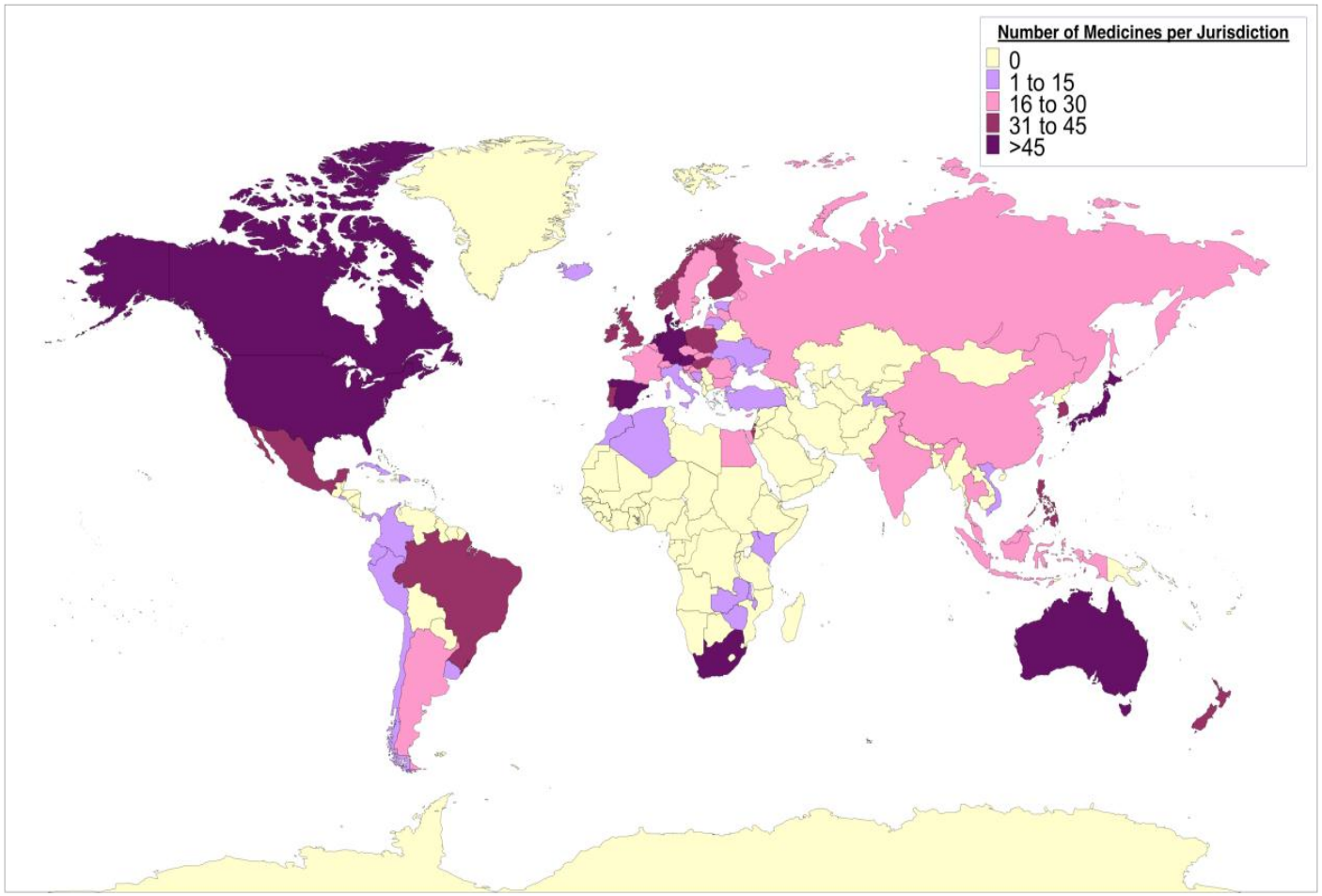
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



The WHO List of Essential Medicines, Updated Patent Landscape (Reader's Digest Version)

Number of medicines patented per jurisdiction for all years. Regional office filings were detected: ARIPO=15, OAPI=17, EAPO=13, EPO=41, WIPO=30.

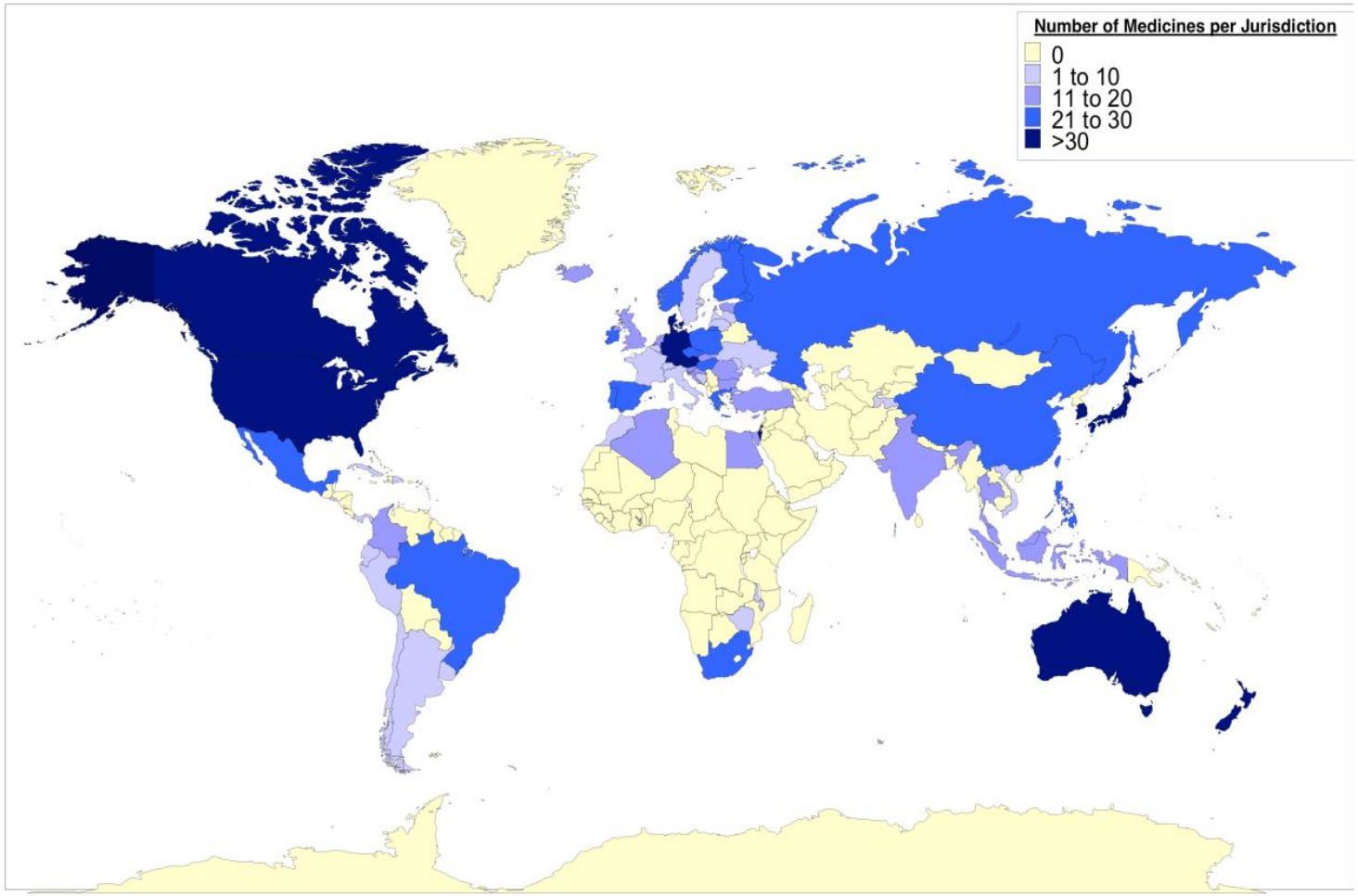
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



The WHO List of Essential Medicines, Updated Patent Landscape (Reader's Digest Version)

Number of medicines patented per jurisdiction post 1990. Regional office filings were detected: ARIPO=14, OAPI=11, EAPO=14, EPO=34, WIPO=30.

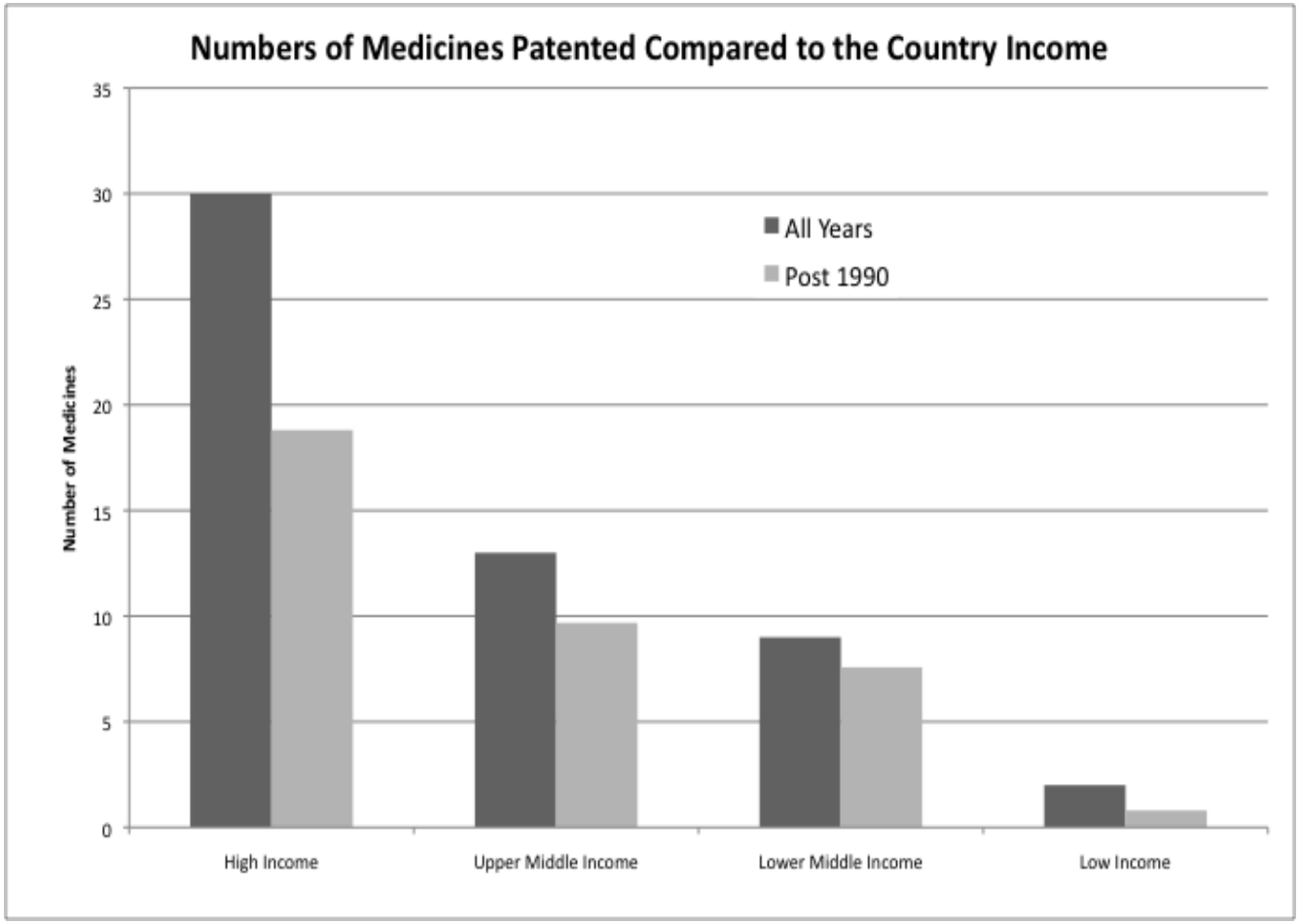
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



The WHO List of Essential Medicines, Updated Patent Landscape (Reader's Digest Version)

Essential Medicines and Their Relationship to World Bank National Income Levels – Post 1990.

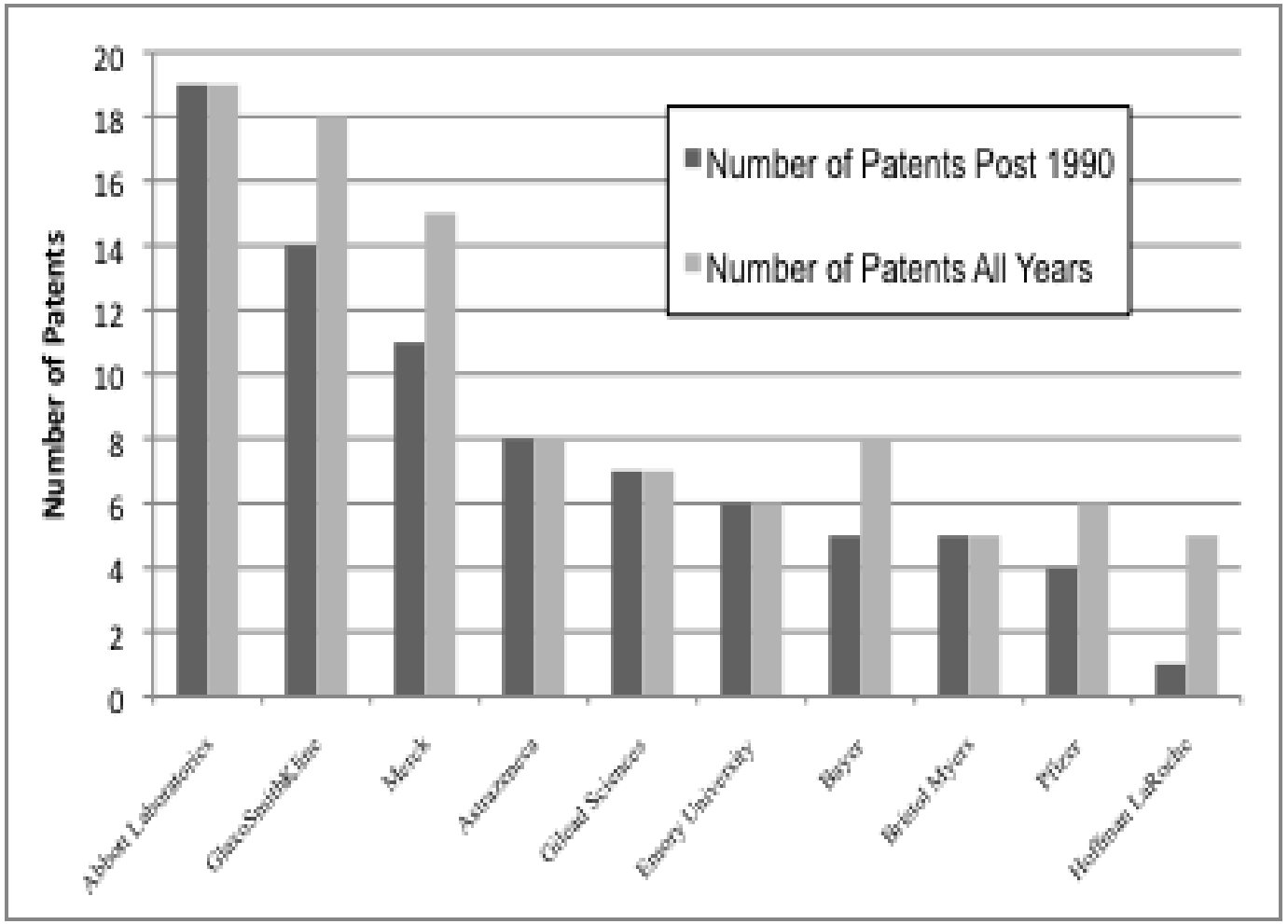
THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



The WHO List of Essential Medicines, Updated Patent Landscape (Reader's Digest Version)

Comparison of Assignee Companies. Assignees were determined from the 166 unique patent documents.

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW



The WHO List of Essential Medicines, Updated Patent Landscape (Reader's Digest Version)

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Conclusions and Key Implications

A standardized protocol is a critical tool for periodic identification and analyses of patents appurtenant to updates of the WHO EML. Said protocol should be made available, and indeed taught to, all Member States, with particular focus on the developing nations.

Caution in assessing FTO in any given jurisdiction should be the *modus operandi*; a stepwise approach which proceeds from a standardized protocol to more diligent research, e.g., analyzing patentee portfolios or in-country paper-based patent searches, is strongly recommended. Hasty assumptions based on preliminary data are neither judicious nor prudent.

The WHO List of Essential Medicines, Updated Patent Landscape (Reader's Digest Version)

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Conclusions and Key Implications

Data presented in the ITTI EML patent study support the proposition that global patenting trends follow economic development and markets; this is a dynamic and fluid situation across the world; patentees will likely file patent applications in more countries as viable economic markets expand accordingly.

The WHO List of Essential Medicines, Updated Patent Landscape (Reader's Digest Version)

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY
UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW

Conclusions and Key Implications

Patents *per se* might not be a primary obstacle for access to EML pharmaceuticals in many developing countries, as they are consistently not detected in patent family data from developing nations and regions; yet caution in assessing FTO is always necessary.

More recent EML pharmaceuticals appear to have greater global patent filings, which is not inconsistent with generally increasing global trends in patenting activity.

Acknowledgments

Professor Jon Cavicchi
Dr. Kevin Clark
Dr. David Pflugh
Dr. Cole Duncan
Ms Aarushi Gupta
Ms Spoorthy Gudavalli
Mr. Matt Curran
Mr. Ian Mullet
Dr. Anatole Krattiger
Dr. Richard Laing

THE FRANKLIN PIERCE Center for INTELLECTUAL PROPERTY

UNIVERSITY of NEW HAMPSHIRE SCHOOL of LAW