BIOGRAPHICAL SKETCH

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NAME: Schurdak, Mark E.

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

POSITION TITLE: Associate Professor in Computational and Systems Biology

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
University of Miami, Miami, FL	BS	05/82	Biology
Baylor College of Medicine, Houston, TX	PhD	06/87	Pharmacology

A. Personal Statement

My formal training is in pharmacology and I have practical experience in the innovation of novel screening approaches, complex biological assay development and implementation using QC methods. I have over 20 years of experience in the development and implementation of assays for high-throughput screening (HTS) and hit-to-lead (HtL) campaigns in the biotech and large pharmaceutical companies. As a Group Leader in the high-throughput screening group at Abbott, I instituted the first high-throughput ADME/Tox group at Abbott, and established siRNA and high content screening (HCS) capabilities. Early high-throughput ADME/Tox capabilities were essential for prosecuting hit-to-lead projects and involved structured implementation, QC, and data analysis. This experience grounded me in industrial development including the use of validation statistics and QC methods. Following the successful implementation of multiple HCS and ADME/Tox assays in the HTS group, I moved to the hit-to-lead (HtL) group where I led the biology efforts on projects for oncology and immunology. I directly managed the efforts of two projects and delivered lead series to the respective therapeutic projects for further lead development. Two lead series for one of those projects were advanced to lead optimization and preclinical stages of development under my guidance. Key to the success of these projects were my critical data analysis, creative problem solving approaches, and expertise in assay development for designing selectivity and orthogonal assays to demonstrate the MOA of lead compounds. I was active in other projects within the HtL group, consulting on strategies and implementing assays to identify lead compound series for advancement to lead optimization. In the Early Pain Discovery group within Abbott's department of Neuroscience I was a lead biologist identifying novel therapeutic targets for pain, and developing and implementing HTS and HtL screening campaigns for six projects. Compounds from one of these projects were moved into lead optimization and preclinical animal studies. Upon moving to the University of Pittsburgh Drug Discovery Institute (UPDDI) I took the position of Director of Operations and assumed the role of Scientific Coordinator for the Pittsburgh Special Applications Center, which is part of the NCI NExT Chemical Biology Consortium, and of Director for the University of Pittsburgh Cancer Institute's Chemical Biology Facility. In these positions I coordinated the efforts of multiple groups and managed projects to successful conclusions. At the UPDDI, I have implemented HCS for several projects including STAT3 in head and neck cancer, NR4A1 for ovarian cancer, HSV-1 latency in iPSC derived neurons, and neuroprotection in Huntington's disease. I lead the Huntington's Disease Quantitative Systems Pharmacology (QSP) program integrating clinical, computational and experimental analyses, including development of iPSC derived cell based assays, to gain a comprehensive understanding of disease pathology with which to inform effective therapeutic approaches for disease management. I am also involved in developing and applying informatics software tools for drug discovery and development including development of novel statistics to identify and measure heterogeneity in cell-based assays (PHI – Pittsburgh Heterogeneity Indices).

Finally, I am leading the efforts to expand the Microphysiology Database to integrate experimental, reference, and clinical data for multiple microphysiologic organ and disease models, and enable tools to assess the reproducibility and predictability of these models as part of a Cooperative Agreement with NCATS, Texas A&M, MIT, and the IQ Consortium.

B. Positions and Honors

Positions and Employment

1987 – 1990 Postdoctoral Fellow, Dept. of Oncology and Virology, Hoffmann La Roche, Inc., Nutley, NJ
1990 – 1996 Sr. Scientist, Dept. Molecular and Cell Biology, PharmaGenics, Inc., Allendale, NJ
1996 – 1998 Sr. Research Pharmacologist, Dept. of Combinatorial Chemistry, Abbott Labs., Abbott Park, IL
1998 – 2006 Group Leader, High-throughput Screening, Abbott Labs., Abbott Park, IL
2006 – 2009 Res. Invest. Pharmacologist, Dept. Target and Lead Discovery, Abbott Labs., Abbott Park, IL
2009 – 2011 Sr. Scientist III, Dept. Neuroscience, Early Pain Discovery, Abbott Labs., Abbott Park, IL
2011 – present Associate Professor, Dept. Computational and Systems Biology, University of Pittsburgh, Pittsburgh, PA
2011 – present Director of Operations, University of Pittsburgh Drug Discovery Institute
2015 – present Director of the University of Pittsburgh Cancer Institute Chemical biology Facility

Other Experience and Professional Memberships

American Association for the Advancement of Science
American Chemical Society
American Association for Cancer Research
Society for Laboratory Automation and Screening
Society for Biomolecular Screening (1999 – 2001)

Honors

1982 Outstanding Academic Achievement, University of Miami, Miami, FL
2000 Chairman's Award for the invention of Continuous Format High Throughput Screening Technology, Abbott Laboratories, Abbott Labs, Abbott Park, IL
2001 Volwiler Society award for outstanding research team: ARCS Screening Technology Development Team, Abbott Labs, Abbott Park, IL
2002 Advanced Technology I^3 award for Affinity Selection Screening team, Abbott Labs, Abbott Park, IL
2004 Spot award for developing high throughput siRNA screening, Abbott Labs, Abbott Park, IL
2004 Advanced Technology I^3 award for siRNA Target Discovery, Abbott Labs, Abbott Park, IL
2005 Spot award for assisting in the development of the HT-ADME team, Abbott Labs, Abbott Park, IL
2006 Advanced Technology I^3 award for High Content Analysis, Abbott Labs, Abbott Park, IL
2008 Spot award for personal commitment, dedication, and performance on the HTL team, Abbott Labs, Abbott Park, IL

C. Contribution to Science

1. Most of my scientific career has been in the Pharmaceutical industry innovating solutions to increase the efficiency of the early drug discovery process. I have developed two breakthrough technologies for ultra-high throughput screening of small molecules in large combinatorial library mixtures and discrete compound collections. The continuous format high throughput screening technology led to the invention and patenting of the μARCS technology (pat. no. 5,976,813) and enabled thousands of compounds to be screened in enzymatic, ELISA, or cell-based assays within the standard 96-well footprint. This technology further enabled the screening of large numbers of compounds in 3D-cell culture. The affinity selection mass spectrometry technique enabled the screening of over 36,000 compounds per single run for binding to targets and has been the primary assay for numerous therapeutic discovery campaigns.

a. Schurdak, M.E., Voorbach, M.J., Gao, L., Cheng, X., Comess, K.M., Rottinghaus, S.M., Warrior, U., Truong, H.N., Burns, D.J., and Beutel, B.A. (2001), Complex Gel Permeation Assays for Screening Combinatorial Libraries. J. Biomolecular Screening, 6: 313-323.
b. Comess, K.M., Trumbull, J.D., Park, C., Chen, Z., Judge, R.A., Voorbach, M.J., Coen, M., Gao, L., Tang, H., Kovar, P., Cheng, X., Schurdak, M.E., Zhang, H., Sowin, T., and Burns, D.J. (2006), Kinase Drug Discovery by Affinity Selection / Mass Spectrometry (ASMS): Application to DNA Damage Checkpoint Kinase Chk1. J. of Biomolecular Screening, 11:755-764.
c. Comess, K.M., Schurdak, M.E., Voorbach, M.J. Coen M., Trumbull, J.D., Yang, H., Gao, L., Tang, H., Cheng, X., Lerner, C.G., McCall, J.O., Burns, D.J., and Beutel, B.A. (2006), An Ultra-Efficient Affinity-Based High Throughput Screening Process: Application to Bacterial Cell Wall Biosynthesis Enzyme MurF. J. of Biomolecular Screening, 11:743-754.

2. While traditional target-centric drug discovery approaches have been successful they are costly and inefficient, and often result in <10% of candidates succeeding in the clinic. I am part of the team that is pioneering the development of Quantitative Systems Pharmacology (QSP) as an alternative drug discovery approach which combines iterative experimental and computational analyses to understand disease progression and design effective therapeutic strategies. I led the team that has successfully implemented QSP to understand novel approaches to rescue neuronal cells from the cytotoxic effects of mutant huntingtin in Huntington Disease.
   a. Pei, F., H. Li, M. J. Henderson, S. A. Titus, A. Jadhav, A. Simeonov, M. C. Cobanoglu, S. H. Mousavi, T. Shun, L. McDermott, P. Iyer, M. Fioravanti, D. Carlisle, R. M. Friedlander, I. Bahar, D. L. Taylor, T. R. Lezon, A. M. Stern and M. E. Schurdak (2017). "Connecting Neuronal Cell Protective Pathways and Drug Combinations in a Huntington's Disease Model through the Application of Quantitative Systems Pharmacology." Sci Rep 7(1): 17803.
   b. Stern, A. M., M. E. Schurdak, I. Bahar, J. M. Berg and D. L. Taylor (2016). "A Perspective on Implementing a Quantitative Systems Pharmacology Platform for Drug Discovery and the Advancement of Personalized Medicine." J Biomol Screen. 21(6): 521-534. (Cover article).

3. Identifying potential PK liabilities early in the lead discovery process enables better decisions to be made in selecting and pursuing lead series. I pioneered and directed the high-throughput ADME screening group within the HTS group. My team and I developed cost effective, high throughput analyses for caco permeability, CYP enzyme inhibition, metabolic stability and aqueous solubility. This early work provided the foundation for the formation of an independent HT-ADME group which became a critical function for all early drug discovery efforts.

4. High Content Analysis (HCA) represents an efficient and more physiologically relevant system with which to test and understand the effects of agents on a biological system. At Abbott I instituted HCA capabilities in the HTS group and directed the development and implementation of high content screening assays for cancer, neuroscience, metabolic disease, and molecular toxicology research projects. The development of the HCA phospholipidosis assay achieved more than 17-fold increased efficiency in assessing phospholipidosis toxicity of lead compounds, and enabled routine testing to guide lead optimization efforts for several projects. Similarly, routine screening of project compounds for neuroprotective effects were enabled by the development of a novel Alzheimer's disease neurotoxicity model using HCA. Oncology projects also relied on the quantitative HCA analysis of compounds for guiding SAR and selecting leads to advance into animal studies. For one of the oncology projects, the HCA analysis provided critical clues as to the cellular MOA which enabled the team to move forward after reaching an impasse. In addition to designing and developing HCA assays my expertise extends into the analysis and interpretation of HCA data. At Pitt, I am part of a team that includes some of the inventors of HCA, and we have developed quantitative methods to recognize heterogeneity in HCA analyses and which can be integrated into projects to guide the interpretation of the underlying biology. Understanding heterogeneity of response to bioactive compounds is a critical factor for designing and developing effective therapeutic strategies.
   a. Hu, M., Schurdak, M.E, Puttfarcken, P.S., Kouhen, R.E., Gopalakrishnan, M., and Li, J. (2007), High Content Microscopy Analysis of Ab_{1-42}-induced Neurite Outgrowth Reduction in Rat Primary Cortical Neurons: Neuroprotective Effects of a7 Neuronal Nicotinic Receptor Ligands. Brain Research, 1151:227-235. (Cover article)

b. Schurdak, M.E., Vernetti, L.A., Abel. S.J., and Thiffault, C. (2007), Adaptation of an In Vitro Phospholipidosis Assay to an Automated Image Analysis system. Toxicology Mechanisms and Methods, 17:77-86.
c. Thiffault, C., Gagne, G.D., Schurdak, M.E., Blomme, E.A.G., and Fagerland, J.A., (2006), Microscopic techniques to evaluate phospholipidosis in vitro: Application to drug discovery. Microscopy and Microanalysis, 12:, 1634-1635.
d. Gough AH, Chen N, Shun TY, Lezon TR, Boltz RC, Reese CE, Wagner J, Vernetti LA, Grandis JR, Lee AV, Stern AM, Schurdak ME, Taylor DL. Identifying and quantifying heterogeneity in high content analysis: application of heterogeneity indices to drug discovery. PLoS One. 2014 Jul 18;9(7):e102678. doi: 10.1371/journal.pone.0102678. eCollection 2014. PubMed PMID: 25036749; PubMed Central PMCID: PMC4103836.
e. Gough A, Shun TY, Taylor DL, Schurdak M. A metric and workflow for quality control in the analysis of heterogeneity in phenotypic profiles and screens. Methods. 2016; 96:12-26.

Complete List of Published Work in SciENcv
SchurdakM_Bibliography

D. Research Support

ACTIVE

R01 DK104847 01 (Madden - Dartmouth) 4/01/2016-3/31/2018
High-Throughput Screening for Dab2 Inhibitors as Stabilizers of CFTR
Role: Co-I
Cystic fibrosis is caused by mutations, the most common of which blocks the production and accelerates the degradation of the CFTR protein. Compounds to restore CFTR production are in clinical trials, and in this proposal we will identify and rigorously evaluate complementary compounds that can slow degradation.

1U24TR001935
University of Pittsburgh Tissue Chip Testing Center 9/22/2016 – 8/31/2018
Role: PI
The goal of this project is to provide an independent validation of the robustness of TCs developed by NIH/NCATS Tissue Chip Consortium.

3U24TR001935-02S1
University of Pittsburgh Tissue Chip Testing Center 9/01/2017 – 8/31/2018
Role: PI
In this supplemental application we are proposing to collaborate with the participants in the Microphysiology Systems for Disease Modeling and Efficacy Testing (MPS-DMET) program to further expand the scope of the MPS-Db in order to support all the disease models in development, to support the disease model developers to integrate the use of the MPS database into their workflow, and to centralize and provide the detailed designs, testing data and application data for the disease models developed under this program.

W81XWH-17-0502 09/01/2017 – 09/30/2020
Mechanism of systemic inflammation-associated endothelial and epithelial cell dysfunction following acute pancreatitis, trauma, and burns
Role: Co-I
The aim is to fractionate and analyze human serum using cultured vascular endothelial cells and epithelial cell lines with origin in the intestine as bioassays. Multiple approaches are planned to evaluate four leading candidate molecules, and to determine both pathogenic mechanisms (e.g. direct toxicity or second messenger mediated) and to test potential mechanism-directed therapies to protect human cells from dysfunction and death.

Completed

SAP#4100068731 **01/01/15 – 12/31/17**
PA Department of Health
Determining mechanisms of disease progression using Quantitative Systems Pharmacology (QSP) (Stern)
Role: Co-Investigator
A major goal is to demonstrate the broad applicability of QSP; accordingly, we aim to determine the value of QSP to enable the development of novel therapeutic strategies in a set of diverse diseases.

NExT-CBC Project ID #1015(Grandis) **03/01/2013-08/31/2013**

NCI
Role: Project Manager
CBC S08-221 Task Order 6 “Discovery and optimization of inhibitors of STAT3 activation for the treatment of squamous cell carcinoma of the head and neck”. Task Element 5

The orphan receptor NR4A1 – novel target for ovarian cancer therapy?
WCRC/CTSI (NIH) **07/01/2012 – 06/30/2013**
Role: PI
Develop HTS/HCs assay to examine the relationship between NR4A1 expression and sub-cellular localization and apoptosis.

NExT-CBC RFP S11-030 (Taylor) **02/24/2011 – 06/30/2015**

NCI
Role: Scientific Coordinator
Task Order 8: Task Order Administrative Support

Bill and Melinda Gates Foundation **11/01/2012 – 10/31/2015**
OPP1068374
Proposal on new biomarkers for HIV incidence measurement (Burke)
Role: Co-I
This project will use a new transformational technology to develop an assay to accurately estimate the incidence of HIV infections.

Understudied orphan receptors – novel treatment targets in ovarian cancer (Oesterreich)
DOD **09/01/2014 – 8/31/2015**
Role: Co-I
This project will characterize the role of NR4A1 ovarian cancer cells and tumor tissue samples, and develop a phenotypic, high-throughput assay to identify compounds that modulate NR4A1 function.

Stanley Foundation **11/01/2014 – 12/31/2016**
Testing Biomarkers for Schizophrenia Based on Infectious Exposure and Host
Role: Co-Investigator
Using our iPSC-based platform, a multi-stage screen will be used to identify compounds that reduce or eliminate quiescent infection of neurons.

W81XNH-14-1-0376 (Whitcomb) **09/22/2015 – 09/21/2016**
DOD
Acute pancreatitis as a model to predict transition of systemic inflammation to organ failure in trauma and critical illness
Role: Co-I
Our experimental approach is designed to understand and predict progression from systemic inflammation to multi-organ dysfunction syndrome.