

BIOGRAPHICAL SKETCH

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NAME Maldonado, Rosa A.		POSITION TITLE Associate Professor of Biology	
eRA COMMONS USER NAME (credential, e.g., agency login) ramaldonado			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Central University of Venezuela - UCV, Caracas	B.Sc. Biology	07/89	Biology
Federal University of Rio de Janeiro-UFRJ, Brazil, and Northwestern U. Medical School, Chicago,	D.Sc.	08/96	Molecular Biology
University of Dundee, Dundee, UK	Wellcome Trust Fellow	05/99	Molecular Parasitology
University of Sao Paulo – USP, Sao Paulo, Brazil	Post-Doctor	12/03	Molecular Parasitology

A. Personal Statement

The focus of my research is developing novel immune- and chemotherapy tools to treat Chagas disease and leishmaniasis. I have over 25 years background in chemotherapy and molecular parasitology research, I feel suited to be the PI in the planned research. My previous work have provided the scientific community with the validation and characterization of novel chemotherapeutic targets for Chagas disease, the characterization of novel anti-*Trypanosoma cruzi* and *Leishmania major* drugs as well as potential vaccines to protect against Chagas disease recently published in *Vaccine*. Our preliminary results showed the highly antiparasitic activity of the compound NC2459. However, the low water solubility of the compound was a limitation. In this study we propose to develop and test NC2459 oral formulation. I am convinced that a combination of chemo and immunotherapy is the best approach to cure chronic ChD. In order to test this hypothesis propose to combine the best two molecules that I have characterized in the last, which are MASP (vaccine candidate) and NC2459 (novel chemotherapeutic agent). The funding of this proposal will greatly advance the PI's research. My goal is to take my discoveries from the bench to the clinic, In this regard, I have already established interaction with groups in Brazil and Bolivia, where future clinical trial could be performed. The participation in this proposal of my collaborator and subcontractor Dr. Xie is very important in order to obtain the drug formulation that could be used in these studies. Furthermore, the result generated with the funding of this proposal will be used to build new proposal and will allow the PI further her research competitiveness and the transition to non-SCORE support.

- 1) Miguel A. Vasquez, Eva Iniguez, Umashankar Das, Stephen M. Beverley, Linda J. Herrera, Jonathan R. Dimmock, **Rosa A. Maldonado** (2015) Evaluation of some α,β -unsaturated ketones as anti-trypanosomal agents. *Antimicrob. Agent and Chemother.* 59(6): 3598-35600.
- 2) Serna, C., Lara, J.A., Rodrigues, S.P., Marques, A.F., Almeida, I.C., **Maldonado, R.A.** (2014) A synthetic peptide from *Trypanosoma cruzi* mucin-like associated surface protein as candidate for a vaccine against Chagas disease. *Vaccine*, 32(28):3525-32. *PMCID: PMC4058865*

B. Positions, Honors

- 1989-1991 Research Assistant, Institute of Tropical Zoology, Faculty of Sciences, Central University of Venezuela, Caracas, Venezuela, Supervisor: Gilberto Payares
- 1992-1996 Doctoral Fellow, Institute of Biophysics Carlos Chagas Filho, Federal University of Rio de Janeiro (UFRJ) and Northwestern University Medical School, Chicago, U.S.A.

Program Director/Principal Investigator (Last, First, Middle): Maldonado, Rosa A.

- 1997 Research Assistant, University of Dundee, Department de Biochemistry, Dundee, Scotland, UK,
1997-1999. Wellcome Trust International Post-Doctoral Fellow, Division of Molecular Parasitology and Biological Chemistry, Department of Biochemistry, University of Dundee, UK,
1999- 2003. Post-Doctoral Fellow, Department of Parasitology, Institute of Biomedical Sciences, University of São Paulo (USP), São Paulo, SP, Brazil.
2004 Visiting Assistant Professor, Integrated Center for Gene Therapy (CINTERGEN), Federal University of Sao Paulo (UNIFESP), Sao Paulo, SP, Brazil, Feb-Sep 2004.
2004- 2010 Assistant Professor, Dept. of Biological Sciences, University of Texas at El Paso (UTEP), El Paso, TX.
Sept 2010- Associate Professor, Department of Biological Sciences, University of Texas at El Paso (UTEP), El Paso, TX.

Honors

- 1982-1989 Undergraduate scholarship Central University of Venezuela
1992-1996: Ph.D. fellowship, Consejo Venezolano de Investigaciones Cientificas y Tecnologicas (CONICIT), Venezuela.
1997-1999: Post-Doctorate, International Research Fellow, The Wellcome Trust, United Kingdom.
1999-2003: Post-Doctorate, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Sao Paulo, Brazil.
1998- Member of Brazilian Society of Protozoology (SBPz).
2004- Member of American Society of Microbiology (ASM).
2005- Member of Society for Advancement of Chicanos and Natives Americans in Sciences (SACNAS).
2005- Member of SIGMA Xi, The Scientific Research Society.
2005- Member of American Society of Parasitology.
2005-2007 Member of Infectious diseases and Immunology graduate committee, UTEP.
2006-2008 Member of Admissions & Academic Standards Committee, UTEP.
2006 Reviewer, NIH NIGMS-MBRS.
2006- Member of Union and Bookstore Committee, UTEP.
2007-2010 Alternate Senator at UTEP
2007 Honorary member of the Golden Key International Honour Society, UTEP chapter.
2008-2012 SIGMA Xi Membership Committee.
2008- Faculty advisor of the ASM Student Chapter at the University of Texas at El Paso
2010-2012 Host mentor for the ASM Microbiology Undergraduate Research Fellowship program.
2011-2013 President of the American Society for Microbiology Rio Grande Branch.
2012- Program Director UTEP Bridges to Baccalaureate-NIH.
2012- Member of Undergraduate Curriculum Committee, UTEP.
2012-2014 Vice President of the Bridges PD&CO.
2014-2015 Interim President of the Bridges PD&CO

C. Contribution to Science

1. Drug discovery and vaccine development

My research is concentrated on the development of novel treatments for Chagas disease and leishmaniasis. In this regard, my laboratory has characterized several lead compounds as well as vaccine candidates. In this regard, the publications and four patents (two US non-provisional in active prosecution and two provisional patents) indicated below documents my contribution in the field.

- a. Title: Mucin-Associated Surface Protein as a Novel Vaccine Candidate Against Chagas Disease. US/PCT Application PCT/US14/57124. Disclosure date: October 28, 2014. Inventors: Rosa A. Maldonado, Carylinda Serna, Igor C. Almeida. Status: PCT application filed.
Publication number: 20150086583; Filed: September 24, 2014; Publication date: March 26, 2015; Status: Non-provisional US patent

- b. Title: Antiparasitic effect of Bis[3,5-bis(benzylidene)-4-oxo-1-piperidinyl]amided derivatives. Provisional U.S. patent No. 14/684,300. PCT/US15/25482. Filing date: April 10, 2015. Inventor: Maldonado, Rosa; Vasquez, Miguel A.; Dimmock, Jonathan R.; and Das, Umashankar. Status: Active Prosecution (Non-provisional US patent).
- c. Title: Glycoconjugate Vaccine for Leishmaniasis. Provisional U.S. patent No. 62/136,993. Filing date: March 23, 2015. Inventors: Maldonado, Rosa; Almeida, Igor C.; Michael, Katja. Status: Provisional Filed.
- d. Title: One pot synthesis of substituted 5,5,7,7-tetramethyl-4,5,6,7-tetrahydrothieno[2,3-c]pyridine scaffold and their biological evaluation against L-Major and T-Cruzi. Provisional U.S. patent No. 62/173,845. Filing date: June 10, 2015. Inventors: Maldonado, Rosa; Skouta, Rachid. Status: Provisional Filed.
- 1) Herrera, L. J., Brand, S., Santos, A., Nohara, L.L., Harrison, J., Neil Norcross, N., Thompson, S, Smith, V., Gilbert, I.H., Lema, C., Varela-Ramirez, A., Almeida, I.C., **Maldonado, R.A.** (2016) Validation of *N*-myristoyltransferase as potential chemotherapeutic target in Chagas Disease. *Accepted with minor revisions in PLOS Pathogen*
 - 2) Iniguez, E.A., Perez, A., Maldonado, R.A., Skouta, R. (2015) Novel arylalkylamine compounds exhibits potent selective antiparasitic activity against *Leishmania major*. *Bioorganic & medicinal chemistry letters*. NIHMSID 735915
 - 3) Vasquez, M.A., Iniguez, E., Das, U., Beverley, S. M., Herrera, L.J., Dimmock, J. R., **Maldonado, R.A.** (2015) Evaluation of some α,β -unsaturated ketones as anti-trypanosomal agents. *Antimicrob. Agent and Chemother.* 59(6): 3598-35600.
 - 4) Serna, C., Lara, J.A., Rodrigues, S.P., Marques, A.F., Almeida, I.C., **Maldonado, R.A.** (2014) A synthetic peptide from *Trypanosoma cruzi* mucin-like associated surface protein as candidate for a vaccine against Chagas disease. *Vaccine*, 32(28):3525-32. *PMCID: PMC4058865*
 - 5) Iniguez, E., Sánchez, A., Vasquez, M.A., Martínez, A., Olivas, J., Sattler, A., Sánchez-Delgado, R. A. and **Maldonado, R.A.** (2013) The Metal-Drug Synergy: New Ruthenium^{II} Complexes of Ketoconazole are Highly Active against *Leishmania major* and *Trypanosoma cruzi* and Non-toxic to Human or Murine Normal Cells. *J. Biol. Inorg. Chem.* 18:779-790. *PMCID: PMC3783607*
 - 6) Martínez, A., Carreon, T., Iniguez, E.A., Anzellotti, A., Sánchez, A., Tyan, M., Sattler, A., Herrera, L., **Maldonado, R.A.**, Sánchez-Delgado, R.A. (2012) Searching for New Chemotherapies for Tropical Diseases: Ruthenium-Clotrimazole Complexes Display High *in vitro* Activity against *Leishmania major* and *Trypanosoma cruzi* and Low Toxicity Toward Normal Mammalian Cells. *J. Med. Chem.* 55: 3867-3877. *PMCID:PMC3375397*
 - 7) Lara, D, Yanshu Feng, Bader, J., Savage, P.B., **Maldonado, R.A.** (2010) Anti-trypanosomatid activity of ceragenins. *J. Parasitology*, 96(3):638-42. *PMCID: PMC2891*
 - 8) Ramos, E.I., Luise Krauth-Siegel, Garza, K., Martinez L., **Maldonado, R.A.** (2009) 2,3-diphenyl-1,4-naphthoquinone: a potential chemotherapeutic agent against *Trypanosoma cruzi*. *J. Parasitology*, 95: 461-466. *PMCID:PMC2929754*
 - 9) **Maldonado, R.A.** Kuniyoshi, R.K., Linss, J., Almeida, I.C. (2006) Molecular and biochemical characterization of oleate desaturase in trypanosomatids. *J. Parasitology*, 92: 1064-1074
 - 10) **Maldonado, R.A.** and Fairlamb, A.H. (2001) Cloning of a pyruvate phosphate dikinase from *Trypanosoma cruzi*. *Mol Biochem Parasitol*, 112, 183-191.
 - 11) **Maldonado, R.A.**, Mirzoeva, S., Godsel, L.M., Lukas, T.J., Goldenberg, S., Watterson, D.M. and Engman, D.M. (1999) Identification of calcium binding sites in the trypanosome flagellar calcium-acyl switch protein. *Mol Biochem Parasitol*, 101, 61-70.
 - 12) **Maldonado, R.A.**, Linss, J., Thomaz, N., Olson, C.L., Engman, D.M., Goldenberg, S. (1997) Homologues of the 24-kDa flagellar Ca(2+)-binding protein gene of *Trypanosoma cruzi* are present in other members of the Trypanosomatidae family. *Exp Parasitol.* 1997 Jul;86(3):200-5
 - 13) **Maldonado, R.A.**, Molina, J., Payares, G. and Urbina, J.A. (1993) Experimental chemotherapy with combinations of ergosterol biosynthesis inhibitors in murine models of Chagas' disease. *Antimicrob Agents Chemother*, 37, 1353-1359.
 - 14) Urbina, J.A., Lazard, K., Marchan, E., Visbal, G., Aguirre, T., Piras, M.M., Piras, R., **Maldonado, R.A.**, Payares, G. and de Souza, W. (1993) Mevinolin (lovastatin) potentiates the antiproliferative effects of

Program Director/Principal Investigator (Last, First, Middle): Maldonado, Rosa A.

ketoconazole and terbinafine against *Trypanosoma (Schizotrypanum) cruzi*: in vitro and in vivo studies. *Antimicrob Agents Chemother*, 37, 580-591.

Lipid metabolism of *Giardia lamblia*

- 1) Tavis L. Mendez, Atasi De Chatterjee, Trevor T. Duarte, Felipe Gazos-Lopes, Leobarda Robles-Martinez, Debarshi Roy, Jianjun Sun, **Rosa A. Maldonado**, Sukla Roychowdhury, Igor C. Almeida, and Siddhartha Das (2013) Glucosylceramide Transferase Activity is Critical for Encystation and Viable Cyst Production by an Intestinal Protozoan, *Giardia lamblia*. *J Biol Chem*. 288(23):16747-60. PMID: PMC3675608
- 2) Hernandez, Y., Shpak, M., Duarte, T, Mendez, T.L., **Maldonado, R.A.**, Roychowdhury, S., Rodrigues, M. and Das, S. (2008) Novel Role of Sphingolipid Synthesis Genes in Regulating Giardial Encystation. *Infect Immun*. 76(7): 2939-49. PMID: PMC2446683.

Molecular and biochemical characterization of antimicrobial peptides.

- 1) Esteves E, Fogaça AC, **Maldonado R**, Silva FD, Manso PP, Pelajo-Machado M, Valle D, Daffre S.(2009) Antimicrobial activity in the tick *Rhipicephalus (Boophilus) microplus* eggs: Cellular localization and temporal expression of microplusin during oogenesis and embryogenesis. *Dev. Comp. Immunol*. 33(8):913-9.
- 2) Barbosa, F.M., Daffre, S., **Maldonado, R. A.**, Miranda, A., Nimrichter, L. and Rodrigues, M. L. (2007) Gomesin, a peptide produced by the spider *Acanthoscurria gomesiana*, is a potent anti-cryptococcal agent that also acts in synergism with fluconazole. *FEMS Microbiol Lett*, 274(2):279-86.

Ecology and epidemiology of infectious diseases

- 1) Buhaya, M., Galvan, S., **Maldonado, R.A.** (2015). Incidence of *Trypanosoma cruzi* Infection in Triatomine Bugs Collected at Indio Mountains Research Station. *Acta Tropica* 150:97-99.
- 2) Mendes Nascimento, E.M., Gehrke, F.S., **Maldonado, R. A.**, Colombo, S., Da Silva, L.J. and Schumaker, T. Tizu Sato (2005) Identification of brazilian spotted fever infection by polymerase chain reaction in a patient from São Paulo state. *Mem. Inst. Oswaldo Cruz* 100: 277-279.

***All my publications are available at:**

<http://www.ncbi.nlm.nih.gov/sites/myncbi/rosa.maldonado.1/bibliographahy/40214914/public/?sort=date&direction=ascending>

Manuscripts in preparation:

1. Sebastian Montalvo, Elizabeth Calzada, Cristina Gutierrez, Omonike Olaleye and **Rosa A. Maldonado** Inhibitors of Methionine Aminopeptidase-1 as a potential chemotherapeutic agent against *Leishmania major*.
2. Claudia Manriquez Roman, Jose A. Orozco, Eva Iniguez, Adam Vera, Doug Watts and **Rosa A. Maldonado**. Evaluation of Chagas' disease in Wild and Domestic Reservoir in El Paso County – Texas.

D. Research Support

Ongoing Support

R25 (NIH/NIGMS) Maldonado (PI) 06/01/2015 - 05/31/2019
Bridges to the Baccalaureate Program (Renewal)
The goal of this study is to promote the successful transition of minority (primarily Mexican-American) students with biomedical interests from the community college to the university and to improve their completion of a baccalaureate degree.

Completed Research Support

2R25GM049011-10 (NIH/NIGMS) Maldonado (PI) 09/01/2011 - 05/31/2015
Bridges to the Baccalaureate Program
The goal of this study is to promote the successful transition of minority (primarily Mexican-American) students with biomedical interests from the community college to the university and to improve their completion of a baccalaureate degree
UTEP-IDR PI Sep 2013 – Aug 2014

Program Director/Principal Investigator (Last, First, Middle): Maldonado, Rosa A.

Novel Tools for Parasite Targeting and Delivery of a Chemotherapeutic Drug

Amount (total): \$20,000

Overall goal: To improve drug delivery system

NIH/NCRR/ARRA - Grant Number U54RR022762 Maldonado (PI)

Oct 2010 – June 2012

HTS for discovery of novel anti-trypanosomal agents

Amount (total): \$25,000

Overall goal: To identify potential MetAP inhibitors with antiparasitic activity against *L. major*, *T. cruzi* and *T. brucei*

NIH/BBRC- Grant Number Maldonado (PI)

Oct 2011 – June 2012

Evaluation of the Antiparasitic Activity of Metal-Based Azoles

Amount (total): \$25,000

Overall goal: Evaluate the anti-*T. cruzi* activity of a novel serie of Ruthenium-azole complexes seeking for new treatment for Chagas disease.

NIH/MBRS/SCORE Grant ID # 2S06GM00812-37 Maldonado (PI)

Jun 2007-May 2011

Oleate desaturase: Novel drug target for Chagas disease

Amount (total): \$ 585.000

Overall goal: Characterization and validation of potential chemotherapeutic targets, and development of new drugs to treat Chagas' disease.

HMI Grant ID number 52005908 Maldonado (Co-PI)

Sept 2006 - Aug 2010

2006 Undergraduate Science Education Program

Amount (total): \$375,000 direct each year, 1.5 million total over four years

Overall goal: Involve the student in a meaningful research opportunity through the development of an undergraduate research center and curriculum, which will give research experience to all students majoring in Microbiology or Biology-Biomedicine at UTEP.