CURRICULUM VITAE - 2016 IVO P.TORRES FILHO, MD, PhD

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INSTITUTION	DEGREE	Completion Date	FIELD OF STUDY
State University of Rio de Janeiro	M.D.	12/1981	Medicine
Federal University of Rio de Janeiro	M.S.	05/1984	Physiology and Biophysics
Federal University of Rio de Janeiro	Ph.D.	05/1988	Physiology and Biophysics
University of California, San Diego	Postdoctoral	04/1994	Physiology and Biophysics

A. Personal Statement

Our research helps to understand physiological mechanisms taking place at the level of the microcirculation in health and disease by applying novel techniques and methods. Various experimental strategies are used to investigate the pathophysiology of specific cardiovascular conditions and their treatment. We also aim to develop new tools for diagnosis and interventions against these conditions. We focus on hemorrhagic shock, and factors that affect the local distribution of oxygen and blood flow in the microcirculation. A major area of study is endothelial cell function, notably factors affecting glycocalyx structure and function *in vivo*.

We have developed and extensively used noninvasive techniques for measuring glycocalyx thickness and oxygenation *in vivo*. A key and unique component of our approach is to integrate traditional systemic physiological parameters, blood biomarkers, and microvascular variables such as microvascular permeability, leukocyte-endothelial interactions, platelet-endothelial interactions, and local blood flow measurements in addition to *in vivo* glycocalyx determinations.

Our focus is on translational physiology, and the main questions are related to treatment of ischemia and shock, primarily on mechanisms at the level of the microcirculation. We have run an independent, fully funded laboratory for several years.

B. Positions and Honors

Positions and	Employment
2001-2002	Visiting Associate Professor, Department of Physiology, VCU Medical Center, Virginia
	Commonwealth University
2002-2003	Visiting Associate Professor, Department of Anesthesiology, VCU Medical Center,
	Virginia Commonwealth University
2003-2010	Associate Professor, Department of Physiology and Biophysics, Department of
	Emergency Medicine, VCU Medical Center, Virginia Commonwealth University
2010-2011	Associate Professor, Department of Internal Medicine,
	VCU Medical Center, Virginia Commonwealth University
2011-present	Research Physiologist, Damage Control Resuscitation Group, US Army Institute of
	Surgical Research, JBSA Fort Sam Houston, TX

Other Experience and Professional Memberships

1986-present	The Microcirculatory Society, Inc. (Development Committee <i>member</i> , 2011-2015)
1989-present	American Physiological Society
2000-2008	M.S. Thesis Committees: B. Dalcin (2000); L. Torres (2001); D. Williams (2004); M.
	Barker (2005); G Alexander (2006); P. Meliagros (2008)

2001-2010	Ph.D. Comprehensive Exam and Thesis Committees: L. Torres (2001, 2005); J. Moll (2007, 2008); W. Nugent (2007, 2010); B Song (2009, 2010); M. Connery (2009)
2007-2008	Scientific Advisory Board, Oxyvita, Inc.
2009-2010	Scientific Advisory Board, Oxygen Biotherapeutics, Inc
2009	Ad Hoc Reviewer for Am J Physiol, Shock, J Appl Physiol, Critical Care, J Trauma Acute
	Care Surg, Resuscitation, J Mil Medicine
2009	Invited Member of the Peer Review Board of the Combat Casualty Care Blood Research
	Program, United States Army Medical Research and Material Command
2009-2010	Faculty member of the review/selection committee for the VCU-HHMI summer scholars
2009-2010	Faculty member of the review/selection committee for the VCU Department of
	Physiology and Biophysics Summer Undergraduate Research Program
2011-present	SHOCK Society
2014-present	Advisor, The National Academies of Sciences, NRC Research Associateship Programs

Awards and Honors

1983	National Nuclear Energy Commission (CNEN - Brazil), Travel Award
1984	Outstanding Teacher Award, Physiology, School of Dentistry, UERJ, Brazil
1985-1991	National Research Council (CNPq - Brazil), Principal Investigator
1988	Outstanding Teacher Award, Physiology, Institute of Biology, UERJ, Brazil
1991-1992	National Research Council (CNPq - Brazil), Post-Doc Award
1992-1993	National Institutes of Health (USA), Fogarty International Center, Post-Doc Award
1993	Radiation Research Society, Travel Award for the 41st Annual Meeting
1993	The Microcirculatory Society, Inc. (USA), IPM Innovative Instrumentation Award
1993-1994	The Pew Charitable Trusts, Latin American Fellows Program, Post-Doc Award
1999	The Pew Charitable Trusts, Latin American Fellows Program, Travel Award
2002	The Pew Charitable Trusts, Latin American Fellows Program, Travel Award
2010-2012	National Institutes of Health (USA), Sickle Cell Disease BTRP Scholar Award

C. Contribution to Science

1. <u>In vivo evaluation of microvascular glycocalyx and its modulation.</u> Changes in endothelial glycocalyx has been attempted in different scenarios and using various techniques. Our unique and innovative approach allows the glycocalyx to be measured in vivo while critical local and systemic physiological variables to be simultaneously monitored and recorded. Using this approach, we have been studying *endothelial glycocalyx, venular blood flow, and coagulation function* after various resuscitation strategies in animals subjected to hemorrhagic shock. More recently, we showed (using various fluids) that glycocalyx degradation products correlate with changes in glycocalyx thickness changes measured in vivo and therefore may be useful as surrogate of microvascular glycocalyx changes during hemorrhage/resuscitation.

Torres, L.N., Sondeen, J.L., Ji, L., Dubick, M.A. and **Torres Filho** I.P. – *Evaluation of resuscitation fluids on endothelial glycocalyx, venular blood flow, and coagulation function after hemorrhagic shock in rats.* Journal of <u>Trauma and Acute Care Surgery 75(5):759-766, 2013</u>.

Torres Filho I.P., Torres, L.N., Sondeen, J.L., Polykratis, A. and Dubick, M.A. – *In vivo evaluation of venular glycocalyx during hemorrhagic shock in rats using intravital microscopy*. <u>Microvascular Research 85(1):128-133, 2013</u>.

Torres, L.N., Sondeen, J.L., Dubick, M.A. and **Torres Filho** I.P. – *Systemic and microvascular effects of resuscitation with blood products after severe hemorrhage in rats*. Journal of Trauma and Acute Care Surgery <u>77(5):716-723, 2014</u>.

Torres Filho I.P., Torres, L.N., Salgado, C., and Dubick, M.A. – *Plasma syndecan-1 and heparan sulfate correlate with microvascular glycocalyx degradation in hemorrhaged rats after different resuscitation fluids*. <u>Am.</u> J. Physiol. Heart Circ. Physiol. 310(11):H1468-H1478, 2016.

2. <u>Microvascular responses to hemorrhagic hypotension</u>. For decades, our work has been directed to using intravital microscopy to study the microvascular responses following hemorrhagic hypotension. Initially, under guidance of Prof. Paul Johnson, we published an extensive study of muscle microcirculatory responses during hypotension, disclosing differential behavior of differently sized arterioles as well as venules. Since then, we demonstrated a variety of mechanisms that participate of the pathophysiological response following hemorrhagic shock such as vasomotion as well as redistribution of blood flow and PO2. More recently we demonstrated for the first time *in vivo* that hemorrhage degrades the microvascular glycocalyx. As noted above, these demonstrations required technical innovations. Although the findings are relatively recent, they are highly significant because they also provide important tools for studying new resuscitation strategies for hemorrhagic shock.

Torres Filho, I.P., Boegehold, M., Bouskela-Torres, E., House, S. and Johnson, P.C. – *Microcirculatory responses in cat sartorius muscle to hemorrhagic hypotension*. <u>Am. J. Physiol.</u> <u>257:H1647-H1655, 1989</u>.

Torres Filho, I.P., Contaifer, D., Jr., Garcia, S. and Torres, L.N. – *Vasomotion in rat mesentery during hemorrhagic hypotension*. <u>Life Sciences 68(9):1057-1065, 2001</u>.

Torres Filho, I.P., Contaifer, D.,Jr., Garcia, S. and Torres, L.N. – *Effects of hypertonic saline solution on mesenteric microcirculation*. <u>Shock 15(5):353-359, 2001</u>.

Torres, L.N., **Torres Filho**, I.P., Barbee, R.W., Tiba, M.H., Ward, K.R. and Pittman, R.N. – *Systemic responses to prolonged hemorrhagic hypotension.* <u>Am. J. Physiol. Heart Circ. Physiol. 286(5):H1811-</u><u>H1820, 2004</u>.

Torres, L.N., Pittman, R.N. and **Torres Filho**, I.P. – *Microvascular blood flow and oxygenation during hemorrhagic hypotension*. <u>Microvascular Research 75(2):217-226, 2008</u>.

Torres Filho, I.P., Torres, L.N. and Pittman, R.N. – *Early physiological responses to hemorrhagic hypotension*. <u>Translational Research 155(2):78-88, 2010</u>.

Tiba, M.H., Draucker, G.T., Barbee, R.W., Terner, J.T., **Torres Filho** I.P., Romfh, P, Vakhshoori, D. and Ward, K.D. – *Tissue oxygenation monitoring using resonance Raman spectroscopy during hemorrhage*. Journal of Trauma and Acute Care Surgery 76(2): 402-408, 2014.

3. Development of innovative methods for non-invasive measurement of oxygenation: Tissue/microvascular PO2 and Raman microspectroscopy. I have developed and extensively used noninvasive techniques for measuring oxygen tension (PO₂) in microvessels and in interstitial spaces using quenching phosphorescence. I also employed Raman spectroscopy to measure oxygen saturation (SO₂) in microvessels and in the surface of various organs. Collectively, the significance of my work in this field is highlighted by the relatively high citation of the articles in oxygenation that to date sum over 810 citations.

Phosphorescence Quenching (PO₂)

Torres Filho, I.P. and Intaglietta, M. – *Microvessel* pO₂ *measurements by phosphorescence decay method.* Am. J. Physiol. Heart Circ. Physiol. 265(4):H1434-H1438, 1993.

Torres Filho, I.P., Leunig, M., Yuan, F., Intaglietta, M. and Jain, R. – *Non-invasive measurement of microvascular and interstitial pO*₂ *profiles in a human tumor in SCID mice*. <u>Proc. Natl. Acad. Sci. USA</u> <u>91(6):2081-2085</u>, 1994.

Kerger, H., **Torres Filho**, I.P., Rivas, M., Winslow, R.M. and Intaglietta, M. – *Systemic and subcutaneous microvascular oxygen tension in awake syrian golden hamsters.* <u>Am. J. Physiol. Heart Circ. Physiol.</u> <u>268(2):H802-H810, 1995</u>.

Torres Filho, I.P., Kerger, H. and Intaglietta, M. – pO_2 measurements in arteriolar networks. <u>Microvasc. Res.</u> <u>51(2):202-212, 1996</u>.

Torres Filho, I.P., Spiess, B.D., Barbee, R.W., Ward, K.R. and Pittman, R.N. – *Experimental analysis of critical oxygen delivery*. <u>Am. J. Physiol. Heart Circ. Physiol. 288(3):H1071-H1079, 2005</u>.

Torres Filho, I.P., Spiess, B.D., Barbee, R.W., Ward, K.R. and Pittman, R.N. – Systemic responses to hemodilution after transfusion with stored blood and with hemoglobin-based oxygen carrier. <u>Anesthesia & Analgesia 100(4):912-920, 2005</u>. (Editorial by KK Tremper on 100:910-11, 2005)

Ward, K.R., Ivatury, R.R., Barbee, R.W., Terner, J., Pittman, R.N., **Torres Filho**, I.P. and Spiess, B. – *Near infrared spectroscopy for evaluation of the trauma patient: A technology review.* <u>Resuscitation 68(1):27-44</u>, 2006.

Ward, K.D., Tiba, M.H., Ryan, K.L., **Torres Filho**, I.P., Rickards, C.A., Witten, T., Soller, B.R., Ludwig, D.A. and Convertino, V.A. – *Oxygen transport characterization of a human model of progressive hemorrhage*. <u>Resuscitation 81(8):987-993, 2010</u>.

Raman Spectroscopy (SO₂)

Torres Filho, I.P., Terner, J., Pittman, R.N., Somera, L.G. and Ward, K.R. – *Hemoglobin oxygen saturation measurements using resonance Raman intravital microscopy*. <u>Am. J. Physiol. Heart Circ. Physiol.</u> <u>289(1):H488-H495, 2005</u>.

Ward, K.R., **Torres Filho**, I.P., Barbee, R.W., Torres, L.N., Tiba, M.H., Reynolds, P.S., Pittman, R.N., Ivatury, R.R. and Terner, J. – *Resonance Raman spectroscopy: a new technology for tissue oxygenation monitoring.* <u>Crit. Care Med. 34(3):792-799, 2006</u>. (Editorial by GC Kramer et al. 34:924-5, 2006)

Ward, K.R., Barbee, R.W., Reynolds, P.S., **Torres Filho**, I.P., Tiba, M.H., Torres, L.N., Pittman, R.N. and Terner, J. – *Oxygenation monitoring of tissue vasculature by resonance Raman spectroscopy*. <u>Analytical Chemistry 79(4):1514-1518, 2007</u>.

Torres Filho, I.P., Terner, J., Pittman, R.N., Proffitt, E.K. and Ward, K.R. – *Measurement of hemoglobin oxygen saturation using Raman microspectroscopy 532 nm excitation*. J. Appl. Physiol. 104(6):1809-1817, 2008.

Tiba, M.H., Draucker, G.T., Barbee, R.W., Terner, J.T., **Torres Filho** I.P., Romfh, P, Vakhshoori, D. and Ward, K.D. – *Tissue oxygenation monitoring using resonance Raman spectroscopy during hemorrhage*. Journal of <u>Trauma and Acute Care Surgery 76(2): 402-408, 2014</u>.

Torres Filho I.P., Nguyen, N.M., Jivani, R., Terner, J., Romfh, P., Vakhshoori, D.P. and Ward, K.D. – Oxygen saturation monitoring using resonance Raman spectroscopy. Journal of Surgical Research 201(2):425-431, 2016.

D. Research Support

Ongoing Research Support

Torres Filho (PI)

Combat Casualty Care Research Program - U.S. Department of Defense

"Optimizing Pre-hospital Resuscitation Strategies for Tissue Stabilization after Trauma and Hemorrhagic Shock in Rats"

This project explores using combinations of compounds to improve tissue stabilization after hemorrhagic shock in rats.

Role: PI

Completed Research Support (Past Three Years)

Torres Filho (PI)

Combat Casualty Care Research Program - U.S. Department of Defense

"The role of Endothelial Glycocalyx in the Pathophysiology of Hemorrhagic Shock after

Resuscitation Therapy with Plasma Compared to Standard Resuscitation Fluids in Rats."

The purpose of this project was to investigate the potential role of different resuscitation fluids to modulate microvascular glycocalyx following hemorrhagic shock injury.

Role: PI

Torres Filho (PI)

2012-2014

2012-2014

Combat Casualty Care Research Program - U.S. Department of Defense

"Effect of Hemorrhagic Shock / Fluid Resuscitation on In Vivo Thrombus Formation and Platelet Adhesion."

The goal of this project was to determine the effect of hemorrhagic hypotension on thrombus formation and platelet adhesion using an in vivo model of changes in the microcirculation. Role: PI

Torres Filho (PI)

2012-2014

Combat Casualty Care Research Program - U.S. Department of Defense

"Effects of complement inhibitors, Syk inhibitor and Bradykinin Type 2 receptor antagonist on morbidity and mortality in mice after hemorrhagic shock and trauma."

This project focused on the role of *complement inhibitors* in the treatment of hemorrhagic shock using a mouse model.

Role: Co-Investigator

2015-2017