BIOGRAPHICAL SKETCH

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NAME: Karyn A. Esser

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

POSITION TITLE: Professor and Chair of Physiology and Aging

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
Wake Forest University, Winston-Salem	BS	05/1979	Math: Biology
University of Nevada, Las Vegas	M.Ed.	06/1981	Human Exercise Physiology
University of Michigan, Ann Arbor	Ph.D.	01/1990	Kinesiology
Children’s Medical Research Foundation	Post-doc	07/1993	Muscle Genetics

A. Personal Statement As an academic scientist, my lab has been working in the area of skeletal muscle adaptation for many years. During the first part of my career, my research was focused on understanding the molecular mechanisms that underly adult skeletal muscle adaptation to both endurance training (e.g. fiber type) and resistance training (e.g. hypertrophy). One example of this work is our publication; Baar and Esser (1999) in which we were the first group to implicate activation of the mTOR/mTORC1 pathway as a critical node for hypertrophic growth of skeletal muscle after high force contractions.

My lab has been largely focused on the regulation of transcription and gene expression in skeletal muscle and it was our first unbiased expression profiling experiment that identified circadian clock genes changing in response to muscle contractions (Chen et al., 2002). From that observation, we started a line of research to focus on circadian rhythms, molecular clock and skeletal muscle homeostasis. My lab used genetic models of circadian disruption (*Bmal1* KO/Clock mutant mice) to show that skeletal muscle exhibits profound weakness, altered fiber type, increased fibrosis and disrupted mitochondria similar to what is shown in aging skeletal muscle/sarcopenia. We currently use inducible skeletal muscle specific genetic mouse models to test the function of the endogenous clock in adult mice. We have learned that disruption of the endogenous molecular clock in skeletal muscle, through targeted loss of *Bmal1*, leads to a similar phenotype to muscle aging with loss of muscle strength, altered insulin sensitivity, substrate metabolism, fiber type changes and fibrosis. Currently the preclinical arm of my lab is pursuing the transcriptional mechanisms that link the circadain clock and clock output with muscle homeostasis, the role of exercise as a time cue for muscle clocks and how healthy muscle supports systemic resilience.

In addition to my lab, I have been an active member of the NIH funded Molecular Transducers of Physical Activity Consortium (MoTrPAC) in which we are using multi-omics data sets with well defined acute exercise and exercise training in rats (18 tissues) to discover exercise specific pathways/molecules important for systemic health benefits. I also lead and contribute to clinical studies in muscle aging and I am co-Director of the NIA funded UF Older Americans Independence Center. Lastly, I am a contributing scientist to the NIA funded multicenter Studies of Muscle Mobility and Aging (SOMMA) project and also a co-I on the R01 studying exercise response heterogeneity in aging (co-I with Bamman, Miller and Bodine).

Ongoing projects that I would like to highlight include:
1) R01AR079220 Role: PI: 3/2021-03/2026
Circadian Clock and Muscle Health

2) P30 AG028740. Esser MPI: Manini, MPI). 4/2022-3/2027
Claude D. Pepper Older Americans Independence Center (OAIC)

3) R01 AG059416 Role - site PI: Cummings PI. 09/2024-09/2029
Study of muscle, mobility, and aging (SOMMA)

4) R01AG1551353 Role, co-I (Bamman, Miller and Bodine, MPI). 09/1/24 - 09/30/2028
Multidimensional predictive modeling to understand mechanisms of exercise response heterogeneity in older adults

Selected Citations

a) Ehlen, JC, Brager AJ, Baggs J, Pinckney L, Gray, CL, DeBruyne JP, **Esser, KA**, Takahashi JS and Paul KN. Bmal1 function in skeletal muscle regulates sleep. eLife, 20;6. pii: e26557. doi: 10.7554/eLife.26557, 2017. PMCID:PMC5574702

b) Amar D, Gay NR, Beltran MJ …. **Esser, KA**, MoTrPAC study group (I am one of 6 corresponding authors). Temporal dynamics of the multi-omic response to endurance exercise training across tissues. *Nature.* 2024 May;629(8010):174-183. doi: 10.1038/s41586-023-06877-w.

c) Gutierrez-Monreal MA, Wolff CA, Rijos, EE, Viggars MR, Douglas CM, Pagala V, Peng J, Hunt LC, Ding H, Demontis F, Huo Z and **KA Esser**. Targeted Bmal1 restoration in muscle prolongs lifespan with systemic health effects in aging model. *JCI Insight 2024 Oct 1;9(22):e174007.*

d) Viggars MR, Berko HE, Hesketh SJ, Wolff CA, Gutierrez-Monreal MA, Martin RA, Jennings IG, Huo Z, **Esser KA**. Skeletal muscle BMAL1 is necessary for transcriptional adaptation of local and peripheral tissues in response to endurance exercise training. *Mol Metab* 2024. doi: 10.1016/j.molmet.2024.101980

B. Positions and Scientific Appointments

2024-2025	Interim Chair – Department of Anatomy and Cell Biology, University of Florida
2022-	Chair – Department of Physiology and Aging, University of Florida
2022-	Co-Director – University of Florida Older Americans Independence Center (OAIC)
2015-2019	Board of Scientific Counselors NIH:NIAMS
2015	Preeminence Professor – Department of Physiology and Functional Genomics, University of Florida
2015	Associate Director for Basic Muscle Biology; Institute of Myology, University of Florida
2013-2015	Appointed Faculty member, UK Research Foundation Board of Directors
2011	University of Kentucky Research Professor
2010-2015	Director, Center for Muscle Biology, University of Kentucky
2009-2015	Professor – Department of Physiology, University of Kentucky
2007-2015	Director, Core Facility, Mouse exercise training and testing, University of Kentucky
2004-2009	Associate Professor – Department of Physiology, University of Kentucky
1999	Fellow, American College of Sports Medicine
1999-2004	Associate Professor – School of Kinesiology, University of Illinois, Chicago
1993-1999	Assistant Professor - School of Kinesiology, University of Illinois, Chicago

Other Professional Contributions and Honors

2025	Grand Rounds, Michael Hughes Memorial Lecture, Washington University, St. Louis
2024	John and Margaret Faulkner Lectureship, Department of Physiology, University of Michigan
2022	UF College of Medicine Outstanding Research Scientist Award in Basic Sciences, Univ Florida
2021	Guest Editor, PNAS
2019	Organizer for ACSM World Congress on Exercise, Circadian Rhythms and Sleep
2018	Editorial Board, Physiological Reviews
2017-2024	External Advisory Board member for the Indiana Center for Musculoskeletal Health
2016-present	External Advisory Panel, Michigan Integrative Musculoskeletal Health P30 Core Center
2016-2020	Regular member NIH/SMEP study section

2015-present. Executive Committee member for the NIH Common Fund program, Molecular Transducers of Physical Activity in Humans,
2015-present External Advisory Board, Physiology Department, Baylor College of Medicine
2015 NIH Biomarker Workshop: NHLBI, NIA, and Sleep Research Society.
2014 Organizer ACSM Integrative Physiology of Exercise meeting; 09/2014
2013 Meeting Organizer ASBMR: Cutting Edge Discoveries in Muscle Health and Disease:
2013 NIAMS Scientific Retreat: Circadian rhythms and skeletal muscle, May 2013
2011-2014 Associate Editor, American Journal of Physiology: Cell
2011 Invited panel member for review of the Nordic Sports Sciences: 5/2011
2008-2012 NIAMS AMS committee, standing member 10/2008-10/2012
2009 Elected Organizer, Frontiers in Myogenesis, 5/2009.
2003-2006 Regular member, Skeletal Muscle Biology and Exercise Physiology (SMEP) study section Chair SMEP study section 3/2005-7/2006
2001-2003 Regular member NIH/Skeletal Muscle Biology study section 11/2001-6/2003
2000-2001 Regular member NIH/RAP study section 6/2000-6/2001

C. Contributions to Science

1) Transcriptional regulation of skeletal muscle phenotype. My lab has been studying the molecular basis of skeletal muscle adaptation to exercise for over 20 years. These studies involved use of different models of skeletal muscle adaptation (regeneration, innervation, hypertrophy) with the use of molecular and biochemical assays to define transcriptional regulation of genes critical for phenotype changes. One example of our work is where we merged understanding of the physiological parameters through which innervation regulates slow fiber type with *in vivo* transfection approaches to define cis elements necessary for slow gene expression. My lab was also an early advocate for use of unbiased approaches in physiological studies, such as expression profiling, to understand transcriptional responses more systematically

a) **Esser, K.,** T. Nelson, V. Lupa-Kimball and E. Blough. The CCAC box and MEF2 sites within the myosin light chain 2 slow promoter cooperate in regulating slow nerve-specific transcription in skeletal muscle. Vol.274(17) 12095-12102 J. Biol. Chem. 1999.
b) Zhang, X., S. Patel, J. McCarthy, A. Rabchevsky, D. Goldhamer and **K.A. Esser**. A non-canonical E-box within the MyoD core enhancer is necessary for circadian expression in skeletal muscle. *Nucleic Acids Research*, 40(8):3419-30, 2012. PMCID:PMC3333858
c) Hodge BA, Zhang X, Gutierrez-Monreal MA, Cao Y, Hammers DW, Yao Z, Wolff CA, Du P, Kemler D, Judge AR, **Esser KA**. MYOD1 functions as a clock amplifier as well as a critical co-factor for downstream circadian gene expression in muscle. *Elife*. 2019 Feb 21;8. pii: e43017. doi: 10.7554/eLife.43017. PMCID: PMC6398978

2_ Regulation of skeletal muscle hypertrophy. Early on my lab established a reputation for publications that were leading the field on the topic of high force contractions and muscle hypertrophy. Early studies using distinct models of muscle contractions provided the data to suggest that the mTORC1 pathway is necessary for skeletal muscle hypertrophy (Baar and Esser, 1999). Subsequent studies demonstrated that mTORC1 signaling in response to high force muscle contractions occurred independent of IGF1 and other well-known growth factor pathways. Not only has this body of work been important for understanding signaling pathways specific to different types of exercise, but it has provided important findings for our understanding of the temporal dynamics of the signaling and transcriptional changes following an acute bout of exercise.

a) Baar, K., and **K. Esser**. Activation of p70s6k correlates with skeletal muscle hypertrophy in the rat. Am J Physiol Cell Physiol. 276 (1): C120-C127, 1999.
b) Hornberger, T., R. B. Hunter, S. Kandarian and **K. Esser**. Differential regulation of translation factors in atrophying muscle. Am. J. Physiol.: Cell 281:C179-C187, 2001.
c) Nader, G. and **K. Esser**. Intracellular signaling specificity in skeletal muscle in response to different modes of exercise. *J. Appl. Physiol*. 90(5):1936-42, 2001
d) Kirby TJ, Lee JD, England JH, Chaillou T, **Esser KA**, McCarthy JJ. Blunted hypertrophic response in aged skeletal muscle is associated with decreased ribosome biogenesis. J Appl Physiol 119(4):321-327, 2015. PMCID: PMC4538281

3) Role of the molecular clock in skeletal muscle and systemic homeostasis. My lab has pioneered the understanding of the role of the molecular clock and circadian rhythms on skeletal muscle phenotype and function starting with our early publication in PNAS. Continued work in this area work has also led to exciting outcomes linking muscle health to systemic health. Our studies combine fundamental measures of animal circadian behavior, with inducible mouse genetic models, use of real time bioluminescence assays with the circadian reporter mouse (mPER2:LUC) or stably transfected C2C12 myotubes cultures to study clock function. My lab's work has defined that the molecular clock functions in skeletal muscle as a cell autonomous and self-sufficient mechanism. We have documented that loss of the muscle clock is sufficient to induce weakness and features like aging muscle. We also have shown that loss of muscle clock leads to altered sleep homeostasis.

Most recently, we have starting experiments to define circadian clock function in human primary muscle with in vitro real time bioluminescence assays. For these studies we have lentiviral vectors with either the Bmal1-luciferase or Per2-luciferase to probe both the positive and negative arms of the core clock mechanism. We have been able to find differences in clock phase across samples of young adult samples and will be applying these tools to studies of aging and exercise responsiveness.

a) Ehlen, JC, Brager AJ, Baggs J, Pinckney L, Gray, CL, DeBruyne JP, **Esser, KA**, Takahashi JS and Paul KN. Bmal1 function in skeletal muscle regulates sleep. eLife, 20;6. pii: e26557. doi: 10.7554/eLife.26557, 2017. PMCID:PMC5574702
b) Schroder EA, Harfmann BD, Zhang X, Srikuea R, England JH, Hodge BA, Wen Y, Riley LA, Yu Q, Christie AD, Smith JD, Wolf Horrell EM, Mula J, Peterson CA, Butterfield TA, and **Esser KA.** Intrinsic Muscle Clock is Necessary for Musculoskeletal Health, J. Physiol. 15;593(24):5387-404 2015. PMCID: PMC4704520
c) Riley, LA, Zhang X, Douglas CM, Mijares JM, Hammers DW, Wolff CA, Wood NB, Olafson HR, Du P, Labeit S, Previs MJ, Wang ET and **Esser KA**. The skeletal muscle circadian clock regulates titin splicing through RBM20. *Elife*. 2022 Sep 1;11:e76478. doi: 10.7554/eLife.76478. PMID: 36047761 PMCID: PMC9473687
d) Gutierrez-Monreal MA, Wolff CA, Rijos, EE, Viggars MR, Douglas CM, Pagala V, Peng J, Hunt LC, Ding H, Demontis F, Huo Z and **KA Esser**. Targeted Bmal1 restoration in muscle prolongs lifespan with systemic health effects in aging model. *JCI Insight*. 2024.

4) Exercise, circadian rhythms and health. Work from my lab determined that exercise training during the rest phase was sufficient to cause a 2-3hr shift in the phase of the circadian clock mechanism in muscle. We have also demonstrated that the impact of time of exercise and the clock depends on the specific clock phase at the time of exercise. These results highlighted that exercise timing served as a bone fide environmental cue for the clock mechanism.

Our most recent work has determined that the molecular response to exercise, either a single bout or training, requires an intact circadian clock mechanism. Loss of muscle clock function led to a diminished acute exercise response with dampened responses in well-known exercise genes including PGC1a and Nr4a3. Mice without a functional muscle clock adapted to exercise training but there was a large divergent remodeling of the transcriptional and metabolomic adaptations in muscle with no functional clock. Additionally, we found that the adaptations in peripheral tissues, that had functional circadian clocks, were also impacted with an increased signature of inflammation. These results highlight the importance of the circadian clock mechanism for the transcriptional and metabolic responses to exercise. In addition, they reinforce the importance of the muscle exercise responses for the system.

a) Wolff, G and **K.A. Esser**. Scheduled Exercise Phase Shifts the Circadian Clock in Skeletal Muscle. Med. Sci in Sports and Exercise, 44(9):1663-70, 2012 PMCID: PMC3414645
b) Amar D, Gay NR, Beltran MJ …. **Esser, KA**, MoTrPAC study group (I am one of 6 senior authors). Temporal dynamics of the multi-omic response to endurance exercise training across tissues. *Nature.* 2024 May;629(8010):174-183. doi: 10.1038/s41586-023-06877-w.
c) Viggars, MR, Berko HE, Hesketh SJ, Wolff CA, Gutierrez-Monreal MA, Martin RA, Jennings IG, Huo Z and **KA Esser**. Skeletal muscle BMAL1 is necessary for transcriptional adaptation of local and peripheral tissues in response to endurance exercise training. Molecular Metabolism, Volume 86, 2024

d) Erickson ML, Blackwell TL, Garcia RE, Mau T, Cawthon PM, Cummings SR, Farsijani S, Sparks LM, Noone J, Glynn NW, Newman AB, **Esser KA**. Rest Activity Rhythms and their Association with Cardiorespiratory Fitness and Walking Energetics in Older Adults: Study of Muscle, Mobility and Aging. *Med Sci Sports Exerc*. 2025 Apr 18. doi: 10.1249/MSS.0000000000003730.

5) Contributions through the MoTrPAC consortium and Studies of Muscle, Mobility and Aging (SOMMA) group.
I have been working within the MoTrPAC consortium for 10 years. My lab was one of 3 preclinical sites that performed very defined exercise interventions with 6mo and 18mo old F344 male and female rats. Beyond the tissue collections, we have been actively involved in the analysis of the multi-tissue, multi-omics findings. This work has resulted in my lab gaining expertise in large dataset handling, working with established informatics pipelines for RNAseq, ATACseq and ChIPseq data as well as handling differential analysis outputs from metabolomics and proteomics cores. We have now integrated these skills for work across all research projects in the lab.

My lab has also been the site for the RNA processing for bulk RNAseq and now single nuclei RNA seq along with ATAC seq (10X platform) for the SOMMA study. The initial SOMMA period led to >800 samples being prepped for RNAseq with subsequent analysis. In the second round of SOMMA we will continue our bulk RNAseq for new subjects while applying single nuclei techniques to a targeted cohort. My lab has the technical and computational expertise for these studies and we continue to apply new molecular tools for deeper understanding of aging and muscle health.

My lab has always made the omics data from these studies publicly available after the first publication. I looking forward to application of these approaches to address questions ranging from targeted cell specific omic changes to multi-tissue, multiplatform systems physiology questions.

a) Chen, Y-W, G. Nader, K. Baar, M. Fedele, E. Hoffman, and **K.Esser**. Response of rat muscle to acute resistance exercise defined by transcriptional and translational profiling. J. Physiol:London. 545: 27-41 2002
b) Terry, EE, Zhang X, Hoffmann C,Hughes, LD, Lewis SA , Li J, Wallace MJ, Riley LA, Douglas CA , Gutierrez-Monreal M, Lahens N, Gong, M, Andrade, F, **Esser, KA** and ME Hughes. Transcriptional profiling reveals extraordinary diversity among skeletal muscle tissues. eLife May 29;7. 2018 PMCID: PMC6008051
c) Nair, VD, Vasoya, M, Nair V., Smith, G. Pincas, H, Ge, Y, Douglas, CM, **Esser, KA**, Sealfon, SC. Differential analysis of chromatin accessibility and gene expression profiles identifies cis-regulatory elements in rat adipose and muscle. Genomics, 113(6):3827-3841, 2021
d) Amar D, Gay NR, Beltran MJ, …. **Esser KA***, MoTrPAC study group. Temporal dynamics of the multi-omic response to endurance exercise training across tissues. ***one of the corresponding authors.** *Nature*, 2024 May;629(8010):174-183. doi: 10.1038/s41586-023-06877-w.

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