

INCT-NanoBiofar

**National Institute of Science and Technology in
Nanobiopharmaceutics**

ANNUAL ACTIVITY REPORT 2009

INCT NANOBIOFAR

1. [Home](#)
2. [About INCT-NanoBiofar](#)
 - [Partners](#)
 - [Associated partners](#)
3. Research
 - [Basic/ Technological](#)
 - [Application Driven](#)
4. [Activities](#)
5. [Facilities](#)
6. Publications
 - [Publication List](#)
7. Patents
 - [Applications](#)
 - [Granted](#)
8. [Technology Transfer](#)
9. [Summary of Annual Activities](#)
10. [Pictures](#)

Welcome

[Back](#)

The National Institute in Science and Technology in Nanobiopharmaceutics (NanoBiofar) was created in 2008 as part of the government initiative to move forward and to a higher step its effort in promoting scientific and biotechnological development in Brazil.

NanoBiofar has as main focus the development of new pharmaceutical products based on incremental and radical innovation using especially nanotechnology.

The Institute mission is to facilitate a nanobiotechnology network of people and facilities to enhance existing academic research, pursue unique cross-disciplinary research and education initiatives, and to foster the entrepreneurship and the interaction of academy with the private-sector in the pharmaceutical area.

As a part of its initiatives Nanobiofar helped the Physiology and Pharmacology PhD program of the Federal University of Minas Gerais to launch the innovative Professional Science Master's program in Biopharmaceutical Innovation to meet the future workforce needs of a growing bioscience industry. The INCT-Nanobiofar investigators are participating actively in the program as advisors of projects aimed to generate novel and innovative processes and products. In addition they are responsible for many disciplines and for the field of Intellectual Property of the Professional Master program.

Our research facilities distributed in our network of laboratories and research centers are dedicated to supporting innovation in drug development and drug delivery based on a multidisciplinary research team. The main translational research platform of the Institute is the novel protective arm of the renin-angiotensin system, the ACE2/Ang-(1-7)/Mas axis. The Principal Investigators of Nanobiofar were notably involved in the development of the newer concept of the RAS, a system importantly involved in cardiovascular and renal function and pathophysiology. Nanoformulations of the heptapeptide Angiotensin-(1-7) have been developed by investigators of Nanobiofar and are now protected by patents recently issued in USA, China and India. These innovative products are currently being tested experimentally and in patients, for the treatment of cardiovascular and metabolic disorders. Two partnerships with Brazilian Pharmaceutical / Technological Industries (União Química and Scitech) were established for the development of innovative products based on nanocarriers for Angiotensin-(1-7) and other receptor Mas agonists.

Our international science collaborative program focuses on advanced genetic engineering and drug development and delivery. The Nanobiofar international network comprises the Kidney Research Center at Ottawa Health Research Institute- University of Ottawa-Canada, the Max-

Delbruck Center for Molecular Medicine in Berlin, the MIT in Boston-USA, the Erasmus University in Netherlands and the Center for Aging and Regeneration – CARE in Chile.

Our Institute can also deliver professionally managed contract research services to industry in the areas of Drug Formulation, Pre-clinical Pharmaceutical Analysis and Intellectual Property Protection. Part of these services is under the responsibility of LABFAR, a unit of our Institute devoted to contract research services. Pharmaceutical companies which use/used LABFAR services include Daiichi-Sankyo (Japan), COMPUGEN (Israel) and Biolab (Brazil).

Basic /Technological Research

[Back](#)

NanoBiofar has assumed the role of enabling multidisciplinary and multinational research collaborations aimed to develop novel therapeutic formulations of drugs, and devices. One of the goals is to overcome both the geographical fragmentation of researchers and the limited communication across previously discreet scientific disciplines such as chemistry, biology, physics and medicine.

Many intersection research studies are currently being performed. The [publication list](#) illustrates the broad range of interaction among NanoBiofar investigators.

APPLICATION DRIVEN

Clinical Trial (Phase II) of Ang-(1-7) in preeclampsia

The discovery of new components of the renin angiotensin system (RAS), opened the possibility to explore new ways to influence its activity. Until recently only angiotensin converting enzyme inhibitors (ACEi), AT1 receptor blockers (BRA) were used as therapeutic tools. More recently direct renin inhibitors were launched in the market. The identification of Ang(1-7) receptor Mas and of the angiotensin converting enzyme 2 (ACE 2), opened new possibilities for the treatment of cardiovascular and kidney diseases. In this context, preeclampsia is a disease in which the RAS is involved on its pathogenesis. Recently based in the studies done at the Hypertension Laboratory of UFMG and on evidences from the literature, it was demonstrated that the mismatch between the vasodilator Ang-(1-7)/Mas axis and the Ang II/ AT1 vasoconstrictor axis plays an important role in the development of this disease. We are currently exploring the possibility that administration of Ang-(1-7) to preeclamptic patients could ameliorate preeclampsia. The clinical protocol "The therapeutic use of Ang-(1-7) in preeclampsia treatment", was approved by the Research Ethics Committee from the Hospital das Clínicas of UFMG (COEP/UFMG 562/07) and by National Research Ethics Committee (CONEP/Brasília 0562.0.203.000-07). We expect that the trial will be completed in about four months.

Principal Investigators: *Robson Augusto Souza dos Santos, MD, Antônio Carlos Vieira Cabral, MD,, Henrique Vítor Leite,MD; Marco Túlio Vilaça Castagna,MD; Zilma Silveira Nogueira Reis ,MD; Elizabeth Portugal Pimenta Velloso,PhD, RenataLúcia Vieira Pimente, MSc.*

“Clinical Study (Phase I) of Pharmacokinetic and Tolerability of a New Oral Formulation of Angiotensin-(1-7) Included in HP β -Cyclodextrin in Healthy Volunteers”

We are waiting for the approval of this clinical protocol by the Research Ethics committee of the “Hospital das Clínicas” of UFMG. The results of this clinical trial will be the basis for future clinical studies aimed to evaluate the effect of angiotensin-(1-7) in cardio-metabolic diseases.

Principal Investigators: Robson Augsto Souza dos Santos, MD; Sérgio Henrique Sousa Santos, PhD; Rodrigo Bastos Fóscolo, MD; Antônio Ribeiro de Oliveira Junior, MD.

BIOINOVA PROJECT: Development of Drug Eluting Stents Based on Angiotensin-(1-7) included in Biodegradable Polymers.

This project is a collaborative effort of NanoBiofar and the Biotechnology Company Scitech.

PUBLICATION LIST

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Activities

Events

● **RENIN-ANGIOTENSIN SYSTEM SYMPOSIUM**

The Institute organized a satellite symposium of the Joint Meeting SBH/IASH 2009 with the participation of many invited speakers from abroad. Different novel aspects of the renin-angiotensin system were discussed in the symposium. The symposium had more than 400 participants.

FINAL PROGRAM

RENIN ANGIOTENSIN ALDOSTERONE SYSTEM SATELLITE SYMPOSIUM

AUGUST 4, 2009 Tuesday

Date: August, 4

Hour: 2:00 - 6:00pm

Symposium Venue: Ouro Minas Hotel

2:00 - 3:30pm Prorenin/Renin/(P)RR/Renin Inhibition

Chairs: Jan Danser (Rotterdam - The Netherlands)

Geneviève Nguyen (Paris France)

2:00 - 2:30pm Diabetes, Renin System Blockade and the State of the Blood Supply to the Kidney and the Eye

Norman Hollenberg (Brigham and Women's Hospital, Boston, Massachusetts USA)

2:30 - 3:00pm The Rise in Renin During Renin Inhibition: Cause and Consequences

A.H. Jan Danser (Division of Pharmacology, Vascular and Metabolic Diseases, Department of Internal medicine, Erasmus

MC, Rotterdam - The Netherlands)

3:00 - 3:30pm The (Pro)Renin Receptor: Biology and Roles in Pathophysiology
Geneviève Nguyen (Institut National de la Santé et de la Recherche Médicale, Unit 833 and Collège de France, Paris France)

3:30 - 4:00pm Animal Models with Altered (Pro)Renin Receptor Expression
Michael Bader (Max-Delbrueck-Center, Berlin Germany)

4:30 - 6:00pm ACE2-Angiotensin(1-7)-Mas Axis

Chairs: Mariella Gironacci (Buenos Aires Argentina)

Robson Santos (Belo Horizonte Brazil)

2

4:30 - 5:00pm ACE2-Angiotensin(1-7)-Mas Axis: an Overview
Robson Santos (Department of Physiology, Federal University of Minas Gerais, Belo Horizonte, MG Brazil)

5:00 - 5:30pm Angiotensin-(1-7) and Protection from Hypertensive Remodeling in Mice

Timothy L. Reudelhuber (Clinical Research Institute of Montréal (IRCM), Montréal Canada)

5:30 - 6:00pm Role of ACE2 in Cardio-Pulmonary Pathophysiology
Mohan K. Raizada (Department of Physiology and Functional Genomics, University of Florida, College of Medicine, Gainesville, Florida USA)

6:00 - 6:30pm Contrasting Roles of the Renin-Angiotensin System in Maternal Uterus and Fetal Placenta in Normal and Preeclamptic Pregnancy
Bridget Brosnihan (Wake Forest Univ. Health Sciences, Winston-Salem USA)

AUGUST 5, 2009 Wednesday

Date: August, 5

Hour: 8:00am - 12:00pm

Symposium Venue: Ouro Minas Hotel

8:00 - 10:00am Amino peptidase A-Angiotensin III-AT2 Receptor-Bradykinin B2 Receptor-EDHF Axis

Chairs: Michael Bader (Berlin Germany)

João Pesquero (São Paulo Brazil)

8:00 - 8:30am Regulation of Renal Sodium Excretion by Angiotensin III and AT2 receptors

Robert Carey (Division of Endocrinology and Metabolism, Department of Medicine, University of Virginia Health System, Charlottesville, VA USA)

8:30 - 9:00am Orally Active Amino peptidase A Inhibitors Reduce Blood Pressure: a New Strategy for Treating Hypertension

Catherine Llorens-Cortes (Institut National de la Santé et de la Recherche Médicale, Unit 691 and Collège de France, Paris France)

9:00 - 9:30am Angiotensin AT2 Receptor Agonism a New Pharmacological Concept for Anti-Inflammation and Tissue-Protection?

Ulrike Steckelings (Center for Cardiovascular Research, Charité-Universitätsmedizin Berlin, Berlin Germany)

9:30 - 10:00am Kinin Receptors and Obesity. A New Role for Kinins
3

João B Pesquero (Department of Biophysics, Universidade Federal de São Paulo, São Paulo Brazil)

10:15 - 12:15pm ACE-Angiotensin II-AT1 Receptor-Aldosterone-Mineralocorticoid Receptor Axis

Chairs: Timothy Reudelhuber (Montreal Canada)

Gabriel Navar (New Orleans USA)

10:15 - 10:45am ACE and AT1 Receptor Function as Angiotensin II-Independent Mechanotransducers

Jose Krieger (Heart Institute/Univ. São Paulo Med School, São Paulo Brazil)

10:45 - 11:15am Structural Aspects Related to AT1 Receptor Activation

Claudio Costa-Neto (Department of Biochemistry and Immunology Faculty of Medicine at Ribeirão Preto University of São Paulo, São Paulo - Brazil)

11:15 - 11:45pm Networking Between Angiotensin II and Aldosterone

Rhian Touyz (Kidney Research Centre, Ottawa Health Research Institute, University of Ottawa, Ontario Canada)

11:45 - 12:15pm Effects of Aldosterone on Coronary Function

Claude Delcayre (INSERM Unit 942 Université Paris-Diderot, Hôpital Lariboisière, Paris France)

• SBH/IASH 2009 Meeting

The coordinator of the INCT-NanoBiofar, Prof. Robson Santos, was the president of the XVII congress of the Brazilian Society of Hypertension and the XVIII scientific session of the Interamerican Society of Hypertension (Belo Horizonte, August 4-8, 2009). Many investigators of the Institute participated in the organizing committee and as speakers in the meeting. NanoBiofar provided air tickets and cover hotel expenses of many speakers from abroad. Details of the meeting can be found at:

http://itpack31.itarget.com.br/uploads/hi2/arquivos/Programacao_Final_02-08-2009noite1.pdf

Education and Training

- **UFMG & SCHOOLS PROGRAM**

The institute is given support to the program UFMG& Schools directed to elementary school students. Prof. Andrea Macedo, investigator of NanoBiofar is one of the coordinators of this educational program. The aim of this program is to teach basic science concepts to young students serving as a motivational activity as well.

- **Workshops**

Two workshops were organized in the period. One of them (November 23-24, 2009) with two invited speakers from the center of excellence in aging and regeneration (CARE, Chile): Dr. Carlos Vio and Enrique Brandan. An agreement for a collaborative project involving NanoBiofar and CARE was made, at the end of the workshop. The first workshop held at Chemistry Department (March 12, 2009) was organized to discuss the research activities scheduled for the first (2009) period.

- **Hypertension League**

The Institute has an Academic Hypertension League (LAH-UFMG). The league has many educational and preventive activities over the year, including the organization of regional events for detection of hypertension.

- **Professional Master Program in Biopharmaceutics Innovation**

As a part of its initiatives Nanobiofar helped the Physiology and Pharmacology PhD program of the Federal University of Minas Gerais to launch the innovative Professional Science Master's program in Biopharmaceutical Innovation to meet the future workforce needs of a growing bioscience industry. The INCT-Nanobiofar investigators are participating actively in the program as advisors of projects aimed to generate novel and innovative processes and products. In addition they are responsible for many disciplines and for the field of Intellectual Property of the Professional Master program. A course of good laboratory practice is part of the professional master program.

PATENTS APPLICATION- BRAZIL

[Back](#)

Filing date: 15/01/2009

Application in Brazil: C1 0206336-0

Filing date: 17/01/2008

Application Number: C1 0206336-0

Title: COMPLEXOS SUPRAMOLECULARES DE ALTA ESTEQUIOMETRIA EM SISTEMAS NANOAGREGADOS CONSTITUÍDOS POR CLOREXIDINA OU TETRACICLINA INCLUÍDOS EM CICLODEXTRINA

Inventors: Ruben Dario Sinisterra Millan, Maria Esperanza Cortes Segura, Michel Victor Furtado Araujo, Andre Luiz Pataro

Filing date: 15/01/2009

Priority in Brazil: PI 0800596-6

Filing date: 31/01/2008

Application Number: PI 0800596-6

Title: MÉTODO PARA A POTENCIALIZAÇÃO DA FUNÇÃO ERÉTIL ATRAVÉS DO USO DAS COMPOSIÇÕES FARMACÊUTICAS DE TOXINA Tx2-6 DA ARANHA PHONEUTRIA NIGRIVENTER

Inventors: Ruben Dario Sinisterra Millan, Adriano Monteiro Castro Pimenta, Maria Elena Lima Perez Garcia, Romulo Cerqueira Leite, Luciana Franco Lanza, Kenia Pedrosa Nunes, Marcelo Diniz

Filing date: 15/01/2009

Priority in Brazil: PI 0800606-7

Filing date: 13/02/2008

Application Number: PI 0800606-7

Title: USO DE ANGIOTENSINA-(1-7)- β -HPCD, ANÁLOGOS OU DERIVADOS PARA O TRATAMENTO DE CONDIÇÕES CARDÍACAS

Inventors: Ruben Dario Sinisterra Millan, Robson Augusto Souza Santos, Anderson Jose Ferreira, Fulvia Dias Marques.

Filing date: 15/01/2009

Priority in Brazil: PI 0800585-0

Filing date: 13/02/2008

Application Number: PI 0800585-0

Title: PEPTÍDIO DES-[ASP1]-[ALA1]- AGONISTA DA ANGIOTENSINA-(1-7) E COMPOSIÇÕES FARMACÊUTICAS PARA TRATAMENTO DE DOENÇAS

Inventors: Ruben Dario Sinisterra Millan, Robson Augusto Souza Santos, Anderson Jose Ferreira

Filing date: 15/01/2009

Priority in Brazil: PI 0801542-2

Filing date: 18/03/2008

Application Number: PI 0801542-2

Title: MODIFICAÇÃO, REDUÇÃO DA ESTRUTURA PRIMÁRIA E SÍNTESE DE PEPTÍDEOS HIPOTENSIVOS PRESENTES NO VENENO DE ESCORPIÃO PARA OTIMIZAÇÃO NA UTILIZAÇÃO DOS MESMOS COMO FÁRMACOS

Inventors: Robson Augusto Souza Santos, Adriano Monteiro Castro Pimenta, Maria Elena Lima Perez Garcia, Carlos Ribeiro Diniz (Falecido), Marie France Martin Eauclaire, Pierre Edouard Bougis, Thiago Verano Braga

Filing date: 15/01/2009

Priority in Brazil: PI 0802009-4

Filing date: 30/04/2008

Application Number: PI 0802009-4

Title: FORMULAÇÃO FARMACÊUTICA À BASE DE ALOE VERA PARA CAPEAMENTO DIRETO EM POLPA DENTÁRIA E COMO MATRIZ PARA TRANSPORTE DE FÁRMACOS E/OU CÉLULAS

Inventors: Ruben Dario Sinisterra Millan, Maria Esperanza Cortes Segura, Alfonso Gala Garcia

Filing date: 15/01/2009

Priority in Brazil: PI 0802806-0

Filing date: 22/07/2008

Application Number: PI 0802806-0

Title: USO DO PEPTÍDEO ANGIOTENSINA-(1-7), SEUS ANÁLOGOS, AGONISTAS OU DERIVADOS PARA O TRATAMENTO DE CONDIÇÕES DOLOROSAS

Inventors: Robson Augusto Souza Santos, Igor Dimitri Gama Duarte, Aline Conceição Oliveira Costa

Filing date: 15/01/2009

Priority in Brazil: PI 0901877-8

Filing date: 19/05/2009

Application Number: PI 0901877-8

Title: PROCESSO DE OBTENÇÃO DE NANOAGREGADOS NA BASE DOS ANTAGONISTAS DO RECEPTOR AT1 COM CÁTIOS METÁLICOS

Inventors: Ruben Dario Sinisterra Millan, Maria Esperanza Cortes Segura, Angelo Marcio Leite Denadai, Izabela Mariane Pampolini Daniel, Luan Alves Lopes Carneiro

Filing date: 15/01/2009

Priority in Brazil: PI 0902242-2

Filing date: 30/06/2009

Application Number: PI 0902242-2

Title: PROCESSO DE OBTENÇÃO DE NANOAGREGADOS NA BASE DOS ANTAGONISTAS DO RECEPTOR AT1 COM CÁTIOS METÁLICOS

Inventors: Mauro Martins Teixeira, Robson Augusto Souza Santos, Katia Daniela Silveira

Filing date: 15/01/2009

Priority in Brazil: 14090005008 (Protocol)

Filing date: 06/11/2009

Application Number: 14090005008 (Protocol)

Title: PROCESSO DE PREPARAÇÃO DE UM SISTEMA DE LIBERAÇÃO CONTROLADA DE CLOREXIDINA E SEUS COMPOSTOS DE INCLUSÃO, A PARTIR DE CIMENTO RESINOSO, PRODUTO E USO

Inventors: Ruben Dario Sinisterra Millan, Maria Esperanza Cortez, Eliete Marçal Guimaraes Raso

INTERNATIONAL PATENTS APPLICATION

Filing date: 18/12/2008

Priority in Brazil: PI 0602372-0

Priority Date: 18/05/2006

Publication Number:

Publication Date:

Application Number: Europa PCT/BR2007/000160

Title: COMPOSITE PREPARATION PROCESS ON A BASIS OF BIOCERAMICS AND BIODEGRADABLE OR NON BIODEGRADABLE POLYMERS, CEMENTING AND/OR CARRIER SUBSTANCES CONTAINING ENCAPSULATED OR NON-ENCAPSULATED MICRO OR NANOPARTICULATED ANTIBIOTICS AND ANGIOTENSIN (1-7) FOR TISSUE RESTITUTION AND PRODUCTS THEREFROM

Inventors: Robson Augusto Souza dos Santos, Rubén Dario Sinisterra Millan, Maria Esperanza Cortés Segura, André Luiz Parato, Michele Fabiane de Oliveira, Miriam Teresa Paz Lopes, Regina Maria de Marco Truchetti Maia

Filing date: 30/01/2009

Priority in Brazil: PI 0800596-6

Priority Date: 31/01/2008

Publication Number: WO/2009/094742

Publication Date: 06/08/2009

Application Number: PCT/BR2009/000040

Title: TOXIN OF THE SPIDER PHONEUTRIA NIGRIVENTER FOR TREATMENT OF ERECTILE DYSFUNCTION

Inventors: Maria Elena de Lima Perez Garcia, Rubén Dario Sinisterra Millán, Kênia Pedrosa Nunes, Rômulo Leite, Luciana Franco Lanza, Marcelo Ribeiro Vasconcelos Diniz, Marta do Nascimento Cordeiro, Adriano Monteiro de Castro Pimenta, Michael Richardson, Maria do Carmo Valentim

Filing date: 13/02/2009

Priority in Brazil: PI 0800585-0

Priority Date: 13/02/2008

Publication Number: WO/2009/100513

Publication Date: 20/08/2009

Application Number: PCT/BR2009/000046

Title: "PEPTIDE DES-[ASP1]-[ALA1], ANGIOTENSIN-(1-7) AGONIST AND PHARMACEUTICAL COMPOUNDS FOR THE TREATMENT OF DISEASES"

Inventors: Robson Augusto Souza dos Santos, Anderson José Ferreira, Rubén Dario Sinisterra

Filing date: 22/07/2009

Priority in Brazil: PI0802806-0

Priority Date: 22/06/2008

Publication Number: WO/2010/009524

Publication Date: 28/01/2010

Application Number: PCT/BR2009/000217

Title: USE OF THE PEPTIDE ANGIOTENSIN (1-7) AND ITS ANALOGUES, AGONISTS OR DERIVATIVES FOR THE TREATMENT OF PAINFUL CONDITIONS

Inventors: Robson Augusto Souza dos Santos, Igor Dimitri Gama Duarte, Aline Conceição Oliveira Costa

Filing date: 30/12/2009

Priority in Brazil: C 10200751-7

Priority Date: 02/07/2007

Publication Number:

Publication Date:

Application Number: EUA PCT/BR2008/000023

Title: PHARMACEUTICAL COMPOSITIONS COMPRISING SEMICARBAZONES AND THIOSEMICARBAZONES AND METHOD FOR TREATING INFLAMMATORY, PAINFUL AND FEBRILE CONDITIONS AND PREVENTING SIGNS AND SYMPTOMS

Inventors: Heloisa de Oliveira Beraldo, Márcio de Matos Coelho, Rubén Dario Sinisterra Millan, Maria Carolina Doretto

Filing date: 31/12/2009

Priority in Brazil: C 10200751-7

Priority Date: 02/07/2007

Publication Number:

Publication Date:

Application Number: INDIA PCT/BR2008/000023

Title: PHARMACEUTICAL COMPOSITIONS COMPRISING SEMICARBAZONES AND THIOSEMICARBAZONES AND METHOD FOR TREATING INFLAMMATORY, PAINFUL AND FEBRILE CONDITIONS AND PREVENTING SIGNS AND SYMPTOMS

Inventors: Heloisa de Oliveira Beraldo, Márcio de Matos Coelho, Rubén Dario Sinisterra Millan, Maria Carolina Doretto

Filing date: 27/07/2009

Priority in Brazil:

Priority Date:

Publication Number:

Publication Date:

Application Number: BRASIL PCT/BR2008/000022

Title: PHARMACEUTICAL COMPOSITIONS AND METHODS FOR TREATING ERECTILE DYSFUNCTION.

Inventors: Ruben Dario Sinisterra Millan, Robson Augusto Souza dos Santos, Frederic Jean Georges Frezard, Andrey Christian da Costa Gonçalves, Rodrigo Araujo Fraga da Silva

Filing date: 27/07/2009

Priority in Brazil:

Priority Date:

Publication Number:

Publication Date:

Application Number: EUA PCT/BR2008/000022

Title: PHARMACEUTICAL COMPOSITIONS AND METHODS FOR TREATING ERECTILE DYSFUNCTION.

Inventors: Ruben Dario Sinisterra Millan, Robson Augusto Souza dos Santos, Frederic Jean Georges Frezard, Andrey Christian da Costa Gonçalves, Rodrigo Araujo Fraga da Silva

Filing date: 20/08/2009

Priority in Brazil:

Priority Date:

Publication Number:

Publication Date:

Application Number: Europa PCT/BR2008/000022

Title: PHARMACEUTICAL COMPOSITIONS AND METHODS FOR TREATING ERECTILE DYSFUNCTION.

Inventors: Ruben Dario Sinisterra Millan, Robson Augusto Souza dos Santos, Frederic Jean Georges Frezard, Andrey Christian da Costa Gonçalves, Rodrigo Araujo Fraga da Silva

Filing date: 30.04.2009

Priority in Brazil: PI 0504978-4

Priority Date: 30/09/2005

Publication Number:

Publication Date:

Application Number: EUA PCT/BR2006/000233

Title: PROCESS FOR THE PREPARATION OF COMPOUNDS OF AT1 RECEPTOR ANTAGONISTS WITH ANGIOTENSIN-(1-7), ANALOGUES THEREOF AND/OR MIXTURES OF THESE SYSTEMS, PHARMACEUTICAL COMPOSITIONS THEREOF AND USE OF THEIR DERIVATIVE PRODUCTS

Inventors: Cynthia Fernandes Ferreira Santos, Robson Augusto Souza dos Santos, Ivana Silva Lula, Frederico Barros de Sousa, Pedro Pires Goulart Guimarães, Rubén Dario Sinisterra Millan, Angelo Márcio Leite Denadai

Filing date: 31.03.2009

Priority in Brazil: PI 0602366-5

Priority Date: 26/04/2006

Publication Number:

Publication Date:

Application Number: EUA PCT/BR2007/000100

Title: USE OF MAS-G-PROTEIN-COUPLED RECEPTOR AGONISTS IN THE TREATMENT OF THE METABOLIC SYNDROME, ITS COMPONENTS AND ITS COMPLICATIONS

Inventors: Robson Augusto Souza dos Santos, Sergio Henrique Sousa Santos, Jaqueline Isaura Alvarez Leite, Marina Matos de Moura, Andrea Siqueira Haibara, Luciana Rodrigues Fernandes, Rubén Dario Sinisterra Millan, Michael Bader, Natalia Alemina

INTERNATIONAL PATENTS GRANTED

Filing date: 5/11/2002

Priority in Brazil: PI0105509-7

Priority Date: 5/11/2001

Application Number: 10/494,756

Title: PROCESS OF PREPARATION OF FORMULATIONS OF THE PEPTIDE ANGIOTENSIN-(1-7) AND ITS ANALOGUES, AGONISTIC AND ANTAGONISTS USING CYCLODEXTRINS, LIPOSSOMES AND BIODEGRADABLE POLYMERS AND/OR MIXTURES AND PRODUCTS THEREOF

Inventors: Rubén Dario Sinisterra Millan, Frederic Jean Georges Frezard, Ana Paula Nadu, Robson Augusto Souza dos Santos

Filing date: 5/11/2002

Priority in Brazil: PI0105509-7

Priority Date: 5/11/2001

Application Number: 1214/CHENP/2004

Title: PROCESS OF PREPARATION OF FORMULATIONS OF THE PEPTIDE ANGIOTENSIN-(1-7) AND ITS ANALOGUES, AGONISTIC AND ANTAGONISTS USING CYCLODEXTRINS, LIPOSSOMES AND BIODEGRADABLE POLYMERS AND/OR MIXTURES AND PRODUCTS THEREOF

Inventors: Rubén Dario Sinisterra Millan, Frederic Jean Georges Frezard, Ana Paula Nadu, Robson Augusto Souza dos Santos

Filing date: 5/11/2002

Priority in Brazil: PI0105509-7

Priority Date: 5/11/2001

Application Number: 02824013.8

Title: PROCESS OF PREPARATION OF FORMULATIONS OF THE PEPTIDE ANGIOTENSIN-(1-7) AND ITS ANALOGUES, AGONISTIC AND ANTAGONISTS USING CYCLODEXTRINS, LIPOSSOMES AND BIODEGRADABLE POLYMERS AND/OR MIXTURES AND PRODUCTS THEREOF

Inventors: Rubén Dario Sinisterra Millan, Frederic Jean Georges Frezard, Ana Paula Nadu, Robson Augusto Souza dos Santos

Filing date: 9/4/2002

Priority in Brazil: PI 0102252-0

Priority Date: 10/4/2001

Application Number: 2,444,145

Title: PREPARATION OF FORMULATIONS OF ANGIOTENSIN II AT1 RECEPTORS ANTAGONISTS FOR THE TREATMENT OF ARTERIAL HYPERTENSION, OTHER CARDIOVASCULAR ILLNESSES AND ITS COMPLICATIONS

Inventors: Rubén Dario Sinisterra Millan, Frederic Jean Georges Frezard, Washington Xavier de Paula, Robson Augusto Souza dos Santos

Filing date: 9/4/2002

Priority in Brazil: PI 0102252-0

Priority Date: 10/4/2001

Application Number: 578949

Title: PREPARATION OF FORMULATIONS OF ANGIOTENSIN II AT1 RECEPTORS ANTAGONISTS FOR THE TREATMENT OF ARTERIAL HYPERTENSION, OTHER CARDIOVASCULAR ILLNESSES AND ITS COMPLICATIONS

Inventors: Rubén Dario Sinisterra Millan, Frederic Jean Georges Frezard, Washington Xavier de Paula, Robson Augusto Souza dos Santos

Filing date: 9/4/2002

Priority in Brazil: PI 0102252-0

Priority Date: 10/4/2001

Application Number: 02810681.4

Title: PREPARATION OF FORMULATIONS OF ANGIOTENSIN II AT1 RECEPTORS ANTAGONISTS FOR THE TREATMENT OF ARTERIAL HYPERTENSION, OTHER CARDIOVASCULAR ILLNESSES AND ITS COMPLICATIONS

Inventors: Rubén Dario Sinisterra Millan, Frederic Jean Georges Frezard, Washington Xavier de Paula, Robson Augusto Souza dos Santos

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[Back](#)

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- Lady Davis Research Institute - McGill University (Canada);
- Laboratory of Biophysics - Institute of General and Molecular Biology, N. Copernicus University (Poland).
- CYL Pharmazeutika GmbH (Austria).
- Compugen *Ltd* (Israel)
- Erasmus University (Netherland)

FACILITIES

[Back](#)

Facilities for research at the INCT-NanoBiofar include:

- Cell Culture rooms
- Molecular Biology laboratories, including RT-PCR
- Stem cell research facility
- Western Blot facilities
- RIA Assay facility
- High resolution echocardiography
- Elisa Assay facility
- Telemetry unit
- Drug delivery formulations
- Bio-analytic instrumentation
- *In vivo* and *in vitro* cardiovascular facilities
- Physical-chemical analysis facility

EQUIPMENTS

Some of the equipments disponible for the network are listed below:

- 1) High Resolution Echocardiography - VEVO 2100
- 2) Li-Cor – Fluorescence Scanner for Western Blot
- 3) Potencial Zeta Zetasiser
- 4) Spectrofluorimeter for microplates and cuvet
- 5) Simultaneous thermogravimetry modulus (Tga-Dta) - Dtg-60
- 6) Nano Itc 2g System With Hastelloy Cylindrical Cell
- 7) PCR Life Express 96 with temperature gradient (Tc - 96thg)
- 8) Ultraviolet Uv-B Transiluminator
- 9) Powerlab 4/30

- 10) Activity Wheel and Activity Wheel Software**
- 11) Micropipette Puller (Twist) - Harvard Apparatus**
- 12) PowerEase 500 P C System Kit for WB – Invitrogen**
- 13) DataScience Telemetry Equipment (36 telemetry sensors)**
- 14) Nuclear Magnetic Resonance Spectroscopy**
- 15) Infrared Spectroscope**

Technology Transfer

Nanobiofar has made technology transfer agreements with two companies. With Scitech the objective is to use a technology protected by patents issued in US, India and China to produce Eluting Stents (see granted patents list) . With União Química the objective is to finalize the Phase I/II clinical trial in preeclamptic patients using an intravenous formulation of Ang-(1-7) and to start a Phase III study. An orally active formulation of Ang-(1-7) will be also tested for treatment of hypertension and cardio-metabolic diseases. In addition a technology based on an ongoing collaboration with investigators of the University of Gratz in Austria, will be transferred to the Austrian company CYL, this year.

SUMMARY OF ANNUAL ACTIVITIES

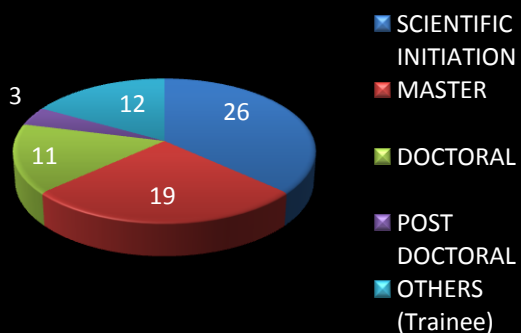
RESULTS	
A- RESEARCH INDICATORS	
TECHNICAL-SCIENTIFIC PRODUCTION	
DESCRIPTION	AMOUNT
BOOKS	3
BOOKS CHAPTERS	8
MANUSCRIPTS PUBLISHED IN NATIONAL SCIENTIFIC JOURNALS	14
MANUSCRIPTS PUBLISHED IN INTERNATIONAL SCIENTIFIC JOURNALS	148
ABSTRACT PRESENTED AT NATIONAL CONFERENCES	13
ABSTRACT PRESENTED AT INTERNATIONAL CONFERENCES	23
PATENT	
PRODUCTS	14
PROCESSES	7
GRANTED	6
B- HUMAN RESOURCES INDICATORS	
HUMAN RESOURCES FORMATION	
DESCRIPTION	AMOUNT
COMPLETED:	
SCIENTIFIC INITIATION	26
MASTER	19
DOCTORAL	11
POSTDOCTORAL	12
IN PROCESS:	
SCIENTIFIC INITIATION	43
MASTER	30
DOCTORAL	42
POSTDOCTORAL	15
OTHER	8
C- INDICATORS OF KNOWLEDGE AND TECHNOLOGY TRANSFER	
PRODUCTION DESCRIPTION	
DESCRIPTION	AMOUNT
SCIETCH	1
UNIÃO QUÍMICA	1

D- INDICATORS OF EDUCATION AND SCIENCE DISSEMINATION	
PRODUCTION DESCRIPTION	
DESCRIPTION	AMOUNT
TELEVISION NEWS PROGRAMS ABOUT HYPERTENSION	5
MAGAZINES AND NEWSPAPERS NOTES / COVERAGE	12

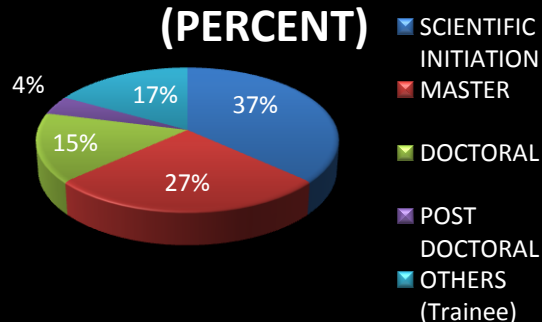
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[Back](#)

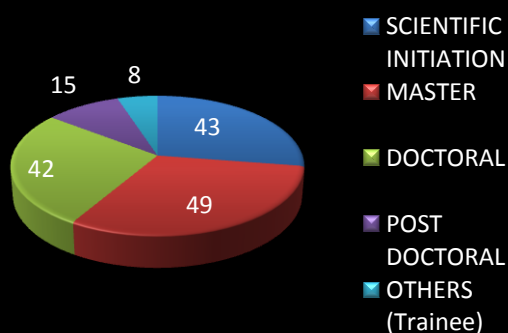
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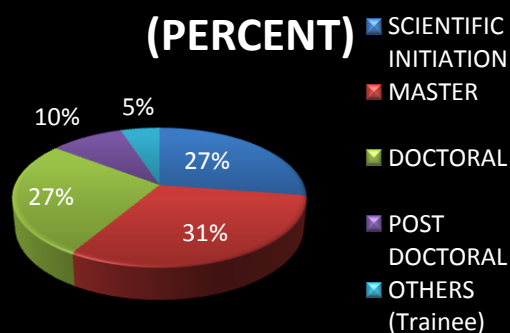
COMPLETED (PERCENT)



IN PROGRESS



IN PROGRESS (PERCENT)



FEDERAL UNIVERSITY OF MINAS GERAIS

[Back](#)



FEDERAL UNIVERSITY OF UBERLÂNDIA – MG



INSTITUTE OF CARDIOLOGY – FUC - RS



FEDERAL UNIVERSITY OF OURO PRETO - MG



ADDITIONAL PICTURES

