# Clair Crewe, Ph.D.

Assistant Professor
Department of Cell Biology and Physiology
Department of Internal Medicine, Division of Endocrinology, Metabolism and Lipid Research
Washington University School of Medicine
Clair.Crewe@wustl.edu

# **EDUCATION, POSTGRADUATE TRAINING, AND FACULTY APPOINTMENTS**

2021 – Present 2019 – 2021	Assistant Professor, Washington University School of Medicine Assistant Instructor at the University of Texas Southwestern Medical Center Training with Dr. Philipp Scherer
2015 – 2019	Postdoctoral Fellow at the University of Texas Southwestern Medical Center
2009 – 2015	Postdoctoral training with Dr. Philipp Scherer University of Oklahoma Health Sciences Center Ph.D. Biochemistry and Molecular Biology Doctoral research with Dr. Luke Szweda
2005 – 2009	Oklahoma Christian University  B.S. Biology

#### **PUBLICATIONS**

# **Primary Research Articles**

Joffin, N, Gliniak, CM, Funcke, JB. Paschoal VA, **Crewe C**, Chen S, Gordillo R, Kusminski CM, Oh DY, Geldenhuys WJ, Scherer PE. Adipose tissue macrophages exert systemic metabolic control by manipulating local iron concentrations. *Nat Metab* (2022). https://doi.org/10.1038/s42255-022-00664-z

Borcherding N, Jia W, Giwa R, Field RL, Moley JR, Kopckey BJ, Chan MM, Yang BQ, Sabio JM, Walker EC, Osorio O, Bredemeyer A, Pietka T, Alexander-Brett J, Morley SC, Artyomov MN, Abumrad NA, Schilling J, Lavine K, **Crewe C**, Brestoff JR. (2022) Dietary Lipids Inhibit Mitochondria Transfer to Macrophages to Divert Adipocyte-derived Mitochondria to Blood for Distribution to Distant Organs. **Cell Metabolism**. *Aug 30:S1550-4131(22)00353-9. doi: 10.1016/j.cmet.2022.08.010. Epub ahead of print. PMID: 36070756.* 

**Crewe C,** Chen S, Bu D, Gliniak CM, Asterholm IW, Yu XX, Joffin N, de Souza CO, Funcke JB, Oh DY, Varlamov O, Robino JJ, Gordillo R, Scherer PE. (2022) Deficient Caveolin-1 Synthesis in Adipocytes Stimulates Systemic Insulin-independent Glucose Uptake via Extracellular Vesicles. **Diabetes**. db220035. https://doi.org/10.2337/db22-0035

**Crewe C,** Funcke JB, Li S, Joffin N, Gliniak CM, Ghaben AL, An YA, Sadek HA, Gordillo R, Akgul Y, Chen S, Samovski D, Fischer-Posocszky P, Kusminski CM, Klein S and Scherer PE.

- (2021) Extracellular vesicle-based Interorgan Transport of Mitochondria from Energetically Stressed Adipocytes. **Cell Metabolism.** 33(9): 1853-1868 e1811.
- Zhu Y, Li N, Huang M, Bartels M, Dogné S, Zhao S, Chen X, **Crewe C**, Straub L, Vishvanath L, Zhang Z, Shao M, Yang Y, Gliniak CM, Gordillo R, Smith GI, Holland WL, Gupta RK, Dong B, Caron N, Xu Y, Akgul Y, Klein S, Scherer PE. 2021 Adipose tissue hyaluronan production improves systemic glucose homeostasis and primes adipocytes for CL-316,243-stimulated lipolysis. **Nature Communications**. 12(1):4829. doi: 10.1038/s41467-021-25025-4.
- Zhang Z, Funcke JB, Zi Z, Zhao S, Straub LG, Zhu Y, Zhu Q, **Crewe C**, An YA, Chen S, Li N, Wang MY, Ghaben AL, Lee C, Gautron L, Engelking LJ, Raj P, Deng Y, Gordillo R, Kusminski CM, Scherer PE. (2021) Adipocyte iron levels impinge on a fat-gut crosstalk to regulate intestinal lipid absorptionn and mediate protection from obesity. **Cell Metabolism**. 33(8):1624-1639.e9. doi: 10.1016/j.cmet.2021.06.001.
- Joffin N, Paschoal VA, Gliniak CM, **Crewe C**, Elnwasany A, Szweda LI, Zhang Q, Hepler C, Kusminski CM, Gordillo R, Oh DY, Gupta RK, Scherer PE. (2021) Mitochondrial metabolism as a key regulator of the fibro-inflammatory and adipogenic stromal subpopulations in white adipose tissue. **Cell Stem Cell**. 28(4):702-717.e8.doi: 10.1016/j.stem.2021.01.002.
- Kusminski CM, Ghaben AL, Morley TS, Samms RJ, Adams AC, An Y, Johnson JA, Joffin N, Onodera T, **Crewe C**, Holland WL, Gordillo R, Scherer PE. (2019). A Novel Model of Diabetic Complications: Adipocyte Mitochondrial Dysfunction Triggers Massive β-Cell Hyperplasia. *Diabetes*. db190327.
- An YA, **Crewe C**, Asterholm IW, Sun K, Chen D, Zhang F, Shao M, Funcke JB, Zhang Z, Straub L, Yoshino J, Klein S, Kusminski CM, Scherer PE. (2019) Dysregulation of Amyloid Precursor Protein Impairs Adipose Tissue Mitochondrial Function and Promotes Obesity. *Nature Metabolism*. 1, 1243–1257 doi:10.1038/s42255-019-0149-1
- Zhang Z, Shao M, Hepler C, Zi Z, Zhao S, An YA, Zhu Y, Ghaben A, Wang MY, Li N, Onodera T, Joffin N, **Crewe C**, Zhu Q, Vishvanath L, Kumar A, Xing C, Wang QA, Gautron L, Deng Y, Gordillo R, Kruglikov I, Kusminski CM, Gupta RK, Scherer PE. (2019). Dermal Adipose Tissue has High Plasticity and Undergoes Reversible Dedifferentiation in Mice. *JCI*. 10.1172/JCI130239
- **Crewe C.**, Zhu Y., Paschoal VA., Joffin N., Ghaben AL., Gordillo R., Oh DY, Liang G., Horton JD., and Scherer PE. (2019). SREBP-regulated Adipocyte Lipogenesis is Dependent on Substrate Availability and Redox Modulation of mTORC1. *JCI Insight*. 10.1172/jci.insight.129397
- Bu D., **Crewe C.**, Kusminski CM., Gordillo R., Ghaben AL., Kim M., Park J., Deng H., Xiong W., Liu XZ., Lonning PE., Halberg N., Rios A., Chang Y., Gonzalez A., Zhang N., An Z., Scherer PE. (2019). Human Endotrophin as a Driver of Malignant Tumor Growth. *JCI Insight*. 10.1172/jci.insight.125094
- **Crewe C.**, Joffin N., Rutkowski J.M., Kim M., Zhang F., Towler D.A., Gordillo R., Scherer P.E. (2018). An Endothelial to Adipocyte Extracellular Vesicle Axis Governed by Metabolic State. *Cell*. 175(3):695-708.e13.

**Crewe C.**, Schafer C., Lee I., Kinter M., Szweda LI. (2017) Regulation of pyruvate dehydrogenase kinase 4 in the heart through degradation by the Lon protease in response to mitochondrial substrate availability. *J. Biol. Chem.* 292 (1), 305-312

Asterholm I.W., Kim J., Rutkowski J.M., Tao C., **Crewe C.**, and Scherer PE. (2016). Pathological Type-2 Immune Response, Enhanced Tumor Growth, and Glucose Intolerance in Retnlβ (RELMβ) Null Mice: A Model of Intestinal Immune System Dysfunction in Disease Susceptibility. *American Journal of Pathology*. 186(9) 2404-16.

**Crewe, C.**, Kinter, M., and Szweda, L. I. (2013) Rapid Inhibition of Pyruvate Dehydrogenase: An Initiating Event in High Dietary Fat-Induced Loss of Metabolic Flexibility in the Heart. **PLoS ONE** 8, e77280

#### **Literature Reviews**

**Crewe C.** (2022) Energetic Stress-induced Metabolic Regulation by Extracellular Vesicles. *Comprehensive Physiology.* Accepted.

**Crewe C** (2022) The Challenges of Interrogating Adipose Tissue Extracellular Vesicle Functions in Physiology. *Commun. Biol.* Jun 14;5(1):581. doi: 10.1038/s42003-022-03511-9. PMID: 35701664.

Stratman A.N., **Crewe C.**, and Stahl P. (2022) The microenvironment- a general hypothesis on the homeostatic function of extracellular vesicles. **FASEB BioAdvances**. DOI: 10.1096/fba.2021-00155

**Crewe C.**, Scherer P.E. (2021) Intercellular and Interorgan Crosstalk through Adipocyte Extracellular Vesicles. *Rev Endocr Metab Disord*.https://doi.org/10.1007/s11154-020-09625-x

**Crewe C.**, An Y., and Scherer PE (2017). The Ominous Triad of Adipose Tissue Dysfunction: Inflammation, Fibrosis and Angiogenesis. *JCI*. 127(1) 74-82.

Yi Z., **Crewe C.**, Scherer P.E. (2016). Hyaluronan in adipose tissue: Beyond dermal filler and therapeutic carrier. **Science Translational Medicine**. 8 (323), 323ps324.

Rindler, P. M., **Crewe, C. L.**, Fernandes, J., Kinter, M., and Szweda, L. I. (2013) Redox Regulation of Insulin Sensitivity Due to Enhanced Fatty acid Utilization in the Mitochondria. *American Journal of Physiology - Heart and Circulatory Physiology* 305, H634-H643

#### **INVITED SEMINARS**

- 2022 "Adipocyte Energetic Stress Induces Mitochondria-derived EV Production to Regulate Systemic Metabolism". Full talk at the **Exosomes/Microvesicles Keystone Symposia**, **Santa Fe**, NM.
- 2022 "Extracellular Vesicle-mediated Regulation of Metabolism." **Duke Molecular Physiology Institute, Duke, Durham**, NC.

- 2022 "Extracellular vesicle-based Interorgan Transport of Mitochondria from Energetically Stressed Adipocytes" **Helmholtz Diabetes Conference**, **Munich**, Germany.
- 2022 "Extracellular vesicle-based Interorgan Transport of Mitochondria from Energetically Stressed Adipocytes" American Heart Association-Basic Cardiovascular Sciences Scientific Sessions, Chicago, IL.
- 2021 "Extracellular vesicle-based Interorgan Transport of Mitochondria from Energetically Stressed Adipocytes" Research Seminar Series, Center for Perioperative Medicine (CPM), **UT Health Houston**, TX
- 2021 "Mitochondria-containing Exosomes from Energetically Stressed Adipocytes Precondition the Heart to Protect Against oxidative Damage". **Leducq Foundation Webinar Sessions on Cardiac Function and Regeneration.**
- 2021 "Inter-Organ Crosstalk Through Adipose Tissue Exosomes" Endocrine Society Annual Meeting, **ENDO 2021** (Virtual due to the SARS-CoV-2 outbreak)
- 2021 "Exosome-Based Interorgan Transport of Mitochondria from Energetically Stressed Adipocytes". Full talk at Exosomes/Microvesicles Keystone Symposia, Banff, Canada (Canceled due to the SARS-CoV-2 outbreak)
- 2020 "Adipocytes Undergoing Energetic Stress Release Mitochondria-containing Exosomes that Trigger Hormetic Oxidative Stress in the Heart" Short talk at **Mitochondrial Biochemistry/ROS Keystone Symposia, Whistler**, Canada (Canceled due to the SARS-CoV-2 outbreak)
- 2020 "Inter-Organ Cross Talk Through Adipose Tissue Exosomes" Endocrine Society Annual Meeting, AOCE-SICEM 2020, Seoul, Korea (Virtual due to the SARS-CoV-2 outbreak)
- 2020 "Inter-Organ Crosstalk Through Adipose Tissue Exosomes" Endocrine Society Annual Meeting, **ENDO 2020, San Francisco**, CA (Canceled due to the SARS-CoV-2 outbreak)
- 2019 "Adipocytes Undergoing Mitochondrial Stress Release Exosomes that Modulate Cardiomyocyte Energetic and Redox State" Emerging Luminaries in Nutrition, Exercise and Metabolism. Indiana University-Bloomington, IN
- 2019 "Adipocyte Oxidative Stress Induces Mitochondrial-Derived Extracellular Vesicle Production to Regulate Systemic Metabolism" Short talk at **Obesity Keystone Symposia**, **Banff**, Canada
- 2018 "An Endothelial to Adipocyte Extracellular Vesicle Axis Governed by Metabolic State", Rising Stars Symposium, **U of Utah Health, Salt Lake City**, UT
- 2016 "Transcellular and Inter-organ Trafficking of Adipose Tissue-derived Particles", NIH, Bethesda, MD
- 2016 "Endotrophin Neutralizing Monoclonal Antibodies for Breast Cancer Treatment" **UT Health, Houston**, TX
- 2012 "A Potential Adaptive Response of Cardiac Mitochondria to High Dietary Fat: Rapid Inhibition of Pyruvate Dehydrogenase", Pierre and Marie Curie University, Paris, France

## **ACADEMIC AND PROFESSIONAL HONORS**

- 2022 Nominee for The Helmholtz Young Investigator in Diabetes (HelDi) award.
- 2014 Graduate Research Education and Technology (GREAT) Symposium College of Medicine Graduate Student Association (COMGSA) Travel Award Recipient
- 2014 Graduate College Award for Scientific Achievement
- 2013 GREAT Symposium COMGSA Travel Award Recipient
- 2013 GREAT Symposium Oklahoma Medical Research Foundation Travel Award Recipient
- 2012 Oklahoma Medical Research Foundation Scientific Travel Award Recipient

2012 Provost's Travel Award Recipient

2011 GREAT Symposium COMGSA Travel Award Recipient

2011 Harold Hamm Diabetes Center Research Symposium Travel Award Recipient

2010 Oklahoma Medical Research Foundation Barrett Scholarship Recipient

2009 Dean's Award Recipient from Oklahoma Christian University

2007 Outstanding Sophomore Award Recipient Oklahoma Christian University

#### **GRANTS**

2019 – Present	K99/R00 Pathway to Independence Award NIDDK (Crewe/Scherer). Extracellular Vesicle-mediated Regulation of Metabolism.
2017 – 2019	F32 Postdoctoral Fellowship NIDDK (Crewe/Scherer). <i>Uncovering New Regulatory Mechanisms of Adiponectin Expression: Cooperation Between the Adipocyte and Adipose Tissue Microenvironment.</i>
2016 – 2017	T32 Training Grant

## PROFESSIONAL MEMBERSHIPS AND SERVICE

## **Scientific Societies**

2022 – present	Kern Lipid Conference Board of Directors.
2020 - present	Sigma XI
2019 – present	Endocrine Society
2017 – 2019	American Diabetes Association
2013 – 2016	American Society for Biochemistry and Molecular Biology
2011 – 2014	American Association for the Advancement of Science

## **Journal Reviewer**

Nature

Nature Metabolism

**Nature Communications** 

Cell Reports

Science Signaling

Molecular Metabolism

**Diabetes** 

Aging Cell

**STAR Protocols** 

Immunology and Regenerative Medicine