REQUEST FOR APPLICATIONS: Brigham/Harvard ROSA Center SCORE Travel Fellowships

To foster collaboration between SCORE sites and enable early career scientists to learn new technical skills and/or enhance SCORE collaborations, the ROSA Center will award 4 SCORE Travel Fellowships (TF) in the 2025-26 academic year:

2 ROSA Associate scientists to visit external SCORE sites, and
2 for SCORE sites to send fellows/faculty to the Brigham/ Harvard ROSA Center site.

Award of up to $3,000 for travel-related costs.

Eligibility Criteria: Brigham/Harvard ROSA Center candidates visiting other SCORE programs ('outbound TF fellows') must a have a Harvard Medical School appointment as a Research Fellow, Instructor or Assistant Professor in the current or upcoming academic year. Inbound Fellows visiting the Brigham/Harvard ROSA Center should hold an equivalent position at their home institution. Senior faculty, at the Associate Professor level or above, will not be eligible for the Fellowship.

Applicants: Affiliates of the SCORE are encouraged to apply. Project leads will be asked to identify others that are eligible/would benefit from this Exchange Fellowship.

Application Process:

1. A brief ½ page application detailing the requested SCORE site; objectives of the visit; biosketch; and host investigator(s) to visit with letter from the host institution indicating willingness to participate.
2. A preliminary budget and budget justification for travel related expenses (up to $3,000).

Selection Process:

The Brigham/Harvard ROSA Center SCORE will have a Travel Fellowship Subcommittee select the Fellows each year based on an overall ranking of applications. Selection criteria will include:

1. Investigator qualifications with a focus on opportunities for early career investigators to acquire new technical skills and foster collaboration and knowledge transfer across the SCORE Consortium.
2. Potential to use the knowledge gained to advance a current pilot project, a potential pilot project application, or an NIH research application or related to the overall aims of the SCORE programs.

Reporting: A one page report of the activities and outcomes of the visit, along with an expense report and a brief survey one month post visit will be required. The TE subcommittee will review survey and report data.

For more information, contact Mara Hampson or the Brigham/Harvard ROSA Center CEC directors Kathy Rexrode and Janet Rich-Edwards.

Timeline: Applications will be accepted on a rolling basis.

Applications should be submitted to Mara Hampson.

Details on the SCORE sites and projects can be found below and on the SCORE Centers spreadsheet.

National SCORE Sites and CEC Leads:

Site	Title of SCORE	CEC Lead(s)
Augusta University	Improving Awareness of Women with Hypertension: ROAR (Rural, Obese, At Risk)	Daria Ilatovskaya, Ph.D.
BWH	Brigham/Harvard Center for Reproductive Outcomes of Stress and Aging (ROSA Center)	Kathryn Rexrode, M.D., M.P.H., & Janet Rich-Edwards, M.P.H., Sc.D.
Cedars-Sinai Medical Center	The Microvascular Aging and Eicosanoids - Women's Evaluation of Systemic Aging Tenacity (MAE-WEST) ("You are never too old to become younger!") Specialized Center of Research Excellence	Noel Bairey Merz, M.D.
Emory University	Emory Specialized Center of Research Excellence (SCORE) on Sex Differences	Marcia Holstad, Ph.D., and Kelli Stidham Hall, Ph.D

Johns Hopkins University	Sex and Age Differences in Immunity to Influenza (SADII)	Wendy Bennett, M.D.
MGH	Sex Differences in Major Depression: Impact of Prenatal Stress- Immune and Autonomic Dysregulation	Stuart A. Tobet, Ph.D., Joshua Roffman, M.D., Jordan W. Smoller, M.D., Sc.D., and Albert Hofman, M.D., Ph.D.
Mayo Clinic	Sex-Specific Effects of Endocrine Disruption on Aging and Alzheimer's Disease	Virginia M. Miller, Ph.D.
Medical University of South Carolina	MUSC Specialized Center of Research Excellence on Sex Differences	Kathleen T. Brady, M.D., Ph.D.
UCLA P1	Sex Differences in Cardiometabolic Health and Disease	Arthur P. Arnold, Ph.D., and Stephanie Correa, Ph.D.
UCLA P2	Sex Related Differences in Brain Gut Microbiome Interactions in Irritable Bowel Syndrome	Emeran Mayer, M.D., & Lin Chang, M.D.
University of Colorado	Bioenergetic and Metabolic Consequences of the Loss of Gonadal Function	Judith G. Regensteiner, Ph.D.
Yale University	Yale-SCORE on Sex Differences in Alcohol Use Disorder	Ismene Petrakis, M.D.

More details on each of the SCORE sites and projects can be found at this link:

https://orwh.od.nih.gov/sex-gender/orwh-mission-area-sex-gender-in-research/specialized-centers-of-research-excellence-on-sex-differences-u54-clinical-trial

Centers	Director(s)	Grant	Title	Research projects:	Research Projects: 2	Research Projects: 3	Research Projects: 4	Career Enhancement Core	Sleep Resource Core	Resource Support Core	Resource Support Core2
Augusta University	Jennifer Sullivan, Ph.D.	U54HL169191	Improving Awareness of Women with Hypertension: ROAR (Rural, Obese, At Risk)	Type: Basic Science and Clinical Lead: Jennifer Sullivan, Ph.D.	Type: Basic Science and Clinical Lead: Erin Taylor, Ph.D.	Type: Basic Science and Clinical Lead: Michael Ryan, Ph.D.				Type: Leadership Administrative Core Leads: Jennifer Sullivan, Ph.D. & Michael Ryan, Ph.D.	
Brigham and Women's Hospital	Hadine Joffe, M.D., M.Sc. (hjoffe@bwh.harvard.edu)	U54AG062322	Brigham/Harvard Center for Reproductive Outcomes of Stress and Aging (ROSA)	Type: Clinical. Leads: Hadine Joffe, M.D., M.Sc., & Pamela Mahon, Ph.D.	Type: Population. Leads: Emily Oken, M.D., M.P.H., & Jorge Chavarro, M.D., M.S., Sc.D.	Type: Basic. Leads: Ursula Kaiser, M.D., & Victor Navarro, Ph.D.		Type: Career Enhancement Core Leads: Kathryn Rexrode, M.D., M.P.H. (krexrode@bwh.harvard.edu), & Janet Rich-Edwards, M.P.H., Sc.D. (jr33@partners.org)	Type: Sleep Resource Core Lead: Elizabeth Klerman, M.D., Ph.D.	Type: Leadership Administration Core Leads: Hadine Joffe, M.D., M.Sc., & JoAnn Manson, M.D., M.P.H., Dr.PH	
Cedars-Sinai Medical Center	Noel Bairey Merz, M.D. (Noel.BaireyMerz@cshs.org), & Susan Cheng, M.D., M.P.H., M.M.Sc. (susan.cheng@cshs.org)	U54AG065141	The Microvascular Aging and Eicosanoids - Women's Evaluation of Systemic Aging Tenacity (MAE-WEST) ("You are never too old to become younger!") Specialized Center of Research Excellence	Type: Population. Leads: Lead: Susan Cheng, M.D., M.P.H., M.M.Sc. Co-Investigators: Priya Palta, Ph.D., M.H.S., & Eugene Rhee, M.D..	Type: Clinical. Lead: Noel Bairey Merz, M.D. Co-Investigators: Chrisandra Shufelt, M.D., Janet Wei, M.D., Carl Pepine, M.D., Eileen Handberg, Ph.D., ARNP, Michael Nelson, Ph.D., M.S., & Jeffrey Wertheimer, Ph.D.	Type: Basic. Lead: John Shyy, Ph.D. Co-Investigator: Sonia Sharma, Ph.D.		Lead: Noel Bairey Merz, M.D. (Noel.BaireyMerz@cshs.org) Co-Investigators: Mariko Ishimori, M.D., Joshua Pevnick, M.D., & Denis Magoffin, M.D.		Type: Biostatistics & Informatics Core Co-Leads: Susan Cheng, M.D., M.P.H., M.M.Sc., & Andre Rogatko, Ph.D. Co-Investigator: Marcio Diniz, Ph.D.	Type: Eicosanoids Profiling Core Lead: Mohit Jain, M.D., Ph.D. Co-Investigator: Jeramie Watrous, Ph.D.
Emory University	Igho Ofotokun, M.D. (iofotok@emory.edu), and Lisa B. Haddad, M.D.	U54AG062334	Emory Specialized Center of Research Excellence (SCORE) on Sex Differences	Type: Neuro–hypothalamic–pituitary–adrenal axis. Leads: Gretchen Neigh, Ph.D., and Vasiliki Michopoulos, Ph.D.	Type: Musculoskeletal. Leads: M. Neale Weitzmann, Ph.D., and Igho Ofotokun, M.D.	Type: Cardiovascular. Leads: Arshed Quyyumi, M.D., and Leslee J. Shaw, Ph.D.		Co-Directors: Marcia Holstad, Ph.D. (nurmmcd@emory.edu), and Kelli Stidham Hall, Ph.D. (kelli.s.hall@emory.edu)			
Johns Hopkins University	Sabra L. Klein, Ph.D. (sklein2@jhu.edu)	U54AG062333	Sex and Age Differences in Immunity to Influenza (SADII)	Title: Sex differences in longitudinal humoral immunity against influenza in the frail elderly. Lead: Dr. Sean Leng	Title: Sex differences in immune responses to vaccine and circulating strains of influenza in health care workers. Lead: Dr. Andrew Pekosz	Title: Genetic and hormonal mechanisms of sex differences in immune responses and influenza vaccine efficacy in young and aged mice. Lead: Dr. Sabra Klein		Director: Wendy Bennett, M.D. (wendy.bennett@jhmi.edu)			

Massachusetts General Hospital/Harvard Medical School	Jill M. Goldstein, Ph.D. (jill_goldstein@hms.harvard.edu), & Stuart Tobet, Ph.D. (Stuart.Tobet@ColoState.EDU)	U54MH118919	Sex Differences in Major Depression: Impact of Prenatal Stress- Immune and Autonomic Dysregulation	Title: Impact of Sex on Prenatal Stress-Immune Programming of Depression and Autonomic Dysregulation. Lead: Jill M. Goldstein, Ph.D.	Title: Sex-Dependent Impact of Transcutaneous Vagal Nerve Stimulation on the Stress Response Circuitry and Autonomic Dysregulation in Major Depression Leads: Vitaly Napadow, Ph.D., & Ronald G. Garcia, M.D., Ph.D.	Title: Sex Differences in Fetal Programming by Glucocorticoids: Adult Hypothalamus and Autonomic Nervous System Leads: Stuart A. Tobet, Ph.D., and Taben Hale, Ph.D.		Co-Leads: Stuart A. Tobet, Ph.D., Joshua Roffman, M.D., Jordan W. Smoller, M.D., Sc.D., and Albert Hofman, M.D., Ph.D.	Co-Leads: Vitaly Napadow, Ph.D., & Hang Lee, Ph.D.	
Mayo Clinic	Kejal Kantarci, M.D., M.S. (kantarci.kejal@mayo.edu) and Michelle M. Mielke, Ph.D. (mmielke@wakehealth.edu)	U54AG044170	Sex-Specific Effects of Endocrine Disruption on Aging and Alzheimer's Disease	Title: Effects of bilateral salpingo-oophorectomy on physical and cognitive aging. PI: Michelle M. Mielke, Ph.D. Co-Investigators: Walter A. Rocca, M.D., Julie A. Fields, Ph.D., and Nathan K. LeBrasseur, Ph.D.	Title: Effects of bilateral salpingo-oophorectomy on imaging biomarkers of Alzheimer's disease and cerebrovascular diseases. PI: Kejal Kantarci, M.D. Co-Investigator: Kent R. Bailey, Ph.D.	Title: Effects of bilateral ovariectomy on the biology of physical and cognitive aging in mice. PI: Nathan K. LeBrasseur, Ph.D. Co-Investigators: Marissa J. Schafer, Ph.D., and Sundeep Khosla, M.D.		Director: Virginia M. Miller, Ph.D. (miller.virginia@mayo.edu)	Type: Resource Support Core-Clinical Director: Ekta Kapoor, M.B.B.S.	
Medical University of South Carolina	Aimee L. McRae-Clark, Pharm.D. (mcraeal@musc.edu), and Kevin Gray, M.D. (raykm@musc.edu)	U54DA016511	MUSC Specialized Center of Research Excellence on Sex Differences	Title: Sex differences in the interface between cannabis use and stress among emerging adults MPIs: Kevin Gray, M.D. and Rachel Tomko, Ph.D.	Title: Impact of stress and craving on return to cannabis use in postpartum women MPIs: Kathleen Brady, M.D., Ph.D., and Connie Guille, M.D. Co-Investigator: Roger Newman, M.D.	Title: Sex differences in risk of cognitive decline in older cannabis users MPIs: Aimee McRae-Clark, Pharm.D. and Andreana Benitez, Ph.D.	Title: Preclinical component PI: Rachel Penrod-Martin, Ph.D. Co-I: Onder Albayram, Ph.D.	Director: Kathleen T. Brady, M.D., Ph.D. (bradyk@MUSC.EDU)	Type: Human Translational Bioinformatics Core MPIs: Nathaniel Baker, M.S. and Brian Neelon, Ph.D. Co-I: Rachel Tomko, Ph.D.	Type: Leadership Administrative Core Director: Aimee McRae-Clark, Pharm.D.
University of California, Los Angeles (1)	Karen Reue , Ph.D. (reuek@g.ucla.edu)	U54HL170326	Sex Differences in Cardiometabolic Health and Disease	Title: Epigenetic sex determinants of cardiometabolic disease and prevention Lead: Karen Reue, Ph.D.	Title: Gene-by-sex interactions in heart failure with preserved ejection fraction (HFpEF) Lead: Jake Lusis, Ph.D.	Title: The impact of estrogen receptor alpha on cardiomyocellular metabolism and health Lead: Andrea Hevener, Ph.D.		Lead: Arthur P. Arnold, Ph.D. (arnold@ucla.edu) and Stephanie Correa, Ph.D. (stephaniecorrea@g.ucla.edu)	Type: Human Translational Bioinformatics Core Lead: Hooman Allayee, Ph.D.	
University of California, Los Angeles (2)	Emeran Mayer, M.D. (emayer@ucla.edu), & Lin Chang, M.D. (linchang@mednet.ucla.edu)	U54DK123755	Sex Related Differences in Brain Gut Microbiome Interactions in Irritable Bowel Syndrome	Title: The primary objective of this project is to examine the role of brain–gut microbiome interactions in mediating IBS and constipation symptoms during menses and menopause. Co-Leads: Lin Chang, M.D., & Arpana Gupta, Ph.D.	Title: Sex-related differences in structure, function, and connectivity of central arousal and salience networks involving brain stem nuclei are involved in IBS symptom generation. Co-Leads: Jennifer Labus, Ph.D., & Benjamin Ellingson, Ph.D.	Title: The primary object of this project is to examine sex-related differences in the effect of cognitive behavioral therapy on emotional arousal and salience circuits and the role of the gut microbiome. Co-Leads: Emeran Mayer, M.D., & Bruce Naliboff, Ph.D.		Emeran Mayer, M.D. (emayer@ucla.edu), & Lin Chang, M.D. (linchang@mednet.ucla.edu)	Type: Data Processing and Analysis Core Co-Leads: Arpana Gupta, Ph.D., Jennifer Labus, Ph.D., & Jonathan Jacobs, M.D., Ph.D. Co-Investigators: Lisa Kilpatrick, Ph.D., & Swapna Joshi, Ph.D.	

University of Colorado - Anschutz Medical Campus	Wendy M. Kohrt , Ph.D. (Wendy.Kohrt@ucdenver.edu) and Kerrie Moreau, Ph.D (kerrie.moreau@cuanschutz.edu)	U54AG062319	Bioenergetic and Metabolic Consequences of the Loss of Gonadal Function	Title: Cardiometabolic Consequences of the Loss of Ovarian Function PI: Kerrie Moreau, Ph.D. Co-Investigators: Daniel Bessesen, M.D.; Vienna Brunt, Ph.D.; Wendy Kohrt, Ph.D.; Margaret Wierman, M.D.	Title: Intersection of Exercise and Estrogen in Weight Regain After Weight Loss PI: Paul S. MacLean, Ph.D. Co-Investigators: Matthew Jackman, Ph.D.; Travis Nemkov, Ph.D.; Darleen Sandoval, Ph.D.; Rebecca Scalzo, Ph.D.; Kartik Shankar, Ph.D.	Title: Suppression of ERα Signaling in HSCDAs Increases Adiposity via KYN, AhR PI: Dwight J. Klemm, Ph.D.	Director: Judith G. Regensteiner, Ph.D. (JUDY.REGENSTEINER@CUANSCHUTZ.EDU)	
Yale University	Sherry McKee, Ph.D. (sherry.mckee@yale.edu)	U54AA027989	Yale-SCORE on Sex Differences in Alcohol Use Disorder	Lead: Sherry McKee, Ph.D.	Lead: Kelly Cosgrove, Ph.D.	Co-Leads: Marina Picciotto, Ph.D., & Yann Mineur, Ph.D.	Lead: Ismene Petrakis, M.D. (ISMENE.PETRAKIS@YALE.EDU)	Co-Leads: Ralitza Gueorguieva, Ph.D., & Ismene Petrakis, M.D.

Augusta University

Title	Improving Awareness of Women with Hypertension: ROAR (Rural, Obese, At Risk)
Director(s)	Jennifer Sullivan, Ph.D.
Abstract	About 19 million deaths were attributed to cardiovascular disease (CVD) globally in 2020, an increase of ~20% from 2010; heart disease remains the leading cause of death for men and women in the United States. Hypertension is a major modifiable risk factor for CVD, and it has been suggested that eliminating hypertension would reduce CVD mortality by 30.4% in men and 38.0% in women. Although young women are considered "protected" from hypertension and the associated cardiovascular (CV) risk relative to age-matched men, the elimination of hypertension is projected to have a larger impact on CVD mortality in women. Importantly, the highest risk of death from hypertension is in the U.S. rural South, and specific subsets of women are particularly vulnerable to developing hypertension and CVD, including Black women. A critical barrier to limiting premature death from CVD is lack of awareness surrounding the risks of CVD. Our overall goal is to transform academic and community understanding of sex as a biological variable (SABV) in the consideration of hypertension. We will achieve this goal through rigorous research, creation and dissemination of innovative educational content, development of strategic partnerships, and enhanced community engagement in the Southeast U.S.

Title	Research Project 1: Basic Science and Clinical
Lead(s)	Jennifer Sullivan, Ph.D.
Abstract	Compared with age-matched men, young women are protected from hypertension and end organ damage. Yet, increasing epidemiological evidence suggests that this protection is compromised by chronic consumption of saturated fat. This project will determine whether activation and recruitment of immune cells in response to a chronic high-fat diet abolishes CV protection in females and will explore the mechanisms mediating increases in BP.

Title	Research Project 2: Basic Science and Clinical
Lead(s)	Erin Taylor, Ph.D.
Abstract	Systemic lupus erythematosus (SLE) disproportionately affects young women and markedly increases the prevalence of hypertension, and ultimately CV and renal disease, which are major causes of mortality in both this population and the U.S. Clinical data indicate that rates of obesity are increased in patients with SLE, and even in the absence of an overweight or obese body-mass index (BMI), patients with SLE have altered fat deposition and increased visceral adiposity compared to BMI-matched controls. This project will determine whether obesity in SLE leads to excess adipose tissue inflammation and elevated leptin levels that both promote B and T cell dysfunction, leading to disease pathogenesis and progression.

Title	Research Project 3: Basic Science and Clinical
Lead(s)	Michael Ryan, Ph.D.
Abstract	As noted above, SLE increases the prevalence of hypertension, and ultimately CV and renal disease; yet the mechanisms underlying the prevalent hypertension remain unclear. This project will determine whether a feedforward mechanism drives the generation of renal reactive oxygen species (ROS) during SLE, leading to impaired renal vascular function and increased tubular sodium reabsorption. This cycle involves the presence of neutrophil extracellular traps (NETs) that increase cell stress signals including high-mobility group protein 1 (HMGB1), TLR4 mediated mitochondrial dysfunction, and ROS production

Title	Career Enhancement Core
Lead(s)	Daria Ilatovskaya, Ph.D.
Abstract	The Career Enhancement Core will work to (1) develop a foundation for long-term relationships among the research, medical, and lay communities in Georgia, Mississippi, and South Carolina and (2) bring greater awareness to the risk of CVD in women and the consideration of SABV in the control of hypertension through education, mentorship, strategic partnerships, and training of community-engaged researchers. The CEC will develop and implement several programs and tools to increase awareness of the risks associated with CVD and uncontrolled hypertension, and will increase interest in the study of SABV. Such activities will include SABV Workshop for Researchers, SABV Mentoring Academy, training of undergraduate and medical students in how to perform SABV research, mini-sabbaticals for pre- and postdoctoral scholars to gain training in SABV-related techniques, pilot grants from early career investigators, outreach into local schools and colleges to increase awareness and promote SABV research opportunities, community engagement, a qualitative needs assessment to identify barriers to seeking/obtaining CV health care among at-risk women, a dedicated medical illustrator to develop educational materials on CVD across the health span of women, and a Blood Pressure Checks for Women campaign that will place BP monitoring equipment in nail and hair salons in Augusta and Athens, Ga., Columbia, S.C., and Jackson, Miss., to empower women to monitor their BP.

Title	Leadership Administrative Core
Lead(s)	Jennifer Sullivan, Ph.D. & Michael Ryan, Ph.D.
Abstract	The Leadership Administrative Core will provide vital support for all ROAR programmatic activities, ROAR Leadership and project investigators, faculty, and staff to ensure program success. This support will include (1) providing direction, oversight, support, and assessment of the entire program including the three research projects and the Career Enhancement Core, (2) coordinate communication and collaboration across the three ROAR institutions, and (3) work with the SCORE Consortium to maximize our impact, expand opportunities for trainees, and promote new collaborations in SABV in CVD.

Title	Brigham/Harvard Center for Reproductive Outcomes of Stress and Aging (ROSA)
Director(s)	Hadine Joffe, M.D., M.Sc (hjoffe@bwh.harvard.edu)
Abstract	Older women experience dramatic changes in the hypothalamic-pituitary-gonadal (HPG) axis and female reproductive hormones, producing vasomotor symptoms (VMS), sleep problems, cognitive changes, and cardiometabolic risks, which increase susceptibility to cardiovascular disease (CVD) and dementia. VMS occur in 85% of women and persist in one-third for 10+ years after menopause, potentially leading to prolonged disruption of quality of life, sleep disturbance, cardiometabolic risk, and extended VMS treatment, conferring further risk for CVD and dementia. Such health outcomes may also be influenced by stress exposures across the lifespan and during pregnancy, which may exert their effects through neural mechanisms. The Brigham and Women's Hospital (BWH) and Harvard Medical School (HMS) SCORE is advancing our understanding of stress exposures and neural regulation of reproductive aging health outcomes, and catalyzing growth of translational women's health and sex-differences research in aging women. We are pursuing novel translational science through three Projects.

Title	Research Project 1: Clinical Science
Lead(s)	Hadine Joffe, M.D., M.Sc., & Pamela Mahon, Ph.D.
Abstract	This project is defining evoked stress responsivity, stress-related activation of neural networks on functional brain imaging, and GABA concentrations as markers of VMS occurrence and persistence, including compounding effects of poor sleep and stress exposures.

Title	Research Project 2: Population Science
Lead(s)	Emily Oken, M.D., M.P.H., & Jorge Chavarro, M.D., M.S., Sc.D.
Abstract	This project is determining whether perimenopausal women with higher exposure to social stressors across the lifespan and physiological stressors across pregnancy have greater cardiometabolic risk and sleep-related, cognition-related, and neuropsychiatric symptoms.

Title	Research Project 3: Basic Science
Lead(s)	Ursula Kaiser, M.D., & Victor Navarro, Ph.D.
Abstract	This project is characterizing the role of kisspeptin, neurokinin, and dynorphin (KNDy) neurons and upstream GABAergic neurons in mediating the effects of stress and corticosteroids on the HPG axis, VMS, and sleep disturbances in a rodent model. These scientific efforts receive critical support from the site's cores.

Title	Sleep Resource Core
Lead(s)	Elizabeth Klerman, M.D., Ph.D.
Abstract	The Sleep Resource Core provides equipment for recording and expertise for the analysis of objective and subjective sleep metrics in human and animal research projects.

Title	Career Enhancement Core
Lead(s)	Kathryn Rexrode, M.D., M.P.H. (krexrode@bwh.harvard.edu), & Janet Rich-Edwards, M.P.H., Sc.D. (jr33@partners.org)
Abstract	This core is promoting early-career investigators interested in sex differences researchers by supporting scholars, pilot projects, travel exchange fellowships, and a robust educational program.

Title	Leadership Administrative Core
Lead(s)	Hadine Joffe, M.D., M.Sc., & JoAnn Manson, M.D., M.P.H., Dr.PH.
Abstract	This core provides scientific and administrative oversight and engages across the SCORE Consortium. Building on existing, fruitful collaborations, this outstanding interdisciplinary team of investigators—leaders in women's health, sleep medicine, neuroimaging, neuroendocrinology, stress science, cognition, cardiometabolic risk, and reproductive epidemiology—is leveraging robust resources at the Connors Center for Women's Health and Gender Biology and across synergistic women's health and sleep programs at BWH.

Title	The Microvascular Aging and Eicosanoids - Women's Evaluation of Systemic Aging Tenacity (MAE-WEST) ("You are never too old to become younger!") Specialized Center of Research Excellence
Director(s)	Noel Bairey Merz, M.D. (Noel.BaireyMerz@cshs.org), & Susan Cheng, M.D., M.P.H., M.M.Sc. (susan.cheng@cshs.org)
Abstract	The Cedars-Sinai Medical Center (CSMC) SCORE Program proposes that sexual dimorphism in both local and systemic eicosanoid variation contributes to sex differences in microvascular dysfunction and, in turn, to sex differences in age-related multi-organ disease. Motivated by MAE-WEST's early findings and the need to understand the determinants and drivers of sex differences in age-related disease outcomes, the goal is to form a robust and sustainable structure of academic activities centered on systematically interrogating sex differences in the relationships among eicosanoids, microvascular dysfunction, and age-related end-organ disease, with an initial focus on the microvascular aging effects on brain, heart, and kidney function. The overarching objective of MAE-WEST is to enhance our understanding of sex differences in microvascular and chronic multi-organ diseases and, in turn, enable effective interventions through interdisciplinary science, education, and advocacy.

Title	Research Project 1: Population Science
Lead(s)	Susan Cheng, M.D., M.P.H., M.M.Sc.
Co-I(s)	Priya Palta, Ph.D., M.H.S., & Eugene Rhee, M.D.
Abstract	The goal of Project 1 is to examine longitudinal variation in circulating eicosanoid levels in relation to age-related alterations in microvascular function in end-organ (cardiovascular, neurocognitive, renal) disease traits in large-community cohorts.

Title	Research Project 2: Clinical Science
Lead(s)	Noel Bairey Merz, M.D.
Co-I(s)	Chrisandra Shufelt, M.D., Janet Wei, M.D., Carl Pepine, M.D., Eileen Handberg, Ph.D., ARNP, Michael Nelson, Ph.D., M.S., & Jeffrey Wertheimer, Ph.D.
Abstract	The goal of Project 2 is to prospectively enroll and deeply phenotype a cohort of women and men to assess the relation of eicosanoids with organ-specific and global burden of microvascular disease, as well as their response to a trial of intensive medical therapy with Food and Drug Administration–approved agents (statins and ACEIs/ARBs).

Title	Research Project 3: Basic Science
Lead(s)	John Shyy, Ph.D.
Co-I(s)	Sonia Sharma, Ph.D.
Abstract	The goal of Project 3 is to study the mechanistic role of sex-specific eicosanoid signaling on human endothelial cell function and on microvascular function in experimental models of organ-specific disease as well as whole organism aging.

Title	Biostatistics & Informatics Core
Lead(s)	Susan Cheng, M.D., M.P.H., M.M.Sc., & Andre Rogatko, Ph.D.
Co-I(s)	Marcio Diniz, Ph.D.
Abstract	The Biostatistical & Bioinformatics Core provides dedicated end-to-end support and resources for efficiently managing and analyzing eicosanoids data generated from diverse human, animal, and cell biospecimens in relation to microvascular aging traits across the Cedars-Sinai SCORE site, including both project work and trainee pilot studies. While leveraging the expertise offered by an exceptional group of statistical epidemiologists, biostatisticians, bioinformaticians, and data scientists, the core activities are integrated with complementary resources across the SCORE site.

Title	Eicosanoids Profiling Core
Lead(s)	Mohit Jain, M.D., Ph.D.
Co-I(s)	Jeramie Watrous, Ph.D.

Abstract	The Eicosanoids Profiling Core provides dedicated high-throughput mass spectrometry eicosanoid profiling services for the diverse human, animal, and cell biospecimens that will be generated from across the SCORE site's studies. The core is specifically optimized to enable the application of robust and reproducible measure of up to 500 eicosanoids per sample across thousands of samples from any given project. Additionally, the core provides an accurate and unified framework for standardizing and integrating high-dimensional eicosanoids data across multiple projects. While leveraging the expertise offered by an exceptional group of analytical chemists, mass spectrometrists, structural biologists, and computational biologists, the core activities are integrated with complementary resources across the SCORE site.

Title	Career Enhancement Core
Lead(s)	Noel Bairey Merz, M.D. (Noel.BaireyMerz@cshs.org)
Co-I(s)	Mariko Ishimori, M.D., Joshua Pevnick, M.D., & Denis Magoffin, M.D.
Abstract	The Cedars-Sinai Career Enhancement Core provides mentoring from a diverse body of high-caliber faculty mentors who bring scientific expertise and career mentoring experience from across multiple fields and institutions. The core also facilitates all trainee projects using services and resources available from across an inter-institutional collaborative. The core centers all activities on the overarching goal of developing the next generation of translational investigators equipped to lead the discovery and implementation of interventions aimed at eliminating sex disparities in health, in sync with the goals of both this SCORE site and the overarching mission of the SCORE program as a whole. The core also serves as a hub for education in and dissemination of innovative translational research methods, results, and best practices for scientific and clinical audiences at large.

Title	Emory Specialized Center of Research Excellence (SCORE) on Sex Differences
Director(s)	Igho Ofotokun, M.D. (iofotok@emory.edu), and Cecile Lahiri, M.D., MSc (cdelill@emory.edu)
Abstract	The Emory SCORE is focused on the influence of biological sex on microbial–host–pathogen interactions, using HIV as a model for probing the nature of these interactions. The working hypothesis is that HIV-induced inflammation co-acts with that induced by estrogen insufficiency to heighten the inflammatory state among women living with HIV, thereby worsening age-related comorbidities in this population. The long-term goal of the Emory SCORE is to develop a program to serve as a regional hub for studying the influence of biological sex on the outcomes of infectious diseases and for promoting the normalization of sex as a biological variable (SABV) in research.

Title	Neuro–hypothalamic–pituitary–adrenal axis
Lead(s)	Gretchen Neigh, Ph.D., and Vasiliki Michopoulos, Ph.D.
Abstract	The goal of the project is to identify factors contributing to HIV-associated chronic inflammation in women. These studies are critical for providing the framework needed to design therapeutic strategies aimed at resolution of the chronic inflammation in women living with HIV.

Title	Musculoskeletal
Lead(s)	M. Neale Weitzmann, Ph.D., and Igho Ofotokun, M.D.
Abstract	The project will test the hypothesis that enhanced fracture risk observed in women living with HIV is caused by the collision between HIV/antiretroviral therapy–induced inflammation and that induced by estrogen insufficiency as women living with HIV age.

Title	Cardiovascular
Lead(s)	Arshed Quyyumi, M.D., and Leslee J. Shaw, Ph.D.
Abstract	The goal of the project is to assess the combined immune effects of HIV and estrogen status described in Project 1 and Project 2 on cardiovascular health as assessed by endogenous reparative/regenerative capacity (circulating progenitor cells) and the development/progression of subclinical coronary (CT angiography) and carotid artery (MRI) atherosclerosis in women living with HIV compared with HIV-negative controls.

Title	Career Enhancement Core
Lead(s)	Marcia Holstad, Ph.D. (nurmmcd@emory.edu), and Kelli Stidham Hall, Ph.D. (kelli.s.hall@emory.edu)
Abstract	The role of the Career Enhancement Core (CEC) is to prepare the next generation of women's health researchers to capitalize on Emory's considerable strengths in prevention science, infectious disease research, clinical and translational research, basic immunology, and antiviral drug development within the context of the National Institutes of Health's (NIH) recently outlined steps to promote sex considerations in the design and conduct of all research, including the basic sciences.

Title	Sex and Age Differences in Immunity to Influenza (SADII)
Director(s)	Sabra L. Klein, Ph.D. (sklein2@jhu.edu)
Abstract	The Sex and Age Differences in Immunity to Influenza (SADII) SCORE is positioned to transform our understanding of the role of biological sex, gender, and aging on immune responses to influenza vaccination, which has global public health implications, affecting millions of people worldwide. The overarching hypothesis: Female-biased vaccine-induced immunity to influenza viruses is age-dependent and reflects both hormonal and genetic differences between the sexes that impact immune responses (i.e., both effector and memory) to influenza vaccine antigens. The SADII SCORE brings together investigators focused on (1) seasonal influenza vaccination in an existing age- and sex-stratified human population, (2) animal models that can test hypotheses and mechanisms of action that are inferred from studies in human populations, and (3) the contributions of age, frailty, sex, and gender to vaccine outcomes using quantitative and qualitative statistical models.

Title	Sex differences in longitudinal humoral immunity against influenza in the frail elderly
Lead(s)	Dr. Sean Leng
Abstract	This research project is led by Dr. Sean Leng, in collaboration with the Johns Hopkins University Older Americans Independence Center. The goal of this project is to provide a detailed analysis of sex and gender differences in humoral immunity and adverse reactions to seasonal influenza vaccines in combination with age and frailty in an existing longitudinal cohort of older individuals.

Title	Sex differences in immune responses to vaccine and circulating strains of influenza in health care workers
Lead(s)	Dr. Andrew Pekosz
Abstract	This research project is led by Dr. Andrew Pekosz, in collaboration with the Johns Hopkins Center of Excellence in Influenza Research and Surveillance (JH-CEIRS). The study will characterize the number and transcriptional activity of B cells, as well as humoral immune responses and adverse reactions, following receipt of seasonal influenza vaccines. The study will be focused on men and women between the ages of 18 and 45, to provide an age- and sex-stratified cohort to assess sex differences in vaccine responses among adults.

Title	Genetic and hormonal mechanisms of sex differences in immune responses and influenza vaccine efficacy in young and aged mice
Lead(s)	Dr. Sabra Klein
Abstract	This research project is led by Dr. Sabra Klein. The goal of the project is to uncover the genetic, hormonal, and age-associated changes in B cells that mediate sex and age differences in vaccine-induced immunity to influenza. This will be accomplished by a systematic evaluation of the effects sex hormones and genes encoded by sex chromosomes have on the antibody response to influenza vaccination.

Title	Career Enhancement Core
Lead(s)	Wendy Bennett, M.D. (wendy.bennett@jhmi.edu)

Abstract

The SADII Career Enhancement Core (CEC) is led by Dr. Wendy Bennett, in collaboration with the Johns Hopkins Center for Women's Health, Sex, and Gender Differences. Aims include: Providing collaboration, networking, dissemination, and mentoring opportunities; Providing pilot grant funding for early-stage investigators (i.e., investigators at the level of assistant professor or below), with emphasis on diversity of candidates, interested in incorporating sex differences into their clinical, translational, or basic science research in the broad area of immunology (e.g., asthma and allergy, autoimmunity, cancer, infectious diseases, inflammation, microbiome, and vaccines); Integrating educational opportunities focused on teaching skills and methods for incorporating sex as a biological variable and gender considerations when planning, analyzing, and reporting data, as well as research dissemination activities in regard to a broad range of existing training programs (e.g., KL2 and BIRCWH programs); Evaluating the effectiveness of the SADII CEC in expanding learning opportunities, dissemination of sex and gender research, mentorship, and funded research

Title	Sex Differences in Major Depression: Impact of Prenatal Stress- Immune and Autonomic Dysregulation
Director(s)	Jill M. Goldstein, Ph.D. (jill_goldstein@hms.harvard.edu), & Stuart Tobet, Ph.D. (Stuart.Tobet@ColoState.EDU)
Abstract	The scientific mission of the Massachusetts General Hospital–Harvard Medical School SCORE site is to identify stress–immune pathway abnormalities, beginning in fetal development, that have shared adverse consequences for sex differences in brain circuitry regulating mood, stress, and risk for major depressive disorder (MDD) comorbid with autonomic and neurovascular dysfunction and cardiovascular disease risk in midlife. It is facilitating transdisciplinary, translational collaborations among basic and clinical investigators to enhance our understanding of the impact of sex on MDD and central and peripheral autonomic and vascular function and develop a novel noninvasive neuromodulation therapeutic targeted to the neural–cardiac interface in a sex-selective manner. Further, it aims to serve as an interdisciplinary resource to train and disseminate findings about sex differences in MDD, autonomic dysregulation, and cardiovascular risk to the scientific and medical communities, policymakers, and the public.

Title	Impact of Sex on Prenatal Stress-Immune Programming of Depression and Autonomic Dysregulation
Lead(s)	Jill M. Goldstein, Ph.D.
Abstract	The goal of the project is to test the hypothesis that immune pathway abnormalities beginning in fetal development are associated with sex-dependent impacts on the stress response circuitry in the brain that result in lifelong recurrent MDD and with dysregulation of hormonal and immune responses to stress and autonomic and neurovascular dysfunction in midlife. This is possible, given the unique 60-year-plus follow-up of a prenatal cohort of offspring now turning 57–62 years of age in whom the researchers conduct adult multi-modal imaging and deep clinical phenotyping and assays of blood-based biomarkers in prenatal development and midlife.

Title	Sex-Dependent Impact of Transcutaneous Vagal Nerve Stimulation on the Stress Response Circuitry and Autonomic Dysregulation in Major Depression
Lead(s)	Vitaly Napadow, Ph.D., & Ronald G. Garcia, M.D., Ph.D.
Abstract	This project will test the hypothesis that expiratory-gated transcutaneous vagus nerve stimulation (tVNS) can effectively modulate specific brain stem–cortical pathways of the stress response circuitry and attenuate cardiophysiologic and neurovascular dysfunction in recurrent MDD in a sex-dependent manner. Case subjects in project 1 will be assessed in project 2, as well.

Title	Sex Differences in Fetal Programming by Glucocorticoids: Adult Hypothalamus and Autonomic Nervous System
Lead(s)	Stuart A. Tobet, Ph.D., and Taben Hale, Ph.D.
Abstract	The overall goal of this project is to identify the cellular and physiological pathways that are affected by overexposure to glucocorticoids (or maternal stress) and implicated in long-term, sex-selective alterations in anxiety- and depressive-like behaviors, neuroendocrine function, and autonomic (e.g., cardiovascular) responses to stress in the offspring. Results will identify brain regions or vasculature and their connectivity that are responsible for the sex-biased developmental alterations in behavioral, endocrine, and autonomic responses in adulthood. Causal mechanisms involving the renin-angiotensin system will be specifically tested. Further, the project will evaluate the use of a tVNS device (in parallel to project 2) to restore autonomic function and behavioral responses in adult rats that were exposed to stress in utero.

Title	Resource Support Core

Lead(s)	Vitaly Napadow, Ph.D., & Hang Lee, Ph.D
Abstract	The Resource Support Core (RSC) will provide infrastructure and tools to enable a cohesive approach to the collection, analysis, storage, and sharing of data across the SCORE site's projects. The RSC will also provide expert support in areas such as biostatistics, transcutaneous vagus nerve stimulation, and advanced autonomic and neuroimaging analyses. Establishing a unified approach will enhance the quality of all studies, allowing each project to inform the others in potentially significant ways and enabling valuable exploratory analyses through the pooling of data and translations between human and animal studies.

Title	Career Enhancement Core
Lead(s)	Stuart A. Tobet, Ph.D. (stuart.tobet@colostate.edu), Joshua Roffman, M.D.(jroffman@mgb.org), Jordan W. Smoller, M.D., Sc.D.(jsmoller@mgb.org), and Albert Hofman, M.D., Ph.D. (ahofman@hsph.harvard.edu)
Abstract	The Career Enhancement Core (CEC) will contribute to training the next generation of scientists and clinician-scientists as leaders in the fields of women's health and sex differences in medicine. They will be empowered to contribute to understanding sex-dependent vulnerabilities to mood and anxiety disorders and associated cardiometabolic diseases. To enhance the careers of SCORE trainees, the CEC will specifically (1) integrate levels of training and thought about etiologic mechanisms at basic and clinical levels for sex differences and for gender and health disparities at the policy level, (2) mentor trainees from a team perspective that exposes them to different levels of analysis from mentors with complementary expertise, (3) provide access to material and faculty resources that will enhance the success of the candidates, and (4) provide seed funding to supplement work with preclinical studies that will ultimately translate to human studies.

Title	Sex-Specific Effects of Endocrine Disruption on Aging and Alzheimer's Disease
Director(s)	Kejal Kantarci, M.D., M.S. (kantarci.kejal@mayo.edu) and Michelle M. Mielke, Ph.D. (mmielke@wakehealth.edu)
Abstract	The Mayo Clinic Specialized Center of Research Excellence (SCORE) on Sex Differences promotes interdisciplinary approaches to advancing translational research on sex differences in health and disease. Research bridges results from basic science projects to clinical studies. The goal of the Mayo Clinic SCORE on Sex Differences is to understand how female-specific conditions associated with major hormonal shifts (e.g., menarche, pregnancy, and menopause) affect physical and cognitive decline in women as they age. During the first funding period (2012–2018), the Mayo Clinic SCORE's research focused on how the sex-specific conditions of hypertensive pregnancy disorders and natural menopause, with and without menopausal hormone therapy, affected the risk of cardiovascular disease and cognitive decline. In this renewal application, the Mayo Clinic SCORE will extend these investigations to an extreme model of endocrine disruption: premenopausal bilateral salpingo-oophorectomy (BSO). About 1 in 8 women in the United States undergo BSO before reaching natural menopause. Although premenopausal BSO confers protection against ovarian cancer, it is associated with increased all-cause mortality, dementia, Alzheimer's disease (AD) pathology, cardiovascular disease, skin aging, and sexual dysfunction. Given the large number of aging women with a history of premenopausal BSO, there is an urgent need to understand the long-term physical and cognitive outcomes to empower women considering prophylactic BSO to make more informed decisions. The central hypothesis of the Mayo Clinic's SCORE renewal is that the abrupt endocrine disruption caused by premenopausal BSO will accelerate pathological aging processes that manifest as reductions in physical and cognitive function and in AD. This hypothesis will be tested through three interrelated translational projects, which are supported by three interdependent cores.

Title	Effects of bilateral salpingo-oophorectomy on physical and cognitive aging
Lead(s)	Michelle M. Mielke, Ph.D.
Co-I(s)	Walter A. Rocca, M.D., Julie A. Fields, Ph.D., and Nathan K. LeBrasseur, Ph.D.
Abstract	The primary objective of Project 1 is to determine whether premenopausal bilateral salpingo-oophorectomy (BSO) is associated with accelerated aging as measured by a higher frailty score, a greater decline in physical and cognitive function, and higher plasma levels of senescence-associated secretory phenotype (SASP) proteins compared with referents. The SASP proteins are also used as the primary aging biomarker in Project 3.

Title	Effects of bilateral salpingo-oophorectomy on imaging biomarkers of Alzheimer's disease and cerebrovascular diseases
Lead(s)	Kejal Kantarci, M.D.
Co-I(s)	Kent R. Bailey, Ph.D.
Abstract	The primary objective of Project 2 is to assess the effects of premenopausal bilateral salpingo-oophorectomy (BSO) on neuroimaging measures of Alzheimer's disease and cerebrovascular pathology and to determine whether APOE-ε4 modifies these effects. In addition, the relationship between the neuroimaging biomarkers and the cognitive outcomes measured in Project 1 will be determined.

Title	Effects of bilateral ovariectomy on the biology of physical and cognitive aging in mice
Lead(s)	Nathan K. LeBrasseur, Ph.D.
Co-I(s)	Marissa J. Schafer, Ph.D., and Sundeep Khosla, M.D.

Abstract	As a mechanistic complement to the human projects, Project 3 will use mice, with the primary objective of determining the effects of ovariectomy (OVX) on cellular senescence, senescence-associated secretory phenotype (SASP), and measures of physical and cognitive function that parallel those in Projects 1 and 2. In addition, the temporal sequence and tissue-specific effects of estrogen replacement therapy on cellular senescence will be determined.

Title	Resource Support Core - Clinical
Lead(s)	Ekta Kapoor, M.B.B.S.
Abstract	The Resource Support Core – Clinical will provide centralized, coordinated support, management, and oversight for the human studies of the SCORE (Projects 1 and 2). Specific functions include recruiting, screening, consenting, and enrolling study participants; coordinating and completing clinical and neuroimaging visits; and maintaining and managing a shared database.

Title	Career Enhancement Core
Lead(s)	Virginia M. Miller, Ph.D. (miller.virginia@mayo.edu)
Abstract	The Career Enhancement Core (CEC) will provide career enrichment, leadership training, and funds to support ancillary studies of the main projects to stimulate new interest in sex differences and women's health. The Mayo Clinic SCORE will serve as a vital hub for education and dissemination of innovative sex-based translational research methods, results, and best practices. The Mayo Clinic SCORE's integrated approach for research, training, and education is consistent with the goals of the SCORE on Sex Differences program and ensures continuing research in areas of women's health and sex differences by training the workforce of the future.

Title	MUSC Specialized Center of Research Excellence on Sex Differences
Director(s)	Aimee L. McRae-Clark, Pharm.D. (mcraeal@musc.edu), and Kevin Gray, M.D. (raykm@musc.edu)
Abstract	The MUSC Specialized Center of Research Excellence (SCORE) on Sex Differences has been highly productive for 20 years. In addition to convening a multidisciplinary group of investigators to work closely together to explore sex differences in substance use disorders and the relationship between stress and drug use, the MUSC SCORE has provided a fertile training ground for new investigators and has attracted senior investigators to apply their skills to sex-specific research. The specific aims of this SCORE are to support and enhance translational scientific collaborations among the investigators conducting primary and pilot research projects, catalyze further growth of interdisciplinary sex-based research on the MUSC campus, continue foundational research training for early-career investigators dedicated to sex-focused translational research, and promote strategic partnerships to enhance the translation and dissemination of SCORE findings and other relevant research to improve health outcomes. During the renewal period, we are continuing to reach across the MUSC campus, South Carolina, and the nation through cross-SCORE collaborations and other initiatives focused on dissemination of research findings to improve health outcomes. The science within our research group includes four tightly integrated research projects. To address critical public health needs, these research projects investigate sex differences in cannabis use disorders across the lifespan, focusing on populations with recent rapid increases in cannabis use and potential vulnerability to sex-disparate harms of cannabis (i.e., emerging adults, postpartum women, and older adults).

Title	Sex differences in the interface between cannabis use and stress among emerging adults
Lead(s)	Kevin Gray, M.D. and Rachel Tomko, Ph.D.
Abstract	The interface between cannabis use and stress is a particularly important focus for sex differences research in emerging adults. Given the dynamics at play during this critical stage when cannabis use is most prevalent, developmentally informed research is needed to guide tailored clinical interventions. This study applies rigorous and innovative methods to elucidate sex differences in the nexus of cannabis use and stress among emerging adults with cannabis use disorder to guide the development of tailored treatments.

Title	Impact of stress and craving on return to cannabis use in postpartum women
Lead(s)	Kathleen Brady, M.D., Ph.D., and Connie Guille, M.D.
Co-I(s)	Roger Newman, M.D.
Abstract	Although most women who use cannabis will reduce their cannabis use during pregnancy, almost all women will return to cannabis use postpartum. Longitudinal studies are needed to examine the relationships between stress, progesterone, and return to cannabis use in postpartum women. This study will help to inform the development of targeted interventions that prevent postpartum return to cannabis use and improve women's health.

Title	Sex differences in risk of cognitive decline in older cannabis users
Lead(s)	Aimee McRae-Clark, Pharm.D. and Andreana Benitez, Ph.D.
Abstract	Cannabis is the most frequently used illicit substance by older adults, and its use among persons ages 50+ is rising. Little is known about the potential harms of cannabis use in this population, such as the impact on cognitive decline and risk for Alzheimer's disease and related dementias, and whether sex differences in stress and hormones influence these risks. This project will study cannabis-using older men and women to answer these questions to inform public health messaging on cannabis use and to identify potential clinical interventions for older adults.

Title	Preclinical component
Lead(s)	Rachel Penrod-Martin, Ph.D.
Co-I(s)	Onder Albayram, Ph.D.

Abstract	Legalization of cannabis products for recreational use has increased rates of cannabis use and cannabis use disorder across multiple vulnerable groups, including adolescents/young adults, pregnant women, and older adults. Despite legalization, the neurobiological impacts of acute and chronic cannabis use, and how they are affected by sex and age, largely remain uninvestigated. This component, and the associated Clinical Projects 1-3, will investigate how the active components of cannabis impact learning and memory, relapse behavior, and brain function at the molecular level in vulnerable populations.

Title	Career Enhancement Core
Lead(s)	Kathleen T. Brady, M.D., Ph.D. (bradyk@MUSC.EDU)
Abstract	The SCORE Career Enhancement Core (CEC) provides a formal, intensive program of mentored clinical and translational research training and career development activities to promote junior scholars in the area of sex-based clinical and translational research focused on the impact of stress on human health. Training scientists with an understanding of the role of sex in the etiology and pathophysiology of specific disease states will enable optimization of the personalized approaches to diagnosis and treatment that are essential to improving the health of both men and women.

Title	Leadership Administrative Core
Lead(s)	Aimee McRae-Clark, Pharm.D.
Abstract	The Leadership Administrative Core (LAC) is the hub of the MUSC SCORE, serving as the central coordinating point for all SCORE activities. It influences each of the research projects and Center cores and brings together the various components to form a cohesive, functioning unit. The LAC also oversees SCORE outreach, collaboration, and evaluation efforts.

Title	Biostatistical Resource Core
Lead(s)	Nathaniel Baker, M.S. and Brian Neelon, Ph.D.
Co-I(s)	Rachel Tomko, Ph.D.
Abstract	The Biostatistical Resource Core provides centralized support to the entire MUSC SCORE team of investigators and strives to promote synergy in terms of study design and analyses across projects and other shared resources. It also contributes to the career enhancement mission of the MUSC SCORE.

Title	Sex Differences in Cardiometabolic Health and Disease
Director(s)	Karen Reue , Ph.D. (reuek@g.ucla.edu)
Abstract	The objective of our SCORE on “Sex Differences in Cardiometabolic Health and Disease” is to identify factors that determine sex-specific cardiometabolic disease risk, which may lead to better diagnosis and treatment for both sexes. A unique feature of our program is the investigation of sex differences from multiple perspectives, including effects of estrogen, of XX vs. XY sex chromosome genes, and of genetic variation among individuals. Our program consists of three research projects and three cores, and employs preclinical mouse models, human induced pluripotent stem cell lines (iPSCs), and existing human population datasets (genomic, transcriptomic, proteomic, and metabolomic) to translate findings from our model systems to humans.

Title	Epigenetic sex determinants of cardiometabolic disease and prevention
Lead(s)	Karen Reue, Ph.D.
Abstract	Sex impacts the development of obesity and related cardiometabolic disorders. Sex also influences adverse responses to statin drugs, which are widely prescribed to prevent cardiovascular disease. We have identified genes on the sex chromosomes (X and Y) that have differential expression levels between males and females and impact cardiometabolic traits. We will define the mechanisms by which sex-biased action of these genes influences adipocyte biology, whole body energy balance, and statin-related adverse effects. Results will provide potential targets for intervention in cardiometabolic disease and adverse drug effects.

Title	Gene-by-sex interactions in heart failure with preserved ejection fraction (HFpEF)
Lead(s)	Jake Lusis, Ph.D.
Abstract	This project seeks to understand the mechanisms underlying increased prevalence of HFpEF in women compared to men. Using a “systems genetics” approach and a panel of genetically distinct mouse strains, the goals are to understand sex differences in HFpEF traits at the molecular level, including the role of gonadal hormones and sex chromosomes, and to create sex-specific biologic networks that can be generalized to humans. Recent findings implicate sex differences in the action of a mitochondrial enzyme as causal for HFpEF, and further studies will characterize the role of mitochondrial dysfunction in HFpEF.

Title	The impact of estrogen receptor alpha on cardiomyocellular metabolism and health
Lead(s)	Andrea Hevener, Ph.D.
Abstract	Reductions in estrogen receptor alpha are associated with cardiometabolic disease risk in women and men. This project will test the hypothesis that estrogen receptor alpha action in cardiomyocytes impacts mitochondrial metabolism, cardiac tissue integrity, and heart function. We will address this hypothesis with conditional cardiomyocyte-specific estrogen receptor alpha knockout and overexpression mouse models. Our findings will then be integrated with human data in collaboration with our Human Translational Bioinformatics Core.

Title	Human Translational Bioinformatics Core
Lead(s)	Hooman Allayee, Ph.D.

Abstract	The research projects in our SCORE utilize model systems (inbred and genetically modified mouse strains, human induced-pluripotent stem cells) to study mechanisms of sex differences in cardiometabolic disease. The Human Translational Bioinformatics Core will serve as a hub for computational and in silico analyses that translate data from model systems to cardiometabolic traits in humans using established analytical pipelines and large human multi-omics datasets from multi-ancestry cohorts.

Title	Career Enhancement Core
Lead(s)	Lead: Arthur P. Arnold, Ph.D. (arnold@ucla.edu) and Stephanie Correa, Ph.D. (stephaniecorrea@g.ucla.edu)
Abstract	The Career Enhancement Core proposes an integrated set of educational and research support activities to foster development of research in women's health and sex as a biological factor, especially related to sex differences in cardiometabolic disease. The CEC will administer a Pilot & Feasibility grant program for post-doc and faculty researchers, and will educate undergraduate and graduate student researchers about sex as a biological factor through courses, a hands-on laboratory 'bootcamp,' and a curated video library.

Title	Sex Related Differences in Brain Gut Microbiome Interactions in Irritable Bowel Syndrome
Director(s)	Emeran Mayer, M.D. (emayer@ucla.edu), & Lin Chang, M.D. (linchang@mednet.ucla.edu)
Abstract	This SCORE proposal aims to gain a better understanding of the role of the gut microbiome and female sex hormones in the modulation of brain–gut microbiome interactions in two of the most common disorders of the gastrointestinal tract, irritable bowel syndrome (IBS) and chronic functional constipation. These disorders are more prevalent in women than men, and their pathophysiology is not completely understood. While there are some treatments available to treat symptoms, the majority of patients report lack of satisfaction with current treatments. The proposed studies will compare brain–gut microbiome interactions in (1) women with IBS and healthy women during low estrogen states (perimenstrual, postmenopausal), (2) women and men with IBS and healthy women and men, and (3) premenopausal women with normal and slow transit constipation and healthy women. In addition, the proposed studies will study gut microbial and brain mechanisms underlying the effectiveness of cognitive behavioral therapy in women and men with IBS. Results obtained from the proposed studies are likely to provide significant insights on the pathophysiology and treatment of these disorders.

Title	The primary objective of this project is to examine the role of brain–gut microbiome interactions in mediating IBS and constipation symptoms during menses and menopause
Lead(s)	Lin Chang, M.D., & Arpana Gupta, Ph.D.
Abstract	This grant will provide new insights into the pathogenesis of IBS and normal transit constipation (symptoms of constipation in the absence of changes in transit or defecation), which are highly prevalent gastrointestinal disorders that occur more commonly in women and are associated with a significant health care and economic burden, decreased quality of life, and lack of satisfactory treatment. The proposed studies expand novel insights gained from our preliminary data into the role of sex as a biological variable in altered brain–gut microbiome interactions and clinical symptoms of IBS and normal transit constipation. These insights have the potential to identify endophenotypes within women with IBS and chronic constipation that can lead to the development of novel treatment approaches.

Title	Sex-related differences in structure, function, and connectivity of central arousal and salience networks involving brain stem nuclei are involved in IBS symptom generation
Lead(s)	Jennifer Labus, Ph.D., & Benjamin Ellingson, Ph.D.
Abstract	Even though IBS is now considered a brain–gut disorder, the underlying biological mechanisms and the role of sex-related differences are not completely understood. By studying men and women with IBS and healthy women and men, we propose to study sex-related differences in the structure and function of brain networks that are relevant for IBS and to characterize the modulation of these networks by gut microbial metabolites and estrogen. The results from the proposed studies are likely to identify novel targets for IBS drug development, with particular relevance for female patients.

Title	The primary object of this project is to examine sex-related differences in the effect of cognitive behavioral therapy on emotional arousal and salience circuits and the role of the gut microbiome.
Lead(s)	Emeran Mayer, M.D., & Bruce Naliboff, Ph.D.
Abstract	Cognitive behavioral therapy is an effective treatment for IBS, but the biological mechanisms underlying its effectiveness and the role of biological sex are not known. The proposed study aims to examine the role of the gut microbiome and its interactions with brain and brain stem regions, as well as clinical and behavioral variables, and determine the role of biological sex in these interactions and in clinical outcomes. The results from this study have the potential to identify subgroups of patients highly responsive to therapy, as well as underlying biological mediators.

Title	Data Processing and Analysis Core

Lead(s)	Arpana Gupta, Ph.D., Jennifer Labus, Ph.D., & Jonathan Jacobs, M.D., Ph.D.
Co-I(s)	Lisa Kilpatrick, Ph.D., & Swapna Joshi, Ph.D.
Abstract	The Data Processing and Analysis Core will provide the advanced microbiome, metabolomics, and neuroimaging tools and technologies necessary to analyze the interactions of neurobiological and molecular mechanisms underlying the brain–gut microbiome axis, sex differences in this system, the influence of hormones on this system, and how cognitive behavioral therapy alters this system. Elucidation of brain–gut microbiome pathways cannot be achieved by analysis of microbiome and neuroimaging data sets in isolation. Integration of these distinctive omics data sets to find biologically meaningful relationships represents a frontier in bioinformatics that will be critical to identifying novel diagnostic and therapeutic targets for IBS.

Title	Career Enhancement Core
Lead(s)	Emeran Mayer, M.D. (emayer@ucla.edu), & Lin Chang, M.D. (linchang@mednet.ucla.edu)
Abstract	The Career Enhancement Core (CEC) will be responsible for implementing innovative programs to enhance collaborations, training, education, recruitment of new investigators, and community outreach. The CEC will oversee the pilot and feasibility programs to provide seed grant funding, the recruitment and mentoring of young investigators, organization of educational conferences, and community outreach. Involvement of underrepresented minority students and trainees in research on women's health and sex as a biological variable will be encouraged. The CEC will closely interact with UCLA's Sex Differences in Metabolism SCORE.

Title	Bioenergetic and Metabolic Consequences of the Loss of Gonadal Function
Director(s)	Wendy M. Kohrt , Ph.D. (Wendy.Kohrt@ucdenver.edu)
Abstract	The overarching scientific goal of the SCORE is to address gaps in knowledge of the impact of gonadal aging on the regulation of energy homeostasis and metabolism by conducting mechanistically driven research across the basic-to-clinical translational spectrum. The scientific premise is that gonadal aging, through the accompanying decline in sex hormones, mediates biological changes that increase risk for chronic disease. Importantly, because gonadal failure is inevitable in women in mid-life, but rare in men until much later in life, this meets the objective of the SCORE Program to study sex differences that impact women's health. A new scientific focus in the current award period is on the tryptophan-kynurenine (TRP-KYN) pathway because of the emerging evidence that it regulates energy homeostasis, metabolic function, and the aging process. The overarching educational objective is to engage new investigators in research aligned with the focus of the SCORE. The SCORE will provide mentored career development and training on how to conduct research that appropriately addresses sex as a biological variable.

Title	Cardiometabolic Consequences of the Loss of Ovarian Function
Lead(s)	Kerrie Moreau, Ph.D.
Co-I(s)	Daniel H. Bessesen, M.D., Edward L. Melanson, Ph.D., Kerrie L. Moreau, Ph.D., and Margaret E. Wierman, M.D.
Abstract	Project 1 will determine novel mechanisms by which the loss of ovarian function contributes to vascular endothelial dysfunction and increased abdominal visceral adipose tissue (VAT) in women. We contend that ovarian estradiol (E2) withdrawal impairs endothelial function 1) directly through increasing reactive oxygen species (ROS) and inflammation and reducing NO bioavailability, and 2) indirectly through the accumulation of abdominal VAT and the release of adipose tissue-derived adipokines. Additionally, because of emerging evidence for the role of TRP-KYN in cardiometabolic dysfunction and the aging process, the project will investigate whether dysregulation of systemic and tissue-specific TRP-KYN metabolism mechanistically contributes to increased abdominal VAT and vascular endothelial dysfunction with E2 withdrawal.

Title	Suppression of ERα Signaling in HSCDAs Increases Adiposity via KYN, AhR
Lead(s)	Dwight Klemm, Ph.D.
Abstract	Recent evidence suggests that diet-induced obesity requires the interaction between the metabolic intermediate, kynurenine (KYN), and its aryl hydrocarbon receptor (AhR). Preliminary SCORE data show that the enzyme that catalyzes KYN production in adipose tissue, indoleamine dioxygenase 1 (IDO1), and AhR are expressed at significantly higher levels in hematopoietic stem cell-derived adipocytes (HSCDAs) than in conventional mesenchymal stem cell-derived adipocytes. Project 3 will investigate whether the loss of estrogen signaling via ERα stimulates the production of HSCDAs and their subsequent production of KYN and AhR, and promotes weight gain, increased adiposity, and related metabolic dysfunction.

Title	Career Enhancement Core
Lead(s)	Judith G. Regensteiner, Ph.D. (JUDY.REGENSTEINER@CUANSCHUTZ.EDU)

Abstract

The Career Enhancement Core (CEC) of the Colorado SCORE is focused on providing career enhancement for researchers in the innovative, growing field of sex differences research. The objectives of the CEC are to 1) develop and support a cadre of accomplished early career researchers in the thematic focus of the SCORE, and 2) provide a curriculum that meets the career enhancement needs of early career faculty scientists focused on translational science in the study of sex differences. Objective 1 will be carried out by selecting a SCORE Scholar through peer review who will be focused on developing a career in sex differences research. The SCORE Scholar will have at least 75% protected research time and project support. In addition, relevant pilot projects will be awarded (by peer review) to 2 to 4 promising scientists per year. For Objective 2, SCORE Scholars and Pilot Awardees will participate in an innovative career enhancement program including team mentoring, hands-on research experience and curricular training in academic skills, career development skills and methods by which to study sex differences from the Ludeman Family Center for Women's Health Research as well as a weekly works in progress session run by the Investigations in Metabolism, Aging, Gender, and Exercise (IMAGE) group of the Colorado Multidisciplinary Center on Aging.

Title	Yale-SCORE on Sex Differences in Alcohol Use Disorder
Director(s)	Sherry McKee, Ph.D. (sherry.mckee@yale.edu)
Abstract	The Yale-SCORE on Sex Differences in Alcohol Use Disorder (AUD) brings together a team of leading basic and clinical science experts to pursue an interdisciplinary, translational, cross-species program of research aimed at identifying novel therapeutics to address the recent surge in rates of AUD in women. Over the past 10 years, rates of AUD in women have increased by 84%, translating to 10.5 million women across the United States. Alcohol use is the third-leading cause of preventable morbidity and mortality in the United States, and women drinkers experience exacerbated health risks associated with alcohol consumption when compared with men. Food and Drug Administration–approved medications for AUD were primarily developed with samples of men, and none targets factors that differentially maintain drinking in women. A considerable body of data identifies that women are more likely to drink to regulate negative affect and stress, whereas men are more likely to drink for alcohol-related positive reinforcement. Our primary aim is to use a neurobiologically informed approach to expedite the development of sex-appropriate therapeutics targeting stress and negative affect, which differentially maintain drinking in women.

Title	Project 1
Lead(s)	Sherry McKee, Ph.D.
Abstract	The primary aim of Project 1 is to examine sex differences in guanfacine’s effect on counteracting stress- and stimulation-based drinking behavior in the laboratory and improving clinical outcomes during a subsequent treatment phase.

Title	Project 2
Lead(s)	Kelly Cosgrove, Ph.D.
Abstract	The primary aim of Project 2 is to examine whether chronic alcohol consumption is associated with reductions in microglia and synaptic density and whether the impairment varies by sex. By sharing subjects with Project 1, we will examine sex differences in neurochemical markers of neurodegeneration in the living brains of patients with AUD and their relationship to critical clinical outcomes.

Title	Project 3
Lead(s)	Marina Picciotto, Ph.D., & Yann Mineur, Ph.D.
Abstract	The primary aim of Project 3 is to identify and translate sex differences in the neurobiological mechanisms studied across Projects 1 and 2. Project 3 will examine the effects of stress and pharmacological targets on neuronal activity in the amygdala, neuroinflammation, and metabolism.

Title	Resource Core
Lead(s)	Ralitza Gueorguieva, Ph.D., & Ismene Petrakis, M.D.
Abstract	This core will provide research-related resources to the animal and human projects, including management of regulatory issues, comprehensive recruitment, a core battery, data management, and project design and statistical methods that incorporate state-of-the-art SABV approaches.

Title	Career Enhancement Core
Lead(s)	Ismene Petrakis, M.D. (ISMENE.PETRAKIS@YALE.EDU)
Abstract	This core will provide qualified junior faculty members with salary support and translational team mentorship to enhance their research career development focused on sex as a biological variable (SABV) and alcohol use. Core activities include translational team mentorship, a pilot program, a curriculum dedicated to education on SABV and sex differences in alcohol use, professional development experiences, and training in leadership skills.