BIOGRAPHICAL SKETCH

NAME: Jill A. Macoska

POSITION TITLE: Distinguished University Professor of Science and Mathematics

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Kent State University, Kent, OH	B.A	05/78	Physical Anthropology
City University of New York, New York, NY	M. Phil.	05/86	Chemistry/Biochemistry
City University of New York, New York, NY	Ph.D.	05/88	Chemistry/Biochemistry
Harvard University, Cambridge, MA	Postdoctoral	05/88-10/89	Molecular Genetics
Michigan Cancer Foundation, Detroit, MI	Postdoctoral	10/89-06/91	Cancer Genetics

A. Personal Statement

I have led peer-reviewed and NIH-funded research for the past 25 years focused on elucidating the molecular genetic alterations and dysfunctional inter- and intra-cellular signaling mechanisms that promote urinary tract (kidney, bladder, prostate) pathobiology. I work extensively in the areas of prostate and kidney cancer to understand the basic biological mechanisms governing tumor initiation and progression, and to identify biomarkers and new therapeutics of clinical utility. Research in the Macoska laboratory is currently focused on: 1) Defining the mechanisms through which dysfunctional interactions between cell types within the tissue microenvironment develop, and how these dysfunctional interactions contribute to pathobiology in the urinary tract; 2) Exploring the concept of periurethral fibrosis as a pathobiology promoting male lower urinary dysfunction; 3) Elucidating genomic alterations contributing to upper and lower urinary tract pathobiologies; 4) Understanding how the intersection of lifestyle and genetic predisposition contributes to health disparities in diverse populations 5) Translating laboratory-based knowledge to the development of clinically efficacious biomarkers and therapeutics.

B. Positions and Honors

Professional Experience

1991-2000 Research Associate, Lecturer, Assistant Professor, The University of Michigan, Department of Surgery, Section of Urology
1996-2001 Associate Editor, Basic Science Section, *Urology*
2000-2010 Director, University of Michigan Comprehensive Cancer Center Affymetrix and cDNA Microarray Facility
2000-2002 Member, Executive Committee, Society for Basic Urologic Research
2000-2002 Member, NIH Small Business Innovation Research (SBIR) in Genetic Sciences Study Section
2001-2012 Faculty Member, Program in Bioinformatics (now the Center for Computational Medicine and Bioinformatics).
2001-2010 Associate Professor w/tenure, The University of Michigan, Department of Urology
2002-2006 Associate Director, Prostate/Urologic Oncology Program, University of Michigan Comprehensive Cancer Center
2003-2008 Associate Chair, Department of Urology, University of Michigan
2004-2008 Charter Member, NIH Cancer Genetics Study Section
2004-2012 Faculty Member and Associate Graduate Program Director, Cell and Molecular Biology Graduate Program, The University of Michigan
2007 Participant, NIDDK Prostate Basic and Clinical Research Strategic Planning Meeting
2007-2010 Director, University of Michigan Urology Research Training Program
2008-2010 Chief, Division of Laboratory Research, Department of Urology, University of Michigan
2010-2012 Charter Faculty Member, Cancer Biology Graduate Program, The University of Michigan
2010-2012 Professor w/tenure, The University of Michigan, Department of Urology

2010-2013 Secretary, the Society for Basic Urologic Research
2012-Present Associate Editor, *The Prostate*
2013-Present Alton J. Brann Endowed Chair and Distinguished University Professor of Science and Mathematics, University of Massachusetts Boston
2013-Present Director, Center for Personalized Cancer Therapy, University of Massachusetts Boston
2013-Present Presidential Scholar, the Dana-Farber/Harvard Cancer Center
2014-Present Director, University of Massachusetts Boston Genomics Core
2013-2014 Vice-President, the Society for Basic Urologic Research
2014-2015 President, the Society for Basic Urologic Research
2016-Present Chair, University of Massachusetts Boston Institutional Animal Care and Use Committee
2019 *Ad Hoc* Member, NIH/NIDDK Advisory Council

Honors

1974 Salutatorian, St. Joseph Academy High School
1978 Magna Cum Laude
1979 Phi Beta Kappa
1985 Beatrice Goldstein Konheim Graduate Scholarship in the Life Sciences, City University of New York
1991-1993 Ph.D. Scholar, American Foundation for Urologic Disease (AFUD)
1995-1996 New Investigator Research Award American Foundation for Urologic Disease/Searle
1996-1997 Society for Basic Urologic Research/Merck Young Investigator Award
2012 Society for Women In Urology/ Society for Basic Urologic Research Award for Excellence in Urologic Research
2015 2015 "Woman to Watch", Boston Business Journal
2020 Commonwealth of Massachusetts 2020 Citation for Outstanding Performance

C. Contributions to Science

1. The finding that the prostates of aging men exhibited an inflammatory phenotype led my group to hypothesize that fibrosis, which occurs consequent to inflammation, might comprise a *previously unrecognized pathobiology* contributing to lower urinary dysfunction (LUTD). We first showed that periurethral tissues from men with LUTD, as measured by elevated American Urological Association Symptom Index (AUASI) scores, demonstrated significantly higher levels of collagen content and tissue stiffness indicative of fibrosis than tissues from men with low AUASI scores. Subsequent studies revealed that the inflammatory mediator chemokines and interleukins in the prostatic microenvironment dpromoted the expression of pro-fibrotic extra cellular matrix proteins, collagen secretion, fibroblast to myofibroblast phenoconversion, and acquisition of a fibrotic phenotype in the prostate. Further work is focused on elucidating the molecular mechanisms that promote fibrosis in the LUT, the development of diagnostic biomarkers for fibrosis, and the development of anti-fibrotic therapeutics.

a. D'Arcy Q, Gharaee-Kermani M, Zhilin-Roth A, Macoska JA. The IL-4/IL-13 signaling axis promotes prostatic fibrosis. PLoS One. 2022 Oct 6;17(10):e0275064. doi: 10.1371/journal.pone.0275064. PMID: 36201508.
b. Patalano-Salsman S, Rodriguez-Nieves J, Colaneri C, Cotellessa J, Almanza D, Zhilin-Roth A, Riley T, Macoska J. CXCL12/CXCR4-Mediated Procollagen Secretion Is Coupled To Cullin-RING Ubiquitin Ligase Activation. Sci Rep. 2018 Feb 22;8(1):3499. doi: 10.1038/s41598-018-21506-7 PMID: 29472636; PubMed Central PMCID: PMC5823879.
c. Ma J, Gharaee-Kermani M, Kunju L, Hollingsworth JM, Adler J, Arruda EM, Macoska JA. Prostatic fibrosis is associated with lower urinary tract symptoms. J Urol. 2012 Oct;188(4):1375-81. doi: 10.1016/j.juro.2012.06.007. Epub 2012 Aug 17. PubMed PMID: 22906651; PubMed Central PMCID: PMC3485634.

2. In an effort to understand and potentially identify therapeutic targets for prostatic enlargement consequent to aging, our group examined whether aging-associated changes in the stromal cellular components of the prostate gland might disrupt tissue homeostasis and promote proliferation of prostatic epithelium. Work from my group showed that primary stromal fibroblasts from the prostates of older men exhibited transcriptional up-regulation and secretion of inflammatory proteins, including several interleukins and CXC-type chemokines, compared to those from younger men. Interleukins and CXC-type chemokines serve as cytokines to promote the proliferation of prostatic epithelium. This novel finding, that the aging prostate gland

microenvironment was highly inflammatory, formed the basis for subsequent work by my group and others aimed at understanding the etiology of human benign prostatic hyperplasia (BPH).

a. Begley L, Monteleon C, Shah RB, Macdonald JW, Macoska JA. CXCL12 overexpression and secretion by aging fibroblasts enhance human prostate epithelial proliferation in vitro. Aging Cell. 2005 Dec;4(6):291-8. PubMed PMID: 1630048
b. Begley LA, MacDonald JW, Day ML, Macoska JA. CXCL12 activates a robust transcriptional response in human prostate epithelial cells. J Biol Chem. 2007 Sep 14;282(37):26767-74. Epub 2007 Jul 12. PubMed PMID: 17631494.
c. Begley LA, Kasina S, MacDonald J, Macoska JA. The inflammatory microenvironment of the aging prostate facilitates cellular proliferation and hypertrophy. Cytokine. 2008 Aug;43(2):194-9. doi:10.1016/j.cyto.2008.05.012. Epub 2008 Jun 24. PubMed PMID: 18572414; PubMed Central PMCID:PMC2538565.
d. McDowell KL, Begley LA, Mor-Vaknin N, Markovitz DM, Macoska JA. Leukocytic promotion of prostate cellular proliferation. Prostate. 2010 Mar 1;70(4):377-89. doi: 10.1002/pros.21071. PubMed PMID: 19866464; PubMed Central PMCID: PMC3167472.

3. As a Project PI in the University of Wisconsin Madison/University of Massachusetts George M. O'Brien Center for Benign Urology Research I have published several studies in collaboration with Center project and Core PIs to elucidate pathobiologies contributing to male lower urinary tract dysfunction.

a) Macoska JA, Uchtmann KS, Leverson GE, McVary KT, Ricke WA. Prostate Transition Zone Fibrosis is Associated with Clinical Progression in the MTOPS Study. J Urol. 2019 Dec;202(6):1240-1247. doi: 10.1097/JU.0000000000000385. Epub 2019 Jun 12. PMID: 31188728; PMCID: PMC7339116.
b) Wegner KA, Abler LL, Oakes SR, Mehta GS, Ritter KE, Hill WG, Zwaans BM, Lamb LE, Wang Z, Bjorling DE, Ricke WA, Macoska J, Marker PC, Southard-Smith EM, Eliceiri KW, Vezina CM. Void spot assay procedural optimization and software for rapid and objective quantification of rodent voiding function, including overlapping urine spots. Am J Physiol Renal Physiol. 2018 Oct 1;315(4):F1067-F1080. doi: 10.1152/ajprenal.00245.2018. Epub 2018 Jul 4. PubMed PMID: 29972322; PubMed Central PMCID: PMC6230749.
c) Hao L, Greer T, Page D, Shi Y, Vezina CM, Macoska JA, Marker PC, Bjorling DE, Bushman W, Ricke WA, Li L. In-Depth Characterization and Validation of Human Urine Metabolomes Reveal Novel Metabolic Signatures of Lower Urinary Tract Symptoms. Sci Rep. 2016 Aug 9;6:30869. doi: 10.1038/srep30869. PubMed PMID: 27502322; PubMed Central PMCID: PMC4977550.
d) Gharaee-Kermani M, Rodriguez-Nieves JA, Mehra R, Vezina CA, Sarma AV, Macoska JA. Obesity induced diabetes and lower urinary tract fibrosis promote urinary voiding dysfunction in a mouse model. Prostate. 2013 Jul;73(10):1123-33. doi: 10.1002/pros.22662. Epub 2013 Mar 26. PubMed PMID: 23532836; PubMed Central PMCID: PMC5512573.

Complete List of Published Work in NCBI MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/jill.macoska.1/bibliography/public/

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

NIH/NCI 5 U54 CA156734-12 (MPI: Colon-Carmona, Macoska) 09/1/21-08/31/26
Administrative Core; Planning and Evaluation Core; Shared Resources Core
(1/2) The University of Massachusetts, Boston - Dana-Farber/Harvard Cancer Center U54 Comprehensive Partnership for Cancer Disparities Research
Role: PI

NIH/NIDDK U54 DK104310-09 09/24/14-07/31/24
George M. O'Brien Center for Benign Urologic Research (Ricke, PI)
University of Wisconsin Madison - University of Massachusetts Boston
Project 3 (Macoska, Project PI): Persistence of an IL-4/IL-13 Autocrine Loop Promotes Fibrosis-Mediated Urinary Voiding Dysfunction
Role: Project PI

Massachusetts Life Sciences (Macoska, PI) 07/01/20-06/31/21
Spatial Transcriptomics: In Situ Tissue-Based Gene Expression Profiling at the Cellular Level.