



Jonathan Z. Long

Assistant Professor of Pathology

Bio

BIO

Dr. Jonathan Long is an Assistant Professor of Pathology and an Institute Scholar of Stanford ChEM-H (Chemistry, Engineering & Medicine for Human Health). Prior to arriving to Stanford in 2018, Dr. Long completed his Ph.D. in Chemistry at Scripps Research with Benjamin F. Cravatt and his postdoctoral work at Harvard Medical School/Dana-Farber Cancer Institute with Bruce M. Spiegelman. His pioneering contributions in the areas of lipid biochemistry and energy homeostasis have been recognized by numerous awards from the National Institutes of Health and the American Diabetes Association.

At Stanford, the Long laboratory is at the forefront of research in molecular metabolism. The laboratory focuses on circulating metabolite and polypeptide factors that regulate metabolic tissue function. Current research interests include: 1) N-acyl amino acids, a family of circulating lipids that stimulate thermogenesis; 2) endocrine factors that transduce the systemic benefits of physical activity; and 3) mass spectrometry-based approaches for mapping the chemical composition of blood plasma. The long-term goal of this work is to discover new endocrine pathway of energy metabolism that can be translated into therapeutic opportunities for obesity, metabolic disease, and other age-associated chronic diseases.

ACADEMIC APPOINTMENTS

- Assistant Professor, Pathology
- Member, Bio-X
- Member, Cardiovascular Institute
- Faculty Fellow, Stanford ChEM-H

ADMINISTRATIVE APPOINTMENTS

- Member, Stanford Diabetes Research Center, (2018- present)

HONORS AND AWARDS

- NIH Pathways to Independence Award, National Institutes of Health (2015)
- Postdoctoral Research Fellowship, American Diabetes Association (2012)

PROFESSIONAL EDUCATION

- Postdoc, Dana-Farber Cancer Institute and Harvard Medical School (2017)
- PhD, The Scripps Research Institute , Chemistry (2011)
- BA, Columbia University , Biochemistry (2007)

PATENTS

- Spiegelman BM, Long JZ, Lin H, Kamenecka T, Griffin P.. "United States Patent WO/2019/108739 Chemical uncouplers of respiration and methods of use thereof", Dana-Farber Cancer Institute Inc, Jun 6, 2019
- Spiegelman BM, Long JZ. "United States Patent WO2017075329A2 Methods for identification, assessment, prevention, and treatment of metabolic disorders using PM20D1 and N-lipidated amino acids", Dana-Farber Cancer Institute Inc, Oct 28, 2016
- Spiegelman BM, Rao RR, Long JZ. "United States Patent 14762375 Compositions and methods for regulating thermogenesis and muscle inflammation using METRNL and METRN", Dana-Farber Cancer Institute Inc, Jan 21, 2014
- Cravatt BF, Long JZ, Li W, Nomura DK. "United States Patent 12998642 Methods and compositions related to targeting monoacylglycerol lipase", The Scripps Research Institute, Jul 1, 2010

LINKS

- Long Lab Homepage: <http://longlabstanford.org>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Our laboratory focuses on the circulating factors in blood plasma that are secreted by and act on peripheral metabolic tissues. We are especially interested in those that are dynamically modulated by physiologic energy stressors such as nutrient availability, physical activity, or environmental temperature. What are the identities of these molecules? What energy stressors do they respond to? Where are they made? What cell types or tissues do they act on? We use chemical biology and mass spectrometry-based technologies as discovery tools. We combine these tools with classical biochemical and genetic approaches in cell and animal models. Our goal is to uncover new endocrine pathways of organismal energy metabolism. Recent studies from our laboratory have identified a family of cold-regulated circulating lipids that stimulate mitochondrial respiration as well as an exercise-stimulated thermogenic polypeptide hormone. We suspect that many more remain to be discovered. We anticipate that our approach will uncover fundamental mechanisms that control mammalian energy homeostasis. In the long term, we hope to translate our discoveries into therapeutic opportunities that matter for metabolic and other age-associated chronic diseases.

Teaching

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Aurora Alvarez-Buylla, Anthony Cordova, Jason Rodencal

Orals Chair

Benjamin Bell

Postdoctoral Faculty Sponsor

Marta Garcia Contreras, Xuchao Lyu, Maria de los Dolores Moya Garzon

Doctoral Dissertation Advisor (AC)

Veronica Li, Amanda Wiggenhorn, wei wei

Postdoctoral Research Mentor

Marta Garcia Contreras

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biophysics (Phd Program)
- Cancer Biology (Phd Program)

Publications

PUBLICATIONS

- **Proteomics illuminates fat as key tissue in aging** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Long, J. Z.
2020; 117 (19): 10111–12
- **Cooperative enzymatic control of N-acyl amino acids by PM20D1 and FAAH.** *eLife*
Kim, J. T., Terrell, S. M., Li, V. L., Wei, W., Fischer, C. R., Long, J. Z.
2020; 9
- **Family-wide Annotation of Enzymatic Pathways by Parallel InVivo Metabolomics.** *Cell chemical biology*
Kim, J. T., Li, V. L., Terrell, S. M., Fischer, C. R., Long, J. Z.
2019
- **H⁺ transport is an integral function of the mitochondrial ADP/ATP carrier** *NATURE*
Bertholet, A. M., Chouchani, E. T., Kazak, L., Angelin, A., Fedorenko, A., Long, J. Z., Vidoni, S., Garrity, R., Cho, J., Terada, N., Wallace, D. C., Spiegelman, B. M., Kirichok, et al
2019; 571 (7766): 515–+
- **Discovery of Hydrolysis-resistant Isoindoline N-Acyl Amino Acid Analogs that Stimulate Mitochondrial Respiration.** *Journal of medicinal chemistry*
Lin, H., Long, J. Z., Roche, A. M., Svensson, K. J., Dou, F., Chang, M. R., Strutzenberg, T., Ruiz, C., Cameron, M. D., Novick, S. J., Berdan, C. M., Louie, S., Nomura, et al
2018
- **Ablation of PM20D1 reveals N-acyl amino acid control of metabolism and nociception.** *Proceedings of the National Academy of Sciences of the United States of America*
Long, J. Z., Roche, A. M., Berdan, C. A., Louie, S. M., Roberts, A. J., Svensson, K. J., Dou, F. Y., Bateman, L. A., Mina, A. I., Deng, Z., Jedrychowski, M. P., Lin, H., Kamenecka, et al
2018
- **Do Adipocytes Emerge from Mural Progenitors?** *CELL STEM CELL*
Vishvanath, L., Long, J. Z., Spiegelman, B. M., Gupta, R. K.
2017; 20 (5): 585–586
- **Cdkal1, a type 2 diabetes susceptibility gene, regulates mitochondrial function in adipose tissue.** *Molecular metabolism*
Palmer, C. J., Bruckner, R. J., Paulo, J. A., Kazak, L., Long, J. Z., Mina, A. I., Deng, Z., LeClair, K. B., Hall, J. A., Hong, S., Zushin, P. H., Smith, K. L., Gygi, et al
2017; 6 (10): 1212–25
- **The Secreted Enzyme PM20D1 Regulates Lipidated Amino Acid Uncouplers of Mitochondria** *CELL*
Long, J. Z., Svensson, K. J., Bateman, L. A., Lin, H., Kamenecka, T., Lokurkar, I. A., Lou, J., Rao, R. R., Chang, M. R., Jedrychowski, M. P., Paulo, J. A., Gygi, S. P., Griffin, et al
2016; 166 (2): 424–435
- **A Secreted Slit2 Fragment Regulates Adipose Tissue Thermogenesis and Metabolic Function** *CELL METABOLISM*
Svensson, K. J., Long, J. Z., Jedrychowski, M. P., Cohen, P., Lo, J. C., Serag, S., Kir, S., Shinoda, K., Tartaglia, J. A., Rao, R. R., Chedotal, A., Kajimura, S., Gygi, et al
2016; 23 (3): 454–466
- **Endocannabinoid Catabolic Enzymes Play Differential Roles in Thermal Homeostasis in Response to Environmental or Immune Challenge** *JOURNAL OF NEUROIMMUNE PHARMACOLOGY*
Nass, S. R., Long, J. Z., Schlosburg, J. E., Cravatt, B. F., Lichtman, A. H., Kinsey, S. G.
2015; 10 (2): 364–370
- **Blockade of 2-Arachidonoylglycerol Hydrolysis Produces Antidepressant-Like Effects and Enhances Adult Hippocampal Neurogenesis and Synaptic Plasticity** *HIPPOCAMPUS*
Zhang, Z., Wang, W., Zhong, P., Liu, S. J., Long, J. Z., Zhao, L., Gao, H., Cravatt, B. F., Liu, Q.
2015; 25 (1): 16–26

- **Prolonged Monoacylglycerol Lipase Blockade Causes Equivalent Cannabinoid Receptor Type 1 Receptor-Mediated Adaptations in Fatty Acid Amide Hydrolase Wild-Type and Knockout Mice** *JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS*
Schlosburg, J. E., Kinsey, S. G., Ignatowska-Jankowska, B., Ramesh, D., Abdullah, R. A., Tao, Q., Booker, L., Long, J. Z., Selley, D. E., Cravatt, B. F., Lichtman, A. H.
2014; 350 (2): 196-204
- **Meteorin-like Is a Hormone that Regulates Immune-Adipose Interactions to Increase Beige Fat Thermogenesis** *CELL*
Rao, R. R., Long, J. Z., White, J. P., Svensson, K. J., Lou, J., Lokurkar, I., Jedrychowski, M. P., Ruas, J. L., Wrann, C. D., Lo, J. C., Camera, D. M., Lachey, J., Gygi, et al
2014; 157 (6): 1279-1291
- **Monoacylglycerol Lipase Inhibition Blocks Chronic Stress-Induced Depressive-Like Behaviors via Activation of mTOR Signaling** *NEUROPSYCHOPHARMACOLOGY*
Zhong, P., Wang, W., Pan, B., Liu, X., Zhang, Z., Long, J. Z., Zhang, H., Cravatt, B. F., Liu, Q.
2014; 39 (7): 1763-1776
- **A Smooth Muscle-Like Origin for Beige Adipocytes** *CELL METABOLISM*
Long, J. Z., Svensson, K. J., Tsai, L., Zeng, X., Roh, H. C., Kong, X., Rao, R. R., Lou, J., Lokurkar, I., Baur, W., Castellot, J. J., Rosen, E. D., Spiegelman, et al
2014; 19 (5): 810-820
- **Control of experimental spasticity by targeting the degradation of endocannabinoids using selective fatty acid amide hydrolase inhibitors** *MULTIPLE SCLEROSIS JOURNAL*
Pryce, G., Cabranes, A., Fernandez-Ruiz, J., Bisogno, T., Di Marzo, V., Long, J. Z., Cravatt, B. F., Giovannoni, G., Baker, D.
2013; 19 (14): 1896-1904
- **ABHD12 controls brain lysophosphatidylserine pathways that are deregulated in a murine model of the neurodegenerative disease PHARC** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Blankman, J. L., Long, J. Z., Trauger, S. A., Siuzdak, G., Cravatt, B. F.
2013; 110 (4): 1500-1505
- **Dual Fatty Acid Amide Hydrolase and Monoacylglycerol Lipase Blockade Produces THC-Like Morris Water Maze Deficits in Mice** *ACS CHEMICAL NEUROSCIENCE*
Wise, L. E., Long, K. A., Abdullah, R. A., Long, J. Z., Cravatt, B. F., Lichtman, A. H.
2012; 3 (5): 369-378
- **The fatty acid amide hydrolase (FAAH) inhibitor PF-3845 acts in the nervous system to reverse LPS-induced tactile allodynia in mice** *BRITISH JOURNAL OF PHARMACOLOGY*
Booker, L., Kinsey, S. G., Abdullah, R. A., Blankman, J. L., Long, J. Z., Ezzili, C., Boger, D. L., Cravatt, B. F., Lichtman, A. H.
2012; 165 (8): 2485-2496
- **Inhibition of monoacylglycerol lipase attenuates vomiting in *Suncus murinus* and 2-arachidonoyl glycerol attenuates nausea in rats** *BRITISH JOURNAL OF PHARMACOLOGY*
Sticht, M. A., Long, J. Z., Rock, E. M., Limebeer, C. L., Mechoulam, R., Cravatt, B. F., Parker, L. A.
2012; 165 (8): 2425-2435
- **A PGC1-alpha-dependent myokine that drives brown-fat-like development of white fat and thermogenesis** *NATURE*
Bostroem, P., Wu, J., Jedrychowski, M. P., Korde, A., Ye, L., Lo, J. C., Rasbach, K. A., Bostroem, E. A., Choi, J. H., Long, J. Z., Kajimura, S., Zingaretti, M. C., Vind, et al
2012; 481 (7382): 463-U72
- **Endocannabinoid Hydrolysis Generates Brain Prostaglandins That Promote Neuroinflammation** *SCIENCE*
Nomura, D. K., Morrison, B. E., Blankman, J. L., Long, J. Z., Kinsey, S. G., Marcondes, M. C., Ward, A. M., Hahn, Y. K., Lichtman, A. H., Conti, B., Cravatt, B. F.
2011; 334 (6057): 809-813
- **Metabolomics annotates ABHD3 as a physiologic regulator of medium-chain phospholipids** *NATURE CHEMICAL BIOLOGY*
Long, J. Z., Cisar, J. S., Milliken, D., Niessen, S., Wang, C., Trauger, S. A., Siuzdak, G., Cravatt, B. F.
2011; 7 (11): 763-765
- **The Metabolic Serine Hydrolases and Their Functions in Mammalian Physiology and Disease** *CHEMICAL REVIEWS*
Long, J. Z., Cravatt, B. F.

2011; 111 (10): 6022-6063

- **Blockade of Endocannabinoid Hydrolytic Enzymes Attenuates Precipitated Opioid Withdrawal Symptoms in Mice** *JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS*
Ramesh, D., Ross, G. R., Schlosburg, J. E., Owens, R. A., Abdullah, R. A., Kinsey, S. G., Long, J. Z., Nomura, D. K., Sim-Selley, L. J., Cravatt, B. F., Akbarali, H. I., Lichtman, A. H.
2011; 339 (1): 173-185
- **Inhibition of Monoacylglycerol Lipase Attenuates Nonsteroidal Anti-Inflammatory Drug-Induced Gastric Hemorrhages in Mice** *JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS*
Kinsey, S. G., Nomura, D. K., O'Neal, S. T., Long, J. Z., Mahadevan, A., Cravatt, B. F., Grider, J. R., Lichtman, A. H.
2011; 338 (3): 795-802
- **Monoacylglycerol Lipase Exerts Dual Control over Endocannabinoid and Fatty Acid Pathways to Support Prostate Cancer** *CHEMISTRY & BIOLOGY*
Nomura, D. K., Lombardi, D. P., Chang, J. W., Niessen, S., Ward, A. M., Long, J. Z., Hoover, H. H., Cravatt, B. F.
2011; 18 (7): 846-856
- **Reversible Competitive alpha-Ketoheterocycle Inhibitors of Fatty Acid Amide Hydrolase Containing Additional Conformational Constraints in the Acyl Side Chain: Orally Active, Long-Acting Analgesics** *JOURNAL OF MEDICINAL CHEMISTRY*
Ezzili, C., Mileni, M., McGlinchey, N., Long, J. Z., Kinsey, S. G., Hochstatter, D. G., Stevens, R. C., Lichtman, A. H., Cravatt, B. F., Bilsky, E. J., Boger, D. L.
2011; 54 (8): 2805-2822
- **Inhibition of endocannabinoid catabolic enzymes elicits anxiolytic-like effects in the marble burying assay** *PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR*
Kinsey, S. G., O'Neal, S. T., Long, J. Z., Cravatt, B. F., Lichtman, A. H.
2011; 98 (1): 21-27
- **An anatomical and temporal portrait of physiological substrates for fatty acid amide hydrolase** *JOURNAL OF LIPID RESEARCH*
Long, J. Z., LaCava, M., Jin, X., Cravatt, B. F.
2011; 52 (2): 337-344
- **Fatty Acid Amide Hydrolase and Monoacylglycerol Lipase Inhibitors Produce Anti-Allodynic Effects in Mice Through Distinct Cannabinoid Receptor Mechanisms** *JOURNAL OF PAIN*
Kinsey, S. G., Long, J. Z., Cravatt, B. F., Lichtman, A. H.
2010; 11 (12): 1420-1428
- **Chronic monoacylglycerol lipase blockade causes functional antagonism of the endocannabinoid system** *NATURE NEUROSCIENCE*
Schlosburg, J. E., Blankman, J. L., Long, J. Z., Nomura, D. K., Pan, B., Kinsey, S. G., Nguyen, P. T., Ramesh, D., Booker, L., Burston, J. J., Thomas, E. A., Selley, D. E., Sim-Selley, et al
2010; 13 (9): 1113-U111
- **The serine hydrolase ABHD6 controls the accumulation and efficacy of 2-AG at cannabinoid receptors** *NATURE NEUROSCIENCE*
Marrs, W. R., Blankman, J. L., Horne, E. A., Thomazeau, A., Lin, Y. H., Coy, J., Bodor, A. L., Muccioli, G. G., Hu, S. S., Woodruff, G., Fung, S., Lafourcade, M., Alexander, et al
2010; 13 (8): 951-U67
- **Characterization of Tunable Piperidine and Piperazine Carbamates as Inhibitors of Endocannabinoid Hydrolases** *JOURNAL OF MEDICINAL CHEMISTRY*
Long, J. Z., Jin, X., Adibekian, A., Li, W., Cravatt, B. F.
2010; 53 (4): 1830-1842
- **Monoacylglycerol Lipase Regulates a Fatty Acid Network that Promotes Cancer Pathogenesis** *CELL*
Nomura, D. K., Long, J. Z., Niessen, S., Hoover, H. S., Ng, S., Cravatt, B. F.
2010; 140 (1): 49-61
- **Dual blockade of FAAH and MAGL identifies behavioral processes regulated by endocannabinoid crosstalk in vivo** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Long, J. Z., Nomura, D. K., Vann, R. E., Walentiny, D. M., Booker, L., Jin, X., Burston, J. J., Sim-Selley, L. J., Lichtman, A. H., Wiley, J. L., Cravatt, B. F.
2009; 106 (48): 20270-20275
- **Monoacylglycerol Lipase Limits the Duration of Endocannabinoid-Mediated Depolarization-Induced Suppression of Excitation in Autaptic Hippocampal Neurons** *MOLECULAR PHARMACOLOGY*

- Straiker, A., Hu, S. S., Long, J. Z., Arnold, A., Wager-Miller, J., Cravatt, B. F., Mackie, K.
2009; 76 (6): 1220-1227
- **Blockade of 2-Arachidonoylglycerol Hydrolysis by Selective Monoacylglycerol Lipase Inhibitor 4-Nitrophenyl 4-(Dibenzo[d][1,3]dioxol-5-yl(hydroxymethyl)piperidine-1-carboxylate (JZL184) Enhances Retrograde Endocannabinoid Signaling** *JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS*
Pan, B., Wang, W., Long, J. Z., Sun, D., Hillard, C. J., Cravatt, B. F., Liu, Q.
2009; 331 (2): 591-597
 - **Blockade of Endocannabinoid-Degrading Enzymes Attenuates Neuropathic Pain** *JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS*
Kinsey, S. G., Long, J. Z., O'Neal, S. T., Abdullah, R. A., Poklis, J. L., Boger, D. L., Cravatt, B. F., Lichtman, A. H.
2009; 330 (3): 902-910
 - **Characterization of Monoacylglycerol Lipase Inhibition Reveals Differences in Central and Peripheral Endocannabinoid Metabolism** *CHEMISTRY & BIOLOGY*
Long, J. Z., Nomura, D. K., Cravatt, B. F.
2009; 16 (7): 744-753
 - **C-H Bond Functionalization via Hydride Transfer: Synthesis of Dihydrobenzopyrans from ortho-Vinylaryl Alkyl Ethers** *ORGANIC LETTERS*
McQuaid, K. M., Long, J. Z., Sames, D.
2009; 11 (14): 2972-2975
 - **Inhibitors of Endocannabinoid-Metabolizing Enzymes Reduce Precipitated Withdrawal Responses in THC-Dependent Mice** *AAPS JOURNAL*
Schlosburg, J. E., Carlson, B. L., Ramesh, D., Abdullah, R. A., Long, J. Z., Cravatt, B. F., Lichtman, A. H.
2009; 11 (2): 342-352
 - **Discovery and Characterization of a Highly Selective FAAH Inhibitor that Reduces Inflammatory Pain** *CHEMISTRY & BIOLOGY*
Ahn, K., Johnson, D. S., Mileni, M., Beidler, D., Long, J. Z., McKinney, M. K., Weerapana, E., Sadagopan, N., Liimatta, M., Smith, S. E., Lazerwith, S., Stiff, C., Kamtekar, et al
2009; 16 (4): 411-420
 - **Selective blockade of 2-arachidonoylglycerol hydrolysis produces cannabinoid behavioral effects** *NATURE CHEMICAL BIOLOGY*
Long, J. Z., Li, W., Booker, L., Burston, J. J., Kinsey, S. G., Schlosburg, J. E., Pavon, F. J., Serrano, A. M., Selley, D. E., Parsons, L. H., Lichtman, A. H., Cravatt, B. F.
2009; 5 (1): 37-44
 - **In vivo Imaging and differential localization of lipid-modified GFP-variant fusions in embryonic stem cells and mice** *GENESIS*
Rhee, J. M., Purity, M. K., Lackan, C. S., Long, J. Z., Kondoh, G., Takeda, J., Hadjantonakis, A.
2006; 44 (4): 202-218
 - **Genetic and spectrally distinct in vivo imaging: embryonic stem cells and mice with widespread expression of a monomeric red fluorescent protein** *BMC BIOTECHNOLOGY*
Long, J. Z., Lackan, C. S., Hadjantonakis, A. K.
2005; 5