BIOGRAPHICAL SKETCH

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NAME: Gough, Albert

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

POSITION TITLE: 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
University of Michigan, Ann Arbor, Ann Arbor, MI	BS	05/1984	Cellular and Molecular Biology
Carnegie Mellon University, Pittsburgh, PA	PHD	10/1992	Biology/Biophysics

A. Personal Statement

Presently my research is focused in 2 areas that are highly related to this project. First, is the development of, and computational analysis of data from, 3D tissue models in microfluidic devices. We have developed a microfluidic 3D human liver model that uses fluorescent reagents, reporter cells (sentinels) and probes for direct functional readouts. Analyses of a broad array of real-time and off-line biochemical, mass spectrometric, and high content assays are used to profile functional effects and to develop predictive models. A second major area of research is on the relationship between cellular heterogeneity, compound mechanism(s) of action and cell signaling pathways. I have recently published on the use of three indices to characterize heterogeneity, and a QC metric for comparing and monitoring the consistency of cellular distributions in assays, screens and large scale biology projects. My experience and expertise are well suited to these projects. I received my PhD in Biophysics from Carnegie Mellon University where I developed tools and assays using fluorescence microscopy to study single cell physiology. As a Postdoc I served as the Director of Imaging Technology in the Center for Light Microscope Imaging and Biotechnology at Carnegie Mellon University, one of the NSF funded Science and Technology Centers. In that role I led a development project to build an Automated Interactive Microscope for real-time 3D imaging of live biological systems. I later joined Cellomics, to automate light microscopy and enable the analysis of millions of cells under thousands of experimental conditions in a single day, a method now called High Content Screening (HCS). I led the team which developed the first HCS platform, and the following generations of HCS platforms. In 2005, I joined Cellumen with a mission to develop Cellular Systems Biology (CSB) assay panels, using HCS Technology. The goal was to build better predictive models of in vivo toxicity using CSB data from in vitro assay panels. At Cellumen I led the development of classification models to interpret the multiparameter data generated for large pharmaceutical companies, the FDA and the EPA. In 2010 I joined the University of Pittsburgh Drug Discovery Institute.

1. 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.
2. 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.
3. 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.
4. 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;9(7):e102678. PubMed PMID: 25036749; PubMed Central PMCID: PMC4103836.

B. Positions and Honors

Positions and Employment

1992 - 1996	Director of Imaging Technology, Carnegie Mellon University, Center for Light Microscope Imaging and Biotechnology, Pittsburgh, PA
1996 - 1998	Director of Drug Discovery Systems, Cellomics, Inc., Pittsburgh, PA
1998 - 2004	Vice President of Research and Development, Cellomics, Inc., Pittsburgh, PA
2004 - 2005	Biotech Consultant, Metricell, Pittsburgh, PA
2005 - 2010	Vice President Discovery Technology, Cellumen, Inc., Pittsburgh, PA
2010 -	Associate Professor, University of Pittsburgh, Dept of Cellular and Systems Biology, Drug Discovery Institute, Pittsuburgh, PA

Other Experience and Professional Memberships

1986 -	Member, American Society for Cell Biology
1996 - 2013	Member, Society of Biomolecular Sciences
2010 -	Member, International Society of Advancement of Cytometry
2013 -	Member, Society of Laboratory Automation & Screening

Honors

C. Contribution to Science

1. Lack of efficacy and human liver toxicity remain major causes of late stage drug failure. Animal models are still the standard for preclinical studies, even though they have been shown to have poor concordance with human efficacy and toxicity. To address this problem, we have developed a series of human biomimetic, 3D microfluidic liver models that exhibit long-term functioning for modeling diseases and characterizing chronic toxicities (a). The models are components of a platform we developed that includes fluorescent protein biosensors, panels of mechanistic assays, and a web-based Microphysiological Database (MPS-Db). I have been particularly focused on the MPS-Db, which combines assay data from in vitro models with chemical, biochemical, preclinical, and post marketing data to facilitate the design and interpretation of study results, relative to human physiology. Furthermore, the MPS-Db enables the development of computational to predict toxicity of test compounds based on their mechanistic profiles, such as my prior work at Cellumen, where I developed a classifier with >95% specificity and 40-60% sensitivity to predict in vivo toxicity, using cellular data from 2D in vitro assay panels of human derived cells. This approach is currently being extended for integration with the MPS-Db and application to the liver and other organ models.

    a. 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.
    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. 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.

2. One of the greatest challenges in biomedical research, drug discovery and diagnostics is understanding how seemingly identical cells can respond differently to perturbagens including drugs for disease treatment. Although heterogeneity has become an accepted characteristic of a population of cells, in drug discovery it is not routinely evaluated or reported. To address this need I defined a method that can be readily implemented to identify, quantify and characterize heterogeneity in cellular assays to guide decisions during drug discovery and experimental cell/tissue profiling. These heterogeneity indices provide a standardized method that can easily be integrated into small and large scale screening or profiling projects to guide interpretation of the biology, as well as the development of therapeutics and diagnostics. Understanding the heterogeneity in the response to perturbagens will become a critical factor in designing strategies for the development of therapeutics including targeted polypharmacology.

   a. Spagnolo DM, Al-Kofahi Y, Zhu P, Lezon TR, Gough A, Stern AM, Lee AV, Ginty F, Sarachan B, Taylor DL, Chennubhotla SC. Platform for Quantitative Evaluation of Spatial Intratumoral Heterogeneity in Multiplexed Fluorescence Images. Cancer Res. 2017 Nov 1;77(21):e71-e74. PubMed PMID: 29092944; PubMed Central PMCID: PMC5683175.
   b. Gough A, Shun TY, Lansing Taylor D, Schurdak M. A metric and workflow for quality control in the analysis of heterogeneity in phenotypic profiles and screens. Methods. 2016 Mar 1;96:12-26. PubMed PMID: 26476369; PubMed Central PMCID: PMC5200891.
   c. Spagnolo DM, Gyanchandani R, Al-Kofahi Y, Stern AM, Lezon TR, Gough A, Meyer DE, Ginty F, Sarachan B, Fine J, Lee AV, Taylor DL, Chennubhotla SC. Pointwise mutual information quantifies intratumor heterogeneity in tissue sections labeled with multiple fluorescent biomarkers. J Pathol Inform. 2016;7:47. PubMed PMID: 27994939; PubMed Central PMCID: PMC5139455.
   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;9(7):e102678. PubMed PMID: 25036749; PubMed Central PMCID: PMC4103836.

3. I was responsible for the development of the first High Content Screening (HCS) platforms and software systems. HCS was introduced by Cellomics in the mid-1990's as a method for high throughput cell biology that sparked a revolution in image-based cell analysis, going from a handful of measurements from a few hand-picked cells to multiplexed measurements on large populations of cells, providing statistically significant data on objectively chosen cells. The first high content screening system was used at Merck to assay activation of NFkB (Ding, et. al., 1998). HCS is now widely used throughout Drug Discovery and Academic research (Giuliano, et. al. 2006, Giuliano, et. al. 2010).

   a. Gough A, Lezon T, Faeder JR, Chennubhotla C, Murphy R, Critchley-Thorne R, Taylor DL. The molecular basis of cancer. Mendelsohn J, Howley PM, Israel MA, Gray JW, Thompson C, editors. Philadelphia, PA: Saunders/Elsevier; 2015. Chapter 25, High-Content Analysis with Cellular and Tissue Systems Biology: a Bridge between Cancer Cell Biology and Tissue-Based Diagnostics; p.369-392. 863p.
   b. Giuliano KA, Gough AH, Taylor DL, Vernetti LA, Johnston PA. Early safety assessment using cellular systems biology yields insights into mechanisms of action. J Biomol Screen. 2010 Aug;15(7):783-97. PubMed PMID: 20639501.
   c. Giuliano KA, Johnston PA, Gough A, Taylor DL. Systems cell biology based on high-content screening. Methods Enzymol. 2006;414:601-19. PubMed PMID: 17110213.
   d. Giuliano KA, DeBiasio RL, Dunlay TR, Gough AH, Volosky JM, Zock J, Pavlakis GN, Taylor DL. High-Content Screening: A New Approach to Easing Key Bottlenecks in the Drug Discovery Process. Journal of biomolecular screening. 1997 June 01; 2(4):249.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1zi58V50cp4kF/bibliography/48230554/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

G2013-STAR-L1, EPA
Shane Hutsen (PI)
12/01/14-11/30/18
Vanderbilt-Pittsburgh Resource for Organotypic Models for Predictive Toxicology
We propose to replace the primary hepatocytes used in our current device with renewable, validated, adult-like iPSC hepatocytes and develop novel biosensors to AhR, ppar-a, NFkB, PR and others for incorporation into the 4 organoids.
Role: Co-Investigator

1U24TR001935, NIH
Schurdak (PI)
09/22/16-08/31/18
University of Pittsburgh Tissue Chip Testing Center
The goal of this project is to capture, manage and provide all data generated by the Tissue Chip Testing Centers, and to provide an independent validation of the robustness of TCs developed by NIH/NCATS Tissue Chip Consortium.
Role: Co-Investigator

N44TR-18-1011, National Center for Advancement of Translational Sciences
Gough (PI)
02/15/18-02/14/20
Development and Evaluation of the HepaPlate iPS: A High Throughput Organ-on-a-Chip iPS Hepatotoxicity Screening Platform
We will determine the capacity of the HepaPlate iPS to provide a reproducible and robust multiparameter readouts of toxicity, and to facilitate high-throughput screening and detect compound toxicity.
Role: PI

1U01CA204826, NIH
Chennubhotla, Taylor (PI)
05/04/16-02/28/19
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 imaged as multiplexed (< 7 biomarkers) and hyperplexed (> 7 biomarkers) immunofluorescence data.
Role: KP

5U24TR001935-025, NCATS
Schurdak (PI)
09/01/17-08/31/18
Tissue Chip Testing Center-Admin Supplement
The overarching goal of our proposal is to extend the existing MPS-Database design to support all the disease models developed in the MPS-DMET program by integrating clinical and reference data with MPS-DMET experimental data, and thus enhancing the effectiveness of the MPS-DMET program
Role: Co-Investigator