Stanford

# Chad S. Weldy, M.D., Ph.D.

- Postdoctoral Medical Fellow, Cardiovascular Medicine
- Fellow in Medicine
- Resident in Medicine

Curriculum Vitae available Online

## Bio

### BIO

Dr. Chad Weldy is a senior cardiology fellow at Stanford University School of Medicine and a postdoctoral fellow in the lab of Dr. Thomas Quertermous, the William G. Irwin Professor of Medicine at Stanford University. He received his M.D. from Duke University School of Medicine and completed his internal medicine internship, residency, and clinical cardiology training at Stanford University as a member of the Stanford Translational Investigator Program (TIP). Prior to entering medical school, Dr. Weldy received his Ph.D. from the University of Washington and completed a postdoctoral fellowship with the University of Washington, Division of Cardiology where he conducted basic science research investigations within the fields of cardiovascular biology, redox biology, toxicology, and epigenetics. Dr. Weldy has a clinical interest in the field of inherited cardiomyopathies where he treats patients and families within Stanford's Center for Inherited Cardiovascular Disease (SCICD) with Dr. Euan Ashley. As a physician-scientist he works to better understand human genetics, epigenetics, and transcriptional regulation in cardiovascular disease. He has received NIH funding through a Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral Fellowship (Parent F32) and an NIH Loan Repayment Award for his work on single cell biology and atherosclerosis. Within Stanford, he was the recipient of the Gerald Reaven Award for Basic Science from the Division of Cardiovascular Medicine, he has been inducted into AOA from the Stanford School of Medicine, and was the recipient for the Timothy F. Beckett Jr. Award for Best Clinical Teaching from the Department of Medicine.

### CLINICAL FOCUS

- Fellowship - Cardiovascular Medicine
- Fellow

### HONORS AND AWARDS

- NIH Loan Repayment Program (LRP) Award, NIH/NHLBI (July, 2021)
- Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral Fellowship (F32), NIH/NHLBI (July, 2021)
- Gerald Reaven Award for Basic Science, Stanford University (June, 2021)
- Timothy F. Beckett Jr. Award for Best Clinical Teaching by a Medicine Fellow, Stanford University (June, 2021)
- AOA - Alpha Omega Alpha Medical Honor Society, Stanford University School of Medicine (6/2020)
- 2019 Residency Research Travel Award, Stanford University Internal Medicine Residency Program (April, 2019)
- 2014 Paper of the Year Award, Society of Toxicology, Inhalation and Respiratory Specialty Section (March 24, 2014)
- 2014 Postdoctoral Travel Award, Society of Toxicology, Cardiovascular Toxicology Specialty Section (March 25, 2014)
- 1st Place Postdoctoral Presentation Award, Pacific Northwest Association of Toxicologists (September 2013)
- 2012 Innovations in Research Award, University of Washington Center for Ecogenetics and Environmental Health (CEEH) (May 2012)
- Departmental nominee and one of four finalists, University of Washington Graduate School Medal (May 2011)

- Young Investigator Award (YIA), Society for Free Radical Biology and Medicine (SFRBM) (November 2011)
- 1st Place Student/Post Doc Oral Presentation Award, Pacific Northwest Association of Toxicologists (October 2010)
- 2007 Professor Ming-Ho Yu Award: Outstanding Student in Environmental Toxicology, Huxley College of the Environment, Western Washington University (May 2007)

### PROFESSIONAL EDUCATION

- Doctor of Philosophy, University of Washington (2012)
- Doctor of Medicine, Duke University (2017)
- Bachelor of Science, Western Washington University (2007)
- Cardiovascular Med Fellowship, Stanford University Hospitals , Cardiology
- Internal Medicine Residency, Stanford University Hospitals , Internal Medicine (2019)
- Internal Medicine Internship, Stanford University Hospitals , Internal Medicine (2018)
- MD, Duke University School of Medicine , Medicine (2017)
- Postdoctoral Fellowship, University of Washington, School of Medicine, Division of Cardiology , Cardiovascular Biology, Heart Failure, Epigenetics (2014)
- PhD, University of Washington, School of Public Health , Toxicology, Vascular Physiology, Free Radical Biology (2012)
- BS, Western Washington University, Huxley College of the Environment , Environmental Toxicology, Chemistry (2007)

## Research & Scholarship

### CURRENT RESEARCH AND SCHOLARLY INTERESTS

As a physician-scientist in the lab of Dr. Quertermous I work to understand the genetic basis of cardiovascular disease and the transcriptional and epigenomic mechanisms of atherosclerosis. My work is focused across three main areas of cardiovascular genetics and mechanisms of coronary artery disease and smooth muscle biology:

1. CRISPRi screening with targeted perturb seq (TAPseq) to identify novel CAD genes in human coronary artery smooth muscle cells
2. Investigation of the epigenetic and molecular basis of coronary artery disease and smooth muscle cell transition in mice with conditional smooth muscle genetic deletion of CAD genes Pdgfd and Sox9
3. Defining on single cell resolution the cellular and epigenomic features of human vascular disease across vascular beds of differing embryonic origin

My work with Dr. Quertermous is focused on driving discovery in vascular biology by understanding how common genetic variation in humans in complex disease can lead to novel understandings of disease mechanism. With nearly 100,000 GWAS loci discovered across all complex disease, and nearly 300 GWAS loci identified within coronary artery disease, the methods by which GWAS loci are mapped to causal gene is often times limited based proximity to lead SNP without confirmatory functional genomic testing. By using CRISPRi screening in human coronary artery smooth muscle cells with targeted perturb seq (TAPseq), we aim to epigenetically modify specific GWAS loci to then understand enhancer-gene pairs and identify causal CAD genes within the region of a CAD GWAS loci. For identified CAD genes with high confidence for their causality, understanding how CAD genes modify smooth muscle cell state transition within the vascular wall and the epigenomic mechanisms by which this transition occurs is crucial. By using a vascular smooth muscle cell lineage traced mouse model, we can induce smooth muscle specific deletion of CAD genes, Pdgfd and Sox9 to better understand their causal mechanism in vascular disease with single cell RNAseq and single cell ATACseq. Understanding this cell state transition and epigenomic basis of disease is further expanded to human disease with collaboration from our cardiothoracic surgical colleagues. By harvesting human vascular samples at the time of transplant or organ donation, we have the unique ability to understand on a single cell resolution the mechanisms of vascular disease. Importantly, by comparing the cellular gene expression and cell population with scRNAseq in combination with understanding chromatin accessibility on single cell resolution with scATACseq across vascular beds from differing embryonic origin (coronary, ascending aorta, aortic

arch, descending thoracic, infrarenal, carotid artery) we can work to understand why there is differential susceptibility to vascular disease across vascular sites and the epigenomic and transcriptional mechanisms that facilitate this differential susceptibility.

This work attempts to apply multiple scientific research arms to ultimately lead to novel understandings of vascular disease and discover important new therapeutic approaches for drug discovery.

## Publications

### PUBLICATIONS

- **The epigenomic landscape of single vascular cells reflects developmental origin and identifies disease risk loci** *bioRxiv*
  Weldy, C. S., Cheng, P. P., Pedroza, A. J., Dalal, A. R., Sharma, D., Kim, H., Shi, H., Nguyen, T., Kundu, R. K., Fischbein, M. P., Quertermous, T.
  2022
- **Mulibrey Nanism and the Real Time Use of Genome and Biobank Engines to Inform Clinical Care in an Ultrarare Disease.** *Circulation. Genomic and precision medicine*
  Weldy, C. S., Ashley, E. A.
  2021: CIRCGEN121003430
- **Towards precision medicine in heart failure.** *Nature reviews. Cardiology*
  Weldy, C. S., Ashley, E. A.
  2021
- **Circulating whole genome miRNA expression corresponds to progressive right ventricle enlargement and systolic dysfunction in adults with tetralogy of Fallot.** *PloS one*
  Weldy, C. S., Syed, S. A., Amsallem, M., Hu, D., Ji, X., Punn, R., Taylor, A., Navarre, B., Reddy, S.
  2020; 15 (11): e0241476
- **In utero exposure to diesel exhaust particulates is associated with an altered cardiac transcriptional response to transverse aortic constriction and altered DNA methylation** *FASEB Journal*
  Goodson, J. M., Weldy, C. S., MacDonald, J. W., Bammler, T. K., Chien, W., Chin, M. T.
  2017: 4935-4945
- **Neonatal Diesel Exhaust Particulate Exposure Does Not Predispose Mice to Adult Cardiac Hypertrophy or Heart Failure** *INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH*
  Liu, Y., Weldy, C. S., Chin, M. T.
  2016; 13 (12)
- **Myocardial deletion of transcription factor CHF1/Hey2 results in altered myocyte action potential and mild conduction system expansion but does not alter conduction system function or promote spontaneous arrhythmias** *FASEB JOURNAL*
  Hartman, M. E., Liu, Y., Zhu, W., Chien, W., Weldy, C. S., Fishman, G. I., Laflamme, M. A., Chin, M. T.
  2014; 28 (7): 3007-3015
- **In Utero Exposure to Diesel Exhaust Air Pollution Promotes Adverse Intrauterine Conditions, Resulting in Weight Gain, Altered Blood Pressure, and Increased Susceptibility to Heart Failure in Adult Mice** *PLOS ONE*
  Weldy, C. S., Liu, Y., Liggitt, H. D., Chin, M. T.
  2014; 9 (2)
- **In utero and early life exposure to diesel exhaust air pollution increases adult susceptibility to heart failure in mice** *PARTICLE AND FIBRE TOXICOLOGY*
  Weldy, C. S., Liu, Y., Chang, Y., Medvedev, I. O., Fox, J. R., Larson, T. V., Chien, W., Chin, M. T.
  2013; 10
- **Inhalation of diesel exhaust does not exacerbate cardiac hypertrophy or heart failure in two mouse models of cardiac hypertrophy** *PARTICLE AND FIBRE TOXICOLOGY*
  Liu, Y., Chien, W., Medvedev, I. O., Weldy, C. S., Luchtel, D. L., Rosenfeld, M. E., Chin, M. T.
  2013; 10
- **Glutathione (GSH) and the GSH synthesis gene Gclm modulate plasma redox and vascular responses to acute diesel exhaust inhalation in mice** *INHALATION TOXICOLOGY*

Weldy, C. S., Luttrell, I. P., White, C. C., Morgan-Stevenson, V., Cox, D. P., Carosino, C. M., Larson, T. V., Stewart, J. A., Kaufman, J. D., Kim, F., Chitaley, K., Kavanagh, T. J.

2013; 25 (8): 444-454

- **The Glutathione Synthesis Gene Gclm Modulates Amphiphilic Polymer-Coated CdSe/ZnS Quantum Dot-Induced Lung Inflammation in Mice** *PLOS ONE*

  McConnachie, L. A., Botta, D., White, C. C., Weldy, C. S., Wilkerson, H., Yu, J., Dills, R., Yu, X., Griffith, W. C., Faustman, E. M., Farin, F. M., Gill, S. E., Parks, et al

  2013; 8 (5)

- **Glutathione (GSH) and the GSH synthesis gene Gclm modulate vascular reactivity in mice** *FREE RADICAL BIOLOGY AND MEDICINE*

  Weldy, C. S., Luttrell, I. P., White, C. C., Morgan-Stevenson, V., Bammler, T. K., Beyer, R. P., Afsharinejad, Z., Kim, F., Chitaley, K., Kavanagh, T. J.

  2012; 53 (6): 1264-1278

- **DIESEL particulate exposed macrophages alter endothelial cell expression of eNOS, iNOS, MCP1, and glutathione synthesis genes** *TOXICOLOGY IN VITRO*

  Weldy, C. S., Wilkerson, H., Larson, T. V., Stewart, J. A., Kavanagh, T. J.

  2011; 25 (8): 2064-2073

- **Heterozygosity in the glutathione synthesis gene Gclm increases sensitivity to diesel exhaust particulate induced lung inflammation in mice** *INHALATION TOXICOLOGY*

  Weldy, C. S., White, C. C., Wilkerson, H., Larson, T. V., Stewart, J. A., Gill, S. E., Parks, W. C., Kavanagh, T. J.

  2011; 23 (12): 724-735