BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Fiehn, Oliver	Professor
eRA COMMONS USER NAME OLIVERFIEHN	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
Berlin Free University	diploma	1993	Analytical Chemistry
Berlin Technical University	PhD	1997	Analytical Toxicology
Max-Planck Institute Mol. Plant Physiol.	Postdoc	1998-99	Metabolomics

A. Personal Statement

As Director of the NIH West Coast Metabolomics Center at UC Davis I am committed to provide research and services conducting research in metabolomic method developments and biomedical applications. Combined, I oversee the operation of 33 staff using 14 mass spectrometers. I have pioneered developments and applications in metabolomics since 1998 with over 130 publications to date, and am keen to improve these methods with the aim of further standardization and higher content in biochemical information through automatic annotation of metabolites and by using a range of chemical and biochemical database identifiers with every report we generate. For the Metabolomics Society, I have chaired the efforts in standardizing metabolomic reports, and the developments and services in our Center will enable researchers to maximize interpretation of metabolomic findings using a variety of metabolomics, statistical, informatics and genomic approaches.

B. Positions and Honors

Positions and Employment

1994-1997 Research scientist, Technical University of Berlin, Germany
1998-1999 Postdoctoral research scientist, Max-Planck Inst. Molecular Plant Physiology, Potsdam, Germany
1999 Visiting postdoctoral research scientist, Dept. Molecular Biol., University of Wash., Seattle, WA
1999-2004 Research group leader, Max-Planck Inst. Molecular Plant Physiol., Potsdam, Germany
2004-2009 Assoc. Professor, Dept. of Molecular & Cellular Biology, UC Davis Genome Center, CA
2009- Full Professor, Dept. of Molecular & Cellular Biology, UC Davis Genome Center, CA
2012- Director, NIH West Coast Metabolomics Center

Other Experience, Honors and Professional Memberships

2014 Molecular & Cellular Proteomics Lecture Award
2014 Metabolomics Society Lifetime Achievement Award
2012 Phi Lambda Upsilon Rho –Chapter award, Lincoln, NE
2009 Distinguished Scientist Award, CCDG, Chicago
2004-2010, 2013-15 Board of Directors, Metabolomics Society
2008-2010 Treasurer, Metabolomics Society
2006-2011 Editorial Board 'Journal of Biological Chemistry'
2004- Editorial board member 'Metabolomics' and 'Plant Methods'
2010- Editorial board member "Rapid Communication in Mass Spectrometry"
2008, 2009, 2015 Organizer, Metabolomics Society Conference, Boston, Edmonton, San Francisco
2011 Organizer and Chairman, ASMS Asilomar meeting on "Metabolomics"

C. Contribution to Science

Early contributions 1994-1998 were geared at analytical toxicology, specifically in finding unknown organics from complex industrial wastewaters that exerted toxic effects to aquatic organisms. The central theme of this work, identification of unknowns and untargeted analyses, founded the corner stone of postdoctoral and group leader work in Molecular Plant Physiology at the Max-Planck Institute in Germany, then called metabolite

profiling. As group leader in Germany, and then as Professor at UC Davis, this work led to the now flourishing field of metabolomics and its application in biology and medicine.

1. **Development of metabolomics as a technology in biological studies.** The Fiehn laboratory has pioneered metabolomics since 1998. The major idea was to go beyond hypothesis-driven science towards discovery science, broadening the horizon for pleiotropic biological effects and discerning gene functions for orphan genes, novel biochemical pathways and defining metabolic phenotypes, or metabotypes, as central theme of the function of the molecular machinery of cells and organism. We had first used untargeted metabolomics in a seminal publication on plant leaves (Fiehn et al, 2000), opening the door to large scale comparisons of mutant phenotypes by gas chromatography/mass spectrometry. We then added liquid chromatography/mass spectrometry, specifically for hydrophilic metabolites using HILIC techniques and identified many unpublished and novel metabolites discovered in plant phloem (Tolstikov et al, 2003). Realizing the need to link different types of –omics data, we validated protocols to use a single sample for profiling RNA and proteins as well as metabolites, using specific inhibitors and optimized buffer / sample ratios (Weckwerth et al, 2004). More recently, we have focused on workflows for identifying the hundreds of unknown metabolic signals that are typically found in samples (Kumari et al, 2011) of either mammalian or plant or microbial origins. This work remains important to stretch metabolomics to i ts true potential of 'discovery' type work, while robustness and quantifyability becomes an ever more important topic in epidemiological studies.

Fiehn O, Kopka J, Dörmann P, Altmann T, Trethewey RN, Willmitzer L (2000) Metabolite profiling for plant functional genomics. Nature Biotechnology 18: 1157-1161

Tolstikov VV, Lommen A, Nakanishi K, Tanaka N, **Fiehn O** (2003) Monolithic silica-based capillary reversed-phase liquid chromatography/electrospray mass spectrometry for plant metabolomics. Analytical Chemistry 75: 6737-6740

Weckwerth W, Wenzel K, **Fiehn O** (2004) Process for the integrated extraction, identification and quantification of metabolites, proteins and RNA to reveal their co-regulation in biochemical networks. Proteomics 4: 78-83

Kumari S, Stevens D, Kind T, Denkert C, **Fiehn O** (2011) Applying in-silico retention index and mass spectra matching for identification of unknown metabolites in accurate mass GC-TOF mass spectrometry. Analytical Chemistry 83: 5895-5902

2. **Large scale data processing and databases to study metabolism.** Analytical Chemistry was, and partly still is, dominated by reports on single methods and advances in separation. While this view was valid when only a few target molecules were analyzed, metabolomics quickly encountered the challenge to store, compare and disseminate large data sets in publicly available databases that are compliant to data standards developed by community efforts. The Fiehn laboratory takes an active lead in this process and continues to develop and implement novel methods, libraries and databases to improve the status in the field. Given the enormous complexity of metabolism, the Fiehn laboratory now extends libraries of authentic standards to virtual mass spectral predictions, for example for over 200,000 lipids in 29 lipid classes (Kind et al, 2013). Secondly, the laboratory has amassed a 'Rosetta Stone' to translate names and chemical identifiers between over 250 different genomic and chemical databases, termed the Chemical Translation Service (Wohlgemuth et al, 2010). Ultimately, biological interpretations of metabolomic signatures are aided by visualizing all identified metabolites in network graphs via biochemical substrate/product relationships and adding compounds without enzymatic assignments by chemical structure similarities, or by mass spectral similarities (for unknown compounds) (Barupal et al, 2012).

Kind T, Liu K-H, Lee DY, DeFelice B, Meissen JK, **Fiehn O** (2013) LipidBlast in silico tandem mass spectrometry database for lipid identification. Nature Methods 10: 755-758

Wohlgemuth G, Haldiya PK, Willighagen E, Kind T, **Fiehn O** (2010) The Chemical Translation Service—a web-based tool to improve standardization of metabolomic reports. Bioinformatics 26: 2647-2648

Barupal DK, Haldiya PK, Wohlgemuth G, Kind T, Kothari SL, Pinkerton KE, **Fiehn O** (2012) MetaMapp: mapping and visualizing metabolomic data by integrating information from biochemical pathways and chemical and mass spectral similarity. BMC Bioinformatics 13: 99

Kind T, Wohlgemuth G, Lee DY, Lu Y, Palazoglu M, Shahbaz S, **Fiehn O** (2009) FiehnLib: mass spectral and retention index libraries for metabolomics based on quadrupole and time-of-flight gas chromatography/mass spectrometry. Analytical Chemistry 81: 10038-10048

3. **Discovery of metabolic dysfunctions in human health.** Metabolomics serves two overlapping functions: describing metabolic phenotypes to serve as diagnostic tools in the onset and progression of human diseases, and finding the biochemical mechanisms and causes for diseases by assigning differences in genes or protein functions, as well as the effects of nutrition on the metabolic network and microbiota. For example, we were able to pinpoint a probable differences in diabetic and non-diabetic African-Americans by using metabolomics (Fiehn et al, 2010). In cancer metabolism, we discovere metabolic differences in breast tumors and lung cancers, highlighting the critical roles for lipid metabolism (Hilvo et al, 2011) as well as glutamine dependencies (Budczies et al, 2013). We are further actively investigating diseases of the metabolic syndrome, including diabetes and cardiovascular events, specifically focusing on acylcarnitines and nutritional interventions (Fiehn et al, 2010). We also discovered metabolic differences in cell differentiations, for example between pluripotent and embryonic stem cells, for both primary and lipid metabolism (Meissen et al, 2012).

Hilvo M, Denkert C, Lehtinen L, Müller B, Brockmöller S, Seppänen-Laakso T, Budczies J, Bucher E, Yetukuri L, Castillo S, **Fiehn O**, Oresic M (2011) Novel theranostic opportunities offered by characterization of altered membrane lipid metabolism in breast cancer progression. Cancer research 71: 3236-3245

Budczies J, Brockmöller SF, Müller BM, Barupal DK, Richter-Ehrenstein C, Kleine-Tebbe A, Griffin JL, Orešič M, Dietel M, **Fiehn O,** Denkert C (2013) Comparative metabolomics of estrogen receptor positive and estrogen receptor negative breast cancer: alterations in glutamine and beta-alanine metabolism. Journal of proteomics 94: 279-288

Fiehn O, Garvey WT, Newman JW, Lok KH, Hoppel CL, Adams SH (2010) Plasma metabolomic profiles reflective of glucose homeostasis in non-diabetic and type 2 diabetic obese African-American women. PLoS One 5: e15234

Meissen JK, Yuen BTK, Kind T, Riggs JW, Barupal DK, Knoepfler PS, **Fiehn O** (2012) Induced pluripotent stem cells show metabolomic differences to embryonic stem cells in polyunsaturated phosphatidylcholines and primary metabolism. PloS one 7: e46770

4. **Discovery of metabolic mechanisms in plants, algae and microbes.** Mammalian metabolism describes the interaction of food, the microbiome and mammalian organs in a very complex fashion that makes it very difficult to distinguish cause and effects. For example, we have delineated the relative impact of xeno-metabolites originating from gut microbial metabolism in a controlled nutritional study that improved insulin resistance (Campbell et al, 2014). However, in general, studying metabolism is much easier in systems that have less complex interactions, for example in plants. The Fiehn laboratory has shown that some plants have two metabolically very distinct phloem systems, with the classic system delivering carbon loads but the second, extrafascicular system, responsible for defense and communication (Zhang et al, 2010). We have further discovered very specific enzymes that are responsible for repairing damaged or toxic metabolites, for example repairing the dysfunctional form of hydrated NADPH (Niehaus et al, 2014). On a model species, Chlamydomonas reinhardtii, we could demonstrate that these algae cells have systems that sense the total available nitrogen and counteract metabolic responses way before nitrogen resources are depleted, including up-regulation of novel signaling molecules and a stringent response pathway that was previously only shown for prokaryotes (Lee et al, 2012).

Campbell C, Grapov D, **Fiehn O**, Chandler CJ, Burnett DJ, Souza EC, Casazza GA, Gustafson MB, Keim NL, Newman JW (2014) Improved metabolic health alters host metabolism in parallel with changes in systemic xeno-metabolites of gut origin. PloS one 9: e84260

Zhang B, Tolstikov V, Turnbull C, Hicks LM, **Fiehn O** (2010) Divergent metabolome and proteome suggest functional independence of dual phloem transport systems in cucurbits. Proceedings of the National Academy of Sciences 107: 13532-13537

Niehaus TD, Richardson LGL, Gidda SK, ElBadawi-Sidhu M, Meissen JK, Mullen RT, **Fiehn O**, Hanson AD (2014) Plants utilize a highly conserved system for repair of NADH and NADPH hydrates. Plant physiology 165: 52-61

Lee DY, Park J-J, Barupal DK, **Fiehn O** (2012) System response of metabolic networks in Chlamydomonas reinhardtii to total available ammonium. Molecular & Cellular Proteomics 11: 973-988

D. Research Support - Current

Agilent (PI Fiehn, O. - UC Davis) 01/01/07 to 10/30/2016
Metabolomic libraries and methods by mass spectrometry
Goals: Improve metabolite identification by standardized QTOF and GC-quad MS analyses of reference compounds.

NIH / NIEHS ES020819-01 (PI Hockenbery, D - U Washington/Seattle) 09/01/11 to 08/30/2016
Biomarker discovery for mitochondrial toxicants using metabolic footprinting
Goals: To examine mitochondria dysfunction at sub-chemical thresholds, centered on testing fatty acid overload and metabolite biomarker discovery as a result of BDE-47 exposure in mouse hepatocytes.

P20 NIH HL113452 (PI Hazen, S. Cleveland, Fiehn, O. UC Davis; coPI) 06/01/12 to 05/30/2017
Functional Cardio-Metabolomics
Goals: Untargeted metabolomic analysis by GC-TOFMS and LC-QTOFMS from blood plasma of animal models+human cohorts.

NSF MCB 1153491 (PI Hanson U Florida, Fiehn, O. UC Davis; coPI et al) 04/01/12 to 03/31/2016
Metabolite repair – Uncovering the hidden support system for metabolic networks.

NSF MCB - 1139644 (PI Fiehn, O. - UC Davis) 12/01/11 to 11/30/2016
METABOLOMICS: Integrating cheminformatic resources for investigating photoautotrophic and mixtotrophic metabolism in algae
Goals: To implement novel metabolomic databases and tools for compound identification. To screen 10 algal species under different environmental conditions and map metabolomic databases to algal biomass growth.

NIH U24 DK097154 (PI Fiehn, O - UC Davis) 09/01/12 to 08/30/2017
The West Coast Central Comprehensive Metabolomics Resource Core.
Goals: To provide extensive metabolomic services to biological and medical researchers on the West Coast

NIH U01 DK097430 (PI Subramaniam, S. – UCSD, coPI Fiehn, O) 09/01/12 to 08/30/2017
The Metabolomics Data Center and Workbench (MDCW).
Goals: To provide a central data repository for the NIH regional Metabolomics resource cores.

American Seed Research Foundation (PI Bradford – UC Davis) 04/01/13 to 03/31/2016
Respiratory and Hormonal Metabolism Associated with Seed Germination, Vigor and Quality.
Goals: To investigate seed germplasm with respect to metabolomic changes during germination.

NIH / NIDDK (PI Norris, J - U Denver, CO) 09/01/14 to 08/30/2019
Nutrigenetics & -genomics of Vitamin D and Omega-3 Fatty Acids in Type 1 Diabetes
Goals: To test food biomarkers and metabolic signatures in type 1 diabetes cohort research.