BIOGRAPHICAL SKETCH

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NAME: Almeida, Igor C.

eRA COMMONS USER NAME (credential, e.g., agency login): icalmeida

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Northeastern Regional University-URNe/UEPb, Brazil	B.Pharm.	12/1981	Pharmacy
Escola Paulista de Medicina/UNIFESP, Brazil	M.Sc.	07/1989	Molecular Biology
Escola Paulista de Medicina/UNIFESP, Brazil	D.Sc.	07/1994	Microbiol. & Immunol.
University of Dundee, UK	Postdoctoral	11/1998	Molecular Parasitology

A. Personal Statement

My major research focus in the last 28 years has been the immunoglycobiology of the protozoan parasite, *Trypanosoma cruzi*, the causative agent of Chagas disease (ChD). More specifically, I have been studying the structure and biological and immunological roles of glycosylphosphatidylinositol (GPI)-anchored glycoconjugates (i.e., glycoproteins and glycolipids), which are major components of the parasite cell surface. As a result of these studies, we have been developing a synthetic glycan- and peptide-based ChD vaccines and biomarkers (BMKs) for the early assessment of chemotherapy outcome in ChD. Throughout my career, I have also been actively involved in the structural and functional analysis of a variety of biomolecules from different sources and organisms, including parasites, fungi, bacteria, arthropod vectors, and cancer cells, collaborating with several research groups in the U.S., Latin America, and Europe.

Since November 2004, I have been the director of the Biomolecule Analysis Core Facility (BACF) (recently renamed Biomolecule Analysis and Omics Unit (BAOU)), Border Biomedical Research Center (BBRC), UTEP, which is a cutting-edge core facility for *omics* (e.g., proteomics, metabolomics, lipidomics, and glycolipidomics). I would be delighted to serve as director of BAOU in this U54 proposal. Our Unit has an array of mass spectrometry (MS) instruments (i.e., Orbitrap-MS, ESI-LTQ-MS, GC-TSQ-MS, and TSQ-MS) and many other analytical, shared instruments (Biacore, NTA system, Milliplex/Multiplex, nano- and micro-UPLCs, etc.). we have been employing MS-based and other analytical approaches for the analysis of proteins, lipids, and post-translational modifications of proteins (e.g., GPI-anchoring, glycosylation, palmitoylation, SUMOylation, phosphorylation, etc.) from different sources, including pathogens and cancer cells. My extensive expertise in analysis of biomolecules will be at the entire disposal of the current R01 projects within this U54 application.

Publications relevant to the proposed research (*omics*: proteomics, lipidomics, glycolipidomics):

1. Nakayasu ES, Yashunsky DV, Nohara LL, Torrecilhas AC, Nikolaev AV, **Almeida IC** (2009) GPIomics: global analysis of glycosylphosphatidylinositol-anchored molecules of *Trypanosoma cruzi*. ***Mol Syst Biol*** 5: 261
2. Bayona JC, Nakayasu ES, Laverriere M, Aguilar C, Sobreira TJ, Choi H, Nesvizhskii AI, **Almeida IC***, Cazzulo JJ*, Alvarez VE* (2011) SUMOylation pathway in *Trypanosoma cruzi*: functional characterization and proteomic analysis of target proteins. ***Mol Cell Proteomics*** 10: M110 007369. [*corresponding authors]
3. Peng B, Huang X, Nakayasu ES, Petersen JR, Qiu S, **Almeida IC***, Zhang JY* (2013) Using Immunoproteomics to Identify Alpha-enolase as an Autoantigen in Liver Fibrosis. ***J Proteome Res*** 12: 1789-96. [*corresponding authors]

4. Szempruch AJ, Sykes SE, Kieft R, Dennison L, Becker AC, Gartrell A, Martin WJ, Nakayasu ES, **Almeida IC**, Hajduk SL, Harrington JM (2016) Extracellular Vesicles from *Trypanosoma brucei* Mediate Virulence Factor Transfer and Cause Host Anemia. ***Cell*** 164: 246-57

B. Positions and Honors

Positions and Employment

1989-1993	Lecturer in Biochemistry, Albert Einstein Jewish Hospital Nursing School, Sao Paulo, Brazil
1993-1995	Substitute Adjunct Prof., Dept. of Microbiol., Immunol. & Parasitol. (DMIP), University of Sao Paulo (UNIFESP), Escola Paulista de Medicina (EPM), Sao Paulo, Brazil
1995-1996	Visiting Adjunct Prof., DMIP, EPM/UNIFESP, Sao Paulo, Brazil
1999-2004	Assistant Professor, Dept. of Parasitology, University of Sao Paulo (USP), Sao Paulo, Brazil
2000-2004	Research Fellow, Brazilian National Research Council (CNPq), Brazil
2004-2008	Associate Professor (tenure track), Dept. of Biological Sciences, The Border Biomedical Research Center (BBRC), Univ. of Texas at El Paso (UTEP), TX
2008-2010	Associate Professor (with tenure), Dept. of Biological Sciences, UTEP, El Paso, TX
2004-	Director, Biomolecule Analysis Core Facility, BBRC, Dept. of Biological Sciences, UTEP
2005-	Director, NIH/NIGMS Bridges to the Baccalaureate Program at UTEP, El Paso, TX
2005-	Faculty member, Bioinformatics Program, UTEP, El Paso, TX
2010-	Professor, Dept. of Biological Sciences, UTEP, El Paso, TX
2012-2015	Science Without Borders Special Visiting Researcher, Brazilian National Research Council (CNPq), Brazil.

Other Experience and Professional Memberships

2004-	Member, American Society for Biochemistry and Molecular Biology
2005-	Member, American Society for Microbiology
2006-	Member, Glycobiology Society
2009-	Member, Consortium for Functional Glycomics
2012-	Member, Human Proteome Organisation (HUPO)
2013-	Member, International Society for Extracellular Vesicles (ISEV)
2007-2010	NIH ad hoc reviewer for the PTHE, MBRS/SCORE, DDR, and PDPPP Peer Review Committees
2009-2013	NIH regular reviewer for the PTHE Peer Review Committee

Honors

2007	The University of Texas System's Science and Technology Acquisition and Retention Program (STAR) Award
2009	Research Accomplishment Award, College of Science, University of Texas at El Paso
2011	Outstanding Performance Award for Securing Extramural Funding, Office of Research and Projects (ORSP), College of Science (COS), UTEP, spring 2011.
2012	Millionaire Research Award, for expenditures over a million dollars in 2011, Office of Research and Projects (ORSP), College of Science (COS), UTEP, spring 2012.
2013	Distinguished Achievement Award for Research, UTEP, spring 2013
2013	Distinguished Research Accomplishment Award, College of Science, UTEP, spring 2013
2014	Distinguished Research Accomplishment Award Inaugural Lecture, UTEP, spring 2014
2011-	Member, Editorial boards of Parasitology International, and Frontiers in Mycology.
2012-2015	Special Visiting Researcher, Science Without Borders Program, CNPq, Brazil
2015	Outstanding Performance Award for Securing Extramural Funding, Office of Research and Sponsored Projects (ORSP), University of Texas at El Paso (UTEP)
2016	Member of Special Emphasis Panel/Scientific Review Group 2016/05 ZAI1 PA-I (M2) of the National Institutes of Health (NIH)
Oct 2018	Ad-hoc member, Special Emphasis Panel/Scientific Review Group 2019/01 ZRG1 PSE-D (55) R, NIH.
2017-	Guest Associate Editor, PLoS Neglected Tropical Diseases
2017	Fellow, American Academy of Microbiology (AAM), elected in March 2017.

C. Contribution to Science*

1) Protective role of *T. cruzi*-specific anti-α-Gal antibodies in Chagas disease and cutaneous leishmaniasis

My first relevant contribution to science was the discovery of the major and immunodominant parasite molecules, the GPI-anchored mucin-like glycoproteins (or GPI-mucins), which are recognized by the abundant lytic anti-α-Gal antibodies found in patients with acute or chronic CD (Almeida *et al.*, *J Immunol*, 1991; Almeida *et al*., *J Clin Lab Anal*, 1993; Almeida *et al.*, *Biochem J*, 1994). In one of the studies, we were able to show that anti-α-Gal binds to α-galactopyranosyl (α-Gal)-containing epitopes present on *O*-linked oligosaccharides attached to the polypeptide chain of mucins. Interestingly, we observed that these epitopes are exclusively present on mucins purified from the mammal-dwelling trypomastigote stage, but not on mucins from vector-derived stages. These studies have also clearly shown that the lytic anti-α-Gal Abs are able to destroy the parasite by a mechanism which is mostly independent of the complement cascade (Almeida *et al.*, *Biochem J*, 1994; Pereira-Chioccola et al*., J Cell Sci*, 2000). More recently, we have also developing α-Gal-based vaccines for cutaneous leishmaniasis (Iniguez et al., PLOS NTD 2017).

1. **Almeida, I.C.**, Milani, S.R., Gorin, P.A.J., Travassos, L.R. (1991) Complement-mediated lysis of Trypanosoma cruzi trypomastigotes by the human anti-alpha-galactosyl antibodies. ***J Immunology*** 146: 2394-2400. **PMCID: N/A**
2. A**lmeida, I.C.**, Ferguson, M.A.J., Schenkman, S., Travassos, L.R. (1994) Lytic anti-alpha-galactosyl antibodies from patients with chronic Chagas disease recognise novel *O*-linked oligosaccharides on mucin-like GPI-anchored glycoproteins of *Trypanosoma cruzi*. ***Biochem J*** *304*: 793-802. **PMCID: PMC1137404**
3. Pereira-Chioccola, V.L., Acosta-Serrano, A., **Correia de Almeida, I.**, Ferguson, M.A., Souto-Padron, T., Rodrigues, M.M., Travassos, L.R., Schenkman, S. (2000) Mucin-like molecules form a negatively charged coat that protects Trypanosoma cruzi trypomastigotes from killing by human anti-alpha-galactosyl antibodies. ***J Cell Sci*** *113*: 1299-1307. **PMCID: N/A**
4. Iniguez, E., Schocker, N.S., Subramaniam, K., Portillo, S., Montoya, A.L., Al-Salem, W.S., Torres, C.L., Rodriguez, F., Moreira, O.C., Acosta-Serrano, A., Michael, K., Almeida, I.C.,* and Maldonado, R.A.* (2017) An α-Gal-containing neoglycoprotein-based vaccine partially protects against murine cutaneous leishmaniasis caused by *Leishmania major.* ***PLOS Negl. Trop. Dis.***, Oct 25; 11(10):e0006039. doi: 10.1371/journal.pntd.0006039. [*Both corresponding authors]

2) Development of new tools for diagnosis and follow-up of the chemotherapy of Chagas disease

My second important contribution was the development of a serological chemiluminescent-based immunoassay (CL-ELISA), using either an epimastigote lysate (EpEx CL-ELISA) or purified trypomastigote-derived GPI-mucins (also known as AT or F2/3 antigen) (AT CL-ELISA) as antigens for the precise diagnosis of CD (Almeida *et al., J Clin Lab Anal*, 1994; Almeida *et al.*, *Transfusion*, 1997). The AT CL-ELISA also proved to be the first diagnostic tool for the follow-up of chemotherapy of patients with chronic CD (de Andrade *et al., Lancet*, 1996). Based on this study, in 1998 a group of international experts invited by the Pan-American Health Organization (PAHO)/World Health Organization (WHO) decided to recommend the benznidazole treatment of CD in children and adolescents (up to 15 years of age), using the AT CL-ELISA as one of the criteria of cure (OPS/HCP/HCT/140/99, Washington, 32 p., 1998). The development of this assay resulted in two granted patents, one Brazilian (PI 940095-3) and one American (US Patent 6,682,900). The most gratifying outcome from these studies, however, is the fact that different groups in Latin America have been successfully employing the AT CL-ELISA as criterion of cure for the chemotherapy of patients with CD (de Andrade et al., 1996; Torrico et al., 2018). Recently, in collaboration with Dr. Katja Michael (UTEP) we have been synthesizing and testing a series of α-galactosyl-containing glycotopes, found on for the diagnosis and follow-up of CD chemotherapy (Ashmus et al., *Org Biomol Chem,* 2013), as well as potential experimental vaccines (Schocker et al., Glycobiology, 2016).

a. De Andrade, A.L.S.S, Zicker, F., Oliveira, R.M., Silva, S.A., Luquetti, A., Travassos, L.R., **Almeida, I.C.**, Andrade, S.S., Andrade, J.G., Martelli, C.M. (1996) Randomised trial of efficacy of benznidazole in treatment of early *Trypanosoma cruzi* infection. ***Lancet*** 348: 1407-1413. **PMCID: N/A**
b. **Almeida, I.C**, Covas, D.T., Soussumi, L.M.T., Travassos, L.R. (1997) A highly sensitive and specific chemiluminescent enzyme-linked immunosorbent assay for diagnosis of active *Trypanosoma cruzi* infection. ***Transfusion*** *37*: 850-857. **PMCID: N/A**
c. Schocker NS, Portillo S, Brito CR, Marques AF, **Almeida IC**, Michael K (2016) Synthesis of

Galalpha(1,3)Galbeta(1,4)GlcNAcalpha-, Galbeta(1,4)GlcNAcalpha-, and GlcNAcalpha-containing neoglycoproteins and their immunological evaluation in the context of Chagas disease. ***Glycobiology*** 26(1):39-50. **PMCID: PMC4672149**.

d. Torrico, F., Gascon, J., Ortiz, L., Alonso-Vega, C., Pinazo, M.J., Schijman, A., **Almeida, I.C.**, Alves, F. Strub-Wourgaft, N., Ribeiro, I., on behalf of the E1224 Study Group* (2018) Treatment of adult chronic indeterminate Chagas disease: proof-of-concept randomized placebo-controlled study of benznidazole and three E1224 dosing regimens. ***The Lancet Infectious Diseases***, 2018 Jan 15. pii: S1473-3099(17)30538-8. DOI: doi.org/10.1016/S1473-3099(17)30538-8. PMCID: N/A.

3) <u>Structure and immunogenicity of *T. cruzi* GPI anchors and GPI-anchored glycoproteins</u>

Another significant contribution of my research has been the structural and functional/immunological analysis of glycosylphosphatidylinositol (GPI) anchors and GPI-anchored glycoproteins of *T. cruzi*. We have identified *T. cruzi* GPIs as potent activators of the host innate immune system. In a series of studies in collaboration with Profs. Ricardo T. Gazzinelli (Brazil), Luiz R. Travassos (Brazil), and Michael A.J. Ferguson (UK), we established by MS and other analytical techniques, that the mucin-derived GPI moiety, highly purified from trypomastigote GPI-mucins (tGPI-mucins), comprises the minimal structure required for the strong induction of proinflammatory cytokines and nitric oxide by IFN-γ-primed murine macrophages (Almeida *et al., EMBO J*, 2000). The activation of macrophages and dendritic cells by *T. cruzi* GPIs occurs via Toll-like receptor 2 (TLR2)-mediated signaling cascade (Campos *et al*., *J Immunol*, 2001). We have also described the structure and immunogenicity of the trypomastigote-derived small surface antigen (TSSA), which is an excellent marker infection by *T. cruzi* discrete-type unit (DTU) TcII genotype, which is responsible for the majority of infections if the Southern Cone of South America, which includes Argentina, Chile, Uruguay, and Southern Brazil. The implications of our observations are that the activation of TLR2 by GPIs may provide new approaches for immune intervention during the course of severe protozoan infections, such as Chagas disease, leishmaniasis, toxoplasmosis, and malaria, which together affect over a billion people worldwide.

a. **Almeida, I.C.**, Camargo, M.M., Procopio, D.O., Silva, L.S., Mehlert, A., Travassos, L.R., Gazzinelli, R.T., Ferguson, M.A.J. (2000) Highly purified glycosylphosphatidylinositols from *Trypanosoma cruzi* are potent proinflammatory agents. ***EMBO J*** 19: 1476-1485. **PMCID: PMC310217**

b. Campos, M.A., **Almeida, I.C**., Takeuchi, O., Akira, S., Valente, E.P., Procopio, D.O., Travassos, L.R., Smith, J.A., Golenbock, D.T., Gazzinelli, R.T. (2001) Activation of Toll-like receptor-2 by glycosylphosphatidylinositol anchors from a protozoan parasite. ***J Immunol*** *167*: 416-423. **PMCID: N/A**

c. Di Noia, J.M., Buscaglia, C.A., De Marchi, C.R., **Almeida, I.C.**, Frasch, A.C. (2002) A *Trypanosoma cruzi* small surface molecule provides the first immunological evidence that Chagas' disease is due to a single parasite lineage. ***J Exp Med*** *195*: 401-413. **PMCID:** PMC2193624.

d. Buscaglia, C.A., Campo, V.A., Di Noia, J.M., Torrecilhas, A.C., De Marchi, C.R., Ferguson, M.A., Frasch, A.C., **Almeida, I.C.** (2004) The surface coat of the mammal-dwelling infective trypomastigote stage of *Trypanosoma cruzi* is formed by highly diverse immunogenic mucins. ***J Biol Chem*** 279: 15860-15869. **PMCID:** PMC344000

4) <u>Discovery and validation of novel molecular targets for development of a Chagas disease vaccine</u>

Finally, in recent years, my major contribution has been the identification and validation of potential molecular targets for vaccine development. We have been using proteomics approaches, bioinformatics and immunoinformatics for this purpose (Nakayasu et al., *J Proteome Res* 2012; Bayer-Santos et al., *J Proteome Res* 2013). In collaboration with Dr. Rosa A. Maldonado (UTEP), we have validated the proteomics-immunoinformatics approach as a powerful tool for identification of candidates for development of experimental Chagas disease vaccines (Serna et al., Vaccine, 2014). Recently, we were awarded a U.S. patent for the MASPpep vaccine.

1. Nakayasu E.S., Sobreira T.J., Torres R., Ganiko, L., Oliveira, P.S., Marques, A.F., **Almeida, I.C.** (2012) Improved proteomic approach for the discovery of potential vaccine targets in *Trypanosoma cruzi*. ***J Proteome Res*** 11(1): 237−246. DOI: 10.1021/pr200806s. **PMCID: PMC3253764.**
2. Bayer-Santos E, Aguilar-Bonavides C, Rodrigues SP, Cordero EM, Marques AF, Varela-Ramirez A, Choi H, Yoshida N, da Silveira JF, **Almeida IC** (2013) Proteomic analysis of Trypanosoma cruzi secretome: characterization of two populations of extracellular vesicles and soluble proteins. ***J Proteome Res*** 12: 883−897. DOI 10.1021/pr300947g. **PMCID: N/A**
3. 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**

4. Maldonado, R.A., Serna, C., Almeida, I.C. (2017) U.S. Patent No. US 9,566,320, February 14, 2017.

***All my peer-reviewed publications (total of 151) are available at:**
http://www.ncbi.nlm.nih.gov/sites/myncbi/igor.almeida.1/bibliography/40638082/public/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

1U01AI129783-01A1 (NIH/NIAID) ALMEIDA (LEAD PI) 08/17/2018 – 07/31/2023
New Chemotherapy Regimens and Biomarkers for Chagas Disease
Role: Lead PI (MPIs: Gascon, Joaquim; Torrico, Faustino)
The goal of this clinical trial is to test new regimens of the two current drugs for Chagas disease to improve their safety and efficacy, and develop and test novel diagnostic tools (biomarkers) that will provide a more efficient measure of disease state and treatment outcomes.

2G12MD007592-21 (NIH/NIMHD) KIRKEN (PI) 07/01/2014 - 03/31/2019
Border Biomedical Research Center
To provide BBRC faculty, staff and students full access to cutting-edge instrumentation for biochemical and mass spectrometric analysis of biomolecules from organisms of biomedical relevance.
Role: Director, Biomolecule Analysis Core Facility (BACF subproject)

R01AI127554 (NIH/NIAID) LEWIS (PI) 07/01/2017 – 06/30/2021
Glycogen in Bacterial Vaginosis & How Carbohydrates Shape the Vaginal Microbiome
To examine the proteomes of human vaginal specimens in search of the bacterial enzymes that break down carbohydrates and could be involved in bacterial vaginosis, which is associated with higher risks and many serious reproductive health complications in women.
Role: Sub-contract PI

Completed Research Support

NIH/NIAID, Grant # 1R21AI115451-01 ALMEIDA (PI) 12/01/2014 - 11/30/2017
Synthetic neoglycopeptides as Chagas disease vaccines
To synthesize and evaluate in vivo α-Gal-containing neoglycopeptides as vaccines for experimental Chagas disease.
Role: PI

Kleberg Foundation ALMEIDA and VANDERBERG (PIs) 01/01/2014 - 10/30/2017
Novel Vaccine for Chagas Disease: Efficacy Testing in Baboons
To evaluate a synthetic glycan-based vaccine for Chagas disease in baboons.
Role: PI