

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Shalender Bhasin		POSITION TITLE Professor of Medicine	
eRA COMMONS USER NAME SHBHASIN			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
D.A. V. College, Chandigarh (India)	Pre-Med	1970	Pre-Med
All India Institute of Medical Sciences, New Delhi, India	M.B., B.S.	1976	Medicine
Northwestern Univ. Med. School, Chicago	Resident	1978-81	Internal Medicine

A. Personal Statement

As a translational scientist, I lead a large interdisciplinary research program in mechanism elucidation, target validation, preclinical proof-of-concept studies, and randomized trials of function promoting therapies. My expertise in these content areas is reflected in over 250 high quality peer-reviewed manuscripts, 130 book chapters and reviews, two books, and over 650 abstracts. I have conducted numerous NIH-funded complex randomized trials of the effects of exercise, nutritional, and pharmacological interventions in older adults with mobility limitation, sarcopenia, falls, chronic obstructive lung disease, and end stage renal disease.

I have served as an Associate Editor of the Journal of Clinical Endocrinology and Metabolism and the Journal of Andrology, Chair of the Clinical Guidelines Subcommittee of the Endocrine Society, and as the Chair of the American Board of Internal Medicine (Endocrinology and Metabolism). I chaired the Endocrine Society’s expert panel that developed clinical guidelines for testosterone therapy of androgen deficiency syndromes in men. For the past two years, I have led the US Sarcopenia Biomarker Consortium, which aims to develop a consensus evidence-based definition of sarcopenia. My leadership of the Pepper-wide national initiatives, including the STRIDE Trial, the Sarcopenia Biomarker Consortium, and the Multi-Mod Hip Fracture Trials Consortium reflect my deep roots and commitment to the OAIC community.

I have substantial mentoring experience from my previous roles as a T32 PI, OAIC Director, and former Section Chief. I have guided the careers of 8 K awardees, 5 pre-doctoral fellows and 25 postdoctoral fellows, many of whom have gained considerable acclaim on their own.

My expertise in the entire spectrum of translational research in function promoting therapies, my leadership experience as a Section Chief, an OAIC Director, and as chair of national and international committees, and my extensive collaborations with investigators from all around Boston and from other OAICs, make me uniquely qualified to serve as the joint PI of this application.

Positions and Employment

1984 - 1988	Assistant Professor, In-residence, UCLA School of Medicine
1988 - 1994	Associate Professor, In-residence, UCLA School of Medicine
1994 - 2005	Professor of Medicine, In-residence, UCLA School of Medicine
1996 - 2005	Chief, Division of Endocrinology, Metabolism and Molecular Medicine, Drew University
1999 - 2005	Associate Chair for Academic Affairs, Department of Medicine
2003- 2005	Director, Drew-UCLA Reproductive Science Research Center

2005 - 2014 Professor of Medicine, Boston University School of Medicine, and
Chief, Section of Endocrinology, Diabetes, and Nutrition, Boston Medical Center
2008- Director, Boston Claude D. Pepper Older Americans Independence Center
02/2013- Director, Research Program in Men's Health: Aging and Metabolism, Brigham and
Women's Hospital
06/2014- Professor of Medicine, Harvard Medical School
10/2014- Director, The Center for Clinical Investigation, Brigham and Women's Hospital

Other Experience and Professional Memberships

Associate Editor, Journal of Andrology, 1997-2002; Associate Editor, J Clin Endocrinol Metab 1/2005-12/2009; Member, American Board of Internal Medicine (Endocrinology and Metabolism Exam Writing Committee) 7/1/2005-6/1/2011; Chair, Endocrine Society's Expert Panel for Development of Guidelines for Androgen Deficiency Syndromes in Men 6/2005-; Chair, Endocrine Society's Clinical Guidelines Subcommittee 7/1/2008-6/30/2011; Member, the Council of the Endocrine Society 7/1/2011- 7/1/2014 ; Chair, American Board of Internal Medicine, Endocrinology and Metabolism Subspecialty Board 7/1/2011-7/1/2015.

7/2011- ; Chair, NIDDK Ad Hoc Study Section 1999; Protocol Chair, ACTG 5079, 1999-2005. Member, HIV ACE Study Section, 2002-2006; Chair, Ad Hoc Special Emphasis Panel AARV-6, NIDDK RFA on HIV-Associated Lipodystrophy; Temporary Member ASG Study Section, 2005-; President, Western Society for Clinical Investigation 2003; Member, CSR College of Scientific Reviewers 2010-2012; Reviewer, Special Emphasis Panel for Juvenile Protective Factors, 12/2012, 6/2013, 9/2013; 10/2014; K23 review panel 12/23/2014; NIA Special Emphasis Panel for Vitamin D RFA 03/2014; Special Emphasis Panel for HIV and Aging 5/2014, 7/2015, 11/2015

Honors

1976 Graduate of the Year Gold Medal at AIIMS; 1980 Walter Rombach Intern of the Year Award (Northwestern University); 1984 Weitzman Award for the Best Fellow (Harbor-UCLA Medical Center); 1984 Clinical Associate Physician Award 1985-88, 1990 Richard Weitzman Young Investigator Award; 1990 Harbor-UCLA Distinguished Teaching Faculty Award; 1999 Drew Teaching Award; UT Southwestern Medical School GCRC Award for Excellence in Patient-Oriented Research, 2000; Harbor-UCLA GCRC Second Prize for Excellence in Clinical Research 2002; JCEM Pharmacia Finalist Award for Best Clinical Research Paper 2003; Mentor for Annals of Internal Medicine's Early Career Author Award 10/2012; The Endocrine Society's Research Mentor Award (Mentee: Grace Huang); Best Doctors of America 2005, 2011, 2012, 2013, 2014, 2015; The Clinical Investigator Award, the Endocrine Society, 2015.

C. Contributions to Science (reflected in 250 peer-reviewed manuscripts, 130 chapters and reviews, >650 abstracts, and 2 books)

1. Expertise in investigating biologic effects of testosterone in men and women: My laboratory has conducted some of the most important clinical trials of androgens in young and older adults. In a landmark study published in the N Engl J Med, my laboratory provided the first unequivocal evidence that testosterone increases skeletal muscle mass and maximal voluntary strength, even when protein intake and exercise stimulus are standardized, and that resistance exercise training augments the anabolic effects of testosterone. This paper, which has become one of the most cited papers in the androgen field, resolved one of the longest controversy in clinical medicine, whether androgens have anabolic effects on the muscle. Several subsequent papers demonstrated unequivocally that testosterone supplementation increases lean mass and muscle strength in men with chronic illness such as that associated with HIV infection, chronic obstructive lung disease or old age. These findings have spawned a new biotechnology industry around the development of selective androgen receptor modulators as potential anabolic therapies.

My research has clarified the dose response relationships between testosterone and androgen-dependent outcomes. I pioneered the use of the Leydig cell clamp model to suppress endogenous testosterone production (using a GnRH agonist) in healthy young and older men and demonstrated that testosterone dose-response

curves for several androgen-dependent processes are different. These studies uncovered important age-related differences in testosterone's metabolism and action, including age-related differences in testosterone metabolic clearance rates and adverse event profile.

1. Bhasin S, Storer TW, Berman C, Callegari R, Tricker R, Casaburi R. The effects of supraphysiological doses of testosterone on muscle size and strength in normal men. N Engl J Med 335:1-7,1996. PMID: 8637535
2. Bhasin S, Storer TW, Berman N, Hays R, Beall G. Effects of testosterone replacement and resistance exercise in HIV-infected men with weight loss and low testosterone levels. JAMA 283:756-762,2000. PMID: 1068305
3. Basaria S, Coviello A, Travison TG, Storer TW, Farwell WR, Jette A, Eder R, Tennstedt S, Ulloor J, Zhang A, Choong K, Lakshman K, Mazer NA, Miciek R, Krasnoff J, Elmi A, Knapp P, Brooks B, Bhasin G, Appleman E, Aggarwal S, Collins L, LeBrasseur N, Fiore L, Bhasin S. Adverse effects associated with testosterone administration in older men. N Engl J Med 2010;363:109-22. PMID 2059229
4. Bhasin S, Woodhouse L, Casaburi R, Singh AB, Mac R, Dzekov J, Dzekov C, Lee M, Yarasheski K, Sinha-Hikim I, Bhasin S. Older men are as responsive to the anabolic effects of testosterone as young men. J Clin Endocrinol Metab 2005;90:678-88. PMID: 15562020
5. Licinio J, Caglayan S, Ozata M, Yildiz B, de Miranda P, O'Kirwan F, Cohen P, Bhasin S, Krauss R, Veldhuis J, Wagner AJ, DePaoli, Wong M-L. Leptin replacement resolves morbid obesity, diabetes mellitus, and hypogonadism in leptin-deficient mice. Proc Natl Acad Sci USA 2004; 101:4531-6.
6. Basaria S, Harman SM, Travison TG, Hodis H, Tsitouras P, Budoff M, Pencina KM, Vita J, Dzekov C, Mazer NA, Coviello AD, Knapp PE, Hally K, Pinjic E, Yan M, Storer TW, **Bhasin S**. Effects of testosterone administration for 3 years on subclinical atherosclerosis progression in older men with low or low-normal testosterone levels. JAMA 2015;314(6):570-81. PMID: 26262795
7. Spitzer M, Basaria S, Travison TG, Davda M, Mazer N, Knapp P, Collins L, Eder R, Davou P, Mohammed N, Bhasin S. Effect of testosterone on response to phosphodiesterase 5 inhibitor. Ann Intern Med 2012;157:681-91.
8. Snyder PJ, Bhasin S, Cunningham GC, et al. Effects of testosterone on sexual function, physical function and vitality in older men with unequivocally low testosterone levels: a coordinated set of randomized trials. N Engl J Med 2015 in press. PMID not yet assigned.

Contributions to mechanism elucidation and target validation, and to discovery science as it relates to function promoting therapies. My laboratory has provided important insights into the mechanisms by which testosterone and myostatin regulate skeletal muscle mass. We made the important discovery that androgens promote the commitment and differentiation of multipotent stem cells into the myogenic lineage and inhibit their differentiation into the adipogenic lineage. This important discovery provided a unifying explanation for the reciprocal changes in muscle and fat mass observed during androgen supplementation and for the observed increase in muscle satellite cells. Subsequent studies demonstrated that androgens regulate mesenchymal multipotent cell differentiation by binding to AR, and promoting the association of AR with β -catenin and translocation of the AR- β -catenin complex into the nucleus, resulting in activation of T cell factor 4 (TCF-4). The activation of TCF-4 modulates a number of WNT-regulated genes that promote myogenic differentiation and inhibit adipogenic differentiation. My lab has provided direct evidence of the conformational change in androgen receptor protein upon ligand binding; these findings have important implications for SARM design and selectivity. We have elucidated a novel model of DHT action and the role of steroid 5-alpha reductase in men (JAMA 2012). Our studies have clarified the mechanisms by which testosterone stimulates erythropoiesis and corrects anemia of inflammation.

1. Bhasin S, Travison TG, Storer TW, Lakshman K, Kaushik M, Mazer NA, Ngyuen AH, Davda MN, Jara H, Aakil A, Anderson S, Knapp PE, Hanka S, Mohammed N, Daou P, Miciek R, Ulloor J, Zhang A, Brooks B, Orwoll K, Hede-Brierley L, Eder R, Elmi A, Bhasin G, Collins L, Singh R, Basaria S. Effect of testosterone supplementation with and without a dual 5 α -reductase inhibitor on fat-free mass in adult men with suppressed testosterone production: a randomized trial. JAMA 2012;307:931-9. PMID: 22396515

2. Basaria S, Bhasin S. Targeting the skeletal muscle-metabolism axis in prostate-cancer therapy. N Engl J Med 2012;367:965-7.
3. Gonzalez-Cadavid NF, Taylor WE, Yarasheski K, Sinha-Hikim I, Ma K, Ezzat S, Shen R, Lalani R, Asa S, Mamita M, Nair G, Arver S, Bhasin S. Organization of the human myostatin gene and expression in healthy men and HIV-infected men with muscle wasting. Proc Natl Acad Sci USA 1998;95:14938-43. PMID: 9843994
4. Guo W, Bachman E, Li M, Roy CN, Blusztajn J, Wong S, Chan SY, Serra C, Jasuja R, Travison TG, Muckenthaler MU, Nemeth E, Bhasin S. Testosterone administration inhibits hepcidin transcription and is associated with increased iron incorporation into red blood cells. Aging Cell 2013;12:280-91. PMID 23399021
5. Jasuja R, Costello J, Singh R, Jang H, Serra C, Guo W, Collins JC, Bhasin S. Combined Administration of testosterone plus an ornithine decarboxylase inhibitor as a selective prostate-sparing anabolic therapy. Aging Cell 2014.doi: 10:1111/ace.12174 PMID: 18948405.

Leadership Role in National and International Efforts to Define Cut-points for Sarcopenia and to Develop Guidelines for Testosterone Therapy of Men

1. Bhasin S, Espeland MA, Evans WJ, Ferrucci L, Fried LP, Gill TM, Pahor M, Studenski S, Guralnik J, Nayfield S, Romashkin S, Perlstein R, Burke L, Parks M. Indications, labeling, and outcomes assessment for drugs aimed at improving functional status in older persons: a conversation between aging researchers and FDA regulators. Working Group on Functional Outcome Measures for Clinical Trials. J Gerontol A Biol Sci Med Sci. 2009;64:487-91.
2. **Fielding** RA, Vellas B, Evans WJ, **Bhasin S**, Morley JE, Newman AB, Abellan van Kan G, Andrieu S, Bauer J, Breuille D, Cederholm T, Chandler J, Harris T, Kannt A, Keime Guibert F, Onder G, Papanicolaou D, Rolland Y, Rooks D, Sieber C, Souhami E, Verlaan S, Zamboni M. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. J Am Med Dir Assoc 2011;12:249-56.
3. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM; Task Force, Endocrine Society. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2010;95:2536-59. PMID: 20525905
4. Bhasin S, Pencina M, Jasuja GK, Travison TG, Coviello AD, Orwoll E, Wang PY, Nielson C, Wu F, Tajar A, Labrie F, and the EMAS group, Vesper H, Zhang, A, Ulloor J, Singh R, D'Agostino R, Vasani RS. Reference ranges for testosterone in nonobese men generated using liquid chromatography tandem mass spectrometry in a community-based sample of healthy non-obese young men in the Framingham Heart Study and applied to three geographically distinct cohorts. J Clin Endocrinol Metab 2011;96:2430-9 PMID: 21697255

Access to my full bibliography can be obtained at the My NCBI URL:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/shalendar.bhasin.1/bibliography/40528776/public/?sort=date&direction=descending>

D. Research Support: Ongoing

1R01AG048326-01 Bhasin (PI)

Randomized Trial of a Multi-factorial Fall Injury Prevention Strategy

Source: NIA-PCORI

06/01/2014-5/30/2019

Specific Aims: This is an RCT of a risk-factor based multi-factorial fall injury prevention strategy.

Overlap: None

1R01AG037547-01 Bhasin (PI)

Optimizing Protein Intake in Older Americans with Mobility Limitations

Source: NIH-NIA 10/01/2011-10/1/2016

Specific Aim: To establish protein requirements for older Americans

Overlap: None

5U01AG030644-02 (Snyder, Peter, PI)

The Testosterone Trials (Boston Site PI: Bhasin, S)

Source: NIA; 07/1/2009-06/30/2016

Specific Aims: To determine the effects of testosterone on physical function, bone health, vitality, anemia, and sexual dysfunction in older men. Dr. Bhasin serves as the Leader of the Physical Function Trial.

1R43AG045011-A1 (Bhasin, PI of the Academic Partner BWH; Jasuja, PI of the FPT, LLC)

Novel algorithm for free testosterone determination based on a multi-step allosteric model

Source: NIA 03/1/2015-03/31/2016

Specific Aims: This SBIR grant aims to elucidate the molecular mechanisms of testosterone binding to SHBG and develop an algorithm for estimating free testosterone from the binding model.

1R01NR014502 Bhasin (PI)

A Proof-of-Concept Randomized Trial of a Prostate Sparing Selective Androgen Receptor Modulator for Improving Symptoms of Androgen Deficiency in Men with Organ-Localized Prostate Cancer

Funding: NINR 10/1/2015 – 9/30/2020

Specific aims: To determine the efficacy of a Selective Androgen Receptor Modular for improving symptoms of androgen deficiency in men with prostate cancer

Overlap: None

NIA 1U01 AG051421-01 Bhasin (PI)

Muscle Mass and Strength Cutpoints in Persons at Risk of Mobility Disability

Source: NIA 10/1/2015 – 9/30/2017

Specific aims: Establishing cut-points for muscle mass and strength measures to define sarcopenia as a biomarker to identify older adults at risk for physical disability

Bhasin, S (PI): An Investigator-Initiated Proof-of-Mechanism Study

Application of a kisspeptin analog to stimulate the hypothalamic-pituitary axis in older men

Source: Takeda Pharmaceuticals

Specific aims: To determine the role of a kisspeptin analog in stimulating testosterone secretion in older adults

Overlap: None

1R01 DK070534-06 Bhasin (PI)

Mechanisms of Androgen Effects on Body Composition

NIDDK 08/1/04-3/01/16

Specific aims: To determine how testosterone regulates myogenic differentiation of mesenchymal stem cells.

1R43AG52403 SBIR Grant (Bhasin PI of the BWH Academic Partner)

Application of an Activity Monitor to Detect Falls in Older Adults

NIA 10/1/2015-10/1/2017

Specific aims: This is an ancillary study of the STRIDE Trial which will determine the sensitivity and specificity of an activity monitor to detect falls in older adults

Overlap: None

Completed Grants

1R01DK078512 Bhasin (PI)

Mechanisms of Myostatin Action

Agency: NIH/ NIDDK 07/1/2009 – 6/30/2014

Specific aims: To elucidate the mechanisms by which myostatin regulates mesenchymal stem cell differentiation and metabolism.