BIOGRAPHICAL SKETCH

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NAME: Wendy M Kohrt

eRA COMMONS USER NAME (credential, e.g., agency login): wkohrt

POSITION TITLE: Professor of Medicine

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Wisconsin – Stevens Point	BS	05/1977	Math, Physical Education
Arizona State University, Tempe AZ	MS	05/1983	Exercise Science
	PhD	05/1986	Exercise Science
Washington Univ School of Medicine, St Louis MO	Postdoc	05/1989	Integrative Physiology, Gerontology

A. **Personal Statement**

I have had continuous research funding from the NIH and other sponsors as a principal investigator since 1991. My career has been devoted to *clinical research involving exercise, nutrition, hormone, and pharmacologic interventions focused on various aspects of metabolism, including body weight regulation and fat distribution*. I have been the Director of Research for the Division of Geriatric Medicine since 1999. I am currently the PI for NIH U54 and U01 awards and a VA Merit Review and have more than 280 original and solicited research publications. I hold several administrative positions including: *Director of the Energy Balance Assessment Core in the Colorado Nutrition and Obesity Research Center (NORC)*; Senior Associate Director of the Colorado Clinical and Translational Sciences Institute (CCTSI), and Associate Director of the Ludeman Center for Women's Health Research (CWHR).

My research interests in the effects of sex hormones on body weight regulation and fat distribution began fortuitously early in my career. I conducted an intervention trial to evaluate the effects of exercise training and estrogen-based hormone therapy on bone mineral density in postmenopausal women. The supervised exercise intervention stopped after 11 months but the drug intervention continued for an additional 6 months. The fortuitous finding was that hormone therapy attenuated fat regain after the exercise intervention, particularly in the abdominal region. Two other intervention trials published around the same time also found that estrogens appeared to be a key regulator of abdominal fat accumulation in women, which catalyzed my interests in the metabolic actions of estrogens. Since 2012 I have served as the PI/PD for our Specialized Center of Research Excellence (SCORE) on Sex Differences (U54 AG062319), focused on *Bioenergetic and Cardiometabolic Consequences of the Loss of Gonadal Function. The SCORE includes mechanistically driven basic, preclinical, and clinical studies, led by Drs. Dwight Klemm, Paul MacLean, and Kerrie Moreau (all NORC members), to understand how estradiol (and other factors) regulate the proliferation and function of adipocytes in the abdominal region*. The Colorado NORC provides critical support for all of the SCORE projects, which is only one example of the tremendous value the NORC brings to the research enterprise at CU-AMC.

Ongoing Research

NIH U54 AG062319 (Kohrt) 09/20/2012 to 08/31/2028
Colorado Specialized Center of Research Excellence
Role: Center Director, Project PI, Administrative Core Director
Bioenergetic and Metabolic Consequences of the Loss of Gonadal Function

The new scientific focus for the third award period is on the tryptophan-kynurenine pathway as a mediator of bioenergetic regulation. Basic, preclinical, and clinical projects will address knowledge gaps regarding how rate-limiting enzymes and key metabolites in this pathway are altered by the suppression of gonadal function in a manner that increases propensity for abdominal fat gain. The award also includes a Leadership Administration Core and a Career Enhancement Core. The latter will support one SCORE Scholar each year and several pilot project awards.

NIH U01 AR071124 (Kohrt) 12/06/2016 to 06/30/2025
Molecular Transducers of Physical Activity Consortium–Colorado Clinical Center
Roles: PI of Clinical Center; Chair of Steering and Executive Committees
This NIH Common Fund initiative will develop a national resource of molecular responses to physical activity that will advance the understanding of the mechanisms by which physical activity improves health and fitness. The Colorado Clinical Center will support the interventions for the initiative and the generation of biospecimens for molecular interrogation.

P30 DK048520 (MacLean) 01/01/1997 to 07/31/2025
Colorado Nutrition and Obesity Research Center
Role: Director, Energy Balance Assessment Research Center
This resource fosters interactive nutrition and obesity research, training, and education.

UL1 TR002535 (Sokol) 05/01/2018 to 07/31/2030
Colorado Clinical and Translational Sciences Institute
Role: Senior Associate Director, Clinical and Translational Research Resources and Services; Chair, Scientific Advisory and Review Committee
The program incorporates a broad reaching intra- and inter-institutional comprehensive program to enhance clinical and translational research and science, training of clinical and translational scientists, and collaboration with the communities of the state of Colorado and the surrounding region.

K12 HD057022 (Regensteiner/Santoro) 09/24/2007 to 07/31/2027
Building Interdisciplinary Careers in Women's Health
Role: Director of Research
This K12 training grant fosters interdisciplinary careers in women's health research.

U01 NS113851 (Corcos) 09/25/2019 to 07/31/2024
Study in Parkinson Disease of Exercise Phase 3 Clinical Trial: SPARX3
Role: Co-Investigator
The study objective is to establish the efficacy of high-intensity endurance exercise as first-line therapy for recently diagnosed people with Parkinson's disease (PD).

Veterans Administration 10/01/2014 to 09/30/2028
Eastern Colorado GRECC
Role: Associate Director of Research
The research foci of the GRECC include 1) Consequences and Treatment of Obesity in Older Veterans, and 2) Gender Differences in the Health of Older Veterans.

I01 CX002284 10/1/2021 to 09/30/2024
Enhancing Skeletal Adaptation to Exercise by Attenuating the Acute Disruption of Calcium Homeostasis
Role: PI
The major goals are to confirm that the exercise-induced increase in PTH activates catabolic pathways in bone with repeated exercise bouts and determine if anabolic pathways are activated as robustly as the response to pharmacologic PTH. If the latter does not occur, a randomized controlled trial will determine if pre-exercise calcium administration augments skeletal adaptations to exercise.

B. Positions, Scientific Appointments, and Honors

Positions

1999-present	Distinguished (2020) Professor with Tenure (2007), University of Colorado Anschutz Medical Campus, Department of Medicine, Division of Geriatric Medicine, Denver, CO
1991-1995	Research Assistant Professor; Washington University, Department of Internal Medicine and Program in Physical Therapy, St. Louis, MO

1995-1999 Research Associate Professor; Washington University, Department of Internal Medicine and Program in Physical Therapy, St. Louis, MO
1989-1991 Research Instructor; Washington University, Department of Internal Medicine and Program in Physical Therapy, St. Louis, MO

Scientific Appointments

2016-present Chair, Steering Committee and Executive Steering Committee for the *Molecular Transducers of Physical Activity Consortium*; NIH Common Fund Initiative
2016-2020 Member, NIDDK Clinical Obesity Research Panel
2016 Member, NASA Human Exploration Research Opportunity (HERO) grant review panel
2015 Member, NIH Special Emphasis Panel for NIGMS IDeA-CTR applications
2015 Chair, NASA Human Exploration Research Opportunity (HERO) grant review panel
2011 Chair, NIH Special Emphasis Panel 2012/01 ZAG1 ZIJ-5 (J3); competing renewal of Musculoskeletal Health in Aging Men (MrOS)
2011-2013 Chair, NIH Aging Systems and Geriatrics Review Panel
2010 Citation Award, American College of Sports Medicine
2010-2013 Member, NIH Aging Systems and Geriatrics Review Panel
2009-2011 Co-chair, Steering Committee for the Decadal Survey in Life and Physical Sciences Space Research, convened by the Space Studies Board and the Aeronautics and Space Engineering Board, National Research Council of The National Academies
2008-2014 Member, ISIS Fund Network on Sex Differences in Musculoskeletal Health, affiliated with the Society for Women's Health Research
2007-2008 Member, Dept of Health and Human Services, Physical Activity Guidelines Advisory Committee
2007 Member, Advisory Panel for NASA Johnson Spaceflight Center's Exercise Countermeasure Project Bone Workshop
2006 Member, NIH Special Emphasis Panel ZRG1 RPHB-H
2006 Chair, Special Emphasis Panel for NHLBI U01 proposals on "Weight Loss in Obese Adults with Cardiovascular Risk Factors: Clinical Interventions,"
2005-present Fellow, Gerontologic Society of America
2005-2006 Member, NASA Non-advocate Review Panel and Steering Committee for "Bisphosphonates as a Countermeasure to Spaceflight-induced Bone Loss,"
2005-2014 Member, Editorial Board, Medicine and Science in Sports and Exercise
2004 Chair, International Life Sciences Muscle & Exercise Panel to review experiments for NASA and other international space agencies
2003-2004 Member, NIH *Musculoskeletal Rehabilitation Sciences* study section
2003 University of Colorado Department of Medicine Outstanding Research Faculty Award
2002-2004 Chair, Writing Group for the American College of Sports Medicine Position Stand on Physical *Activity and Bone Health*
2000-2003 Member, NIH *Geriatric and Rehabilitative Medicine* study section
1999-2004 Associate Editor, *Exercise and Sports Sciences Reviews*
1999-2004 Member, Editorial Board, *Journal of Applied Physiology*
1999-2003 Editor, *Yearbook of Sports Medicine*
1993-present Fellow, American College of Sports Medicine

Honors

2024 University of Colorado Anschutz Medical Campus, Department of Medicine *Excellence in Research* Award
2023 University of Colorado Anschutz Medical Campus *Joseph Addison Sewall Award*
2022 University of Colorado Anschutz Medical Campus, Department of Medicine *Innovator Award*
2021-2023 Vice President, American College of Sports Medicine
2019 Honor Award, Environmental and Exercise Physiology Section, American Physiological Society (first woman to receive this award)
2016-present Inaugural Nancy Anschutz Endowed Chair in Women's Health Research
2013 Endocrine Society National Meeting Plenary Lecture; San Francisco, CA
2012 J.B. Wolffe Memorial Lecture; Keynote Address for the 2012 annual meeting of the American College of Sports Medicine; San Francisco, CA
2012-2015 Visiting Professorship, Ritsumeikin University, Kyoto, Japan

2011 Herbert A deVries Research Award from the Council on Aging and Adult Development, American Association for Physical Activity and Recreation
2007 Distinguished Alumnus Award, University of Wisconsin-Stevens Point

C. Contributions to Science

C.1 Metabolic Actions of Estrogens

I have been studying the metabolic actions of estrogens for 30 years. One of my first studies in this area investigated the interactive effects of estrogens and exercise on bone metabolism in postmenopausal women. One of the intriguing findings from that study was that, over the 6 months after the completion of the exercise training intervention, women who had been assigned to the estrogen treatment arm seemed to be protected against fat gain. That observation led to the focus in my lab on the metabolic and bioenergetic actions of estrogens. There is compelling evidence from basic (e.g., transgenic deletion of estrogen receptors) and preclinical (e.g., surgical removal of ovaries; OVX) studies that estradiol is a potent regulator of energy balance. Animals that lack functional estrogen receptors or undergo OVX have an accelerated accumulation of fat, which is predominantly abdominal and leads to insulin resistance and dyslipidemia. The system-level mechanisms for the disruption in energy balance in response to a decline in estrogen signaling include 1) a decrease in energy expenditure due to a decreased basal metabolic rate, 2) a further decrease in energy expenditure due to a decline in spontaneous physical activity, and 3) in some species, an increase in energy intake. These changes are prevented in the OVX model by treatment with estradiol. Our Specialized Center of Research Excellence (SCORE) on Sex Differences (U54 AG062319), which is currently one of only 11 SCOREs around the country sponsored by the NIH Office of Research on Women's Health, is focused on the metabolic and bioenergetic consequences of the loss of gonadal function. The clinical project supported by the SCORE, for which I serve as PI, is focused on mechanisms by which the loss of estradiol leads to increased abdominal adiposity and metabolic dysfunction. During the first award period of the SCORE, we found that ovarian suppression (i.e., gonadotropin releasing hormone analog treatment in premenopausal women) suppresses resting energy expenditure (REE) by ~50 kcal/d. The decline in REE is prevented by concurrent estradiol treatment, demonstrating that it is an estrogen-mediated effect. Ovarian suppression also resulted in an increase in intra-abdominal adiposity, and this, too, was prevented by estradiol treatment. Most recently, the focus has been on isolating actions of follicle-stimulating hormone from those of estradiol.

a. Libby AE, Solt C, Jackman M, Sherk V, Foright RM, Johnson GC, Nguyen TT, Breit M, Hulett N, Rudolph M, Roberson PA, Wellberg E, Jambal P, Scalzo RL, Higgins J, Kumar TR, Wierman ME, Pan Z, Shankar K, Klemm DJ, Moreau KL, Kohrt WM, MacLean PS. Effects of follicle-stimulating hormone on energy balance and tissue metabolic health after loss of ovarian function. *Am J Physiol Endocrinol Metab* 2024 2024 326:E626-E639 PMID 38536037
b. Gavin KM, Melanson EL, Hildreth KL, Gibbons E, Bessesen DH, Kohrt WM. A randomized controlled trial of ovarian suppression in premenopausal women: no change in free-living energy expenditure. *Obesity* 2020 28:2125-2133 PMCID PMC7653843
c. Mijakovac A, Juric J, Kohrt WM, Kristic J, Kifer D, Gavin KM, Miskec K, Frkatovic A, Vuckovic F, Pezer M, Vojta A, Nigrovic PA, Zoldos V, Lauc G. Effects of estradiol on immunoglobulin G glycolsylation: mapping of the downstream signaling mechanism. *Front Immunol* 2021 doi: 10.3389/fimmu.2021.680227 PMC8186398
d. Kohrt WM, Wiermen ME. Preventing fat gain by blocking follicle-stimulating hormone. *N Eng J Med* 377:293-295, 2017

C.2 Novel Factors That Influence Bone Metabolism

One of my research interests is on novel factors that influence musculoskeletal adaptations to exercise. The studies described below highlight the experience of my lab in translating mechanistic findings from basic or preclinical studies to clinical research to determine the physiological relevance to humans.

We were the first to evaluate in humans whether use of non-steroidal anti-inflammatory drugs (NSAIDs) before or after exercise sessions impairs musculoskeletal adaptations to exercise. The scientific rationale for this work was the evidence from basic (cells) and preclinical (animal) studies that the bone formation response to mechanical stress was markedly impaired when NSAIDs were present before mechanical loading but not when NSAIDs were introduced after loading. Our first proof-of-concept study supported a similar effect in young women, demonstrating that taking ibuprofen after exercise session had more favorable effects on bone mineral density (BMD) than taking it before. This study provided the foundation for a larger trial of ibuprofen use before

vs after exercise sessions in older women and men. In contrast to the initial study, taking ibuprofen either before or after exercise tended to attenuate increases in hip BMD in older women. Although the magnitude of the effect was as hypothesized, the results did not achieve statistical significance because variability was higher than expected. Further research in this area is needed, because the beneficial effects of exercise on bone health may be compromised by the use of NSAIDs.

The other novel line of research in this focus area involves the disruption of calcium homeostasis by exercise. Some athletes, such as cyclists, have been observed to have BMD levels that are below normal. Although it is commonly believed this is because they participate in weight-supported exercise (as opposed to weight-bearing), we have found that cyclists lose BMD at an accelerated rate of 1% to 2% per year. We postulate that the disruption of calcium homeostasis during exercise contributes to this loss. The working model portends that serum calcium declines during exercise (e.g., consequent to dermal loss), which leads to an increase in parathyroid hormone (PTH) and the stimulation of bone resorption to mobilize skeletal calcium. We demonstrated that dermal calcium loss was not the trigger for this metabolic cascade, because serum PTH and CTX (marker of bone resorption) begin to increase after only 10 minutes of exercise, before appreciable dermal calcium loss has occurred. However, we confirmed our hypotheses that relative vigorous endurance exercise triggers a decline in serum calcium and increases in PTH and CTX, and that these changes occur in young and older, trained and untrained, women and men during weight-supported or weight-bearing endurance exercise. Further, the provision of supplemental calcium before and during exercise attenuates the increases in PTH and bone resorption. Because PTH can, paradoxically, have either catabolic or anabolic effects on bone, this line of research must be expanded to determine whether exercise-induced increases in PTH are favorable or unfavorable.

a. Wherry SJ, Swanson CM, Kohrt WM. Acute catabolic bone metabolism response to exercise in young and older adults: a narrative review. *Exp Gerontol* 2022 doi: 10.1016/j.exger.2021.111633 PMC10103539
b. Kohrt WM, Wolfe P, Sherk VD, Wherry SJ, Wellington T, Melanson EL. Swanson CM, Weaver CM, Boxer RS. Dermal calcium loss is not the primary determinant of PTH secretion during exercise. *Med Sci Sports Exerc* 2019 51:2117-2124 PMC6746591
c. Kohrt WM, Wherry SJ, Wolfe P, Sherk VD, Wellington T, Swanson CM, Weaver CM, Boxer RS. Maintenance of serum ionized calcium during exercise attenuates parathyroid hormone and bone resorption responses. J Bone Miner Res 33:1326-1334, 2018 PMC5838616
d. Wherry SJ, Blatchford PJ, Swanson CM, Wellington T, Boxer RS, Kohrt WM. Maintaining serum ionized calcium during brisk walking attenuates the increase in bone resorption in older adults. *Bone* 2021 doi: 10.1016/j.bone.2021.116108 PMC8478867

C.3 Mentoring Activities

I view my activity as a research mentor as one of my important contributions to science. Since 1991, I have mentored or co-mentored 41 PhD-trained and 24 MD-trained research fellows from several departments/divisions (Geriatric Medicine, General Internal Medicine, Endocrinology, Infectious Diseases, Cardiology); the majority have established independent research careers. I serve as a senior faculty mentor on several institutional training grants: Integrative Physiology of Aging (T32 AG000279); Nutrition (T32 DK007658); Sleep and Circadian (T32 HL149646); Colorado Building Interdisciplinary Research Careers in Women's Health (K12 AR084226); and Colorado Clinical and Translational Sciences Institute KL2 (UM1 TR004399). I have served as mentor or co-mentor for 29 postdoctoral fellows supported by a T32 award, 8 supported by an F32 award, and 22 supported by a NIH K or VA CDA award.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/wendy.kohrt.1/bibliography/40700553/public/?sort=date&direction=ascending