A. Personal Statement

The Renin Angiotensin Angiotensinogen System (RAAS) has become a target to control the development and progression of hypertension. My laboratory is keen to reveal new targets that could aid in the development of therapeutics to control oxidative stress, kidney injury and high blood pressure in this devastating disease using unique approaches. My laboratory found a new function for the transcriptional regulator Sox6 in renin expression during juxtaglomerular cell recruitment and renal artery stenosis induced renovascular hypertension, oxidative stress and kidney damage. We are developing an innovative approach that includes: 1) the generation of a transgenic mouse, the C57BL6 Ren1d^{Cre/Sox6^{fl/fl}}, which lacks the expression of Sox6 in renin expressing cells; 2) human induced pluripotent stem cells derived kidney organoids to establish the mechanism of renin expression control by Sox6; 3) mice cage systems that capture synchronized metabolic information, coupled to 4) biochemical and cellular assays. It is known that RASTen frequency increases in elderly patients, and affects patients with diabetes, aortoiliac occlusive disease, coronary artery disease (CAD), or hypertension. This proposal will advance our understanding of the biological factors involved in the kidney response during renovascular hypertension and the role of the Sox6-Renin-prorenin-prorenin receptor axis during renal artery stenosis. Discerning the link between Sox6 and renin may uncover a new therapeutic target for the treatment of hypertension and kidney injury induced by renal artery stenosis as well as kidney damage induced by oxidative stress, a prevalent insult on other kidney and cardiovascular diseases. The publications more relevant to this application are:


B. Positions and Honors

Positions and Employment

2009 - 2015 Postdoctoral Fellow, Duke University, Durham, NC
2015 - 2016 Research Instructor, Vanderbilt University Medical Center, Nashville, TN
2016 - Assistant Professor, Vanderbilt University Medical Center, Nashville, TN

Other Experience and Professional Memberships
2010 - Member, American Heart Association
2016 - Member, American Society of Nephrology
2016 - Member, American Society of Physiology

Honors
1995 First Prize in the Fourth National Award in Developing of Enterprises. Awarded to the project Industrial production of annatto colorant., Medellin Chamber of Commerce
1996 Fellowship to 7th Annual International Course of Biotechnological Process UNAM. Awarded by United Nations (One slot per country in Latin America), United Nations
1998 Training – Fellowship on Biofiltration Technologies. Universidad Autonoma de Mexico (UNAM), Colciencias - Colombia
2002 First place in Research Symposium. Chemistry Department., University of Wisconsin - Milwaukee
2002 Victor Vega Scholarship for outstanding academic achievement., University of Wisconsin - Milwaukee
2006 Chair Award Gordon Research Conference: “Drug carriers in medicine and biology”, Gordon conference
2007 American Society of Hematology (ASH), Travel Award, American Society of Hematology
2016 The Council on Hypertension Trainee Advocacy Committee and The International Society of Hypertension New Investigator Committee. Onsite Trainee Poster Award, AHA Hypertension Scientific Sessions 2016, American Heart Association

Service Commitments
2006-2007 School of Medicine Student Senator to GSS Case Western Reserve University
2006-2008 Representative to Case Western Reserve University Faculty Senate Committee on Research
2008 Student Representative to School of Medicine Case Western Reserve University Strategic Planning Task Force
2017 VUMC R01 Grant Review Studio: participated as an expert to evaluate a R01 resubmission
2017 American Society of Nephrology (ASN) kidney week 2017 Abstract reviewer
2017 American Heart Association Fellowship reviewer
2019 Selected as Programs to Increase Diversity Among Individuals Engaged in Health Related Research - Cardiovascular Health-Related Research (PRIDE-CVD) Scholar

C. Contribution to Science
1. Established a new role for the transcription factor Sox6 in renin expression control: We identified a population of renal mesenchymal stromal cells (MSC) in the adult kidney. We found that these renal MSCs can be differentiated to JG like cells by cAMP in vitro. These cells may serve as a new model to test renin expression regulation in vitro. Renal MSC were transplanted into the adult kidney and differentiated to JG cells during JG cells expansion induced by low sodium diet and captopril treatment. We also found that these cells expand and differentiate to JG cells aiding to the kidney response to blood pressure changes and reestablishment of homeostasis. My laboratory elucidated a new role for the transcriptional regulator Sox6 in renin expression control during pathophysiological conditions, including hypertension and kidney damage induced by renal artery stenosis.
2. **Developed a new cellular tracking mechanism for in vivo tracking of MSC:** We determined that the nano-start technology can be used to track MSCs in vivo. This new technology could be used to track transplanted cells in clinical settings to determine the therapeutic effects after transplantation. **Uncovered that Cox2-PGE2-EP4 pathway plays a key role in the activation of renal MSC during JG cells expansion:** We found that the Cox2-PGE2-EP4 pathway plays an important role in the activation of renal CD44+ mesenchymal stromal cell-like cells during conditions of juxtaglomerular cell expansion. Renal MSC differentiate to JG cells after expansion and recruitment to the glomerulus.


3. **Determined that c-Kit positive cardiac progenitor cells play an essential role in cardiac regeneration in response to the b-catenin-Wnt modulator Sfrp2:** The ability of resident c-Kit(+) cells to regenerate damaged heart tissue is highly controversial. However, it remains an open question as to whether these cells play a role in cardiac regeneration in response to specific stimuli. We found that Sfrp2 substantially stimulated differentiation of c-Kit(+) cells into cardiomyocytes and were associated with restored cardiac function. More over, we showed that selective ablation of c-Kit(+) cells resulted in complete inhibition of c-Kit(+) cell differentiation into cardiomyocytes in response to Sfrp2. Sfrp2 induced increased muscle mass and improved cardiac function were completely blocked. We were the first to provide definitive evidence that c-Kit(+) cells, in response to specific stimuli, are essential in the generation of cardiomyocytes and improved cardiac function following MI.


e. **Identified key apoptosis regulators in cancer cells:** during my graduate studies my thesis involved revealing novel mechanisms by which cancer cells evade apoptosis. While normal and cancer cells are vastly different cell types, they both restrict apoptosis to survive long-term. I found the pro-apoptotic protein Bax interacts with Interferon Gamma Receptor 2 (IFGR2) and is kept in his inactive form. At the same time I studies the interaction of the DNA repair protein Ku70 that inhibits Bax activation. These two mechanisms of apoptosis control play a role in cancer cells avoiding of cell death. Using the Bax binding domain of Ku70 and IFGR2 we develop a new series of small peptides able to bind and inhibit Bax induction of apoptosis, hence their name BIP. These peptides are able to inhibit apoptosis and a series of them have the capacity to transduce proteins into the cytosol of mammalian cells. BIP are a good tool to deliver cargo into cells without toxicity.
The C-terminus of interferon gamma receptor beta chain (IFNgammaR2) has antiapoptotic activity as a Bax inhibitor. Cancer Biol Ther. 2009 Sep;8(18):1771-86. PubMed PMID: 19657228; PubMed Central PMCID: PMC2927208.


Complete List of Published Work in My Bibliography (total of 24 publications):

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Active

Programs to Increase Diversity Among Individuals Engaged in Health Related Research - Cardiovascular Health-Related Research (PRIDE-CVD) Small Research Project
Gomez, Jose (PI)
11-01-2019 – 10-31-2020
Discerning the function of Sox6 in aortic aneurysm development
Role: PI

1K01HL135461-01
National Heart, Lung, and Blood Institute
01/01/2017 - 12/31/2021
Sox6 Role in Renin Expression During Juxtaglomerular Cells Expansion
Role: PI

Pending

1 R01 HL149868-01
National Heart, Lung, and Blood Institute
07/01/2020 – 06/30/2025
SOX6: A new modulator of renin expression and hypertension induced by atherosclerosis of the renal artery
Role: PI

Completed (last 5 years)

AHA - Scientist Development Grant (Gomez JA, PI) 07/01/16 – 12/31/17
16SDG29880007
New role of Sox6 in renin expression during Juxtaglomerular cell expansion.
The grant was declined once the NHLBI K01 award started.

Vanderbilt University Medical Center Faculty Research Scholars Program (Gomez JA, PI) 07/01/16 – 06/30/17