# JESSICA M. BERTHIAUME, PH.D.

Case Western Reserve University
Dept. of Physiology & Biophysics
School of Medicine, E518/E534J
10900 Euclid Avenue
Cleveland, Ohio 44106
jessica.berthiaume@case.edu
+1 216.368.4183
ORCID: 0000-0003-1479-5177

## EDUCATION

| | | |
|---|---|---|
| **Doctor of Philosophy (Ph.D.), Toxicology** | University of Minnesota | 2006 |
| **Master of Science (M.S.), Chemistry,** | Univ. of Minnesota, Duluth | 2002 |
| **Bachelor of Science (B.S.), Biochemistry & Mol. Biology** | Univ. of Minnesota, Duluth | 1999 |

## ACADEMIC APPOINTMENTS & FOCUS

**Adjunct Instructor, Case Western Reserve University, Physiology & Biophysics** **2013-present**
Adaptive signaling that regulates cardiac energy metabolism in the normal and injured heart.

**Postdoctoral Scholar, Case Western Reserve Univ., Dept. of Nutrition** **2012-2013**
*Mentors: Drs. Guofang Zhang & Henri Brunengraber*
Metabolic disposition of oxidized lipid species in the heart.

**Postdoctoral Fellow, Case Western Reserve Univ., Physiology & Biophysics** **2007-2013**
*Mentor: Dr. Margaret P. Chandler*
Functional and metabolic effects of high dietary fat in the infarcted heart.

**Graduate Research Assistant, University of Minnesota, Biochemistry & Mol. Biology** **2000-2006**
*Mentor: Dr. Kendall B. Wallace*
Toxicological mechanisms of xenobiotic-mediated mitochondrial dysfunction.
- Mechanisms of Doxorubicin-Induced Mitochondrial Cardiotoxicity (Doctoral Thesis)
- Effects of Perfluorinated Fatty Acid Analogues on Mitochondrial Biogenesis (Master's Thesis)

## ADMINISTRATIVE APPOINTMENTS

**Interim Director, Neuroscience Rodent Behavioral Core, Case Western Reserve Univ.,** **2018-present**
**Director, Mouse Physiology Phenotyping Core, Case Western Reserve Univ.** **2013-present**

## OVERVIEW OF RESEARCH EXPERTISE

*In vivo* : Cardiovascular pathology models (myocardial infarction, transaortic constriction, streptotozocin-induced diabetes, anthracycline-induced cardiotoxicity) | Echocardiography (Doppler flow) | Invasive hemodynamics (PV loops) | Chronic-indwelling arterial catheterization | Dietary manipulation (high fat, ketogenic, ammonium chloride-induced metabolic acidosis) | Whole animal activity (running wheels)

*Ex vivo* : Working and Langendorff cardiac perfusion models using altered metabolic substrate conditions, ischemia-reperfusion, and altered afterload to investigate changes in metabolism.

Endpoints: $MVO_2$ | Heart rate | LV developed pressure | Cardiac output | Glucose/fatty acid oxidation rates

*In vitro* : Isolated mitochondrial respiration studies | Primary cardiomyocyte culture | Established cell line culture | basic transfection/transduction approaches

*Molecular :* Metabolic enzyme activities | circulating metabolite quantification | semi-targeted metabolomics (GC/LS mass spec) | Immunoblotting & gel shift assays | gene expression profiling (qPCR & microarray analysis)

## TEACHING & ACADEMIC ADVISING

**Medical School, Cardiovascular Block, Case Western Reserve Univ. (CWRU)** **2016-present**
Instructor/facilitator in team-based learning session for 1st year medical students (~60) on Cardiovascular Physiology and clinical case-based problems (contact hrs = 4/yr).

**Physiology Independent Study (PHOL 451), CWRU** **2015-present**
Course Director for graduate independent writing course on select topics in Physiology.

**Physiological Basis for Disease (PHOL 402) CWRU** **2014-2015**
Instructor for discussion-based, team-taught course in cardiovascular section of graduate course (contact hrs = 2).

**Academic Adviser, Medical Master's Program (Physiology & Biophysics) CWRU** **2014-present**
Adviser for large plan B master's program designed to prepare students for entry into healthcare professional programs (MD, DO, Dental, etc.). (contact hrs ~2/wk)

**Medical Physiology (PHOL 481), CWRU** **2013-present**
Instructor for large lecture (~140 students) in the cardiovascular block of departmental Medical Masters in Physiology core curriculum (contact hrs = 4/yr).

**Cardiovascular Physiology (PHOL 514), CWRU** **2011-present**
Instructor for small discussion-based graduate course on Cardiovascular Physiology (contact hrs = 6-10/yr), including evaluation of student performance through exams.

**Nucleic Acids & Proteins (PHOL 456), CWRU.** **2009-2012**
Instructor for graduate level course (small lecture format) with evaluation of student performance via homework, exams, & in-class discussion (contact hrs =13/yr).

**Course Director, Biochemistry (CHEM 3322), University of Minnesota** **2003**
- Developed course materials for upper division undergraduate course (~90 students).
- Delivered weekly lectures & out of class contact time (5hrs/wk, ~75 total contact hrs).
- Devised quizzes & exams for evaluation of student performance.

**Teaching Assistant, Biochemistry Laboratory (CHEM 4363) Univ. of MN** **2000**
**Teaching Assistant, Physical Chemistry Laboratory (CHEM 4374) Univ. of MN** **1999**

## RESEARCH MENTORSHIP

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|---|---|
| Katyayini Sharma, MS student (Physiology & Biophysics), Student Researcher | 2016-2017 |
| Nicole Kochman, Undergraduate Researcher, Senior Capstone project | 2015-2016 |
| Lena Ye, MS student (Physiology & Biophysics), Research Assistant | 2015-2016 |
| Jayant Raikhelkar, MD, University Hospitals, Cardiology Fellow, Research Rotation | 2014-2015 |
| Tyler Caldwell, MS Student (Physiology & Biophysics), Research Assistant | 2014-2015 |
| Evan Rotar, MS Student (Physiology & Biophysics), Research Intern | 2013-2014 |

## HONORS & AWARDS

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| Faculty Reach Out Program Scholar (FROP), Washington Univ., St. Louis, MO | 2014 |
| ASBMB Postdoctoral Travel Award (Annual Meeting, Experimental Biology) | 2013 |
| Annette Boman Fellowship Award, Univ. of Minnesota, Duluth | 2005 |
| NL-SOT Poster Award, 2nd Place | 2004 |
| Best Poster Award, Midwest Chapter of SETAC | 2002 |

## PROFESSIONAL SERVICE

*Journal Reviewer:* JCI, American J. Physiology (Heart, Endocrine), Cardiovascular Pathology, Heart Rhythm, Translational Research, PLoS One, and Toxicology.

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| Case Western Reserve Univ. (CWRU) medical school applicant interviewer | 2017-present |
| Case Western Reserve Univ. (CWRU) Faculty Senate Committee, Postdoctoral Rep. | 2010-2011 |
| CWRU Dept. of Physiology & Biophysics Planning Committee | 2008-present |
| CWRU Dept. Physiology & Biophysics, Postdoctoral Group, | 2008-present |
| Univ. of Minn., Biochemistry & Mol. Biology Graduate Student Journal Club, Chair | 2005-2006 |
| Society of Toxicology (SOT) Student Committee, Secretary | 2005-2006 |
| SOT Student Advisory Committee, Representative | 2004-2006 |
| SOT, Northland Chapter (NL-SOT), Student Representative | 2004-2006 |

## PROFESSIONAL SOCIETY AFFILIATION

| | |
|---|---|
| American Society for Biochemistry & Molecular Biology (ASBMB), member | 2012-present |
| American Heart Association (AHA), member | 2007-present |
| Sigma Xi, member | 2002-present |
| United Mitochondrial Disease Foundation, member | 2005-2008 |
| SOT, Northland Chapter, member | 2000-2007 |
| Soc. of Toxicology (SOT), National, member | 2000-2007 |
| Society of Environmental Chemistry & Toxicology (SETAC), member (Midwest) | 2002-2003 |

## PUBLICATIONS

https://www.ncbi.nlm.nih.gov/sites/myncbi/1h9ZhtoDq6pAG/bibliography/47884234/public/?sort=date&direction=descending

## ORIGINAL RESEARCH ARTICLES (*corresponding authorship, †equal author contribution)

Gonzalez-Vicente A, Hong NJ, Yang N, Cabral PD, Asirwatham J, **Berthiaume JM,** Dominici FP, & Garvin JL. Dietary Fructose Increases the Sensitivity of Proximal Tubules to Angiotensin II in Rats Fed High-Salt Diets. (*in preparation*)

Wang Y†, **Berthiaume JM**† Zhang GF. Dephosphorylation of acyl-CoAs: novel biochemical findings in the ischemic heart. J Mol Cell Card *(under review).*

Gonzalez-Vicente A, Cabral PD, Hong NJ, Asirwatham J, Yang N, **Berthiaume JM,** Dominici FP, & Garvin JL. 2017. Dietary fructose enhances the ability of low concentrations of angiotensin II to stimulate proximal tubule $Na^+$ reabsorption. Nutrients. 9(8), 885.

**Berthiaume JM**, Hsiung H, Austin AB, McBraier SP, Chandler MP, & Rosca MG, 2017. Methylene blue decreases lysine acetylation to alleviate metabolic inflexibility and dysfunction in the diabetic heart. Mol Cell Biochem. 432:7-24.

Xu K, Ye L, Sharma K, Jin Y, Harrison M, Caldwell T, **Berthiaume JM**, Luo Y, LaManna LC, & Puchowicz MA, 2017. Diet-induced ketosis protects against focal cerebral ischemia in mouse. Adv Exp Med Biol. 997:205-213.

Wadosky KM, **Berthiaume JM**, Tang W, Zunga M, Portman MA, Gerdes M, & Willis MS, 2016. MuRF1 inhibits cardiac thyroid hormone signaling by TR$\alpha$ mono-ubiquitination and localization to CAP350. J. Mol. Endocrin. 56(3):273-90.

- *This publication received a "best paper" award (1 of 5) by the Society for Endocrinology (2017)*

Zhou Y, Skelton LA, Xu L, Chandler MP, **Berthiaume JM**, & Boron WF, 2016. Role of Receptor Tyrosine Phosphatase $\gamma$ in sensing extracellular $CO_2$ and $HCO_3^-$. J Am Soc Nephrol. (JASN) 27(9):2616-21.

- *This publication was the subject of an editorial review: Soleimani 2016 JASN. 27:2543-45*

Vazquez E, **Berthiaume JM**, Kamath V, Achike O, Buchanan E, Montano M, Chandler MP, Miyagi M & Rosca MG, 2015. Mitochondrial complex I defect and increased fatty acid oxidation enhance protein lysine acetylation in the diabetic heart. Card Res. 107(4):453-65.

Jin Z†, **Berthiaume JM**†, Li Q, Henry F, Huang Z, Sadhukhan S, Tochtrop GP, Puchowicz M, & Zhang GF, 2014. Catabolism of 4-hydroxy-2(E)-nonenal via omega- and omega-1 oxidation initiated by Cytochrome P450 4A: stimulation by a ketogenic diet. J Biol Chem. 289(46):32327-38.

**Berthiaume JM***, Azam S, Hoit BD, & Chandler MP**,** 2014. Time-dependent alterations in cardioprotection by a high fat diet following myocardial infarction. Physl Rep. 20;2(5)e12019.

Li Q, Zhang S, **Berthiaume JM**, Simons B, & Zhang G, 2014. Novel approaches in LC-MS/MS using MRM to generate a full profile of acyl-CoAs; discovery of dephospho-acyl-CoAs, 2013. J Lipid Res. 55(3):592-602.

Li Q, Sadhukhan S, **Berthiaume JM**, Ibarra RA, Tang H, Deng S, Hamilton E, Nagy LE, Tochtrop GP, & Zhang G, 2013. Beta oxidation-regulated 4-hydroxy-2(E)-nonenal catabolism in the isolated rat heart. Free Radical Biol Med. 58:35-44.

**Berthiaume JM**, Young ME, McElfresh TA, Chen X, Yu X, & Chandler MP, 2012. Normalizing the metabolic phenotype after myocardial infarction; impacts of subchronic high fat feeding. J Mol Cell Card. 53:125-133.

Cheng YH, Li W, McElfresh TA, Chen X, **Berthiaume JM**, Castel L, Yu X, Van Wagoner DR, & Chandler MP, 2011. Changes in myofilament proteins, but not calcium regulation, are associated with a high fat diet-induced improvement in contractile function in heart failure. Am J Physiol Heart Circ Physiol. 301(4):H1438-46.

Christopher BA, Huang H**, Berthiaume JM,** McElfresh TA, Chen X, Croniger CM, Muzic RF, & Chandler MP, 2010. Myocardial insulin resistance induced by high fat feeding in heart failure is associated with preserved contractile function. Am J Physiol Heart Circ Physiol. 299(6):H1917-27.

**Berthiaume JM,** Bray MS, McElfresh TA, Chen X, Azam S, Young ME, Hoit BD, & Chandler MP, 2010. The myocardial contractile response to physiological stress improves with high saturated fat feeding in heart failure. Am J Physiol Heart Circ Physiol. 299(2):H410-21.

**Berthiaume JM,** & Wallace KB, 2007. Persistent alterations to the gene expression profile of the heart subsequent to chronic Doxorubicin treatment. Cardiovasc Toxicol. 7(3):178-91.

Palmeira CM, Rolo AP, **Berthiaume JM,** Bjork JA, & Wallace KB, 2007. Hyperglycemia decreases mitochondrial function: the regulatory role of mitochondrial biogenesis. Tox Appl Pharmacol. 225(2):214-20.

**Berthiaume JM*,** Oliveira PJ, Fariss MW, & Wallace KB, 2005. Dietary vitamin E decreases doxorubicin-Induced oxidative stress without preventing mitochondrial dysfunction. Cardiovasc Toxicol. 5(3), 257-267.

Henry K, Erice A, Balfour HH Jr., Schmeling M, **Berthiaume JM,** & Wallace KB, 2002. Lymphocyte mitochondrial biomarkers in asymptomatic HIV-1-infected individuals treated with nucleoside reverse transcriptase inhibitors. AIDS. 16(18):2485-7.

**Berthiaume JM,** & Wallace KB, 2002. Perfluorooctanoate, perfluorooctanesulfulfonate, and N-ethyl perfluorooctanesulfonamido ethanol; peroxisome proliferation and mitochondrial biogenesis. Tox Letters. 129, 23-32.

Sarkela T, **Berthiaume J,** Elfering S, Gybina A, & Giulivi C, 2001. The modulation of oxygen radical formation by nitric oxide in mitochondria. J Biol Chem. 276, 6945-6949.

## Reviews & Book Chapters

Abdullah M, **Berthiaume JM**, Willis. 2018. TRAF6 as an NF-kappaB-modulating therapeutic target in cardiovascular diseases: at the heart of it all. Trans. Res. 195:48-61.

**Berthiaume JM**, Kudrys JG, Muntean DM, & Rosca MG. 2017 Mitochondrial Redox State and Diabetic Cardiomyopathy. Invited topic review in: Antioxidants & Redox Signaling--Forum review article (*epub ahead of print, doi: 10.1089/ars.2017.7415)*.

Brown DI, Willis, MS & **Berthiaume, JM***. "Influence of Ischemia, Reperfusion, and Hypoxia on Cardiac Metabolism" 2015. T. Doenst & M. Schwarzer (Eds.) In: The Scientist's Guide to Cardiac Metabolism, 1st edition, Chapter 11:155-66.

**Berthiaume JM** Kirk JA, Ranek MJ, Lyon MC, Sheikh F, Jensen BC, Hoit BD, Butany J, Tolend V, Rao V, & Willis MS. "Pathophysiology of Heart Failure and an Overview of Therapies" 2015. J Butany & LM Buja (Eds.) In: Cardiovascular Pathology, 4th edition, Chapter 8:271-324.

**Berthiaume JM,** & Wallace KB, 2007. "Adriamycin-induced oxidative mitochondrial cardiotoxicity". Cell Biol Toxicol. 23(1):15-25.

## Abstracts Presented

### Posters

Sharma K, Ye D, Xu K, **Berthiaume JM**, & Puchowicz MA, 2016. Chronic Ketosis induces changes in metabolic profiles and signaling pathways in mouse brain. *Dept. of Physiology & Biophysics Annual Retreat*.

Xu K, Ye D, Jin Y Sharma K, Harrison MM, Caldwell TR, **Berthiaume JM**, Luo Y, LaManna JC, Puchowicz MA, 2016. Diet-induced ketosis protects against focal cerebral ischemia in mouse. A*nnual meeting of the International Society on Oxygen Transport to Tissue* (ISOTT).

Ye D, Caldwell TR, Sharma K, Harrison MM, Xu K, **Berthiaume JM**, Puchowicz MA, 2016 The ketogenic diet modulates signaling pathways of cell growth and survival in the brain. *Research ShowCase, Annual research symposium, Case Western Reserve University*.

Ye D, Caldwell TR, Xi K, **Berthiaume JM**, Puchowicz MA, 2015. The ketogenic diet induces concentration-dependent alterations in the signaling protein AKT. *Dept. of Physiology & Biophysics Annual Retreat*.

Willis M, **Berthiaume J**, Wadosky K, Tang W, Gerdes M, Portman M. 2015. MuRF1 inhibits cardiac thyroid hormone signaling by TRα mono-ubiquitination and localization to CAP350. *International Society for Heart Research (ISHR)-North American Section Meeting*.

Li Q, **Berthiaume J**, Tochtrop G, Zhang GF. 2014. Catabolism of 4-hydroxynonenal in the rat liver via omega- and omega-1 oxidation. *Fed of Amer Soc for Experimental Biology* (FASEB).

Zhang GF, Li Q, **Berthiaume J**, Kemerer M. 2014. Dephosphorylation of acyl-CoAs in the rat ischemic heart. FASEB.

**Berthiaume JM**, Li Q, Sadhukhan S, Henry F, Tochtrop GP, Brunengraber H, Zhang GF. 2013. Catabolism of 4-hydroxy-2(E)-nonenal (HNE) via omega oxidation in perfused rat livers. FASEB.

**Berthiaume J,** Nieuwoudt S, Chandler M. 2013. Time-dependent functional & metabolic phenotype changes in the heart after myocardial infarction & a high fat diet. SHVM.

**Berthiaume J,** Li Q, Sadhukhan S, Henry F, Tochtrop G, Brunengraber H, Zhang G. 2013. Catabolism of 4-hydroxy-2(E)-nonenal (HNE) via omega (ω) oxidation in perfused rat livers. FASEB.

**Berthiaume J**, Chen X, McElfresh T, Yu X, Chandler M. 2011. High dietary fat promotes a normal metabolic phenotype subsequent to myocardial infarction. *Case Cardiovascular Center Research Retreat*.

**Berthiaume J,** Christopher B, Huang H, Muzic R, and Chandler M, 2010. High Dietary Fat Improves the Metabolic Profile of the Infarcted Heart and Induces Myocardial Insulin Resistance. SHVM.

**Berthiaume J,** Chen X, McElfresh T, and Chandler M, 2010. High Dietary Fat Promotes a Normal Metabolic Phenotype in the Infarcted Rat Heart. FASEB.

**Berthiaume J,** Chen X, McElfresh T, and Chandler M, 2009. High Dietary Fat Promotes a Normal Metabolic Phenotype Subsequent to Cardiac Infarction. SHVM.

**Berthiaume J,** Chen X, McElfresh T, and Chandler M, 2009. Alterations in Energy Substrate Utilization Associated with High Dietary Fat in the Infarcted Rat Heart. FASEB.

**Berthiaume J**, Chen X, McElfresh T, and Chandler M, 2008. Myocardial Functional and Metabolic Parameters in Heart Failure Following Chronic High Fat Feeding. FASEB.

**Berthiaume J**, and Wallace K, 2006. Doxorubicin stimulates mitochondrial biogenesis and downregulates mitochondrial gene targets. *Society of Toxicology annual meeting* (Toxicol Sci).

Rolo A, Peterson L, **Berthiaume J**, and Wallace K, 2006. Bioenergetic phenotype of NRTI-induced mitochondrial cardiomyopathy. Toxicol Sci.

**Berthiaume J,** Oliveira P, Fariss M, and Wallace K, 2005. Failure of dietary vitamin E to prevent doxorubicin-induced cardiac mitochondrionopathy *in vivo*. Toxicol Sci.

Bjork J, **Berthiaume J,** Lau C, Butenhoff J, and Wallace K, 2005. Hepatic gene expression profiles of rats exposed to perfluorooctanesulfonate (PFOS) *in utero*. Toxicol Sci.

Palmeira C, **Berthiaume J,** Bjork J, Rolo A, and Wallace K, 2005. Hyperglycemia-induced oxidative stress activates the hexosamine pathway and inhibits mitochondrial biogenesis. Toxicol Sci.

**Berthiaume J**, Bjork J, and Wallace, K, 2004. Persistent alterations in gene expression following chronic doxorubicin administration in rats. Toxicol Sci.

**Berthiaume J**, and Wallace K, 2002. The impact of perfluorooctyl derivatives on peroxisomal proliferation and mitochondrial biogenesis. Toxicol Sci.

## TALKS

**Berthiaume J,** 2013. Controversies in cardiac metabolism: High fat is (not) detrimental to the failing heart. Invited panel discussion, Society for Heart & Vascular Metabolism, annual meeting.

**Berthiaume J,** 2011. High dietary fat promotes a normal metabolic phenotype subsequent to myocardial infarction. Society for Heart & Vascular Metabolism, annual meeting.

**Berthiaume J,** 2010. Improved myocardial contractile response during hemodynamic stress in heart failure rats fed high fat. Experimental Biology, annual meeting.

**Berthiaume J,** 2005. Doxorubicin cardiotoxicity: the role of reactive oxygen species. Northland Soc. of Toxicology (NL-SOT) annual meeting.

**Berthiaume J,** Bjork J, and Wallace K, 2004. Alterations in gene expression following chronic doxorubicin treatment. United Mitochondrial Disease Foundation (UMDF), annual meeting.

**Berthiaume J,** Oliveira P, Fariss M, and Wallace K, 2004. Failure of tocopherol to prevent doxorubicin-induced cardiac mitochondrionopathy in vivo. United Mitochondrial Disease Foundation (UMDF), annual meeting.

## RESEARCH SUPPORT

**Industry sponsored research by Athersys, inc.** **06/2014-04/2018**

(PI: JM Berthiaume)

*Assessment of MultiStem in Acute Myocardial Infarction in Rats*

Project on stem cell therapy in the infarcted heart; defining impact on cardiac function by serial echocardiographic evaluation.

**NIH-NIDDK R01-DK113197** **06/2017-04/2021**

(PI: Walter Boron, role: Key Personnel)

*Project aimed at defining the role of RPTPγ in whole body pH homeostasis through intracellular signaling pathways*

**NIH Shared Instrumentation Grant, S10** **04/2016**

(PI: Julian Stelzer, role: Key Personnel)

*High Resolution Ultrasound for Small animal Imaging*

**Clinical & Translational Science Collaborative, Core Utilization Pilot Award** **03/2015-8/2015**

(PI: JM Berthiaume)

*Positive metabolic remodeling drives the cardioprotective effect of high fat after myocardial infarction*

Focused pilot grant to evaluate the time-dependent changes in metabolic substrates in the heart following infarction and high dietary fat. The overarching goal of the study is to use a semi-targeted approach to determine the relative quantities of a panel of metabolic intermediates in the injured heart over a time-course to identify early changes that correlate to improvements in cardiac function as assessed by echocardiography and invasive hemodynamic measures.