OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Schisler, Jonathan

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0001-7382-2783

Position Title: Assistant Professor (Tenure track)

Organization and Location: McAllister Heart Institute, Department of Pharmacology, Department of Pathology and Lab Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
The University of North Carolina at Chapel Hill, Chapel Hill, NC, United States	Postdoctoral Fellow	07/2006	12/2010	Cardiovascular
Univ. of Texas Southwestern Medical Center, Dallas, TX, USA	DOCTOR OF PHILOSOPHY	08/2000	05/2006	Biological Chemistry
The University of Toledo, Toledo, OH, USA	MASTER OF SCIENCE	09/1998	06/2000	Bioengineering
The University of Toledo, Toledo, OH, USA	BACHELOR OF SCIENCE	09/1993	06/1997	Biology

Appointments and Positions

2020 - present	Assistant Professor (Tenure track), McAllister Heart Institute, Department of Pharmacology, Department of Pathology and Lab Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC, United States
2025 - present	Faculty Director, PRISM (Postbaccalaureate Research Initiative in Science and Medicine), The University of North Carolina at Chapel Hill, Chapel Hill, NC, United States
2020 - present	Faculty Director, Cardiovascular Physiology and Phenotyping Core, The University of North Carolina at Chapel Hill, Chapel Hill, NC, United States
2016 - 2020	Assistant Professor (Research track), Department of Pathology and Lab Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
2014 - 2020	Assistant Professor (Research track), McAllister Heart Institute, Department of Pharmacology, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
2011 - 2014	Research Instructor, Department of Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
2008 - 2010	AHA postdoctoral fellow (Advisor: Cam Patterson, M.D.), McAllister Heart Institute, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
2006 - 2008	Postdoctoral trainee (Advisor: Cam Patterson, M.D.), Carolina Cardiovascular Biology Center, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
2000 - 2005	Pre-doctoral research fellow (Advisor: Chris Newgard, Ph.D.) Biological Chemistry, The University of Texas Southwestern Medical Center at Dallas, Dallas, TX, USA
1998 - 2000	Graduate teaching assistant (Advisor: Patricia Relue, Ph.D) Bioengineering, The University of Toledo, Toledo, OH, USA
1997 - 1998	Post-baccalaureate research fellow (Advisor: Levy Ulanovsky, Ph.D.) DNA Sequencing Technology, Argonne National Laboratory, US Department of Energy, Lemont, IL, USA
1996 - 1997	Undergraduate honors research student (Advisor: Scott Lesiner, Ph.D) Plant Biology, The University of Toledo, Toledo, OH, USA

Products

Products Closely Related to the Proposed Project

1. Hao X, Hu Z, Li M, Zhang S, Tang M, Hao C, Qi S, Liang Y, Almeida MF, Smith K, Zuo C, Feng Y, Guo M, Ma D, Li S,

Wang Z, Sun Y, Deng Z, Mao C, Xia Z, Jiang Y, Gao Y, Xu Y, Schisler JC, Shi C. E3 ubiquitin ligase CHIP facilitates cAMP and cGMP signalling cross-talk by polyubiquitinating PDE9A. EMBO J. 2025 Feb;44(4):1249-1273. PubMed Central PMCID: PMC11833080.

2. da Silveira WA, Fazelinia H, Rosenthal SB, Laiakis EC, Kim MS, Meydan C, Kidane Y, Rathi KS, Smith SM, Stear B, Ying Y, Zhang Y, Foox J, Zanello S, Crucian B, Wang D, Nugent A, Costa HA, Zwart SR, Schrepfer S, Elworth RAL, Sapoval N, Treangen T, MacKay M, Gokhale NS, Horner SM, Singh LN, Wallace DC, Willey JS, Schisler JC, Meller R, McDonald JT, Fisch KM, Hardiman G, Taylor D, Mason CE, Costes SV, Beheshti A. Comprehensive Multi-omics Analysis Reveals Mitochondrial Stress as a Central Biological Hub for Spaceflight Impact. Cell. 2020 Nov 25;183(5):1185-1201.e20. PubMed Central PMCID: PMC7870178.
3. Almeida MF, Smith K, Garris MA, Sanchez-Hodge R, Colie M, Schisler JC. A protocol to establish and maintain organotypic cerebellar slice culture (OCerSC) from aged mice. PLoS One. 2026;21(4):e0342373. PubMed Central PMCID: PMC13089748.
4. Stewart M, Paththamperuma C, McCann C, Cottingim K, Zhang H, DelVecchio R, Peng I, Fennimore E, Nix JC, Saeed MN, George K, Makaroff K, Colie M, Paulakonis E, Almeida MF, Afolayan AJ, Brown NG, Page RC, Schisler JC. Crystal structures reveal phosphorylation-dependent disruption of the heat shock protein 70-CHIP interface: A compensatory G132N variant restores binding affinity. Cell Stress Chaperones. 2026 May;31(3):100166. PubMed Central PMCID: PMC13090976.
5. Stewart M, Schisler JC. Targeting chaperone modifications: Innovative approaches to cancer treatment. J Biol Chem. 2024 Dec;300(12):107907. PubMed Central PMCID: PMC11599458.

Other Significant Products Highlighting Contributions to Science

1. Malkani S, Chin CR, Cekanaviciute E, Mortreux M, Okinula H, Tarbier M, Schreurs AS, Shirazi-Fard Y, Tahimic CGT, Rodriguez DN, Sexton BS, Butler D, Verma A, Bezdan D, Durmaz C, MacKay M, Melnick A, Meydan C, Li S, Garrett-Bakelman F, Fromm B, Afshinnekoo E, Langhorst BW, Dimalanta ET, Cheng-Campbell M, Blaber E, Schisler JC, Vanderburg C, Friedländer MR, McDonald JT, Costes SV, Rutkove S, Grabham P, Mason CE, Beheshti A. Circulating miRNA Spaceflight Signature Reveals Targets for Countermeasure Development. Cell Rep. 2020 Dec 8;33(10):108448. PubMed Central PMCID: PMC8441986.
2. Schisler JC, Rubel CE, Zhang C, Lockyer P, Cyr DM, Patterson C. CHIP protects against cardiac pressure overload through regulation of AMPK. J Clin Invest. 2013 Aug;123(8):3588-99. PubMed Central PMCID: PMC3726173.
3. Ranek MJ, Oeing C, Sanchez-Hodge R, Kokkonen-Simon KM, Dillard D, Aslam MI, Rainer PP, Mishra S, Dunkerly-Eyring B, Holewinski RJ, Virus C, Zhang H, Mannion MM, Agrawal V, Hahn V, Lee DI, Sasaki M, Van Eyk JE, Willis MS, Page RC, Schisler JC, Kass DA. CHIP phosphorylation by protein kinase G enhances protein quality control and attenuates cardiac ischemic injury. Nat Commun. 2020 Oct 20;11(1):5237. PubMed Central PMCID: PMC7575552.
4. Ravi S, Schuck RN, Hilliard E, Lee CR, Dai X, Lenhart K, Willis MS, Jensen BC, Stouffer GA, Patterson C, Schisler JC. Clinical Evidence Supports a Protective Role for CXCL5 in Coronary Artery Disease. Am J Pathol. 2017 Dec;187(12):2895-2911. PubMed Central PMCID: PMC5718092.
5. Shi CH, Rubel C, Soss SE, Sanchez-Hodge R, Zhang S, Madrigal SC, Ravi S, McDonough H, Page RC, Chazin WJ, Patterson C, Mao CY, Willis MS, Luo HY, Li YS, Stevens DA, Tang MB, Du P, Wang YH, Hu ZW, Xu YM, Schisler JC. Disrupted structure and aberrant function of CHIP mediates the loss of motor and cognitive function in preclinical models of SCAR16. PLoS Genet. 2018 Sep;14(9):e1007664. PubMed Central PMCID: PMC6160236.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

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NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Schisler, Jonathan

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0001-7382-2783

Position Title: Assistant Professor (Tenure track)

Organization and Location: McAllister Heart Institute, Department of Pharmacology, Department of Pathology and Lab Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

Personal Statement

As a tenure-track Assistant Professor who has met and exceeded the UNC School of Medicine "Meet-the-Mark" criteria for promotion to Associate Professor with tenure in the Research area of excellence, I have built and led a thriving, independent program since founding the Schisler Lab in 2014. My program in systems pharmacology and multi-omics integration links protein quality control mechanisms to therapeutic opportunities in cardiovascular, neurodegenerative, and post-viral disease, sustained by continuous competitive funding and national recognition.

I founded the Schisler Lab in 2014 and have performed at a fully independent, tenure-level standard from that point forward. Although my appointment was on the fixed-term research track, the substance of my work was equivalent to tenure-track scholarship by the "Meet-the-Mark" criteria: when my prior mentor retired from research in 2014, I assumed sole intellectual and financial leadership of my program, competed successfully for independent federal funding, and directed an original research agenda as senior author. During 2014–2020 I produced 9 senior-author and 3 first-author original research papers, one first-author review, and two senior-authored reviews, while serving as editor of two major textbooks (*Fibrosis in Disease* and *Endocrinology of the Heart*). I received two NIA R01 awards in 2019 and 2020 and sustained continuous support from NIH, NASA, AHA, and BrightFocus, with national recognition. Together, this record establishes that my qualifying body of tenure-level work began in 2014 and has progressed continuously since.

I transitioned to the tenure track in September 2020. Since then, my lab has delivered five original research papers as senior or co-senior/corresponding author plus three senior reviews in refereed journals, including the 2025 *EMBO J* paper on CHIP-mediated PDE9A ubiquitination and the landmark *Cell* 2020 multi-omics study establishing mitochondrial stress as the central hub of spaceflight impact. My team-science record adds 24 primary research publications since September 2020, with my role annotated in my CV. My post-2020 first/senior-author record alone exceeds the five-publication threshold; with my 2014–2020 productivity, it reflects a sustained, progressive trajectory of independent scholarship that satisfies promotion standards.

My teaching and service leadership are likewise exceptional. I direct three major training programs—the AHA- and NINDS R25-supported MHI-Summer and Carolina Summer Fellowship NEURO Programs, plus the School of Medicine-supported PRISM program (2025–) aligned with UNC's strategic plan—contributing directly to UNC School of Medicine priorities in workforce development and inclusive research training. I have also directly mentored well over 100 undergraduates and post-baccalaureates and six graduate students in multi-omics and disease-focused research. These efforts are reinforced by nine years as a full-time instructor for PHCO732 grant writing and four years leading BBSP902 for first-year biomedical science trainees, plus my role as Faculty Director of the MHI Cardiovascular Physiology and Phenotyping Core since 2020.

Looking ahead, I am positioned to lead the integration of cellular proteostasis and metabolism in aging and disease. With new core R01 funding, expanded spatial-omics platforms, and a robust mentoring pipeline, I am poised to train the next generation of systems pharmacologists as a tenured leader at UNC.

Honors

2024	STAR Mentor Award, UNC-CH Office of Graduate Education
2023	Faculty Mentoring Award Nominee, UNC-CH Women’s Leadership Council
2020	Spaceflight Technologies, Application, and Research Program Selection, NASA
2018	McAllister Heart Institute Junior Investigator Award, UNC Chapel Hill
2017	Outstanding Encouragement of Learning & Development Finalist, UNC at Chapel Hill
2017	McAllister Heart Institute Junior Investigator Award, UNC Chapel Hill

2016	Conference Presentation Travel Award, UNC Center for Global Initiatives
2009	Early Investigator Career Award, Society for Heart and Vascular Metabolism
2008	Postdoctoral Fellowship Award, American Heart Association
2006	Symposia scholarship, Keystone Symposia
2004	Scholarship award, Beta Cell Biology Consortium
2003	Symposia scholarship, Keystone Symposia
2000	Graduate School Organization poster session winner, UT Southwestern Medical Center
1997	Honors in Biology, Cum Laude Graduate with Honors, The University of Toledo
1997	Undergraduate Research Fellowship, Argonne National Laboratory

Contributions to Science

1. Advancing Cellular Regulatory Mechanisms: My foundational work on beta cell proliferation and transcriptional regulation naturally evolved into an interest in post-translational regulatory mechanisms. Central to this research are E3 ligases—enzymes that coordinate substrate protein modification through ubiquitination. This process involves attaching ubiquitin, which alters protein function or leads to degradation. My initial focus in this area was on the E3 ligases CHIP and MuRF1 and their roles in cardiovascular health. A key discovery was the identification of the first human mutation in CHIP, resulting in a multi-organ degenerative disease now known as spinocerebellar ataxia autosomal recessive 16 (SCAR16), and later a dominant form called SCA48—as detailed in Shi's 2014 Human Molecular Genetics paper on ataxia and hypogonadism from loss of CHIP ubiquitin ligase activity and the 2018 PLoS Genetics follow-up on disrupted CHIP structure mediating SCAR16 motor/cognitive deficits in preclinical models. Ongoing research aims to identify molecular substrates of CHIP across diverse biological systems, including the heart and brain, as in our 2013 Journal of Clinical Investigation work on CHIP's protection against cardiac pressure overload via AMPK regulation. The integration of protein quality control pathways, considered crucial in cardiovascular and neuroendocrine systems, highlights the progression of my research program and emphasizes its distinctive contribution to the scientific community.

2. Pioneering Research in Space Biomedicine: My lab has made significant progress in biomedical space research by leveraging the unique space environment to gain new insights into human health and disease. Our collaborations have focused on understanding how microgravity and space radiation affect cellular and molecular processes. This work has led to groundbreaking discoveries, including identifying molecular changes in skin health, demonstrating spaceflight-induced molecular alterations similar to aging, investigating renal dysfunction, and uncovering genetic factors that influence radiation sensitivity. Additionally, we identified a spaceflight-associated microRNA signature—as in Malkani's 2020 Cell Reports on circulating miRNA spaceflight signature revealing countermeasure targets—and highlighted mitochondrial stress as a key factor in spaceflight’s effects, following da Silveira's 2020 Cell comprehensive multi-omics analysis of spaceflight impact. Through international collaborations, our team continues to develop innovative biomedical technologies and therapeutic strategies that benefit both astronauts and patients on Earth.

3. Innovating Cardiac Metabolism Research: At the core of heart failure research, my lab has shed light on the crucial role of cardiac metabolism. We’ve identified ubiquitin ligases as key regulators of signaling proteins that control cardiac metabolism and revealed their new role in mitochondrial quality control, including Ranek's 2020 Nature Communications on CHIP phosphorylation by protein kinase G enhancing protein quality control and reducing cardiac ischemic injury. Our ongoing research explores the mechanisms influencing cardiac energetics, using both genetic and pharmacological models to open the door for new therapies.

4. Integrating Clinical Data with Laboratory Research and Bridging Gaps in Genomic Studies: My lab's innovative approach goes beyond traditional models by incorporating clinically derived datasets to model human disease. This integration enables us to develop and test hypotheses in the wet lab, leading to the discovery of new genes and pathways essential to disease progression. Our expertise in multi-omics has facilitated collaborations with leading research groups, focusing on questions directly relevant to human health. Recognizing the limited access that disadvantaged groups have to genetic advancements and precision medicine, my work also aims to address healthcare disparities that disproportionately impact non-Hispanic whites. By focusing on genomic studies involving African Americans, I am dedicated to improving health in the United States by enriching the genetic research landscape with diverse ancestral backgrounds. For example, our extensive genomic profiling and biomarker analysis have identified the chemokine CXCL5's role in cardio-protection, positioning it as a potential biomarker and therapeutic target for coronary artery disease. This is demonstrated by Ravi's 2017 American Journal of Pathology clinical evidence for CXCL5's protective role in coronary artery disease. Additionally, our research covers other disease areas, including infectious diseases, where we have uncovered key genetic and molecular factors that influence disease susceptibility and progression—as in Greenwald's 2024 mBio paper on how mucus polymer concentration defines Pseudomonas antibiotic response in chronic lung infection. This comprehensive approach ensures that our findings are broadly relevant, ultimately helping to improve health outcomes for diverse populations.

5. Pioneering Beta Cell Biology Research: As a graduate student, my research was at the forefront of beta cell biology, focusing on uncovering the mechanisms controlling beta cell proliferation and glucose-stimulated insulin secretion. At that time, the scientific community lacked genetic and biochemical strategies to increase beta cell mass without impairing their essential functions. My approach focused on transcription factors and their downstream targets, using them as therapeutic agents to expand functional beta cell mass outside the body. This progress has potential applications for islet transplantation therapies. Under the mentorship of my Ph.D. advisor, Dr. Chris Newgard, I developed techniques and methods that have become standard in islet biology research. Dr. Newgard's ongoing research continues to build upon these foundations. The insights gained from this work deepened my interest in novel protein functions and their role in human diseases, paving the way for my future research projects.

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