

BIOENGINEERING

PRESENTS

RELAXIN: CARDIOVASCULAR ACTIONS AND THERAPEUTIC POTENTIAL



THURSDAY, January 23, 2020

12:00 – 1:00 PM

2101 ENGINEERING V

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ABSTRACT:

Relaxin, a 6-kDa peptide hormone in the insulin-relaxin superfamily, has important vascular actions that include potent vasodilation and anti-fibrotic effects. The US Food and Drug Administration (FDA) gave relaxin “breakthrough status” in 2013 and Cleveland Clinic named relaxin as one of the Top 10 Medical Innovations for 2014. Much of our knowledge of relaxin has stemmed from investigations of maternal vascular adaptations to pregnancy. With the discovery of local tissue expression and function of relaxin and relaxin receptor in non-pregnant females and males, relaxin has become even more important in the context of the cardiovascular system. This presentation will focus on discussing our relaxin-related work over the past decade, covering basic physiology to potential therapeutic applications: **(1)** Although our original focus was on relaxin’s vascular actions in the context of pregnancy (*Endocrinology* 145:3289-3296, 2004; *Endocrinology* 147:5126-5131, 2006), we made a surprising discovery that relaxin’s vascular actions are not confined to females; males respond equally robustly (*J. Appl. Physiol.* 98:1013-1020, 2005). Furthermore, relaxin-induced vascular geometric remodeling, and not compositional remodeling, contributes to increased vascular passive compliance under physiological conditions (*J. Appl. Physiol.* 111: 260-271, 2011; *Curr. Hypertens. Rep.* 13:409-420, 2011). **(2)** We provided the first evidence for local relaxin ligand-receptor expression and function in arteries (*FASEB J.* 20:2352-2362, 2006). **(3)** We have been examining relaxin’s cardiac actions and therapeutic potential in the context of two pathologies: relaxin-induced left atrial remodeling and suppression of atrial fibrillation (*Circ. Res.* 113:313-321, 2013) and relaxin-induced left ventricular remodeling and associated functional benefits in the setting of diastolic dysfunction (unpublished data). The cardiovascular actions of relaxin, especially potent systemic and renal vasodilation and potential for improving renal function, were the bases for recent clinical trials (Pre-RELAX-AHF and RELAX-AHF) examining relaxin’s therapeutic efficacy in the setting of acute heart failure.

BIOGRAPHY:

Dr. Sanjeev Shroff is the Distinguished Professor of and Gerald E. McGinnis Chair in the Department of Bioengineering, Swanson School of Engineering and Professor of Medicine in the School of Medicine at the University of Pittsburgh. He is also Chair of the Department of Bioengineering (since September 2013). Prior to joining the University of Pittsburgh in April 2000, Dr. Shroff was a faculty member at the University of Chicago for 17 years in the Department of Medicine (Cardiology Section). Trained as an electrical engineer (B.Tech., Indian Institute of Technology, Kanpur, India and M.Eng., McMaster University, Canada), Dr. Shroff obtained his doctoral degree in Bioengineering from the University of Pennsylvania.

Dr. Shroff’s research is in the cardiovascular arena, with two main focus areas: (1) Contractile and regulatory proteins and post-translational regulation of cardiac contraction. (2) Role of vascular stiffness in cardiovascular function and potential therapeutic applications of vascular stiffness-modifying drugs and/or hormones (e.g., relaxin). His research efforts have been supported by numerous grants from NIH (continuous funding since 1986), AHA, NSF, and industry partners. He was the recipient of the

Established Investigator Award from the AHA (1986-1991) and was elected as a Fellow of the American Physiological Society (1988), Fellow of the American Institute for Medical and Biological Engineering (1999), and Fellow of Biomedical Engineering Society (2007). Recognized by his colleagues and peers as a consummate teacher and mentor, Dr. Shroff received the Carnegie Science Center Award for Excellence (University Educator) in 2007, the Swanson School of Engineering's Outstanding Educator Award in 2010, and University of Pittsburgh Chancellor's Distinguished Teaching Award in 2011. He has mentored 32 students (15 post-doctoral and 17 pre-doctoral), most of whom are pursuing independent research careers in academia or industry. Dr. Shroff has been serving as the Principal Investigator on a NIH-NHLBI pre-doctoral T32 training grant (Cardiovascular Bioengineering Training Program) since 2005 and on the Coulter Translational Research Partnership II grant since 2013. In 2012 Dr. Shroff was named the Distinguished Professor at the University of Pittsburgh, a designation that constitutes the highest honor that the University can accord a member of the professoriate.