BIOGRAPHICAL SKETCH

NAME Ravi Jasuja	POSITION TITLE Director, Translational Research and Discovery, Research Program in Men's Health
eRA COMMONS USER NAME (credential, e.g., agency login) ravijasuja	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MMYY	FIELD OF STUDY
Indian Institute of Technology, Delhi, India	B. Tech.	1988-1992	Engineering
University of Hawaii, Manoa, Honolulu, HI	PhD	1992-1997	Biophysics/Phys. Chem.
Albert Einstein College of Medicine	Fellow	1997-1999	Biophysics/Physiology

A. Personal Statement

My research has focused on understanding the mechanisms of testosterone action at molecular, cellular and physiological levels. Drawing from my training in Engineering, Biophysics, Computational Modeling, and spectroscopy, I have developed a translational research program to study testosterone signaling. Such integrated research approaches are particularly important to characterize pleiotropic molecules like testosterone, which effects development and maturation of several key target tissues including muscle, metabolic and reproductive systems. Accordingly, over the years through extensive collaborations, I have contributed to diverse research problems by incorporating the molecular biophysics, cellular signaling, ex-vivo tissue studies and in-vivo, non-invasive imaging modalities. I established the first preclinical metabolic phenotyping core at the Boston University and now lead it at Brigham and Women's hospital.

The preclinical discovery core (PDC) of the Boston Pepper OAIC was originally implemented as small animal resource core (SARC) under my direction. During the first cycle of funding we realized that investigators were not just looking for a resource to characterize animal models, but needed integrated support in identification of appropriate testing/imaging modalities, development/characterization of genetic models and validation of preclinical research efforts. Accordingly the SARC has evolved into a discovery core from the basic service core as originally conceived. In addition to providing support to investigators, the core has continued to innovate and we are developing new tools by integrating Magnetic Resonance Imaging and Spectroscopy measures for non-invasive characterization of force, energetics, blood flow and oxygen tension in preclinical models. As the developmental project of PDC, we will integrate Diffusion Tensor Imaging with simultaneous measurement of peripheral regional perfusion and skeletal muscle oxygen saturation in response to function promoting anabolic interventions. This new capability being developed in collaboration with the Neuro-Radiology Research unit will enable non-invasive imaging of muscle regeneration and sarcopenic alterations in skeletal muscle with aging and in response to anabolic interventions.

With my complementary expertise in biophysical spectroscopy, non-invasive imaging, metabolic phenotyping and preclinical research, I am uniquely positioned to continue to lead and contribute to the Boston OAIC's mission of research and discovery of function promoting therapies.

B. Positions and Honors.

Professional Experience

03/00 - 05/02	Director, Worldwide Business Development, ArsDigita, Cambridge, MA
05/02- 01/04	DevLogics; e.Solve, Sharon, MA
01/04 – 08/07	Assistant Professor, Charles Drew University and Hospital, Los Angeles, CA.
05/2007-12/2012	Assistant Professor of Medicine, Boston University, Boston, MA
01/2013- present	Director, Translational Research and Discovery, Mens Health: Muscle and Metabolism, Brigham and Women's Hospital, Harvard Medical School

Honors and Awards

10/09: Evans Junior Faculty Merit Award for translational research

12/03: Glaxo Smithkline Scholar

06/03: NSF Fellowship for "Molecular Modeling of Biomolecules", Univ. of Georgia, Atlanta GA.

05/03: NIH fellowhip award for "Mathematics of Biological Complexity", Georgia Institute of Tech., Atlanta.

09/99: Young scientist fellowship by the International Union of Pure and Applied Biophysics, XIII International Biophysics Congress.

05/97-03/99: Belfer followship for Postdoctoral research.

08/88: Awarded Council for Scientific and Industrial Research (C.S.I.R.) of India fellowship for four years of undergraduate study.

11/86: National Talent Search Award by the National Council for the Educational Research and Training for six years of college education in India.

C. Contribution to Science

C1. Collaborative development and characterization of pre-clinical, translational discovery models of functional and metabolic perturbations.

Preclinical research models provide an outstanding opportunity to conduct mechanistic investigations of mediators and markers of disease states. As the director of preclinical discovery component of OAIC and in my own research, I have extensively collaborated with and contributed to the research of investigators addressing diverse research problems. These contributions include studying epigenetic reprogramming of muscle and reproductive function, aging associated alterations in physical function, role of inflammation in metabolic disorders, exercise-induced vascular remodeling and mechanisms of muscle function impairment in acute sepsis. By integrating cellular signaling, genomic profiling and systems biology approaches in preclinical rodent models, we have examined the pathways and determinants signaling in multiple models of aging, chronic and/or acute stress.

1: Jang H, Bhasin S, Guarneri T, Serra C, Schneider M, Lee MJ, Guo W, Fried SK, Pencina K, Jasuja R. The Effects of a Single Developmentally Entrained Pulse of Testosterone in Female Neonatal Mice on Reproductive and Metabolic Functions in Adult Life. *Endocrinology.* 2015 Oct;156(10):3737-46. doi: 10.1210/EN.2015-1117. Epub 2015 Jul 1. PubMed PMID: 26132920.

2: DeFuria J, Belkina AC, Jagannathan-Bogdan M, Snyder-Cappione J, Carr JD, Nersesova YR, Markham D, Strissel KJ, Watkins AA, Zhu M, Allen J, Bouchard J, Toraldo G, Jasuja R, Obin MS, McDonnell ME, Apovian C, Denis GV, Nikolajczyk BS. B cells promote inflammation in obesity and type 2 diabetes through regulation of T-cell function and an inflammatory cytokine profile. *Proc Natl Acad Sci* U S A. 2013 Mar 26;110(13):5133-8. doi: 10.1073/pnas.1215840110. Epub 2013 Mar 11. PubMed PMID: 23479618; PubMed Central PMCID: PMC3612635.

3: Alamdari N, Toraldo G, Aversa Z, Smith I, Castillero E, Renaud G, Qaisar R, Larsson L, Jasuja R, Hasselgren PO. Loss of muscle strength during sepsis is in part regulated by glucocorticoids and is associated with reduced muscle fiber stiffness. *Am J Physiol Regul Integr Comp Physiol*. 2012 Nov 15;303(10):R1090-9. doi: 10.1152/ajpregu.00636.2011. Epub 2012 Sep 26. PubMed PMID: 23019215; PubMed Central PMCID: PMC3517670.

4: Cacicedo JM, Gauthier MS, Lebrasseur NK, Jasuja R, Ruderman NB, Ido Y. Acute exercise activates AMPK and eNOS in the mouse aorta. *Am J Physiol Heart Circ Physiol*. 2011 Oct;301(4):H1255-65. doi: 10.1152/ajpheart.01279.2010. Epub 2011 Jul 1. PubMed PMID: 21724864; PubMed Central PMCID: PMC3197351.

C2. Applications of integrated spectropscopic and computational methods to characterize testosterone binding to signaling and binding proteins in circulation.

I utilized a series of biophysical spectroscopy tools and developed new computational modeling tools to examine ligand induced conformational perturbations in androgen receptor. These tools were further modified to characterize multiple equilibria that dynamically partition free testosterone in serum. With the joint PI Bhasin, we validated these finding in clinical samples to demonstrate that SHBG binding to testosterone exhibits a complex multi-step allostery. The novel computational tools developed in LabView, have been made available to the scientific community.

1. Zakharov MN, Bhasin S, Szafran AT, Mancini MA, Jasuja R. Numerical framework to model temporally resolved multi-stage dynamic systems. *Comput Methods Programs Biomed* 2012;108:750-9. PMID: 2272763
2. Zakharov M, Bhasin S, Travison TG, Wu F, Jasuja R. A multi-step model of testosterone's binding to sex-homrone binding globilin with allostery. *Mol Cell Endocrinol* 2015;399:190-200. PMID: 25240469
3. Zakharov MN, Pillai BK, Bhasin S, Ulloor J, Istomin AY, Guo C, Godzik A, Kumar R, Jasuja R. Dynamics of coregulator-induced conformational perturbations in androgen receptor ligand binding domain. *Mol Cell Endocrinol* 2011;341:1-8. PMID: 21605623
4. Xue R, Zakharov M, Xia B, Bhasin S, Costello J, Jasuja R. EPSLiM: Ensemble Predictor for Short Linear Motifs in Nuclear Hormone Receptors. *Mol Endocrinol* 2014;28:768-77. PMID: 24678734
5. Jasuja S, Ulloor J, Yengo CM, Choong K, Istomin AY, Livesay DR, Jacobs DJ, Swerdloff RS, Mikšovská J, Larsen RW, Bhasin S. Kinetic and thermodynamic characterization of DHT-induced conformational perturbations in androgen receptor ligand binding domain. *Molecular Endocrinol* 2009;23:1231-41. PMID: 19443608

C3. Applications of integrated Biophysical and Computational Methods to the Understanding of multiple signaling processes.

I have contributed to several areas of computational and experimental biophysics by developing new experimental techniques, computational framework for modeling of signal amplification. These methods have been used to quantitate photo-induced electron transfer through DNA, signal amplification in response to chemotactic stimuli and ligand-induced conformational gating. I have also contributed open source software for the scientific community to identify and map the disordered signaling surfaces in proteins.

1. Jasuja R, Lin Y, Trentham DR, Khan S. Response tuning in bacterial chemotaxis. Proc. Natl. Acad. Sci. U.S.A. 1999;96(20):11346–51.

2. Jasuja R, Jameson DM, Nishijo C and Larsen RW. Singlet Excited State Dynamics of molecular Complexes of tetrakis(N-methylpyridyl)prophyrin with DNA nucleotides J. Phys. Chem.1997, 101, 8, 144-50.

3. **Jasuja R**, Hazlett TL, Helms MK, Lee SH, Jameson DM, and Larsen RW. Temperature dependence of photoinduced electron transfer within self-associated porphyrin: guanine monophosphate complexes. *Chem. Phys. Lett*. 2002; 350, 515-521. PMID: 1302992

4. Xue R, Zakharov MN, Xia Y, Bhasin S, Costello JC, **Jasuja R**. Research resource: EPSLiM: ensemble predictor for short linear motifs in nuclear hormone receptors. Mol Endocrinol. 2014 May;28(5):768-77.

5. Zakharov MN, Ulloor J, Bhasin S, Ross JA, Narula NS, Bakhit M, Pillai BK, Kumar R, Jameson DM, **Jasuja R**. Guanidinium chloride-induced spectral perturbations of 4,4'-dianilino-1,1'-binaphthyl-5,5'-disulfonic acid confound interpretation of data on molten globule states. *Anal Biochem*. 2011; 416(1):126-8. PMID 21605623

D. Research Support.

Active:

1. **1R43AG045011-A1 (Role: PI)**
   Novel algorithm for free testosterone determination based on a multi-step allosteric model
   Source: NIA 09/1/2014-08/31/2016
   To characterize the technical performance of the novel algorithm and matrix effects.

2. Mechanisms of anabolic action of testosterone (Role: Co-Investigator, PI:Bhasin)
   11/30/09-3/1/16 (NIDDK)
   The goal of this project is to examine the mechanisms of tissue-specific action of androgens.

3. Novel Peptide-based Therapeutics for Triple Negative Breast Cancer (Role: site PI)
   07/01/2015 – 06/30/2016
   To conduct biophyscial characterization of conformational perturbation in peptide therapeutics.

Completed

1. Metabolic and Inflammatory Stress and the Endothelial Cell (Role: Co-Investigator, PI:Ruderman)
   4/15/09-1/13/14 (NHLBI)
   The goal of this project is to investigate the function of the SirT1/LKB1/AMPK signaling mechanism in the vasculature. They should provide insights as to whether its dysregulation could be the cause of the endothelial cell dysfunction associate wit the metabolic syndrome.

2. Develop quantitative methodologies for assessment of androgenic modulation of muscle and adipose tissue. (Role: PI)
   10/1/09- 12/1/11 (Evans Foundation Research Grant)
   The goal of the project was develop novel translational modalities for quantifying androgenic signal amplification in muscle and adipose tissue.

3. To examine the role of microRNA in neonatal reprogramming by testosterone. (Role: PI)
   8/31/10-09/1/12 (Genome Science Institute)
   The goal of the project was to utilize systems biology approaches to examine the role of miRNA in mediating neonatal androgen responses

4. Mechanism-Based Drug Discovery and characterization of androgen-regulated protein (Project PI)
   8/1/08-7/31/11 (Boston OAIC, Pepper Center, NIA)
   The goal of the project was to examine the mechanisms of pro-myogenic, prostate sparing effect of androgen regulated proteins.