## BIOGRAPHICAL SKETCH

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NAME: Chi Chen

POSITION TITLE: Associate Professor of Nutritional Metabolomics

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| China Pharmaceutical University, Nanjing, China | B.S | 1993 | Pharmacy |
| West China Univ. of Med. Sci., Chengdu, China | M.S | 1998 | Pharmacognosy |
| Rutgers University, New Brunswick, NJ | Ph.D. | 2004 | Pharmaceutical Science |
| National Cancer Institute, NIH, Bethesda, MD | Postdoc | 2008 | Metabolomics |

### A. Personal Statement

My training and research experience cover multiple disciplines in chemistry and biology fields, including metabolomics, lipidomics, toxicology, xenobiotic metabolism, nutritional biochemistry and chemoprevention. My current research interest is on the utilization of metabolomics platform to conduct mechanistic characterization of metabolic changes induced by dietary, chemical and pathophysiological challenges. Using untargeted metabolomics as a discovery tool, my research has generated novel information on the metabolic changes induced by fecal microbiota transplantation in recurrent C. difficile infection patients; the disruption of fatty acid metabolism in chemical-induced hepatotoxicity; ethanol metabolism; metabolic effects of feeding dried distillers grains with solubles (DDGS) and peroxidized lipids to pigs; metabolic responses to DDS-induced ulcerative colitis in mice; and *in vivo* biotransformation of carcinogen and therapeutic agents in wild-type and transgenic mice. Through these projects, I accumulated extensive experience in elucidating and characterizing novel metabolite biomarkers (both endogenous and exogenous compounds) of xenobiotic exposure and pathophysiological disorders through a combination of untargeted metabolomics, targeted metabolite profiling, stable isotope tracing, biochemical analysis, animal models, and intervention treatment.

### B. Positions and Honors

**Professional Positions:**

2005-2008 Visiting Fellow, Laboratory of Metabolism, National Cancer Institute, NIH
2008 Senior Scientist, Schering-Plough Research Institute, Kenilworth, NJ
2008-2014 Assistant Professor, Department of Food Science and Nutrition, University of Minnesota at Twin Cities (30% appointment with Animal Science Department for interdisciplinary collaborations)
2014-present Associate Professor, Department of Food Science and Nutrition, University of Minnesota

**Honors and Awards:**

2002 Excellence in Graduate Research in Biotechnology, American Association of Pharmaceutical Scientists
2007 Keystone Symposia Scholarship in Bioactive Lipids
2007 Post-Doctoral Scientist Award in Drug Metabolism (1st place), American Society of Pharmacology and Experimental Therapeutics (ASPET)
2008 NIH Fellows Award for Research Excellence

**C. Contribution to Science**

1. I started to explore metabolomics in my own research during my postdoctoral training at the Laboratory of Metabolism, National Cancer Institute (NCI), and thereafter made significant contribution to the establishment of a highly productive metabolomics platform in that lab. Through my research works on chemical challenges and genetically-modified animal models, I became proficient in utilizing untargeted metabolomics to identify novel metabolites and metabolic changes after xenobiotic exposure. Novel metabolites and metabolic pathways of acetaminophen, PhIP, and aminoflavone were identified and characterized by untargeted metabolomics in my research projects. The experimental approaches adopted in the projects were summarized in a review on the utilization of LC-MS-based metabolomics in xenobiotic metabolism research. Besides xenobiotic metabolites, endogenous metabolites were also identified as the biomarkers of chemical-induced hepatotoxicity and ulcerative colitis through untargeted metabolomics.
    a. **Chen C**, Krausz KW, Idle JR, Gonzalez FJ. *Identification of novel toxicity-associated metabolites by metabolomics and mass isotopomer analysis of acetaminophen metabolism in wild-type and Cyp2e1-null mice.* J Biol Chem. 283: 4543-59 (2008)
    b. **Chen C**, Ma X, Malfatti MA., Krausz KW, Kimura S, Felton JS, Idle JR, Gonzalez FJ. *A comprehensive investigation of 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) metabolism in the mouse using a multivariate data analysis approach.* Chem Res Toxicol. 20, 531-542 (2007)
    c. **Chen C**, Idle JR, Gonzalez FJ. *LC-MS-based metabolomics in drug metabolism.* Drug Metab Rev. 39: 581-97 (2007)
    d. **Chen C**, Shah YM, Morimura K, Krausz KW, Miyazaki M, Richardson TA, Morgan ET, Ntambi JM, Idle JR, Gonzalez FJ. *Metabolomics reveals that hepatic stearoyl-CoA desaturase 1 downregulation exacerbates inflammation and acute colitis*. Cell Metab. 7: 135-47 (2008)

2. After starting my independent research at the University of Minnesota, I expanded my research to other well-known toxicants and dietary ingredients including alcohol, cocaine, and thermally-stressed vegetable oils. Untargeted metabolomic analysis of urine samples from alcohol-treated mice led to the identification of *N*-acetyltaurine (NAT) as a metabolite of ethanol and a urinary biomarker of ethanol exposure. Through examining the mechanism of NAT biosynthesis, our results suggested that the increase of NAT level could function as an effective indicator of hyperacetatemia. In cocaine project, untargeted metabolomics of urine samples identified species-specific metabolism of cocaine in mouse and rat, two commonly used animal models for cocaine research, while untargeted metabolomics of serum led to the observation of cocaine-induced acylcarnitine accumulation in serum. Subsequent mechanistic investigation suggested that the inhibition of hepatic fatty acid oxidation plays an important role in cocaine-induced hepatotoxicity. In addition to these research activities, we also developed new techniques for LC-MS analysis of metabolome, including the development of 2-hydrazinoquinoline as a derivatization agent for detecting aldehydes, ketones, and carboxylic acids in biological samples.
    a. Yao D, Shi X, Wang L, Gosnell BA, **Chen C**. *Characterization of Differential Cocaine Metabolism in Mouse and Rat through Metabolomics-guided Metabolite Profiling*. Drug Metab Dispos. 41: 79-88 (2013)
    b. Shi X, Yao D, Gosnell BA, **Chen C**. *Lipidomic profiling reveals protective function of fatty acid oxidation in cocaine-induced hepatotoxicity*. J. Lip. Res. 53: 2318-30 (2012)
    c. Shi X, Yao D, **Chen C**. *Identification of N-acetyltaurine as a novel metabolite of ethanol through metabolomics-guided biochemical analysis*. J Biol Chem. 287: 6336-49 (2012)
    d. Lu Y, Yao D, **Chen C**. *2-Hydrazinoquinoline as a derivatization agent for LC-MS-based metabolomic investigation of diabetic ketoacidosis*. Metabolites. 3: 993-1010 (2013)

3. The metabolomics platform in my lab has become a very useful resource for the researchers in the University of Minnesota and other institutions. My past and ongoing collaborations cover metabolic events in diverse biological samples (urine, blood, feces, intestinal content, tissue) in multiple species (human, mouse, rat, pig, cattle, zebrafish) under various chemical, environmental, and pathophysiological challenges (fecal transplantation, morphine treatment, feeding oxidized lipids, algae and oat bran, etc). The capacity of untargeted metabolomics to reveal mechanistic information have been demonstrated in these collaborative studies. For example, through metabolomics, the normalization of bile acid metabolism was observed in recurrent *C. difficile* infection patients undergoing fecal microbiota transplantation (FMT). This observation provides a sound explanation for the therapeutic efficacy of FMT since some secondary bile acids produced by the transplanted microbes can suppress the germination of *C. difficile* spores.

a. Weingarden AR[#], **Chen C**[#], Bobr A, Yao D, Lu Y, Nelson V, Sadowsky MJ, Khoruts A. *Microbiota Transplantation Restores Normal Fecal Bile Acid Composition in Recurrent Clostridium difficile Infection*. Am J Physiol Gastrointest Liver Physiol. 306:G310-9 (2014) (# co-first author)
b. Song R, **Chen C**, Wang L, Johnston LJ, Kerr BJ, Weber TE, Shurson GC. *High sulfur content in corn dried distillers grains with solubles (DDGS) protects against oxidized lipids in DDGS by increasing sulfur-containing antioxidants in nursery pigs*. J Anim Sci. 91: 2715-28 (2013)
c. Liu P, **Chen C**, Kerr BJ, Weber TE, Johnston LJ, Shurson GC. *Influence of thermally oxidized vegetable oils and animal fats on growth performance, liver gene expression, and liver and serum cholesterol and triglycerides in young pigs.* J Anim Sci. 92:2960-70 (2014)

Complete List of Published Work in My Bibliography (total 70 peer-reviewed publications):
http://scholar.google.com/citations?user=dTooB-kAAAAJ&hl=en