BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. ***DO NOT EXCEED FIVE PAGES.***

NAME: **W. Lee Kraus**

eRA COMMONS USER NAME *(credential, e.g., agency login)*: wlkrauscornell99

POSITION TITLE: **Director, Cecil H. and Ida Green Center for Reproductive Biology Sciences**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date	FIELD OF STUDY
Cornell University, Ithaca, NY	B.S.	05/1989	Animal Physiology
University of Illinois, Urbana-Champaign	M.S.	05/1991	Physiol./ Cell, Mol. Biol.
University of Illinois, Urbana-Champaign	Ph.D.	05/1994	Physiol./ Cell, Mol. Biol.
University of Illinois, Urbana-Champaign	Postdoc	12/1994	Molecular Biology
University of California, San Diego	Postdoc	01/1999	Biochem., Mol. Biology

A. Personal Statement

My expertise is in the biophysical, biochemical, molecular, genomic, and proteomic analysis of chromatin structure and signal-regulated transcription, especially as it relates to cancer, reproduction, endocrinology, inflammation, and metabolism. In my lab at Cornell University (1999-2010) and UT Southwestern (2010-present), I have been studying the molecular biology, biochemistry, and genomics of signal-regulated transcription, with a focus on estrogen, cytokine (e.g., TNFα, IFNγ) and nuclear NAD^+ signaling and key mediators of these pathways such as estrogen receptors, NF-κB, C/EBPβ, other transcription factors, and poly(ADP-ribose) polymerases (PARPs). Since 2005, my lab has been using advanced genomics and bioinformatics approaches, including RNA-seq, ChIP-seq, GRO-seq, and ATAC-seq, and I have been instrumental in establishing these methodologies and building the related infrastructure at UT Southwestern. I am a leader in the fields of molecular endocrinology, nuclear receptors, and PARPs. I have been an organizer for international meetings on these topics, and serve as an editor or editorial board member for a number of journals in these areas. I am the founding organizer of the Cold Spring Harbor Laboratory meeting on PARPs and I served as a guest editor for special PARP focus issues in *Molecular Cell* (2016) and *Genes Dev.* (2020). I am also a founder, consultant, and SAB member for Ribon Therapeutics, Inc. and ARase Therapeutics Inc., two companies focused on PARPs/ADPRylation operating in Boston since 2015 and 2020, respectively. I have a strong interest in clinical and translational research, especially as it pertains to cancer, reproductive abnormalities, inflammation-based pathologies, and metabolic diseases.

• Relevant ongoing projects that I would like to highlight include:

R01 DK069710-17 - Kraus (PI) Period: 9/2022 through 7/2026 (4 years)
NIH/NIDDK - “The Role of Nuclear PARPs in Hormone-Regulated Transcription”

R01 DK058110-22 - Kraus (PI) Period: 6/2021 through 5/2025 (4 years)
NIH/NIDDK - “Activity of Nuclear Receptor Coregulators with Chromatin”

R01 CA251943-01 - Kraus (PI) Period: 4/2021 - 3/2026 (5 years)
NIH/NCI - “Role of Transcription Factor ADP-ribosylation in Breast Cancer Biology”

R01 CA229487-03 - Kraus (PI) Period: 8/2018 - 1/2024 (5 years)
NIH/NCI - “Context-Dependent Effects of PARP Inhibitors on Breast Cancer Bone Metastasis”

RP220325-01 - Kraus (PI) Period: 3/2022 - 2/2025 (3 years)
CPRIT - “Loss of Site-Specific ADP-ribosylation of Oncohistones in Cancers”

OC200311-01 - Kraus (PI) Period: 9/2021 - 8/2024 (3 years)
US DOD OCRP - “NAD+ Synthesis, Mono(ADP-Ribosyl)ation, Protein Translation, and Proteostasis in Ovarian Cancer”

NGP10107 - Kraus (PI) Period: 6/2021 - 3/2025 (4 years)
Burroughs Wellcome Fund Next Generation Pregnancy Initiative - “A Multi-Omics Approach to Understanding Human Placenta Gene Expression”

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments:

7/22 - present	Assistant Dean for Research Development, UT Southwestern Medical Center, Dallas.
1/21 to present	Consultant and Scientific Advisory Board Member, Alphina Therapeutics, Inc., New Haven, CT.
11/20 - present	Founder, Consultant, SAB member, and BOD member ARase Therapeutics, Inc., Boston, MA.
9/19 – present	Assistant Director for Basic Science, Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas.
4/17 - 12/21	Guest Professor (4/17-5/19) and Advisory Professor (6/19-12/21), Union Hospital, Tongji Medical College, Huazhong University of Science and Tech., Wuhan, China.
4/15 - present	Founder, Consultant, and SAB member, Ribon Therapeutics, Inc., Boston, MA.
7/10 - present	Professor and Vice Chair for Basic Sciences, Department of Obstetrics and Gynecology, Professor of Pharmacology, UT Southwestern Medical Center, Dallas.
7/10 - present	Professor and Director, Cecil H. and Ida Green Center for Reproductive Biology Sciences, UT Southwestern Medical Center, Dallas.
9/09 to 7/10	Professor, Dept. of Pharmacology, Weill Medical College of Cornell University, New York, NY.
7/09 to 7/10	Professor, Dept. of Molecular Biology and Genetics. Cornell University, Ithaca, NY.
10/06 to 8/09	Associate Professor, Department of Pharmacology, Weill Medical College of Cornell University, New York, NY.
7/04 to 6/09	Associate Professor, Department of Molecular Biology and Genetics. Cornell University, Ithaca, NY.
7/02 to 8/04 & 7/08 to 8/13	Instructor, Summer Short Course on Eukaryotic Gene Expression, Cold Spring Harbor Laboratories, CSH, NY.
9/00 to 9/06	Assistant Professor, Department of Pharmacology, Weill Medical College of Cornell University, New York, NY.
2/99 to 6/04	Assistant Professor, Department of Molecular Biology and Genetics. Cornell University, Ithaca, NY.
1/95 to 1/99	Postdoctoral Fellow, Department of Biology, University of California, San Diego (with Dr. Jim Kadonaga).
5/94 to 12/94	Postdoctoral Research Associate, Department of Physiology and Biophysics, University of Illinois, Urbana-Champaign (with Dr. Benita Katzenellenbogen).

Other Experience and Professional Memberships:

2023-2026	Member, Board of Directors, The Endocrine Society
2021	Chair, dkNET (NIDDK Information Network) External Evaluation Panel (EEP) Meeting (December 13, 2021).
2019 to 2022	Chair, Basic Science Advisory Group, The Endocrine Society.
2019	NHLBI Pulmonary Branch Site Visit review for the Division of Intramural Research, Bethesda, MD (April 29th, 2019).
2018 to 2022	Organizer, 2019, 2021 (virtual), and 2022 FASEB meetings on NAD^+ Metabolism and Signaling (lead organizer 2022).
2018 to 2019	Basic Science Chair, The Endocrine Society, 2019 Annual Meeting.
2014 to 2020	Founding organizer, CSH Laboratory meeting on PARPs and ADP-ribosylation.
2013 to present	Senior Editor, *Molecular Cancer Research*
2013 to 2017	Editor, *Molecular Endocrinology* (and *Endocrinology*)
2013 to 2017	External Scientific Panel, NIDDK Consortium Interconnectivity Network (dkCOIN)
2011 to 2015	Editorial Board, *Trends in Endocrinology and Metabolism.*
2011 to present	Member, The Society for the Study of Reproduction.
2010 to present	Editorial Board, *Transcription.*
2008 to 2010	Lead organizer, 2010 Keystone Meeting on NRs: Signaling, Gene Reg. & Cancer.
2008 to 2019	Editorial Board, *Molecular and Cellular Biology.*
2007 to 2010	Standing Member, NIH Molecular and Cellular Endocrinology (MCE) Study Section.
2007 to 2009	Editorial Board, *Molecular Endocrinology.*
2006 to 2008	Co-organizer, 2008 Keystone Meeting on Nuclear Receptors (NRs): Steroid Sisters.
2001 to present	Abstract reviewer, The Endocrine Society Annual Meeting (2001 to 2010, 2019 to present).

2005 to present	NIH Study Section service: Molecular and Cellular Endocrinology (MCE) Study Section, standing member (four year term: 2007 – 2010); 6 ad hoc sessions for various Study Sections.
2000 to present	Member, The American Society for Microbiology.
Since 1999	Ad hoc reviewer for *Cancer Cell, Cell, Cell Metabolism, EMBO J.*, *EMBO Reports, Genes and Development, Journal of Biological Chemistry, Molecular Cell, Nature, Nature Cell Biology, Nature Communications, Proc. Natl. Acad. Sci. USA., Science*.
1996 to present	Member, The Endocrine Society (Membership Committee, 2003 to 2006; Annual Meeting Steering Committee, 2006 to 2009).
1994 to present	Member, American Association for the Advancement of Science.

Honors:

2014	Endocrine Society's Ernst Oppenheimer Award for research excellence.
2010 to present	Cecil H. and Ida Green Distinguished Chair in Reproductive Biology Sciences, UT Southwestern Medical Center, Dallas.
2008	Cornell University CALS Excellence in Undergraduate Research Mentoring Award.
2007	Endocrine Society's Richard E. Weitzman Memorial Award for research excellence.
2006	Univ. of Illinois, Dept. of Mol. & Integrative Physiology Distinguished Alumni Award.
2004	Cornell University CALS Young Faculty Teaching Excellence Award.
1998 to 2002	Burroughs Wellcome Fund Career Award in the Biomedical Sciences.
1998	American Cancer Society, California Division Postdoctoral Fellowship.
1995 to 1998	NIH Postdoctoral Fellowship in Molecular Biology.

C. Contributions to Science

My research as a student, postdoc, and PI over the past 30 years has contributed to our understanding of the mechanisms of signal-regulated gene transcription, especially related to estrogen, cytokine, and nuclear NAD^+ signaling. My studies, which have been at the forefront of research on chromatin, transcription regulation, nuclear signaling pathways, and genomics, have fundamentally changed our understanding of how signal-regulated transcription factors, coregulator complexes, and histone- and chromatin-modifying enzymes collaborate to modulate chromatin structure and gene expression. This work has provided new insights into the molecular mechanisms that underlie gene regulation in a variety of biological systems, from reproduction and metabolism to cancer and inflammation.
Publications list (148 total): https://pubmed.ncbi.nlm.nih.gov/?term=kraus+wl&sort=date

1) *PARPs, NAD^+, and ADP-ribosylation: Links to Chromatin Structure and Gene Regulation*

Studies of poly(ADP-ribosyl)ation by nuclear poly(ADP-ribose) polymerases (PARPs) enzymes was largely focused on their roles in DNA damage detection and repair in the 1960s through 1990s. In the early 2000s, my lab was one of a small number that began to link PARP-1, an abundant nuclear PARP, to the regulation of chromatin structure and gene expression. Using biophysical, biochemical, and molecular approaches, my lab found that PARP-1 plays keys roles in the modulation of chromatin structure and gene expression in response to extracellular signals, such as those mediated by estrogens, TNFα, and IFNγ. In addition, my lab has taken the lead in understanding how the synthesis of nuclear NAD^+, the substrate for PARP-1, by the nuclear NAD^+ synthase NMNAT-1 controls the gene regulatory functions of PARP-1. These studies have linked cellular metabolic state to signal-regulated transcriptional outcomes and downstream biology.

Kim M.Y., Mauro S.A., Gévry N., Lis J.T., **Kraus W.L.** (2004) Modulation of chromatin structure and transcription by nucleosome-binding properties of PARP-1. *Cell* 119:803-814. PMID: 15607977

Luo, X., Ryu K.W., Kim D.-K., Nandu T., Medina C.J., Gupte R., Gibson B.A., Soccio R.E., Yu Y., Gupta R., **Kraus W.L.** (2017) PARP-1 controls the adipogenic transcription program by PARylating C/EPBβ and modulating its transcriptional activity. *Molecular Cell* 65:260-271. PMCID: PMC5258183

Ryu K.W., Nandu T., Kim J., Challa S., DeBerardinis R.J., **Kraus W.L.** (2018) Metabolic regulation of transcription through compartmentalized NAD^+ biosynthesis. *Science* 360:eaan570 and p. 618. PMCID: PMC6465534

Challa S., Khulpateea B.R., Nandu T., Camacho C.V., Ryu K.W., Chen H., Peng Y., Lea J.S., **Kraus W.L.** (2021) Cytoplasmic NAD^+ synthesis and ribosome ADP-ribosylation inhibit translation and maintain proteostasis in ovarian cancer. *Cell* 184:4531-4546.e26. PMCID: PMC8380725

Huang D., Camacho C.V., Setlem R., Ryu K.W., Parameswaran B., Gupta R.K., **Kraus W.L.** (2020) Functional interplay between histone H2B ADP-ribosylation and phosphorylation controls adipogenesis. *Molecular Cell* 79:934-949.e14. PMCID: PMC7502539.

Gupte R., Nandu T., **Kraus W.L.** (2021) Nuclear ADP-ribosylation drives IFNγ-dependent STAT1α enhancer formation in macrophages. *Nature Comm* 12:3931. PMCID: PMC8225886.

2) *The 'Omics' of PARPs, ADP-ribosylation, and Related Factors*

'Omics' approaches, such as genomics and proteomics, have revolutionized the study if complex biological systems. The application of these methodologies to PARPs, ADP-ribosylation, and related factors, however, has lagged behind other areas of biology. My lab has been instrumental in bringing omics to the PARP field. We have used assays, such as ChIP-seq and GRO-seq, to understand where nuclear PARPs localize across the genome and how they regulate gene expression. In addition, we have developed Click-ChIP-seq, the only method available to identify PARP-specific ADP-ribosylation events across the genome. We have also developed and used the most recent mass spectrometry-based proteomics approaches to identify the ADP-ribosylated proteome. This includes the development of an analog-sensitive PARP approach with clickable NAD^+ analogs PARP-specific ADP-ribosylation events proteome-wide.

Krishnakumar R., Gamble M.J., Frizzell K.M., Berrocal J.G., Kininis M., and **Kraus W.L.** (2008) Reciprocal binding of PARP-1 and histone H1 at promoters specifies transcriptional outcomes. *Science* 319:819-821. PMID: 18258916

Gibson, B.A., Zhang, Y., Jiang, H., Hussey, K.M., Shrimp, J.H., Lin, H., Schwede, F., Yu, Y., and **Kraus, W.L.** (2016) Chemical genetic discovery of PARP targets reveals a role for PARP-1 in transcription elongation. *Science* 353:45-50. PMCID: PMC5540732

Liu, Z., **Kraus W.L.** (2017) Catalytic-independent functions of PARP-1 determine Sox2 pioneer activity at intractable genomic loci. *Molecular Cell* 65:589-603. PMCID: PMC5319724

Kim D-S., Camacho C.V., Nagari A., Malladi V.S., Challa S., and **Kraus W.L.** (2019) Activation of PARP-1 by snoRNAs controls ribosome biogenesis and cell growth via the RNA helicase DDX21. *Molecular Cell.* 75, 1270–1285**.** PMCID: PMC6754283

3) *Nuclear Signaling, Chromatin, and Gene Regulation*

Although the contribution of chromatin to gene regulation was recognized and studied in the 1970s and 1980s, it wasn't until 1996 that Allis, Berger, and colleagues linked the enzymatic modification of histones by coregulators to gene regulatory outcomes. This started a revolution in the field of gene regulation and necessitated new methods to explore transcriptional regulation by physiologically relevant transcription factors and coregulators. My lab has developed and employed a wide variety of biochemical, cellular, genomic, and proteomic approaches to study the nuclear endpoints of cellular signaling pathways, including signal-regulated transcription factor activity, alterations of chromatin structure, and the regulation of RNA Pol II activity. These studies have helped to link the regulation of chromatin with Pol II-dependent transcriptional outcomes.

Acevedo M.L., Lee K.C., Stender J.D., Katzenellenbogen B.S., **Kraus W.L.** (2004) Selective recognition of distinct classes of coactivators by a ligand-inducible activation domain. *Molecular Cell* 13:725-738. PMID: 15023342

Danko C.G., Hah N., Luo X., Martins A., Siepel A., **Kraus W.L.** (2013) Signaling pathways differentially affect RNA polymerase II initiation, pausing, and elongation rate in cells. *Molecular Cell* 50:212-222. PMCID: PMC3640649

Franco H.L., Nagari A., **Kraus W.L.** (2015) TNFα signaling exposes latent estrogen receptor binding sites to alter the breast cancer cell transcriptome. *Molecular Cell.* 58:21-34. PMCID: PMC25752574

Murakami S., Nagari A., **Kraus W.L.** (2017) Dynamic assembly and activation of estrogen receptor α enhancers through coregulator switching. *Genes Dev.* 31:1535-1548. PMCID: PMC5630019

4) *Signal-Regulated Transcriptomes and Non-Coding RNAs*

The past decade has seen an incredible growth of genomic approaches to query gene regulation and the nature of the transcriptome on a global scale. My lab has leveraged new genomic methodologies, including global run-on sequencing (GRO-seq), to explore signal-regulated transcription in multiple cell types. We have also annotated new non-coding RNAs, including long non-coding RNAs (lncRNAs), antisense RNAs, and enhancer RNAs, and have begun to explore their functions. Furthermore, we have used genomic assays to examine the molecular mechanisms that drive signal-regulated transcriptional responses. These studies have characterized: (1) the robust and rapid changes that occur across the genome in response to estrogen and TNFα and (2) the expression of thousands of previously unannotated noncoding RNA transcripts, significantly altering our view of signal-regulated transcriptional responses

Hah N., Danko C.G., Core L., Waterfall J.J., Siepel A., Lis J.T., **Kraus W.L.** (2011) A rapid, extensive, and transient transcriptional response to estrogen signaling in breast cancer cells. *Cell* 145:622-634. PMCID: PMC3099127

Hah N., Murakami S., Nagari A., Danko C.G., **Kraus W.L.** (2013) Enhancer transcripts mark active estrogen receptor binding sites. *Genome Research* 23:1210-1223. PMCID: PMC3730096

Sun M., Gadad S.S., **Kraus W.L.** (2015) Discovery, annotation, and functional analysis of long noncoding RNAs controlling cell cycle gene expression and growth in breast cancer cells. *Molecular Cell.* 59:698-711. PMCID: PMC4546522

Hou T.Y., **Kraus W.L.** (2022) Analysis of estrogen-regulated enhancer RNAs identifies a functional motif required for enhancer assembly and gene expression. *Cell Reports*. 39:110944. doi: 10.1016/j.celrep.2022.110944. PMCID: PMC9246336

5) *Applying Genomics, Bioinformatics, and Computational Biology to the Study of Gene Regulation*

To support the research described in 1 through 4 above, my lab has developed and/or applied a wide variety of genomic tools, including novel computational pipelines designed to integrate, analyze, and visualize data from a wide variety of genomic (and proteomic) platforms. These include groHMM, a hidden Markov model-based algorithm for predicting primary transcription units based on GRO-seq data, and TFSEE, a pipeline for integrating genomic data to identify active enhancers. groHMM has been deposited as an R-based package in Bioconductor for the community to use freely. In addition to generating useful tools, our studies have helped to elucidate new facets of the genome and transcriptome.

Danko C.G., Chae M., Martins A., **Kraus W.L.** (2014) groHMM: GRO-seq Analysis Pipeline. R package version 1.0.0. *Bioconductor*. (Software) - www.bioconductor.org/packages/release/bioc/html/groHMM.html.

Danko C.K., Hyland S.L., Core L.J., Martins A.L., Waters C.T., Lee H.W., Cheung V.G., **Kraus W.L.**, Lis J.T., Siepel A. (2015) Accurate identification of active transcriptional regulatory elements from global run-on and sequencing data. *Nature Methods.* 12:433-438. PMCID: PMC4507281

Chae M., Danko C.G., **Kraus W.L.** (2015) groHMM: A computational tool for identifying unannotated and cell type-specific transcription units from global run-on sequencing data. *BMC Bioinformatics* 16:222. PMCID: PMC4502638

Franco H.L., Nagari A., Malladi V., Li W., Xi Y., Richardson D., Allton K.L., Tanaka K., Li J., Murakami S., Keyomarsi K., Bedford M.T., Shi X., Li W., Barton M.C., Dent S.Y.R., **Kraus W.L.** (2018) Enhancer transcription reveals subtype-specific gene expression programs controlling breast cancer pathogenesis. *Genome Research* 28:159-170. PMCID: PMC5793780

See also: Many of the papers listed in 1 through 4, above.