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 2023-24 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:

September 01, 2024	Applications open
December 01, 2024	Deadline to apply
January 08, 2025	Announce awardees
January 2025-May 2025	Visits occur

Applications should be submitted to Mara Hampson.

Detail 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)
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	Jordan W. Smoller, M.D., Sc.D.
Mayo Clinic	Sex-Specific Effects of Endocrine Disruption on Aging and Alzheimer's Disease	Stacey Winham and Melissa Morrow
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 the Metabolic Syndrome	Arthur P. Arnold, Ph.D.
UCLA P2	Sex Related Differences in Brain Gut Microbiome Interactions in Irritable Bowel Syndrome	Lin Chang, M.D.
University of Colorado	Sex Related Differences in Brain Gut Microbiome Interactions in Irritable Bowel Syndrome	Judith G. Regensteiner, Ph.D.
Yale University	Yale-SCORE on Sex Differences in Alcohol Use Disorder	Ismene Petrakis, M.D.

Centers	Director(s)	Grant	Title	Research projects:	Research Projects: 2	Research Projects: 3	Career Enhancement Core	Sleep Resource Core	Resource Support Core	Resource Support Core2
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.	Kathryn Rexrode, M.D., M.P.H. (krexrode@bwh.harvard.edu), & Janet Rich-Edwards, M.P.H., Sc.D. (jr33@partners.org)	Elizabeth Klerman, M.D., Ph.D.		
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: 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: Clinical. 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: 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 Cecile Lahiri, M.D., MSc (cdelill@emory.edu)	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: Kimbi Hagen (kbs.hagen@emory.edu) and Alicia Smith (alicia.smith@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. Leads: Dr. Sean Leng	Title: Sex differences in immune responses to vaccine and circulating strains of influenza in health care workers. Leads: Dr. Andrew Pekosz	Title: Genetic and hormonal mechanisms of sex differences in immune responses and influenza vaccine efficacy in young and aged mice. Leads: 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. Leads: 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: Robert J. Handa, Ph.D., & Taben Hale, Ph.D.	Jordan W. Smoller, M.D., Sc.D. (jsmoller@hms.harvard.edu)		Co-Leads: Vitaly Napadow, Ph.D., & Hang Lee, Ph.D.	
Mayo Clinic	Kejal Kantarci, M.D., M.S. (kantarci.kejal@mayo.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.	Co-Directors: Stacey Winham (Winham.Stacey@mayo.edu) and Melissa Morrow (morrow.melissa@mayo.edu)		Director: Ekta Kapoor, M.B.B.S.	

Medical University of South Carolina	Aimee L. McRae-Clark, Pharm.D. (mcraeal@musc.edu), and Kathleen T. Brady, M.D., Ph.D. (bradyk@MUSC.EDU)	U54DA016511	MUSC Specialized Center of Research Excellence on Sex Differences	Title: Impact of progesterone on stress reactivity and cannabis use. MPIs: Aimee McRae-Clark, Pharm.D., and Michael Saladin, Ph.D. Co-Investigators: Kevin Gray, M.D., Brian Sherman, Ph.D., and Rachel Tomko, Ph.D.	Title: Impact of lofexidine on anxiety, craving, and opioid use in men and women with opioid use disorder. MPIs: Kathleen Brady, M.D., Ph.D., and Connie Guille, M.D. Co-Investigators: Kelly Barth, D.O., and Jenna McCauley, Ph.D.	Title: Sex differences in the impact of conditioned stress on heroin and cannabis use and seeking. MPIs: Peter Kalivas, Ph.D., and Carmela Reichel, Ph.D. Co-Investigator: Constanza Garcia Keller, Ph.D.	Director: Kathleen T. Brady, M.D., Ph.D. (bradyk@MUSC.EDU)	Type: Biostatistical. MPIs: Viswanathan Ramakrishnan, Ph.D., and Nathaniel Baker, M.S.
University of California, Los Angeles (1)	Karen Reue , Ph.D. (reuek@g.ucla.edu)	U54DK120342	Sex Differences in the Metabolic Syndrome	Title: Sex chromosome effects on metabolic syndrome risk and treatment. Lead: Karen Reue, Ph.D.	Title: Gene-by-sex interactions in mitochondrial functions and metabolic syndrome traits. Lead: Jake Lusis, Ph.D.	Title: The impact of estrogen receptor (ER) in metabolic health. Lead: Andrea Hevener, Ph.D.	Lead: Arthur P. Arnold, Ph.D. (arnold@ucla.edu)	Type: Genomic Technologies. Lead: Matteo Pellegrini, 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.	Lin Chang, M.D. (linchang@mednet.ucla.edu)	Type: DATA PROCESSING AND ANALYSIS. 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	Wendy M. Kohrt , Ph.D. (Wendy.Kohrt@ucdenver.edu)	U54AG062319	Bioenergetic and Metabolic Consequences of the Loss of Gonadal Function	Title: Bioenergetic and metabolic consequences of the loss of gonadal function in women. PI: Wendy M. Kohrt, Ph.D. Co-Investigators: Daniel H. Bessesen, M.D., Edward L. Melanson, Ph.D., Kerrie L. Moreau, Ph.D., and Margaret E. Wierman, M.D.	Title: Mediators of metabolic decline with the loss of gonadal function. PI: Paul S. MacLean, Ph.D. Co-Investigators: Matthew R. Jackman, Ph.D., Michael C. Rudolph, Ph.D., and Elizabeth A. Wellberg, Ph.D.	Title: Sex hormones differentially regulate production of a distinct adipocyte population. PI: Dwight J. Klemm, Ph.D. Co-Investigators: Kathleen M. Gavin, Ph.D., and T. Rajendra Kumar, 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.

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	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	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	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)	Kimbi Hagen (kbs.hagen@emory.edu) and Alicia Smith (alicia.smith@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)	Robert J. Handa, Ph.D., & 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 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 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 (akin to project 2) to restore autonomic function and behavioral responses to stress in rats that were exposed to excess glucocorticoid 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)	Jordan W. Smoller, M.D., Sc.D. (jsmoller@hms.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)
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)	Stacey Winham (Winham.Stacey@mayo.edu) and Melissa Morrow (morrow.melissa@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 Kathleen T. Brady, M.D., Ph.D. (bradyk@MUSC.EDU)
Abstract	The Medical University of South Carolina (MUSC) SCORE is an interdisciplinary research center focused on how sex and gender influence addiction and stress-related disorders. It serves as a focal point for women's health research at MUSC and comprises three core research components—a leadership administrative core, a career enhancement core, and a biostatistics support core—and a pilot project program. The MUSC SCORE's core scientific projects focus on sex and gender differences in the relationship between addiction and stress response using emerging technology in closely aligned clinical and basic science projects. The overarching goals of the center are to support and improve the translational scientific collaborations of the core and pilot research projects, catalyze further growth of interdisciplinary sex- and gender-based research on the MUSC campus, and create strategic partnerships to enhance the translation and dissemination of SCORE findings and other relevant research to improve the health of women and girls.

Title	Impact of progesterone on stress reactivity and cannabis use
Lead(s)	Aimee McRae-Clark, Pharm.D., and Michael Saladin, Ph.D.
Co-I(s)	Kevin Gray, M.D., Brian Sherman, Ph.D., and Rachel Tomko, Ph.D.
Abstract	The goal of Project 1 is to extend previous findings to assess the efficacy of exogenous progesterone administration for reduction in stress cue reactivity among male and female cannabis users.

Title	Impact of lofexidine on anxiety, craving, and opioid use in men and women with opioid use disorder
Lead(s)	Kathleen Brady, M.D., Ph.D., and Connie Guille, M.D.
Co-I(s)	Kelly Barth, D.O., and Jenna McCauley, Ph.D.
Abstract	Project 2 will explore gender differences in the impact of an alpha-2 adrenergic agonist (lofexidine) on the relationships among stress, craving, and drug use in individuals with opioid use disorders (OUDs).

Title	Sex differences in the impact of conditioned stress on heroin and cannabis use and seeking
Lead(s)	Peter Kalivas, Ph.D., and Carmela Reichel, Ph.D.
Co-I(s)	Constanza Garcia Keller, Ph.D.
Abstract	The goal of Project 3 is to test the hypothesis that sex differences in the effects of stress on heroin and cannabis use are related to differences of synaptic plasticity and that pharmacological interventions targeting this plasticity will effectively diminish heroin and cannabis self-administration.

Title	Biostatistical Resource Core
Lead(s)	Viswanathan Ramakrishnan, Ph.D., and Nathaniel Baker, M.S.
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	Career Enhancement Core
Lead(s)	Kathleen T. Brady, M.D., Ph.D. (bradyk@MUSC.EDU)

Abstract	The MUSC SCORE Career Enhancement Core (CEC) will provide a formal, intensive program of mentored clinical and translational research training and career development activities. The program will promote the development of junior scholars in the area of sex- and gender-based clinical and translational research focused on the impact of stress on human health. Training scientists with an understanding of the role of sex and gender in the etiology and pathophysiology of specific disease states will allow for the optimization of personalized approaches to diagnosis and treatment essential to improving the health of both men and women.

Title	Sex Differences in the Metabolic Syndrome
Director(s)	Karen Reue , Ph.D. (reuek@g.ucla.edu)
Abstract	The objective of the UCLA SCORE is to elucidate sex differences in risk factors and treatments for metabolic syndrome (MetSyn) components, such as obesity, insulin resistance/diabetes, dyslipidemia, and fatty liver. Differences between men and women in susceptibility to cardiometabolic disease are well known, but the underlying genetic and physiological mechanisms remain poorly defined. Our goal is to identify factors that determine sex-specific MetSyn risk, which may lead to better diagnosis and treatment for both sexes. A unique feature of the UCLA SCORE is the investigation of sex differences in MetSyn from multiple perspectives, including the impact of having an XX versus an XY sex chromosome complement, interactions between sex and genetic variation, and estrogen effects. This triad converges in the study of how each of these components influences metabolism at the genetic and epigenetic levels.

Title	Sex chromosome effects on metabolic syndrome risk and treatment
Lead(s)	Karen Reue, Ph.D.
Abstract	This project will build on the finding that the presence of XX compared with XY chromosomes increases susceptibility to obesity and related traits. Much of the XX effect is attributable to a specific X chromosome gene that escapes X chromosome inactivation and acts at higher levels in female (XX), compared with male (XY), cells. The effects of this gene dosage on the epigenetic regulation of gene expression, energy balance, and adipose tissue remodeling during obesity will be defined. Also, the XX chromosome effect on increased female risk for diabetes secondary to statin drug therapy will be elucidated, and a dietary co-therapy that may alleviate this sex-biased adverse drug response will be tested.

Title	Gene-by-sex interactions in mitochondrial functions and metabolic syndrome traits
Lead(s)	Jake Lusis, Ph.D.
Abstract	This project seeks to understand the roles of both genetics and sex in metabolic syndrome (MetSyn) traits. Results of a systems genetics approach have implicated sex- and tissue-specific action of specific genes on MetSyn traits. The project will elucidate sex effects on mitochondrial functions in insulin resistance, as well as sex-specific effects of genes that have been implicated in insulin resistance and hepatic steatosis. The gene-by-sex interactions discovered in mice will be tested in tissues from human cohorts.

Title	The impact of estrogen receptor (ER) in metabolic health
Lead(s)	Andrea Hevener, Ph.D.
Abstract	This project will test the hypothesis that muscle estrogen receptor (ER) protects against metabolic dysfunction in mice and women, identify ER regulatory sites across the genome in females and males, and elucidate the effect of ER on the regulation of mitochondrial function. Results may provide proof-of-concept evidence that skeletal muscle ER is an effective therapeutic target to combat metabolic dysfunction and type 2 diabetes.

Title	Genomic Technologies Core
Lead(s)	Matteo Pellegrini, Ph.D.

Abstract	The Genomic Technologies Core provides next-generation sequencing and bioinformatic analysis of transcriptomic RNA sequencing, ATAC-seq, and ChIP-seq data to enhance understanding of molecular mechanisms underlying sex differences in metabolic syndrome. Additional information is available at https://sexdifferencesinmetabolism.ucla.edu .

Title	Career Enhancement Core
Lead(s)	Arthur P. Arnold, Ph.D. (arnold@ucla.edu)
Abstract	The Career Enhancement Core (CEC) proposes an integrated set of educational and research support activities to foster development of research at UCLA in women's health and sex as a biological variable (SABV) in disease, especially related to sex differences in metabolic syndrome. The aim is to spread the word about when and how sex has an important effect on physiology and disease and to teach best practices for investigating sex-biasing factors (e.g., gonadal hormones and sex chromosomes) that affect disease. The CEC intends to seed and incubate fledgling research projects and build an interactive community of investigators at UCLA and nationally that consider women's health and sex differences in their research. Key activities include workshops on clinical and experimental approaches to study SABV, a Pilot and Feasibility grant program to enhance the ability of investigators to perform SABV-relevant research, and lectures by invited speakers who study women's health and SABV, in coordination with UCLA undergraduate programs and courses. Involvement of underrepresented minority students in exciting research on women's health and SABV will be emphasized.

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)	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 University of Colorado Specialized Center of Research Excellence on Sex Differences (CO-SCORE) is thematically focused on bioenergetic and metabolic consequences of the loss of gonadal function. The overarching scientific objective of the CO-SCORE is to advance knowledge of the impact of gonadal aging on the regulation of bioenergetics, abdominal adiposity, and metabolism by conducting mechanistically driven research across the basic-to-clinical translational spectrum. The scientific premise is that gonadal failure mediates biological changes that increase risk for chronic disease. The most well-studied example of this is the accelerated decline in bone mineral density at menopause and the associated osteoporosis risk. However, the extent to which gonadal failure increases risk for chronic diseases other than osteoporosis is poorly understood. The three research projects (basic, preclinical, and clinical) will advance cutting-edge, paradigm-challenging translational research on novel mechanisms postulated to contribute to the increased abdominal adiposity and associated metabolic dysfunction that occur in the estrogen-deficient state.

Title	Bioenergetic and metabolic consequences of the loss of gonadal function in women
Lead(s)	Wendy M. Kohrt, 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 is based on the overarching hypothesis that the loss of gonadal function increases risk for chronic disease. This is particularly relevant to women's health because gonadal failure is inevitable in women in midlife but rare in men until much later in life. Aim 1 in the current award period is to determine whether adipose tissue and systemic glucocorticoid metabolism are regulated by estradiol (E2) in women. Because a goal of the CO-SCORE is to advance paradigm-challenging research on sex differences, Aim 2 will investigate follicle-stimulating hormone (FSH) as a mediator of energy homeostasis and cardiometabolic function. Projects 1, 2 (preclinical), and 3 (basic) will all address gaps in knowledge on whether the effects of E2 deficiency to increase abdominal adiposity are mediated by altered glucocorticoid metabolism and/or increased FSH. Adipose tissue samples from women in Project 1 and from animals in Projects 2 and 3 will be interrogated using similar approaches to accelerate the translational relevance of these areas of research. Finally, because blood and tissue samples from experiments in which we control E2 status are of great value across many disciplines, we will bank specimens from women in Project 1 so they can be used to support external collaborations with SCORE (and other) investigators across the country.

Title	Mediators of metabolic decline with the loss of gonadal function
Lead(s)	Paul S. MacLean, Ph.D.
Co-I(s)	Matthew R. Jackman, Ph.D., Michael C. Rudolph, Ph.D., and Elizabeth A. Wellberg, Ph.D.
Abstract	The overarching scientific objective of the CO-SCORE is to advance our understanding of how gonadal aging affects bioenergetics, abdominal adiposity, metabolism, and disease risk by conducting mechanistically driven research across the basic-to-clinical translational spectrum. CO-SCORE Project 2 will leverage preclinical models and interventions to provide a bidirectional, basic-to-clinical translational bridge between the clinically relevant studies of Project 1 and the basic discovery studies in Project 3. The long-term objective of Project 2 is to work collaboratively with CO-SCORE investigators to develop better strategies for treating and preventing the pathological consequences of gonadal aging, which disproportionately afflict women.

Title	Sex hormones differentially regulate production of a distinct adipocyte population
Lead(s)	Dwight J. Klemm, Ph.D.
Co-I(s)	Kathleen M. Gavin, Ph.D., and T. Rajendra Kumar, Ph.D.
Abstract	The menopausal transition, an unavoidable aging-related phenomenon in women, is accompanied by increased abdominal adiposity and the concomitant incidence of adipose-related comorbidities. We have generated evidence that the cellular composition of adipose tissue (AT) defines the phenotype of each individual depot, determining its overall influence on metabolic health. The premise is that the loss of gonadal hormones alters the cellularity of AT, leading to changes in body fat distribution and worsening metabolic health. We previously discovered a novel lineage of adipocytes in the major white adipose depots of mice and humans generated from bone marrow–derived cells of the hematopoietic lineage rather than conventional mesenchymal precursors. In mice, bone marrow–derived adipocytes (BMDAs) were detected in greater numbers in abdominal fat depots and displayed increased inflammatory cytokine but decreased leptin and mitochondrial lipid oxidation gene expression, suggesting a critical role in influencing metabolic health. Furthermore, ovariectomy (OVX) significantly increased BMDA production, which was attenuated by estradiol (E2) replacement. In addition to declines in E2, menopause and OVX are also characterized by rising follicle-stimulating hormone (FSH) levels. Recent research raises the possibility that the consequences of menopause traditionally attributed to the specific loss of ovarian E≠ are instead caused by the previously unappreciated rise in FSH. Here we test the central hypothesis that E2 and FSH differentially regulate the production of BMDAs, altering the cellular composition of AT and resulting in significant changes in metabolic and inflammatory phenotype. Successful completion of these studies will define the roles of E2 and FSH in controlling the production of BMDAs, which may contribute to postmenopausal metabolic pathology. These data have the tremendous potential to highlight BMDA production as a new therapeutic target and provide novel strategies for the prevention of menopausal and aging-related chronic disease risk.

Title	Career Enhancement Core
Lead(s)	Judith G. Regensteiner, Ph.D. (JUDY.REGENSTEINER@CUANSCHUTZ.EDU)
Abstract	The objectives of the CO-SCORE CEC are to develop and support a cadre of accomplished junior researchers in the thematic focus of the CO-SCORE, “Bioenergetic and Metabolic Consequences of the Loss of Gonadal Function,” and to provide a curriculum that meets the career enhancement needs of postdoctoral research fellows and junior faculty scientists focused on translational science in the study of women’s health and sex differences. The SCORE scholars will receive salary support to protect time for research and funds for research project support. In addition, meritorious pilot projects, selected through peer review, will be awarded to three promising scientists each year. SCORE scholars and pilot awardees will participate in an innovative career enhancement program, including team mentoring, hands-on research experience, and curricular training to cultivate academic skills and career development skills. Trainees will also participate in a summer course featuring relevant topics in endocrinology and receive training in methods and strategies for studying sex as a biological variable (SABV), which is being developed by the SCORE faculty. SCORE scholars and pilot awardees will undergo training with the trainees in the Building Interdisciplinary Research Careers in Women’s Health (BIRCWH) K12, the Colorado Clinical and Translational Sciences Institute (CCTSI) KL2 program, and the Center for Women’s Health Research (CWHR) at the University of Colorado Anschutz Medical Campus. The mentoring, research experience, and curricular training provided by this program will provide pivotal support for the SCORE scholars and pilot awardees as they develop careers in women’s health and sex differences research. Expanding the workforce in this area is critical to the field’s becoming fully realized. Success in this endeavor means that health and disease in women and men will be optimally studied so that medical research benefits everyone to the highest level possible.

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.