BIOGRAPHICAL SKETCH

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NAME: Conklin, Daniel J.

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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
Univ. of Wisconsin-Whitewater, Whitewater, WI	B.S.	05/86	Biology, Chemistry
Univ. of Wisconsin-LaCrosse, LaCrosse, WI	M.S.	08/89	Biology
Univ. of Notre Dame, Notre Dame, IN	Ph.D.	12/95	Cardiovascular Phys.
Univ. of Texas Medical Branch, Galveston, TX	Post-Doc	01/96-07/98	Cardiovascular Toxicol.

B. Position and Honors

Positions

1996-1998 National Institute of Environmental Health Sciences Toxicology Postdoctoral Fellow, University of Texas Medical Branch, Galveston, TX
1998-2002 Assistant Professor, Department of Biology, University of Wisconsin-Eau Claire, Eau Claire, WI
2003 Associate Professor, Department of Biology, University of Wisconsin-Eau Claire, Eau Claire, WI
2003-2009 Assistant Professor, Division of Cardiovascular Medicine, Department of Medicine, University of Louisville, Louisville, KY
2006-2014 Study Section Peer Reviewer, American Heart Association Great Rivers Affiliate (formerly Ohio Valley Affiliate); Vascular and Endothelium Biology 2: Co-Chair, 2011-2012; Chair, 2013-2014
2009 NIEHS R13 Study Section Ad Hoc Peer Reviewer
2009-present Director, Inhalation Facility, Division of Cardiovascular Medicine, Department of Medicine, University of Louisville, Louisville, KY
2009-2015 Associate Professor, Division of Cardiovascular Medicine, Department of Medicine, University of Louisville, Louisville, KY
2010-14 Councilor, Vice-President, President Cardiovascular Toxicology Specialty Section, Society of Toxicology
2011-present Director, Animal Core, Diabetes and Obesity Center, University of Louisville, Louisville, KY
2012-13 NIEHS Cardiovascular and Sleep Epidemiology (CASE) Study Section Peer Review (*ad hoc*)
2012-2016 Associate Editor, *Cardiovascular Toxicology*
2012-present Associate Editor, *Toxicology and Applied Pharmacology*
2013, 2015 NIEHS Systemic Injury of Environmental Exposure (SIEE) Study Section Peer Review (*ad hoc*)
2013-present Director, Tobacco Product Evaluation and Exposure Core, American Heart Association – Tobacco Regulation and Addiction Center (A-TRAC), University of Louisville, Louisville, KY
2014 Search Committee, Chair, Diabetes and Obesity Center, University of Louisville, Louisville, KY
2014 NIEHS Special Emphasis Panel (SEP) Study Section Peer Review (*ad hoc*)
2015 NIH Cancer, Cardiovascular and Sleep Epidemiology Study Section Peer Review (*ad hoc*)
2015-2017 Councilor, Inhalation and Respiratory Specialty Section, Society of Toxicology
2015 Professor, Division of Cardiovascular Medicine, Department of Medicine, University of Louisville, Louisville, KY
2015-present Editorial Board, *Circulation Research*

2016-2018 NIEHS Systemic Injury of Environmental Exposure (SIEE) Study Section Peer Review (permanent member)

Honors

1996 Eli J. and Helen Shaheen Graduate School Award In Science, University of Notre Dame
1998 National Research Service Award (NRSA), National Institutes of Environmental Health Sciences, Postdoctoral Fellowship, University of Texas Medical Branch, Galveston, TX
2003 Academic Research Enhancement Award (R15), National Institutes of Environmental Health Sciences, University of Wisconsin-Eau Claire, Eau Claire, WI
2011 "Top Reviewer" -- Toxicology and Applied Pharmacology
2014 Service Award, Cardiovascular Toxicology Specialty Section, Society of Toxicology

C. Contributions to Science (**bolded** authors indicate trainees)

1. *Comparative Physiology of Vascular Regulation:* Initially, I focused my research on mechanisms of vascular control in non-mammalian vertebrate models primarily fish because fish are the most diverse vertebrate class (>30,000 species), and thus, mechanisms of vaso-control (and ones operative in terrestrial vertebrates) likely evolved in fish. We assessed numerous mechanisms in a variety of species under physiological conditions, and identified vascular responses to classical mammalian vasoactive agents including angiotensin II (a.), arginine vasotocin (AVP in mammals; b.), atrial natriuretic peptide (ANP; c.), and localized vascular acclimation in snakes (spun head-in over weeks in a centrifuge at NASA; d.). Collectively, these data provide an evolutionary context for extant mammalian vaso-control mechanisms.

a. *Conklin, D.J.* and K.R. Olson. 1994. Angiotensin II relaxation of rainbow trout vessels *in vitro*. *Am. J. Physiol.* 266:R1856-R1860. PMID: 8024039.
b. *Conklin, D.J.*, **N.W. Mick** and K.R. Olson. 1996. Arginine vasotocin relaxation of gar (*Lepisosteous spp.*) hepatic vein *in vitro*. *Gen. Comp. Endo.* 104:52-60. PMID: 8921355.
c. Olson, K.R., *D.J. Conklin*, A.P. Farrell, J.E. Keen, Y. Takei, **L. Weaver, Jr**., M.P. Smith and Y. Zhang. 1997. Effects of natriuretic peptides and nitroprusside on venous function in trout. *Am. J. Physiol.* 273:R527-R539. PMID: 9277535.
d. *Conklin, D.J.*, H.B. Lillywhite, K.R. Olson, R. Ballard and A.R. Hargens. 1996. Blood vessel adaptation to gravity in a semi-arboreal snake*. J. Comp. Physiol. B.* 196(7):425-432. PMID: 8617890.

2. *Role of Amine Metabolism in Vascular Control and Pathology:* Several primary amines stimulate vascular relaxation via a vascular-rich semicarbazide-sensitive amine oxidase (SSAO) enzyme that generates equal molar quantities of an amine-specific aldehyde, H_2O_2 and ammonia (NH_3). The enigmatic SSAO is highly expressed in the vasculature and in the presence of allylamine, an exogenous amine, there is a rapid onset of irreversible vasospasm in aorta (a.) and coronary arteries (b.). These studies highlight the potent dual action of amine metabolism mediated by vascular wall SSAO (c.), and in particular revealed that acrolein is a potent vascular toxin capable of inducing vasospasm in isolated human blood vessels (d.) – a highly relevant clinical cause of acute myocardial infarction and coronary artery bypass graft (CABG) failure.

a. *Conklin, D.J.* and P.J. Boor. 1998. Allylamine cardiovascular toxicity: evidence for aberrant vasoreactivity. *Tox. Appl. Pharm*. 148(2):245-251. PMID: 9473532.
b. *Conklin, D.J.,* **C.L. Boyce**, M.B. Trent and P.J. Boor. 2001. Amine metabolism: a novel path to coronary artery vasospasm. *Tox. Appl. Pharm*. 175(2):149-159. PMID: 11543647.
c. *Conklin, D.J.*, **H.R. Cowley**, R.J. Wiechmann, G.H. Johnson, M.B. Trent and P.J. Boor. 2004. Vasoactive effects of methylamine in isolated human blood vessels: Role of semicarbazide-sensitive amine oxidase, formaldehyde, and hydrogen peroxide. *Am.J. Physiol. Heart Circ. Phys*. 286:H667-H676. PMID: 14715500.
d. *Conklin, D.J.*, A. Bhatnagar, **H. Cowley**, G.H. Johnson, R.J. Wiechmann, L.M. Sayre, M.B. Trent and P.J. Boor. 2006. Acrolein stimulates hypercontraction in isolated human blood vessels. *Tox. Appl. Pharm.* 217(3):277-88. PMID: 17095030; PMCID: PMC3487162.

3. *Environmental Cardiology:* Since 1993 and the publication of the '*Harvard Six Cities Study'*, the mechanism by which air pollution increases mortality and enhances cardiovascular disease risk has been an intriguing question. Upon joining Dr. Aruni Bhatnagar in 2003 at the Univ. of Louisville, my research has specifically addressed this larger question by focusing on particulate matter (a.) and aldehydes (b.) present in the environment. Uniquely, our group has identified novel and sensitive cardiovascular-specific biomarkers of

air pollution exposure in mice and humans. To this end, we were the first to show that elevated ambient air pollution decreased the level of circulating stems cells (i.e., endothelial progenitor cells, EPCs), important for cardiovascular health, in both young healthy humans (a.) and mice (a., b.). Moreover, we demonstrated that the mechanisms underlying this effect was a systemic 'VEGF resistance' (c.), and that a similar response is triggered by low-level exposure to acrolein (d.) indicating that air pollution at levels encountered in the real world impacts the physiological regulation of circulating stem cells perhaps depressing vascular repair, and thereby, enhancing cardiovascular disease risk.

a. O'Toole, T.E., Hellmann, J., **Wheat, L.**, Haberzettl, P., **Lee, J.,** *Conklin, D.J.*, Bhatnagar, A. and Pope, C.A., 3rd. 2010. Episodic exposure to fine particulate air pollution decreases circulating levels of endothelial progenitor cells. *Circ. Res.* 107(2):200-203. PMID: 20595651; PMCID: PMC2943671.
b. *Conklin, D.J.*, Barski, O.A., **Lesgards, J-F**., Juvan, P., Rezen, T., Rozman, D., Prough, R.A., Vladykovskaya, E., Liu, SQ., Srivastava, S. and A. Bhatnagar. 2010. Acrolein consumption induces systemic dyslipidemia and lipoprotein modification. *Toxicol. Appl. Pharm.* 243(1):1-12. PMID: 20034506; PMCID: PMC2922677.
c. **Wheat, L.A.,** Haberzettl, P., Hellmann, J., Baba, S.P., **Bertke, M., Lee, J.,** McCracken, J., O''Toole, T.E., Bhatnagar, A. and *Conklin, D.J.* 2011. Acrolein inhalation prevents vascular endothelial growth factor-induced mobilization of Flk-1^+/Sca-1^+ cells in mice. *Arterioscler. Thromb. Vasc. Biol.* 31(7):1598-1606. PMID: 21415405; PMCID: PMC3182098.
d. Haberzettl, P., **Lee, J., Duggineni, D.**, McCracken, J., Bolanowski, D., O'Toole, T.E., Bhatnagar, A. and *D. J. Conklin*. 2012. Exposure to ambient air fine particulate matter prevents VEGF-Induced mobilization of endothelial progenitor cells from the bone marrow. *Environ. Health Pers.* 120(6):848-856. PMID: 22418586; PMCID: PMC3385427.

4. *Role of Aldehyde Metabolism in Cardiovascular Toxicity and Disease Pathogenesis*: Over the last decade, we have documented the relatively high sensitivity of cardiovascular targets to exogenous and endogenous aldehyde exposure, especially responses to acrolein. Moreover, we have explored the metabolic basis of this exquisite cardiovascular sensitivity to aldehyde-induced injury by focusing on the specific contribution that aldehyde metabolism enzymes (aldose reductase, aldehyde dehydrogenase, GST, P450s, a.) makes to acute target organ injury and disease pathogenesis. For example, we study aldehyde-metabolizing enzymes that mediate GSH conjugation of unsaturated aldehydes, such as glutathione *S*-transferase P (GSTP). GSTP modulates aldehyde toxicity under environmentally- and clinically-relevant exposure conditions (i.e., inhaled acrolein, b. tobacco smoke, b.; CY, c.; ischemia-reperfusion, d.), thus, exemplifying the practical strength of our concept and its theoretical underpinnings. Moreover, we have in parallel showed in our animal models that these aldehyde metabolizing enzymes are also protective against the progression toward diabetes, which has important implications for this emerging epidemic.

a. **Amunom, I.**, Stephens, L.J., Tamasi, V., *Conklin, D.J.*, Bhatnagar, A., Srivastava, S., Martin, M.V., Guengerich, F.P. and R.A. Prough. 2007. Cytochromes P450 catalyze oxidation of α,β-unsaturated aldehydes. *Archives of Biochemistry & Biophysics.* 464:187-96. PMID: 17599801; PMCID: PMC1994811.
b. *Conklin, D.J.,* Haberzettl, P., Prough, R.A. and A. Bhatnagar. 2009. Glutathione *S*-transferase P protects against endothelial dysfunction induced by exposure to tobacco smoke. *Am. J. Physiol. Heart Circ. Phys*. 296(5):H1586-97. PMID: 19270193; PMCID: PMC2685347.
c. *Conklin, D.J.*, Haberzettl, P., **Lesgards, J-F**, Prough, R.A., Srivastava, S. and A. Bhatnagar. 2009. Increased sensitivity of glutathione S-transferase P-null mice to cyclophosphamide-induced urinary bladder toxicity. *Jrl. Pharmacol. Expt. Therap.* 331(2):456-69. PMID: 19696094; PMCID: PMC2775270.
d. *Conklin, D.J.,* Y. Guo, P. Haberzettl, B.G. Hill, S.P. Baba, L. Guo, **G. Jagatheesan**, **K. Wetzelberger**, D. Obal, D.G. Rokosh, R.A. Prough, S.D. Prabhu, M. Velayutham, J.L. Zweier, D. Hoetker, D.W. Riggs, S. Srivastava, R. Bolli, and A. Bhatnagar. 2015. Genetic deficiency of glutathione *S*-transferase P increases myocardial sensitivity to ischemia-reperfusion injury. *Circ. Res.* 117(5):437-49. doi: 10.1161/CIRCRESAHA .114.305518. PMID: 26169370. PMCID in process.

Public Bibliography URL:
http://www.ncbi.nlm.nih.gov/sites/myncbi/daniel.conklin.1/bibliography/40915266/public/?sort=date&direction=ascending.

D. Research Support

Ongoing

R01ES027881 Haberzettl (PI) 05/01/2017-04/30/2022
Air Pollution, Circadian Rhythm Disruption and Cardiometabolic Disease
The goal of this project is to test the novel hypothesis that air pollution exposure increases the risk of cardiovascular disease and diabetes via disruption of vascular circadian rhythm. This state of circadian dyssynchrony exacerbates cardiometabolic injury.
Role: Co-Investigator, **Conklin, D.J.**

R01 HL122676-01A1 **Conklin (PI)** 07/01/2015-04/30/2020
Cardiovascular Toxicity of Tobacco Products and Constituents
The goal of these studies is to identify biomarkers of cardiotoxicity in mice and humans associated with exposure to aldehydes present in conventional and electronic cigarettes.

FX-ATRAC-UL-01S **Conklin (PI)** 09/01/2015-06/30/2017 (NCE)
Toxicity and Thermal Degradation of Flavors
(Supplement American Heart Association – Tobacco Regulation and Addiction Center; A-TRAC)
The goal of these studies is to identify toxicity in isolated human cardiovascular cells due to exposure to flavors and their thermal degradation products present in electronic cigarette aerosols.

R01 HL122581-01 Baba (PI) 04/01/2014-03/31/2019
Cardiac Pathophysiology of Histidyl Dipeptides
The goal of these studies is to identify the mechanism by which histidyl dipeptides such as carnosine act to protect against ischemia-reperfusion-induced cardiovascular injury in mice.
Role: Co-Investigator, **Conklin, D.J.**

R01 HL120746 Srivastava (PI) 10/01/2013-09/30/2018
Tobacco Products and Atherosclerotic Disease
The goal of these studies is to examine the effects of harmful and potentially harmful constituents (HPHC) of tobacco on atherosclerosis.
Role: Co-Investigator, **Conklin, D.J.**

P20 GM103492-07 Bhatnagar (PI) 09/01/2013-08/31/2018
Diabetes and Obesity Center -- Center of Biomedical Research Excellence (COBRE)
The goals of this center are to train the new generation of scientists, develop new models and pioneer new techniques to be used in obesity and diabetes research.
Role: Co-Investigator/Core Director, **Conklin, D.J.**

P50 HL120163-03 Bhatnagar and Robertson (co-PIs) 07/01/2013-06/30/2018
American Heart Association – Tobacco Regulation and Addiction Center (A-TRAC)
The goal of these studies is to identify biomarkers of cardiotoxicity associated with exposure to harmful and potentially harmful constituents (HPHC) of tobacco.
Role: Co-Investigator, **Conklin, D.J.,** Director, Tobacco Product Evaluation and Exposure Core (TPEE)

R01 ES019217-01A1 O'Toole (PI) 06/01/2011- 05/31/2017 (NCE)
Endothelial progenitor cells and particulate air pollution
In this study we characterize the quantitative and qualitative properties of stem cell populations in humans and mice exposed to particulate air pollution.
Role: Co-Investigator; **Conklin, D.J.,** Director, University of Louisville Inhalation Facility

Completed

R21HL120050-01A1 Li (PI) 05/01/2014-08/30/2016
MicroRNAs as Biomarkers for Tobacco Exposure and Heart Disease
The goal of these studies is to evaluate the utility of microRNAs in blood as biomarkers of tobacco exposure and tobacco-related cardiovascular injury in mice and humans.

Role: Co-Investigator, **Conklin, D.J.**

R21 ES024030 **Conklin (PI)** 09/01/2013-08/31/2015
Novel Treatments of Acrolein-induced Cardiotoxicity
The goal of these studies is to develop a post-exposure intervention to prevent acute cardiotoxicity of acrolein.

14ATRAC23640000 **Conklin (PI)** 09/01/2014-08/31/2015
AHA Tobacco Regulation and Addiction Center (ATRAC) Pilot Research Grants Program
Electronic Cigarette Aldehydes and Cardiovascular Toxicity
The goal of these studies is to identify biomarkers of cardiotoxicity associated with exposure to harmful and potentially harmful constituents (HPHC) of electronic cigarettes.