Name: Luca Clemente

Email: lclemente@wisc.edu

Major Professor: Ian Bird

Degree Objective: Ph.D. Endocrinology and Reproductive Physiology

Background: BS Genetics, Ohio State University. Biochemistry, Colorado State University

Current Research Project:

Preeclampsia (PE) is a medical condition characterized by hypertension and proteinuria associated with profound endothelial dysfunction. Studies from our lab have shown that growth factors and cytokines in PE subjects are capable of driving the inhibition of gap junction function by inducing Src- and ERK-mediated phosphorylations of connexin 43 (Cx43), resulting in loss of agonist-induced Ca^{2+} bursting necessary for nitric oxide production in uterine vasculature during pregnancy. While many such growth factors (VEGF, bFGF) and cytokines (TNFα, IL-1β, IL6) may be capable of acting on their own receptors to stimulate Src in particular, other cytokines (IL8, IFNγ, TNFα) and hormones (aldosterone, angiotensin II) may also/instead achieve Src activation through transactivation of the epidermal growth factor receptor (EGFR). Normally, inhibition of Ca2+ bursting by EGF in pregnant uterine artery endothelial cells (P-UAECs) is modest, possibly due to low levels of EGFR expression. It occurred to us that, because of its possible transactivation role, defects in EGFR that amplify function may be disproportionately damaging. Where EGFR has been studied in the context of cancer, it has been well-established that overexpression or activating mutation drives cancer progression via Src-dependent as well as Src-independent mechanisms. Since dysregulation of similar 'cancer' signaling pathways has also been observed in the preeclamptic placenta, it seemed likely that dysregulated EGFR signaling in vascular endothelial cells during pregnancy would drive Cx43 dysfunction and the hypertension associated with PE. As a proof of principle, we began characterizing the effects of altered EGFR function on gap junction function. Our original hypothesis—namely, that the overexpression of wild-type or constitutively active mutant EGFR in P-UAECs will induce loss of Ca^{2+} bursting necessary for adaptive vasodilation in pregnancy—has been challenged by recent data. We are continuing to develop new models to explain the confusing role of EGFR signaling pathways in the regulation of vasodilation.

Honors:

2006 Ronald McNair Scholar

2007 UW Summer Research Opportunities Program

Grants Received:

UW Madison SciMed Advanced Opportunity Fellowship

NIH (NICHD) T32 Trainee Endocrinology and Reproductive Physiology Program 2012-2014

Publications:

Wilson AC, Clemente L, Liu T, Bowen RL, Meethal SV, Atwood CS. (2008) Reproductive hormones regulate the selective permeability of the blood-brain barrier. Biochim Biophys Acta. Jun;1782(6): 401-7.

Presentations:

Oral presentation: Clemente L, Prentice M, Handa R. Estrogen receptor β activation inhibits the physiological response to stress via neurons in the paraventricular nucleus. *2006 Ronald E. McNair Scholars California Research Symposium*, UC Berkeley.

Oral presentation: Clemente L, Wilson AC, Atwood CS. Effect of age-related dysregulation of the HPG axis on ZO-1 expression in the blood-brain barrier. *2007 Summer Research Opportunities Program Conference,* University of Wisconsin-Madison.

Poster presentation: Clemente L, Atwood CS. Catecholamine regulation of leydig cell function and spermatogenesis. SciMed GRS Poster Show 2009.

Oral presentation: Clemente L, Ozer BH, Bertics PJ. A novel epidermal growth factor mutant in glioblastoma. Endocrinology and Reproductive Physiology Seminar 2009.

Poster presentation: Clemente L, Ozer BH, Weipz GJ, Bertics PJ. A novel EGF receptor mutation found in brain cancer increases autophosphorylation and alters localization. *2010 Endocrinology and Reproductive Physiology Symposium.*

Oral presentation: Clemente L, Bertics PJ, Bird IM. A comparison of Src and ERK signaling in six epidermal growth factor receptor variants. Endocrinology and Reproductive Physiology Seminar 2012.

Poster Presentation: Clemente L, Bertics PJ, Bird IM. A comparison of the ability of oncogenic EGFR mutants to induce ERK 1/2 phosphorylation in the presence or absence of a Src-selective kinase inhibitor. *2013 Endocrinology and Reproductive Physiology Symposium*.

Oral Presentation: Clemente L, Bertics PJ, Bird IM. Kinase activating and inhibiting mutations in the epidermal growth factor receptor alter the role of Src in the MAPK pathway. Endocrinology and Reproductive Physiology Seminar 2013.

Teaching and Mentorship:

Introduction to General Chemistry Laboratory, 2005. Supervised and instructed students in general chemistry classroom and laboratories. Pueblo Community College, Pueblo, CO.

Ronald McNair Scholar Program, 2008. Designed curriculum and co-lectured the McNair graduate school preparation course. Colorado State University, Fort Collins, CO.