BIOGRAPHICAL SKETCH

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NAME: Vernetti, Lawrence

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

POSITION TITLE: Research Associate Professor

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)	END DATE MM/YYYY	FIELD OF STUDY
Portland State University, Portland, OR	BS	01/1975	Chemistry
Oregon Health Sciences Center, Portland, OR	BS	10/1982	Medical Technology
University of Arizona, Tucson, Az	MS	01/1989	Toxicology
University of Arizona, Tucson, AZ	PHD	12/1992	Pharmacology/Toxicology

A. Personal Statement

I spent the first part of my career as a study monitor at AbbVie (formerly Abbott Laboratories) conducting non-GLP and GLP compliant drug safety trials in mice, rats, dogs and non-human primates. During this time I wrote the IND toxicology summary sections for several compounds, including Ritonavir, which became the first approved protease inhibitor drug for HIV treatment. Later in my pharmaceutical experience, I initiated a screening program to assess candidate drugs for potential liability focusing on the use of mechanism-based measurements using High Content Screening (HCS) image analysis and in vitro liver models. In addition, I initiated a high throughput in vitro drug metabolism assay to rank order compounds by intrinsic clearance. After leaving Abbott Laboratories in 2007, I accepted the position of Director of Cellular Toxicology at Cellumen, in Pittsburgh, PA, a biotech developing an HCS-based predictive toxicology platform. During my tenure at Cellumen, I developed 'scoring' method to populate a drug safety database using an expert-based quantitative assessment of rodent and human adverse findings. The drug safety database eventually grew to over 500 marketed and failed drugs and became the core data set for collaborating computational scientists to train a safety risk predictive algorithm to identify toxic compounds from in vitro profile analysis. In December 2010, I joined the Drug Discovery Institute at University of Pittsburgh to initiate an early drug safety toxicology program. In these positions I used media measurements of liver products and HCS to read sub-cellular chemical fluorescent probes to interrogate pathways of toxicity activation. In 2012, I became an active participate into the development, validation and deployment of a physiologically relevant microfluidic, 3D, multicellular human liver microphysiology system (MPS). Our MPS model is a biomimetic re-construction of the liver sinusoid using 4 key liver cell types in a media flow-through device. The two key features leading to the success of this model was, first, the use of genetically encoded fluorescent protein functional biosensors to provide quantitative, real-time readouts of clinically relevant molecular pathways of toxicity, and, second, the ability to recapitulate zone 3 of the liver, most often the specific area in the sinusoid where toxicity and disease initiate. In 2016, I worked with other scientists in the department to begin development of an MPS liver disease model to follow the progression of non-alcoholic fatty liver disease alone or as a part of metabolic syndrome including co-morbidity of type 2 diabetes. Finally, due to my knowledge as an expert toxicologist and prior experience in computational predictive modeling, I assisted in the design, use and interpretation of compound induced adverse effects for the BioSystics-AP™ (formerly known as the University of Pittsburgh MicroPhysiology Database), a commercial comprehensive platform constructed to design wet bench experiments, manage and analyze data for computational modeling to predict human toxicity, pharmacokinetics, drug efficacy and disease initiation and progression.

Ongoing and recently completed projects related to these goals:

UH2TR004124
Miedel (PI), Role: Co-Investigator
7/1/2022-5/31/2028
Re-engineering a human 3D liver tissue model for non-alcoholic fatty liver disease for drug screening

R44TR003535
Yang, Simulations Plus Inc. (PI), Role: Co-Investigator
3/1/2022-2/28/2024
Software for predicting liver injury from biologics drug candidates using data from a human liver microphysiology system

U01 TR002383
Wikswo, Vanderbilt University (PI), Role: Co-Investigator
8/1/2018 – 7/31/2023
Harnessing human brain and liver microphysiological systems for testing therapeutics for metastatic melanoma

R01 DK0017781
Taylor (PI), Role: Co-Investigator
8/1/2018-4/30/2023 (NCE)
Applying a Human Liver Microphysiology system to Develop Therapeutic Strategies for Non-alcoholic Fatty Liver Disease (NAFLD).

U24TR002632
Schurdak (PI), Role: Co-Investigator
12/5/2020-11/30/2023 (NCE)
Development and Commercialization of the Microphysiology Systems Database as a Sustainable Resource

UH3DK119973
Taylor (PI), Role: Co-Investigator
9/20/2018-7/31/2023
Human Microphysiology Systems Disease Model of Type 2 Diabetes Starting with Liver and pancreatic Islets

Citations:

1. Lefever D, Fen P, Miedel M, DiStefano J, DeBiasio R, Shun, TY, Vernetti L, Soto-Gutierrez A, Monga S, Bataller R, Behari J, Yechoor V; Bahar I, Gough A, Stern, A, Taylor D. A Quantitative Systems Pharmacology Platform Reveals Potential Repurposable Drugs for Nonalcoholic Fatty Liver Disease. Metabolites. 2022 Jun 7;12(6):528
2. Courtney Sakolish; Yu-Syuan Luo; Alan Valdiviezo; Lawrence A. Vernetti; Ivan Rusyn. Prediction of Hepatic Drug Clearance with a Human Microfluidic Four-Cell Liver Acinus MicroPhysiology System. Toxicology. 2021 Nov;463:152954.
3. Albert Gough, Alejandro Soto-Gutierrez, Lawrence Vernetti, Mo R. Ebrahimkhani, Andrew M. Stern, D. Lansing Taylor. Human biomimetic liver microphysiology systems in drug development and precision medicine. Nature Reviews Gastroenterol Hepatol, 2021 Apr;18(4):252-268.
4. Vernetti LA, Senutovitch N, Boltz R, DeBiasio R, Shun TY, Gough A, Taylor DL. A human liver microphysiology platform for investigating physiology, drug safety, and disease models. Exp Biol Med (Maywood). 2016 Jan;241(1):101-14.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

1992 - 2007	Toxicologist/Pharmacologist, Abbott Laboratories, Chicago, IL
2007 - 2019	Director In Vitro Toxicology, Cellumen, Pittsburgh, PA
2010 -	Research Associate Professor, University of Pittsburgh - Pittsburgh, PA, Pittsburgh, PA

Other Experience and Professional Memberships

1982 -	Medical Technologist, ASCP
1990 -	Full Member, SOT
1996 - 2006	Diplomat American Board of Toxicology , DABT

C. Contribution to Science

1. A critical component for the drug discovery success is the early identification of compounds with efficacy and rule out those with poor human pharmacokinetics or the potential to increase human toxicity. However, many of the current animal models used to assess human efficacy and risk are poor predictors. Since 2012, I have been active in developing MPS models as a platform to assess human toxicology, pharmacokinetics and for efficacy and disease research. The University of Pittsburgh Drug Discovery Institute MPS models has been successfully used to identify high risk hepatotoxic compounds from compounds that rarely cause hepatotoxicity. A new, vascularized better biomimetic version of the liver model has been developed to include continuous oxygen and metabolic zonation with inducible immune cell infiltration.
   a. Li X, George SM, Vernetti L, Gough AH, Taylor DL. A glass-based, continuously zonated and vascularized human liver acinus microphysiological system (vLAMPS) designed for experimental modeling of diseases and ADME/TOX. Lab Chip. 2018 Aug 21;18(17):2614-2631. PubMed PMID: 30063238; PubMed Central PMCID: PMC6113686.
   b. Lee-Montiel FT, George SM, Gough AH, Sharma AD, Wu J, DeBiasio R, Vernetti LA, Taylor DL. Control of oxygen tension recapitulates zone-specific functions in human liver microphysiology systems. Exp Biol Med (Maywood). 2017 Oct;242(16):1617-1632. PubMed PMID: 28409533; PubMed Central PMCID: PMC5661766.
   c. Vernetti L, Gough A, Baetz N, Blutt S, Broughman JR, Brown JA, Foulke-Abel J, Hasan N, In J, Kelly E, Kovbasnjuk O, Repper J, Senutovitch N, Stabb J, Yeung C, Zachos NC, Donowitz M, Estes M, Himmelfarb J, Truskey G, Wikswo JP, Taylor DL. Functional Coupling of Human Microphysiology Systems: Intestine, Liver, Kidney Proximal Tubule, Blood-Brain Barrier and Skeletal Muscle. Sci Rep. 2017 Feb 8;7:42296. PubMed PMID: 28176881; PubMed Central PMCID: PMC5296733.
   d. Vernetti LA, Senutovitch N, Boltz R, DeBiasio R, Shun TY, Gough A, Taylor DL. A human liver microphysiology platform for investigating physiology, drug safety, and disease models. Exp Biol Med (Maywood). 2016 Jan;241(1):101-14. PubMed PMID: 26202373; PubMed Central PMCID: PMC4723301.

2. The use of animal models for disease research is coming into increasing resistance from a scientific standpoint. The current animal models for complex, multi-factorial human diseases such as neurodegenerative, cancer and chronic liver diseases can often define a single phenotype or molecular event of a disease but fail to reproduce the spectrum of disease from initiation and progression. As part of the UPDDI liver group, my recent research focus is the use of human-based experimental models of NAFLD and ALD and lessen the need for laboratory animal experimentation.
   a. Argemi J, Latasa MU, Atkinson SR, Blokhin IO, Massey V, Gue JP, Cabezas J, Lozano JJ, Van Booven D, Bell A, Cao S, Vernetti LA, Arab JP, Ventura-Cots M, Edmunds LR, Fondevilla C, Stärkel P, Dubuquoy L, Louvet A, Odena G, Gomez JL, Aragon T, Altamirano J, Caballeria J, Jurczak MJ, Taylor DL, Berasain C, Wahlestedt C, Monga SP, Morgan MY, Sancho-Bru P, Mathurin P, Furuya S, Lackner C, Rusyn I, Shah VH, Thursz MR, Mann J, Avila MA, Bataller R. Defective HNF4alpha-dependent gene expression as a driver of hepatocellular failure in alcoholic hepatitis. Nat Commun. 2019 Jul 16;10(1):3126. PubMed PMID: 31311938; PubMed Central PMCID: PMC6635373.
   b. Taylor DL, Gough A, Schurdak ME, Vernetti L, Chennubhotla CS, Lefever D, Pei F, Faeder JR, Lezon TR, Stern AM, Bahar I. Harnessing Human Microphysiology Systems as Key Experimental Models for Quantitative Systems Pharmacology. Handb Exp Pharmacol. 2019;260:327-367. PubMed PMID: 31201557; PubMed Central PMCID: PMC6911651.
   c. Soto-Gutierrez A, Gough A, Vernetti LA, Taylor DL, Monga SP. Pre-clinical and clinical investigations of metabolic zonation in liver diseases: The potential of microphysiology systems. Exp Biol Med (Maywood). 2017 Oct;242(16):1605-1616. PubMed PMID: 28467181; PubMed Central PMCID: PMC5661767.

3. There is the expectation that data from human cell based experimental models and published databases can be combined through computational approaches to augment and then replace the traditional drug safety and efficacy animal trial with robust predictive models. As a toxicologist, I have reviewed and provided interpreted results from hundreds of preclinical animal studies and clinical trials for database entry. These are crucial in vivo data needed before the computational models can be created for in vitro in vivo extrapolation
   a. Vernetti LA, Vogt A, Gough A, Taylor DL. Evolution of Experimental Models of the Liver to Predict Human Drug Hepatotoxicity and Efficacy. Clin Liver Dis. 2017 Feb;21(1):197-214. PubMed PMID: 27842772; PubMed Central PMCID: PMC6325638.
   b. Gough A, Vernetti L, Bergenthal L, Shun TY, Taylor DL. The Microphysiology Systems Database for Analyzing and Modeling Compound Interactions with Human and Animal Organ Models. Appl In Vitro Toxicol. 2016 Jun 1;2(2):103-117. PubMed PMID: 28781990; PubMed Central PMCID: PMC5119471.
   c. Schurdak M, Vernetti L, Bergenthal L, Wolter QK, Shun TY, Karcher S, Taylor DL, Gough A. Applications of the microphysiology systems database for experimental ADME-Tox and disease models. Lab Chip. 2020 Apr 14;20(8):1472-1492. PubMed PMID: 32211684.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1F71iZNZg8ekf/bibliography/public/