BIOGRAPHICAL SKETCH

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NAME: Taylor, D. Lansing

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POSITION TITLE: Director, University of Pittsburgh Drug Discovery Institute
Distinguished Professor & Allegheny Foundation Professor of 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.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Maryland	BS	05/1968	Zoology
State University of New York at Albany	PHD	05/1973	Cell Biology
Woods Hole Marine Biology Laboratory	Postdoctoral Fellow	1974	Biophysics

A. Personal Statement

I began my academic career as an Assistant Professor at Harvard University and remained at Harvard until 1982, developing and using novel fluorescence-based reagents and imaging technologies to investigate fundamental cellular processes such as cell movements and cell division. I then moved to Carnegie Mellon University as a Professor of Biological Sciences and as Director of the Center for Fluorescence Research in the Biomedical Sciences. In 1991, I became the Director of the National Science Foundation-funded Center for Light Microscope Imaging and Biotechnology, and in 1995, I was named Vice Dean of CMU's Division of Molecular Sciences. I continued to develop reagent and imaging technologies, while applying the technologies to understand fundamental processes in cells and tissues. Alan Waggoner and I co-founded Biological Detection Systems (BDS) to commercialize the multi-color cyanine dyes and research imaging platforms and it was acquired by Amersham-now GE Life Sciences. I left CMU in 1997 to found Cellomics, Inc., the company that developed High Content Screening (HCS). HCS was the foundation for a shift from focusing primarily on generating images to generating large-scale, quantitative image-based data from cells, tissues and small organisms. I was CEO of this company from 1997 through 2003 when it became part of ThermoFisher. I then founded a third company, Cellumen, that developed a predictive safety assessment platform using primary hepatocytes, multiplexed panels of reagents, reference safety databases and computational biology. I was CEO of Cellumen from 2004 until 2010 when it became part of Cyprotex, a British CRO. I also co-founded Cernostics, Inc., a fluorescence-based, tissue systems pathology company that has created a test for selecting at risk Barrett's esophagus patients. I hold >25 U.S. patents, including six focused on cell-based imaging. I returned to academia at the end of 2010 to continue my academic interests that now link large-scale cell, tissue and human, biomimetic, tissue-engineered model profiling with computational and systems biology to optimize drug discovery and diagnostics based on quantitative systems pharmacology. I am also collaborating on the development of computational tools to identify and quantify heterogeneity during drug discovery and development.

B. Positions and Honors

Professional Positions

1974 – 1978	Assistant Professor, Harvard University, Cambridge, MA
1980	Sabbatical, Stanford University, Stanford, CA
1978 – 1982	Associate Professor, Harvard University, Cambridge, MA
1982 – 1997	Professor of Biological Sciences, Carnegie Mellon University, Pittsburgh, PA
1982 – 1991	Director, Center for Fluorescence Research in Biomedical Sciences, Carnegie Mellon University, Pittsburgh, PA
1991 – 1997	Director, National Science Foundation, Science and Technology Center: Center for Light Microscope Imaging and Biotechnology, Carnegie Mellon University, Pittsburgh, PA
1991 – 1995	Co-Founder, Board Member, Scientific Advisor, Biological Detection Systems, Inc., Pittsburgh, PA (multimode microscope and cyanine dyes)

1995 – 1997	Vice Dean, Division of Molecular Sciences, Carnegie Mellon University, Pittsburgh, PA
1997 – 2003	Co-Founder, CEO and Chairman, Cellomics, Inc., Pittsburgh, PA (HCS)
1999 – *present*	Adjunct Professor, Carnegie Mellon University, Pittsburgh, PA
2004 – 2010	Co-Founder, President and CEO, Cellumen Inc., Pittsburgh, PA (Predictive toxicology)
2008 – 2011	Co-Founder and Chairman, Cernostics, Inc., Pittsburgh, PA (Tissue systems pathology)
2010 – *present*	Director, University of Pittsburgh Drug Discovery Institute, Pittsburgh, PA
2010 – *present*	Allegheny Foundation Professor of Computational and Systems Biology
2017 – *present*	Distinguished Professor

Other Experience and Professional Memberships

Corporate

1999 – 2009	Board of Directors, NetHealth Systems, Inc. (Medical IT)
2005 – 2011	Board of Directors, CelSense, Inc. (NMR contrast agents for cell tracking *in vivo*)
2002 – 2011	Board of Directors, Pittsburgh Life Sciences Greenhouse (Regional biotech development-Chairman from 2007-2010)

Academic

1985 – 1989	NIH Molecular Cytology Study Section
1990 – 1993	Biophysical Society Council
1991 – 1995	External Advisory Committee, Los Alamos National Labs, Cytometry Group
1995 – 1998	External Advisory Committee, European Molecular Biology Laboratory
1995 – 1999	External Advisory Committee, Molecular Biotechnology Center, Univ. Washington
2000 – 2006	External Advisory Committee, Mayo Clinic and Foundation, Cancer Center
2010 – 2016	NCI Chemical Biology Consortium Steering Committee
2014 –*present*	Foundation for the NIH Biomarkers Consortium-High Content Data Integration Group

Honors

1990 – 2000	NIH Merit Award
1995	German Society of Cell Biology: Carl Zeiss Lecture Award
1996	Computer World-Smithsonian Award in Science: Developments in Imaging Living Cells
2001	Inclusion of paper in "Landmark Papers in Cell Biology," JG Gall and JR McIntosh, Eds. Cold Spring Harbor Laboratory Press and American Society for Cell Biology, NY
2001	Ernst & Young, PA Entrepreneur of the Year
2002	Carnegie Science Center Awards, Entrepreneur of the Year
2003	National Science Foundation Pioneer Award -- Recognition for leadership in STC program
2004	Pittsburgh Life Sciences Greenhouse Pioneer Award, Creation of Companies
2007	Elected Fellow of American Institute for Medical and Biomedical Engineering (AIMBE)
2007	Society of Biomolecular Sciences Achievement Award for Developing High Content Screening
2011	International Society for Analytical Cytometry: Mack J. Fulwyler Award: Outstanding Innovation in Cytometry-invention or a career of innovative science

C. Contribution to Science

1. Microphysiological systems (MPS) for drug discovery and development. A major challenge has been the development of more physiologically relevant models of normal tissues and disease "systems". The full power of phenotypic discovery and experimental disease models depends on having preferably multiple cell type, human 3D models with microfluidics. **(a)** producing a fully functional, human, 4-cell, biomimetic model of the human liver acinus that takes advantage of fluorescent protein biosensors and a second generation human liver acinus model where zonation is modeled and measured **(b). (c)** We have recently reviewed the liver metatstatic breast cancer niche using MPS**,** the use of microfluidics to build organs on chips and **(d**) We have recently showed the functional coupling of multiple organ MPS. The microfluidic models of human organs promise to revolutionize cell/tissue and organ research.

a. Vernetti L, Senutovitch N, Boltz R, DeBiasio R, Shun TY, Gough A, **Taylor DL.** (2016) A human liver microphysiology platform for investigating physiology, drug safety and disease models. J Exp Biol Med 241: 101-114.

b. Lee-Montiel F, George S, Gough A and **Taylor DL**. (2017). Control of oxygen tension recapitulates zone-specific functions in human liver microphysiology systems. Expt Biol Med (April) DOI: 10.1177/1535370217703978

c. Clark A, Ma B, **Taylor DL**, Griffith L, Wells A. (2016). Liver metastases: microenvironments and ex-vivo models. Exp Biol Med. 241 (15): 1639-1652.

d. 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**. 2017. Functional Coupling of Human Microphysiology Systems: Intestine, Liver, Kidney Proximal Tubule, Blood-Brain Barrier and Skeletal Muscle. Sci Rep. Feb 8;7:42296. PubMed PMID: 28176881

2. High Content Screening (HCS) and Quantitative Systems Pharmacology (QSP). The large amount of time required to acquire, process and analyze large numbers of cell-based image data to obtain statistically relevant data from biological experiments encouraged me to follow the lead from the genomics revolution and to automate the whole process based on the microplate format used in the pharmaceutical industry. I left Carnegie Mellon University to start Cellomics, the company that pioneered HCS based on a large number of patents. The pharmaceutical companies embraced HCS to gain deeper biological insights in the mechansims of disease progression, drug discovery and *in vitro* toxicology. **(a)** HCS has become a standard platform in both academic and pharmaceutical research and development and large image datasets can be explored in phenotypic drug discovery including the identification and quantitation of heterogeneity and is a central component of our QSP platform including modeling **(b-d).**

a. Gough A, Chen N, Shun TY, Lezon T, Boltz R, Reese C, Wagner J, Grandis J, Lee A, Stern A, Schurdak M, **Taylor DL.** (2014). Identifying and quantifying heterogeneity in high content analysis: application of heterogeneity indices to drug discovery. PLoS ONE, 9(7):e102678. PMCID: PMC4103836

b. Stern, AM, Schurdak, ME, Bahar, I, Berg, JM, **DL Taylor**. (2016) A perspective on implementing a quantitative systems pharmacology platform for drug discovery and the advancement of personalized medicine. J Biomol Screen.21: 521-534.

c. Erdem C, Nagle AM, Casa AJ, Litzenburger BC, Wang Y, **Taylor DL**, Lee AV and Lezon TR. (2016). Proteomic screening and lasso regression reveal differential signaling in insulin and insulin-like growth factor I pathways. Mol Cell Proteomics 15:3045-3057 PMID: 27364358

d. Gough A, Stern, AM, Maier J, Lezon T, Shun T-Y, Chennubhotla C, Schurdak ME, Haney SA and **Taylor** DL. (2016). Biologically relevant heterogeneity: Metrics and practical insights. SLAS Discovery 22: 213.

3. Fluorescent analog cytochemistry (FAC) and fluorescent protein biosensors (FPB's). My early work at Harvard focused on developing methods for studying the temporal and spatial molecular dynamics within living cells using fluorescence imaging methods. The introduction of FAC allowed the dynamics of proteins to be followed during normal and abnormal cell functions **(a)** FAC was the fore-runner of fluorescent protein (e.g. GFP) tagging of proteins. A Nature paper focused on FAC was chosen as one of the 42 seminal papers in cell biology in the first 40 years of the American Society of Cell Biology. **(b-c)** The further addition of site-specific tagging of proteins with environmentally sensitive fluorescent probes permitted temporal-spatial measurements of protein activities (fluorescent protein biosensors-FPB's) including phosphorylation**. (d)** These methods played a critical role in stimulating the field of cell biology and then other fields to apply fluorescence-based reagents to study the dynamic proteomics and metabolomics in living cells in culture and in microfluidic devices.

a. Taylor DL and Wang Y-L. (1980). Fluorescently labelled molecules as probes of the structure and function of living cells. Nature (Lond.), 284(5755):405-10.

b. Hahn K, DeBiasio R, **Taylor D**. (1992). Patterns of elevated free calcium and calmodulin activation in living cells. Nature (Lond), 359(6397):736-8.

c. DeBiasio RL, LaRocca GM, Post P, **Taylor DL**. (1996). Myosin II transport, organization, and phosphorylation: evidence for cortical flow/solation-contraction coupling during cytokinesis and cell locomotion. Mol Biol Cell, 7(8):1259-82. PMCID: PMC275977

d. Senutovitch N*, Vernetti, L*, Boltz, R, DeBiasio, R, Gough, A, **Taylor, DL.** (2015) Fluorescent Protein Biosensors Applied to Microphysiological Systems. Exp Biol Med 240: 795-808. PMID: 25990438

4. Quantitative digital imaging microscopy. In parallel to the development of fluorescence-based reagents for living cells, my work also focused on developing the digital imaging tools necessary to acquire, process and analyze the time series, digital image data sets of migrating and dividing cells. All of the early platforms were

built in our lab since the microscope companies lagged in the automation and digital imaging technologies that were needed in our research. Our work and others stimulated the rapid development and application of quantitative, digital imaging microscopy **(a-c),** including early super-resolution microscopy **(d)** in basic and applied research**.**

a. Tanasugarn L, McNeil P, Reynolds GT, **Taylor DL.** (1984). Microspectrofluorometry by digital image processing: measurement of cytoplasmic pH. J Cell Biol, 98(2):717-24. PMCID: PMC2113113

b. Bright G, Whitaker J, Haugland R**, Taylor DL**. (1989). Heterogeneity of the changes in cytoplasmic pH upon serum stimulation of quiescent fibroblasts. J Cell Physiol, 141(2):410-9.

c. Farkas DL, Baxter G, DeBiasio R, Gough A, Nederlof MA, Pane D, Pane J, Patek DR, Ryan KW, **Taylor DL**. (1993). Multimode light microscopy and the dynamics of molecules, cells, and tissues. Ann Rev Physiol, 55:785-817.

d. Lanni F, Bailey B, Farkas DL, **Taylor DL**. (1993). Excitation field synthesis as a means for obtaining enhanced axial resolution in fluorescence microscopes. BioImaging, 1(4):187-96.

5. Tissue systems biology for diagnostics. It became clear that a "tissue systems" biology approach was needed to better harness multiplexed fluorescence for cancer diagnostics. Multiplexed panels of biomarkers for cancer and stromal cells, including the migratory immune system were patented **(a)** and the diagnostics company, Cernostics was co-founded by me to develop a Barrett's esophagus test that is currently in trials. The basic multiplexed fluorescence approach to tissue systems biology has been described **(b-c)** and spatial statistics to define spatial heterogeneity have been developed **(d).** Identifying and quantifying spatial heterogeneity will be central to developing an understanding of metastatic disease progression and the development of useful diagnostic and prognostic tests.

a. Critchley-Thorne RJ, Miller SM,**Taylor DL,** Lingle W. (2009). Applications of cellular systems biology in breast cancer patient stratification and diagnostics. Comb Chem High Through Screen, 12(9):860-9.

b. Pritchard, J., Davison, J., Campbell, B., Repa, K., Reese, L., Nguyen, X., Li, J., Foxwell, T., **Taylor, D.,** Critchley-Thorne, R. (2015). TissueCypher: A systems biology approach to anatomic pathology. J. Pathol. Inform. 1: 48.

c. Gough AG, Lezon T, Faeder JR, Chennubhotla C, Murphy RF, Critchley-Thorne R, **Taylor DL**. (2014). High content analysis and cellular and tissue systems biology: a bridge between cancer cell biology and tissue-based diagnostics. In/The Molecular Basis of Cancer, 4th Ed. (Mendelsohn J, Howley PM, Israel MA, Gray JW, Thompson CB) Elsevier, NY.

d. Spagnolo DM, Gyanchandai R, Al-Kofahi Y, Stern AM, Gough A, Meyer DE, Ginty F, Sarachan B, Fine J, Lee AV, **Taylor DL**, Chennubhotla SC. (2016). Pointwise mutual information quantifies intra-tumor heterogeneity in tissue sections labeled with multiple fluorescent biomarkers. J. Pathol. Inform. 7: 47.

List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/d.lansing.taylor.1/bibliography/45727112/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

P30 CA047904 - NIH — Ferris (PI) — 07/01/15 – 07/31/20
Cancer Center Support Grant/Chemical Biology Facility
The major goal of this grant is to enable UPCI laboratory and clinical investigators to work closely together to identify improved approaches for cancer prevention, diagnosis and treatment.
Role: Scientific Lead

STAR 83573601 - EPA — Taylor (CoPI) — 12/01/14 – 11/30/18
Vanderbilt-Pittsburgh Resource for Organotypic Models for Predictive Toxicology - VPROMPT
Role: Co-Principal Investigator
The liver MPS will be integrated into the Vanderbilt moderate throughput screening platform as a microfluidic device to allow use of the secreted media for: (a) assaying the secretome in near real-time for targeted high content metabolomics; (b) provide liver MPS conditioned media to feed chemical metabolites to the 3 developmental MPS and organoids, and (c); track mechanisms of toxicity in the liver.
Role: Co-investigator

U01CA204826 Chennubhotla, Taylor (PI) 03/01/2016-02/28/2019
NIH
Informatics Tools for Tumor Heterogeneity in Multiplexed Fluorescence Images
This proposal will build and develop interactive software for use by cancer biologists and clinicians to *quantitate, interpret and visualize spatial intra-tumor heterogeneity* (ITH) in tumor tissue samples
Role: Co-Principal Investigator

Commonwealth of PA 4100077084 (Okonkwo) 01/01/2017-12/31/2018
Biomarkers and Drug Discovery Pipeline of TBI-Related Neurogeneration
Our goal is to identify serum, cerebrospinal fluid (CSF), and neuroimaging correlates of TBI-related neurodegeneration and to evaluate neurodegenerative mechanisms and therapeutic targets (to prevent, slow, or reverse pathology) through clinical, computational, and laboratory studies.
Role: Co-Investigator

NIH-SBIR HHSN271201800008C (Mimetas) 2/15/18 – 2/14/2020
Development and Evaluation of the HepaPlate iPS: a high-throughput organ-on-a-chip iPS Hepatotoxicity Screening Platform
The complementary teams at Mimetas and UPDDI propose to develop and demonstrate a 3D liver-on-a-chip platform for high-throughput hepatotoxicity prediction using human IPSC co-culture in a structural arrangement that mimics the liver sinusoid.
Role: Co-Investigator

<u>Completed Research Support</u> (Over last 5 years)

5UH2TR000503-02 (UH3) -NIH Taylor (PI) 07/01/14 – 06/30/17
A 3D biomimetic liver sinusoid construct for predicting physiology and toxicity
Integration of microfluidic devices linking the gut, liver and kidney to create a platform for adsorption, metabolism and excretion and the starting point of distribution.
Role: Principal Investigator

4UH2TR000496-03 -NIH Wells (PI) 07/01/14 – 06/30/17
All Human Microphysical Model of Metastasis Therapy
Propose a system that will provide an all human contextual metastatic micro-environment and one intimately linked to drug metabolism and normal physiological functions of liver that my hider or augment therapy effect.
Role: Co-Investigator

SAP#4100068731 Stern (PI) 01/01/15 – 12/31/18
PA Department of Health
Determining mechanisms of disease progression using Quantitative Systems Pharmacology (QSP)
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.
Role: Co-Investigator

NExT-CBC RFP S11-030 –NCI Taylor (PI) 04/01/11 – 03/30/16
Task Order 8: Administrative Support
The major goal of this funding is to provide support for all Chemical Biology Consortium contract-related activities conducted at the University of Pittsburgh Specialized Application Center.
Role: Principal Investigator

1UH2TR000503-01 - NIH Taylor (PI) 07/01/2012 – 06/30/2014
A 3D biomimetic liver sinusoid construct for predicting physiology and toxicity
The goal of this project is to construct a microfluidic liver module which mimics the functions and responses of the human liver, with readouts designed to indicate both normal liver function and toxic responses.
Role: Principal Investigator