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 over the last 25 years has been the immunoglycobiology of the protozoan parasite, *Trypanosoma cruzi*, the causative agent of Chagas disease. 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-based Chagas disease vaccine and biomarkers (BMKs) for the follow-up of the chemotherapy of CD. Throughout my career, I have also been involved in the structural and functional analysis of a variety of biomolecules from different sources and organisms, including parasites, fungi, bacteria, and arthropod vectors. In these studies, I have been employing mass spectrometry-based approaches and other analytical approaches for the analysis of proteins (proteomics), lipids (lipidomics), and post-translational modifications of proteins (e.g., GPI-anchoring, palmitoylation, SUMOylation, phosphorylation, glycosylation, etc.).

Since November 2004, I have been the director of the Biomolecule Analysis Core Facility (BACF) at the Border Biomedical Research Center (BBRC), UTEP, which is a core facility for proteomics and other *omics* (metabolomics, lipidomics, and glycolipidomics), used by 56 BBRC research groups and numerous external users and collaborators.

In this Administrative Supplement proposal, we are requesting funds for upgrading our current Q Exactive Orbitrap MS (QE) to a newer and more robust instrument, the Q Exactive Plus Orbitrap MS (QE Plus). Our current QE is a critical instrument to many BACF users but is presently non-operational, due to several inherent hardware and electronics issues. The cost to fix the QE is almost the cost to upgrade it to the new generation and much improved QE Plus, which is a state-of-the-art MS without the many issues of the first generation QE. The six projects herein described require large-scale, high-resolution (HR) proteomics, which cannot be achieved with the current QE or the other two MS instruments (LTQ XL and Endura Triple Quadrupole) available in our Core. In my specific project on *T. cruzi* described here, we have been using HR proteomics to compare the six genotypes of the parasite aiming to identify universal peptides and proteins that can targeted for development of a vaccine for Chagas disease.

1. Bayona, J.C.,* Nakayasu, E.S.,* Laverrière, M., Aguilar, C., Sobreira, T.J., Choi, H., Nesvizhskii, A.I., **Almeida, I.C.**,# Cazzulo, J.J.,# Alvarez, V.E.# (2011) SUMOylation pathway in Trypanosoma cruzi: functional characterization and proteomic analysis of target proteins. ***Mol Cell Proteomics*** 10: M110.007369. One of

the highlights of the December MCP issue. PMCID: PMC3237068. [*Equal contributors; #corresponding authors].

2. 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.
3. 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.
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: 246-257. PMCID: PMC4715261

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
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, Journal of Glycomics and Lipidomics, and Frontiers in Mycology.
2012-2015	Special Visiting Researcher, Science Without Borders Program, Brazilian National Research Council (CNPq), Brazil
2015	Outstanding Performance Award for Securing Extramural Funding, Office of Research and Sponsored Projects (ORSP), University of Texas at El Paso (UTEP)

C. Contribution to Science*

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

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*p*)-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).

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. Travassos, L.R., **Almeida, I.C.** (1993) Carbohydrate immunity in American trypanosomiasis. ***Springer Seminars Immunopathology*** *15*: 183-204. **PMCID: N/A**
3. 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**
4. 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**

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. 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).

1. 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**
2. **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**
3. Ashmus, R.A. Schocker, N.S., Cordero-Mendoza, Y., Marques, A.F., Monroy, E.Y., Pardo, A., Izquierdo, L., Gállego, M., Gascon, J., **Almeida, I.C.,*** and Michael, K.* (2013) Potential use of synthetic alpha-galactosyl-containing glycotopes of the parasite *Trypanosoma cruzi* as diagnostic antigens for Chagas disease. ***Org Biomol Chem*** 11(34):5579-83. **PMCID:** N/A [*senior authors]
4. 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**.

3) <u>Structural analysis and immunological activity of *T. cruzi* GPI anchors</u>

Another significant contribution of my research has been the structural and functional/immunological analysis of glycosylphosphatidylinositol (GPI) anchors 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; Ropert et al., *J Immunol* 2001). 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.

1. **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**
2. 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**
3. Ropert, C., **Almeida, I.C.**, Closel, M., Travassos, L.R., Ferguson, M.A.J., Cohen, P., Gazzinelli, R.T. (2001) Requirement of mitogen-activated protein kinases and IkappaB phosphorylation for induction of proinflammatory cytokines synthesis by macrophages indicates functional similarity of receptors triggered by glycosylphosphatidylinositol anchors from parasitic protozoa and bacterial lipopolysaccharide. ***J. Immunol.*** *166*: 3423-3431. **PMCID: N/A**
4. **Almeida, I.C.**, Gazzinelli, R.T. (2001) Proinflammatory activity of glycosylphosphatidylinositol anchors derived from *Trypanosoma cruzi*: structural and functional analyses. ***J Leukoc Biol*** *70*: 467-477. **PMCID: N/A**

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 immunoformatics for this purpose (Buscaglia et al., *J Biol Chem, 2004;* Nakayasu et al., *J Proteome Res* 2012; Bayer-Santos et al., *J Proteome Res* 2013). In a recent publication 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).

1. 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: N/A**
2. 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.**
3. 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: NIHMSID # 583794**
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**

***All my publications 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

NIH/NIAID, Grant # 1R21AI115451-01 ALMEIDA (PI) 12/01/2014 - 11/30/2016
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 - 12/30/2016
Novel Vaccine for Chagas Disease: Efficacy Testing in Baboons
To evaluate a synthetic glycan-based vaccine for Chagas disease in baboons.
Role: PI

1R01GM102689-01A1 (NIH/NIGMS) ENGMAN (PI) 07/01/2013 - 03/31/2017
Global Characterization of Protein Palmitoylation in Trypanosomes
To conduct a global analysis of protein palmitoylation in T. brucei to determine its palmitoylproteomes, identify the substrate profiles and functions of T. brucei palmitoyl acyltransferases, and investigate this class of enzymes as potential targets for trypanocidal chemotherapy.
Role: Sub-contract PI

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)

1R01AI095667-01 (NIH/NIAID) DAS (PI) 07/01/2011 - 07/30/2016
Sphingolipid and Mechanism of Cyst Formation by Giardia
To elucidate the mechanism by which glucosylceramide transferase-1 regulates the biogenesis of encystation-specific vesicles (ESVs) and viability of giardial cysts. My role is to advise and help the PI in designing experiments related to mass spectrometry.
Role: Co-investigator

1R15AI105823-01A1 JOHNSON (PI) 04/01/2014 - 03/31/2017
Mechanisms in viral RNA replication complex assembly: novel targets for antiviral therapy
To examine the role of post-translational modification of the Nodamura virus RNA-dependent RNA polymerase in its localization to viral RNA replication complexes in the cell.
Role: Co-investigator

Completed Research Support

R01AI070655 (NIH/NIAID) ALMEIDA (PI) 06/01/2007 – 05/31/2012
Molecular Composition and Function of *Trypanosoma cruzi* Shed Vesicles
To understand how *T. cruzi* shed vesicles secreted by the parasite are able to interact with host effector (receptor) molecules, leading to cell invasion and continuous escape from host immunity.
Role: PI

5S06GM008012 (NIH/NIGMS/SCORE) ALMEIDA (PI) 06/01/2007 – 05/31/2011
Identification and validation of novel antigenic targets in Trypanosoma cruzi
To validate novel antigenic targets in Trypanosoma cruzi for vaccine development
Role: PI

2R25GM049011-10 (NIH/NIGMS) ALMEIDA (PI) 09/01/2009 – 06/30/2014
Bridges to the Baccalaureate Program
Role: PI (until 06/30/2011) (new PI: Maldonado, Rosa, from 07/01/2011)
To promote the successful transition of minority (primarily Mexican-American) students with biomedical interests from the community college to the university.