BIOGRAPHICAL SKETCH

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NAME: Chi-Liang Eric Yen

eRA COMMONS USER NAME (credential, e.g., agency login): CEYEN01

POSITION TITLE: Associate Professor of Nutritional Sciences

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
Taipei Medical College, Taiwan	B.S.	1991	Nutrition and Health Sciences
University of North Carolina, Chapel Hill, NC	Ph.D.	2000	Nutritional Biochemistry
Gladstone Institute of Cardiovascular Disease, University of California, San Francisco, CA	Postdoctoral Fellow	2003	Molecular Genetics of Lipid Metabolism

A. Personal Statement

I have a long-standing interest in understanding how nutrition impacts health and disease. Our research group studies how intestinal lipid processing modulates systemic energy balance and glycemic control. Using genetically engineered mice, we are examining the physiological functions of a series of fatty acids metabolizing enzymes. To examine metabolic phenotypes in mice, we have established a variety of research techniques, including a state-of-the art shared-use facility for the comprehensive characterization of systemic metabolic processes in conventionally raised as well as germ-free/gnotobiotic mice and rats. Many of our projects involve endocrine functions of the intestine, pancreas, liver, and adipose tissues, while other involve the reproductive functions of mammary glands and uterus. It would be my privilege to have the opportunity to work with graduate students from the Endocrinology and Reproductive Physiology Program.

Ongoing projects that I would like to highlight include:

NIH R01 DK131742-01 12/03/21–11/30/25

Role: Multiple Principal Investigator (Co-MPI: John Rawls of Duke University)
Agency: NIDDK
Project Title: *Microbial regulation of intestinal lipid metabolism and its physiological consequences*

This project is to 1) identify the host and microbial mechanisms by which microbiota suppress fatty acid oxidation in the intestinal epithelium and 2) define the roles of intestinal fatty acid oxidation in fuel selection and differentiation of intestinal epithelial cells, and in mediating the influence of the gut microbiota on systemic energy balance.

NIH R01 DK124696-01 04/23/20–01/31/25

Role: Principal Investigator
Agency: NIDDK
Project Title: *Intestinal lipid processing, bile acid metabolism, and pancreatic islet function*

This project is to determine 1) to what extent a reduction of bacterial BSH activity is necessary and/or sufficient to protect mice against diabetes, 2) the mechanism by which loss of intestinal MGAT2, a triacylglycerol synthesis enzyme, increases plasma conjugated primary bile acids, and 3) the mechanism by which loss of MGAT2 preserves functional pancreatic beta-cells.

NIH S10 OD028739-01 07/01/20–06/31/23

Role: Principal Investigator
Agency: NIH Office of the Director
Project Title: *Small Animal Metabolic Phenotyping Facility*

This Shared Instrumentation for Animal Research (SIFAR) grant is to purchase a cluster of state-of-the-art instruments to enable comprehensive characterization of metabolic processes at the organismal level, including microbiota in small animals.

NIH R13 DK126498-01 07/01/20–6/30/24

Role: Principal Investigator (No-cost extension)
Agency: NIDDK/NHLBI
Project Title: 2020 FASEB SRC "The Intestinal Lipid Metabolism Conference: In Health and Disease"

This proposed project requests funding to support investigators and trainees from under-represented groups in research to attend and present in the 2020 FASEB Science Research Conference, entitled "Intestinal Lipid Metabolism in Health and Disease", of which Dr. Yen is a co-organizer. The grant is deferred as the meeting is being rescheduled, due to the COVID-19 pandemic, to June 25 – 30, 2023.

B. Positions, Scientific Appointments and Honors

Positions and Employment

Associate Professor	07/15-	Department of Nutritional Sciences, University of Wisconsin-Madison
Visiting Scholar	02/22–07/22	Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan
Assistant Professor	09/07–06/15	Department of Nutritional Sciences, University of Wisconsin-Madison
Research Scientist	9/03–8/07	Gladstone Institute of Cardiovascular Disease, San Francisco, CA
Postdoctoral Fellow	7/00–8/03	Gladstone Institute of Cardiovascular Disease, San Francisco, CA
Graduate Res. Asst.	8/95–6/00	Department of Nutrition, University of North Carolina, Chapel Hill, NC

Other Experience and Professional Memberships

2023	Co-organizer, 2023 FASEB Scientific Research Conference on Intestinal Lipid Metabolism
2020	*Ad hoc reviewer*, Integrative Nutrition and Metabolic Processes (INMP) Study Section, NIH
2017	Chair, Spotlight Sessions on Nutrition and Metabolism, Annual meeting of American Society of Biochemistry and Molecular Biology, EB 2018
2016	*Ad hoc reviewer*, Integrative Nutrition and Metabolic Processes (INMP) Study Section, NIH
2014	*Ad hoc reviewer*, Special Emphasis Panel, NIDDK, NIH
2012	*Ad hoc reviewer*, Integrative Nutrition and Metabolic Processes (INMP) Study Section, NIH
2010-2011	Member, Steering Committee, Research Interest Group on Energy and Macronutrient Metabolism, American Society for Nutrition
2009-2010	Co-chair, Mini symposium on Lipid and Fatty Acid Metabolism, American Society of Nutrition, Experimental Biology
2006-	Member, American Society for Biochemistry and Molecular Biology
2004-	Member, American Society for Nutrition (formerly American Society for Nutritional Sciences)

Editorial Board

2015-present	*American Journal of Physiology – Gastrointestinal and Liver Physiology*
2012-2021	*Journal of Lipid Research*

***Ad hoc* reviewer**

AJP–Endocrinology and Metabolism, AJP–Gastrointestinal and Liver Physiology, AJP–Regulatory, Integrative and Comparative Physiology, BBA–Molecular and Cell Biology of Lipids, British Journal of Pharmacology, Cell Reports, Cell Metabolism, Developmental Dynamics, FASEB Journal, Frontiers in Biology, Gastroenterology, International Journal of Obesity, Journal of Biological Chemistry, Journal of Clinical Investigation, Journal of Nutritional Biochemistry, Journal of Pharmacological Sciences, Journal of Physiology, Microbiome, Molecular Metabolism, Nature Communication, Nature Metabolism, Obesity, Physiological Reviews, PLoS ONE

Honors

Scientist Development Grant (2006) American Heart Association, National Program; UCSF Postdoctoral Teaching Fellowship (2005) University of California, San Francisco; Postdoctoral Fellowship Award (2005) American Heart Association, Western States Affiliates; Outstanding Poster Award (2004) Gordon Research Conference on Lipoprotein Metabolism; Travel Award (2004) Workshop on Lipids and the Pathophysiology of Obesity. NIDDK, NIH; Postdoctoral Fellowship Award (2003) American Heart Association, Western States Affiliates; SEBM Young Investigator Award (2003) Society for Experimental Biology and Medicine; American Society for Nutritional Sciences Graduate Student Research Award (2000); Keystone Symposia Scholarship (2002) Keystone Symposium ; Hughes Bryan Outstanding Doctoral Award (2000) University of North Carolina at Chapel Hill; Humphreys Dissertation Fellowship (1999) Graduate School, University of North Carolina at Chapel Hill; Avanti Graduate Student Research Award (1998) 33rd Annual Southeastern Regional Lipid Conference; American Society for Nutritional Sciences Graduate Student Research Award (1998); Nutrition Research Fellowship (1998) Institute of Nutrition, University of North Carolina System; Lineberger Comprehensive Cancer Education Research Fellowship (1996) ; Nutrition Research Fellowship (1997) Institute of Nutrition, University of North Carolina System; Book Coupon Award (1991) Taipei Medical College, Taiwan; Yakult Foundation Scholarship (1990) Yakult Foundation, Taipei, Taiwan

C. Contribution to Science

Nutrient availability and programmed cell death

In my PhD dissertation study, I used deficiency of the nutrient choline in cultured cells and primary neurons as a model to examine the possibility that the long-term effects of nutrition can result from modulating programmed cell death. The work was part of a larger project examining how choline availability during pregnancy in rats modulates memory functions of offspring later in life. This work was one of the first examples demonstrating that nutrient availability modulates apoptosis, and it piqued my interest in lipids as signaling molecules and their metabolizing enzymes.

Yen C-LE, Mar MH, Craciunescu CN, Edwards LJ, Zeisel SH. (2002) Deficiency in methionine, tryptophan, isoleucine, or choline induces apoptosis in cultured cells. ***J. Nutrition.*** 132(7):1840–1847.

Yen C-LE, Mar MH, Meeker, RB, Fernandes A, Zeisel SH (2001) Choline deficiency induces apoptosis in primary cultures of fetal neurons. ***FASEB J.*** 15(10):1704–1710.

Yen C-LE, Mar MH, Zeisel SH (1999) Choline deficiency-induced apoptosis in PC12 cells is associated with diminished membrane phosphatidylcholine and sphingomyelin, accumulation of ceramide and diacylglycerol, and activation of caspases. ***FASEB J.*** 13(1):135–142.

Cloning and identification of mammalian lipid acyltransferases

During postdoctoral training, my work focused on searching for additional mammalian acyl CoA: diacylglycerol acyltransferases (DGATs), predicted by the observation that mice deficient in the only known DGAT enzyme (DGAT1) at that time can synthesize TAG. I was involved in the cloning of the second DGAT and have cloned and identified several additional human and mouse acyltransferases, including two acyl CoA: monoacylglycerol acyltransferases (MGAT1 and MGAT2) and a skin multifunctional acyltransferase that catalyzes the synthesis of acylglycerols, retinyl esters, and waxes. I also showed that DGAT1 possesses MGAT activity and may also function as an acyl CoA: retinol acyltransferase. These findings contributed to annotation of genomes and provided essential information for further examination of the functions of these enzymes.

Yen C-LE*, Brown CH, IV, Monetti M, and Farese RV Jr. (2005) Identification of a human multifunctional O-acyltransferase expressed in the skin that catalyzes the synthesis of acylglycerols, retinyl esters, and waxes. ***J. Lipid Research***. 46(11):2388-97

Yen C-LE*, Monetti M, Burri BJ, and Farese RV Jr. (2005) The triacylglycerol synthesis enzyme DGAT1 also catalyzes the synthesis of diacylglycerols, wax esters, and retinyl esters. ***J. Lipid Research.*** 46(7):1502-11.

Yen C-LE and Farese RV Jr. (2003) MGAT2, a monoacylglycerol acyltransferase expressed in the small intestine. ***J. Biological Chemistry.*** 278(20):18532-7. PMID: 12621063

Yen C-LE, Stone SJ, Cases S, Zhou P, Farese RV Jr. (2002) Identification of a gene encoding MGAT1, a monoacylglycerol acyltransferase. ***PNAS.*** 9(13):8512–8517. PMC124292

Physiological function of acyltransferases

Following the cloning and identification of mammalian acyltransferases, we generated and characterized mice that lack or overexpress the encoding genes to explore their physiological functions. For example, the work on MGAT2 highlighted the role of intestinal lipid metabolism in the regulation of systemic energy balance, which forms the basis for our current research focusing on how MGAT2 inactivation protects against diabetes and understanding the underlying molecular mechanisms. This series of work also discovered additional functions of DGAT1, including detoxification of excess vitamin A through its retinol esterification activity. This additional activity may explain the skin and mammary gland defects observed in mice lacking the enzyme. We also contributed to understanding the *in vivo* functions of MGAT1.

Ma Z, Onorato JM, Chen L, Nelson DW, **Yen C–LE**, Cheng D (2017) Synthesis of neutral ether lipid Monoalkyl-diacylglycero (MADAG) by lipid acyltransferases ***J. of Lipid Research****.* Apr. 18 PMC5454505

Agarwal AK, Tunison K, Dalal JS, **Yen C–LE**, Farese RV Jr, Horton JD, Garg A. (2016) *Mogat1* deletion does not ameliorate hepatic steatosis in lipodystrophic (*Agpat2*$^{-/-}$) or obese (ob/ob) mice. ***J. Lipid Research.*** Apr;57(4):616-30. PMC4808770.

Banh T, Nelson DW, Gao Y, Huang TN, Yen MI, **Yen C–LE*** (2015) Adult-onset deficiency of acyl CoA: monoacylglycerol acyltransferase (MGAT) 2 protects mice from diet-induced obesity and glucose intolerance. ***J. Lipid Research.*** 56(2):379-89. PMC4306691

Yen C–LE, Cheong M–L, Grueter C, Zhou P, Moriwaki J, Wong JS, Hubbard B, Marmor S, and Farese RV Jr. (2009) Deficiency of the intestinal enzyme MGAT2 protects mice from metabolic disorders induced by high–fat feeding. ***Nature Medicine.*** 15:442–446. PMC2786494

The regulation of lipid metabolism and energy balance

Because of our expertise in lipid metabolism and in metabolic phenotyping, we are also involved in collaborative projects related to understanding the regulation of lipid metabolism and energy balance in response to dietary interventions or genetic manipulations. With the support of ….

Lin CJ, Cheng YC, Chen HC, Chao YK, Nicholson MW, **Yen C–LE**, Kamp TJ, Hsieh PC*. (2022) Commensal gut microbiota-derived acetate and propionate enhance heart adaptation in response to cardiac pressure overload in mice. ***Theranostics***; 12(17):7319-7334. doi: 10.7150/thno.76002. PMC9691357.

Pak HH, Haws SA, Green CL, Koller M, Lavarias MT, Richardson NE, Yang SE, Dumas SN, Sonsalla M, Bray L, Johnson M, Barnes S, Darley-Usmar V, Zhang J, **Yen C–LE**, Denu JM, Lamming DW (2021) Distinct Roles of fasting and calories in the metabolic, molecular, and geroprotective effects of a calorie restricted diet. ***Nature Metabolism.*** DOI:10.1038/s42255-021-004660-9. PMC8544824

Li Z, Nguyen JN, Votava JA, Jaimes FB, Ly SM, Brinkman JA, Giorgi MD, Kaul S, Green CL, St. Clair SL, Belisle SL, Rios JM, Nelson DW, Sorci-Thomas MG, Lagor WR, Lamming DW, **Yen C–LE**, Parks BW (2020) Integrative analysis of mouse liver co-expression networks and human lipid GWAS data pinpoints *Sestrin1* as a regulator of cholesterol metabolism. ***Cell Metabolism*** Apr;31(4):741–754. PMC7184639

Kasza I, Adler D, Nelson DW, **Yen C–LE**, Dumas S, Ntambi JM, MacDougald OA, Hernando D, Porter WP, Best FA, Alexander CM (2019) Evaporative cooling provides a major metabolic energy sink. ***Molecular Metabolism***. Sep; 27:47-61. PMC6717770

Complete List of Published Work in My Bibliography:

http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/45491289/?sort=date&direction=ascending