

# 2016 Annual Report





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## HSC CORES Facilities



### **Overall Financial Summary**

#### **Revenue & Expenses**

- The Core Facilities budget for FY16 was \$5.3 million with an expense total of \$5.6 million. Approximately \$3.3 million in expenses went to salaries and benefits while \$2.3 million was spent on equipment and operating supplies.
- In FY16, \$3.5 million in services were billed.



NOTE: Positive cash carry forward balance from FY15 was applied to cost of expenses for FY16. These facilities received no operating support from the VP.



## **Cores Administration**

#### Overview

The Health Sciences Center (HSC) Core Facilities operate under central administration headed by Dr. John Phillips, who reports to Dr. Andy Weyrich. The administrative office is managed by Ms. Brenda Smith, with assistance from Ms. Esther Kim, and Mr. Jeff Ware. The Cores Administration office is responsible for the personnel management, budget preparation, financial affairs, ordering of supplies, and tracking expenses of the Core Facilities. In addition, the administrative office supports general research infrastructure for the research community, for example maintaining the X-ray film developer in the SOM and the research irradiator logging and access requests. All cores operate on a charge-back basis, although the percent recovery of operating expenses for each facility varies greatly, the goal for each HSC Core Facilities is to provide the necessary technology and expertise for successful data generation and analysis for all faculty and students at the University of Utah.

#### Personnel

- John Phillips, Ph.D., Director HSC Core Facilities
- Brenda Smith, Associate Director of Finance
- Esther Kim, Administrative Assistant
- Jeff Ware, Accountant

#### 2016 Annual Update

- The administrative team continues to refine the electronic scheduling and billing services to make as user friendly as possible. In 2016 the system was redesigned to be accessible from mobile devices and streamlined for scheduling events. Following up on feedback from the Annual Survey creating an account within the system has been updated to allow Work Authorization Forms to be electronically created and approved.
- In FY16, the Cores Administration office was successfully able to process billing in 1 business day even though the amount of billed revenue is increasing. The new HSC scheduling/billing system validates chartfields with the University's CIS system which has eliminated the majority of billing errors.
- In FY16 the core had a combined billing of 3.5 million; however, what is most impressive of this past year was the collection rate for billed services was 100%. The internal tracking system that was created lists each account balance in real time. Each director can access the system by logging in and reviewing their reports. The tracking system currently stores fiscal data from 2 years.
- A new website was created for the HSC Cores. <u>www.cores.utah.edu</u>.
- The two new Service/Recharge Centers, (Scalable Analytics and Nuclear Engineering), which are managed through the administrative office are doing well. Nuclear Engineering and Scalable Analytics & Informatics (see new sections for descriptions).
- The third annual retreat was held on September 25<sup>th</sup>. Approximately 100 people attended. Directors had an opportunity to discuss methods for maintaining market share, engaging researchers to provide higher quality data analysis and methods to track usage. Discussions regarding requirements for maintaining logs and copies of original data identified that there is no standardized system currently available; this issue will need to be revisited.
- A new electronic inventory system was created for capital equipment assets. As of August, 2016, there are 29 Organizations, 19 Departments, 1,188 items located in 33 buildings and 298 rooms with a total asset value of \$37.2 million in the system. This system will continue to expand to any group on campus, by request.



#### FY2017 Goals

- Develop a Virtual Genomics Website
- Upgrade the electronic inventory system

#### **Cores Administration Revenue & Expenses**

#### FY16 Expenses: Total \$532,109

The Cores Administration Budget covers the following expenses:

- Salaries/Benefits: \$343,096,
- Fixed Expenses: (such as IT Support, Film Developer, and Irradiator) \$124,000, and
- Unanticipated expenses for the cores: \$65,600

#### FY16 Revenues: Total \$536,357

- VP of Health Sciences Support: \$363,000
- FY16 Revenue Generated from Services: \$173,357



\* This represents the income from the 5% administrative fee charged to each core, based on collected revenue from billed services; legend displays 5% of annual revenue collected for each fiscal year.

#### **Advisory Board Committee**

Last meeting date: January 11, 2016

- Andy Weyrich<sup>1</sup>, Associate Dean for Basic and Translational Sciences
- Joseph Yost<sup>1</sup>, Professor, Neurobiology and Anatomy
- Mark Yandell, Professor, Human Genetics
- John Phillips<sup>1</sup>, Director, Core Facilities
- Dennis Winge<sup>1</sup>, Professor, Hematology
- David Stillman<sup>1</sup>, Professor, Pathology
- Wes Sundquist, Professor, Biochemistry
- Brad Cairns<sup>1</sup>, Professor, Huntsman Cancer Institute
- Carl Wittwer, Professor, Pathology
- Eric Schmidt, Professor, Medicinal Chemistry

#### <sup>1</sup> in attendance



Addendum Faculty Oversight Committee Guidelines can be found for all cores at the following link: <u>http://cores.utah.edu/wp-content/uploads/2015/09/Faculty-Advisory-Committee-Responsibilities-</u> 2.pdf



## Biomedical Image & Data Analysis Core

#### Overview

The mission of the new Biomedical Image and Data Analysis Core (BIDAC) facility is to provide advanced image analysis and visualization services to research laboratories at the University of Utah. We offer services and consulting that range from basic image processing (denoising, image reconstruction, image registration) to more advanced image segmentation and morphometric analysis. BIDAC leverages the computational resources and software development infrastructure of the Scientific Computing and Imaging (SCI) Institute. In partnership with the HSC Core imaging facilities (Cell, Small Animal, EM) we are actively developing new services that are based on the needs of HSC researchers and Core users. As a resource for advanced image and data analysis, our goal is to further the scientific mission of the University of Utah by significantly enhancing the capabilities and competitiveness of HSC research laboratories.

#### Services

BIDAC offers a range of services, **including image processing consulting, training, image analysis, image visualization, software prototyping, and new algorithm development**. Our services are currently offered as hourly consulting. However, for FY 2017, we are actively developing a suite of fixed rate, end-to-end solutions for some of the more common image processing needs.

**New Services** that are under development for 2016-2017 include:

- **Statistical shape modeling (SSM).** SSM is a computational branch of morphometrics that is rapidly becoming a standard tool for modern clinical research and medical device engineering. SSM is also now commonly used in many areas of basic biological research, including genetic phenotyping and neurobiology. BIDAC has significant expertise in SSM and uses custom software for group-wise analysis of both 2D and 3D anatomical shapes.
- Automated image archiving and processing via the XNAT open-source imaging and informatics software platform (www.xnat.org). In partnership with clinical researchers and the Center for High Performance Computing (CHPC), we are developing infrastructure to support local and distributed health sciences research projects that involve image acquisition, collection, and analysis (for example, clinical trials and registries). Our services will include custom automated image processing workflows (such as image quality control) on a PHI-secure XNAT server that is hosted at CHPC.
- **Neuroimage MRI data processing with FreeSurfer.** FreeSurfer (<u>www.freesurfer.net</u>) is a popular open source tool for analysis of brain MRI and includes processing such as skullstripping, subcortical segmentation, fMRI analysis, tractography, and cortical surface reconstruction. We will offer FreeSurfer processing and training for neurobiology research.



• Selective Plan Illumination Microscopy (SPIM) image reconstruction and visualization. The HSC Cell Imaging core has constructed a new microscope for acquiring SPIM data. However, quality 3D reconstructions of SPIM image can require significant computational resources, which BIDAC will begin offering to users of the new SPIM resource. This partnership with Cell Imaging will result in a unique imaging resource at the University of Utah for fluorescence microscopy of live specimens and the study of development.

#### Personnel

- Joshua Cates, PhD, Director
- Clement Vachet, MS, MBA, Associate Director

#### 2016 Annual Update

#### Grant Support

BIDAC performed preliminary work and/or provided letters of support for the following grant submissions:

- NIH R01 & NIH R21/R33 Josh Bonkowsky, PhD, Dept. of Pediatrics
- NIH R21 Michelle Mendoza, PhD, Huntsman Cancer Institute
- Orthopaedics departmental seed grant Heath Henninger, PhD, Dept. Orthopaedics Inter-disciplinary collaborations
- Collaborative projects to enhance imaging capabilities have been performed with the Center for High Performance Computing (CHPC) and with several Health Sciences Cores (directly or involving end-users), including Small Animal Imaging Facility, Cell Imaging Facility and Electron Microscopy Facility.

#### Seed Grant Projects

BIDAC provided limited funding to seed larger project collaborations

- Enhancing capabilities of magnetic resonance imaging repositories for multiinstitutional clinical research (quality control and MR image analysis) - Charles Casper, PhD, Dept. Pediatrics
- Development of an application to automate the removal of patient information from fetal echocardiography images Jeffery Yearley, PhD, Dept. Pediatrics
- Pilot Quality Assessment of Baseline Imaging in the Adult Hydrocephalus Research Network (AHCRN) (quality control and MR image analysis) - Richard Holubkov, PhD, Dept. Pediatrics
- Morphology of the Anteriorly Unstable Shoulder with Hill-Sachs Lesions (shape analysis) - Heath Henninger, PhD, Dept. Orthopaedics
- Informing Design of Percutaneous Osseointegrated Docking Systems for Above Elbow Amputees (shape analysis) Kent Bachus, PhD, Dept. Orthopaedics
- Mechanisms of Serotonergic Regulation for Connectivity Development (mice brain MRI/DWI analysis) - Josh Bonkowsky, PhD, Dept. Pediatrics
- Tacking adipogenesisin vivo (in-vivo cell segmentation & tracking) Sihem Boudina, PhD, Dept. Internal Medicine.





\* Total annual revenue displayed in legend (inaugural year).

#### **Advisory Board Committee**

Last meeting date: May, 2nd 2016

- Edward DiBella, PhD, Prof. Radiology and Imaging Sciences, Associate Director UCAIR
- Florian Solzbacher, PhD, Professor Electrical & Computer Engineering, Director CEI
- Tolga Tasdizen, PhD, Associate Professor Electrical & Computer Engineering

#### Addendum

Faculty Oversight Committee Guidelines: <u>http://www.cores.utah.edu/?page\_id=3725.</u>







## **Cell Imaging Facility**

#### Overview

The Cell Imaging Facility provides training and consultation on the use of confocal microscopy, widefield automated microscopy, two-photon, and software analysis tools for quantitative analysis of image data. The facility has Three Olympus FV1000 Spectral confocals, two Nikon A1 confocals, and a Multi-photon confocal from Prairie. In addition, two Nikon Ti automated microscope and a spinning disk confocal are available for live cell imaging. A Zeiss Axioscan Z1 slide scanner is available for automated archiving of histology and fluorescence data. Automated microscopes with one of four different stage incubators are available (CO2, temperature, humidity, one with Hypoxia) and also available for live cell imaging. Nikon Elements, Metamorph, Imaris and Volocity software are available for 2D and 3D analysis of image data.

#### Services

The training and equipment provided by the facility is aimed at reducing the startup time and degree of expertise necessary for an individual user to design and execute experiments requiring microscopy and image processing.

#### Equipment

#### **HSC Location**

- Olympus FV1000 Confocal Microscope
- Nikon A1 Confocal Microscope
- Nikon A1R Confocal Microscope
- Prairie Multi-Photon Confocal Microscope
- Zeiss Axioscan Z1 automated slide scanner with 100 slide loader
- EVOS FL Widefield Microscope
- Nikon Ti Automated Microscope
- SPIM light sheet microscope

#### HCI Location

- Nikon Ti Automated Microscope
- Nikon Ti Automated Microscope with Spinning disk confocal
- Ibidi stage incubator with C02, temperature and hypoxia control

#### SMBB Location

Olympus FV1000 Confocal Microscope

#### **Biology ASB Location**

- Olympus IX81 Automated Microscope
- Olympus FV1000 Confocal Microscope
- Vutara super resolution and Optera Swept Field Confocal

#### Personnel

- Christopher Rodesch, Ph.D., Director
- Michael J. Bridge, Ph.D., Research Associate
- Michael Redd, Ph.D., Research Associate



#### 2016 Annual Update New Services

- SPIM microscopy is available for independent users or run by Mike Redd
- Branch core locations in Biology ASB230, SMBB and Huntsman Cancer Institute are now online.

#### **New Equipment**

- Huntsman Cancer Center Location now has a Spinning Disk Confocal and an automated Widefield Microscope with a Stage incubator with controls for C02, O2 (hypoxia) and temperature.
- Ibidi Hypoxia controller and stage incubator: labtek, Ibidi and well plate adaptors allow incubation with hypoxia shift, C02, temperature and gyn
- Biology Location has an Olympus FV1000 confocal with 405, 488, 543, 633 and an automated widefield scope as well
- SMBB location has an automated FV1000 confocal with 405, 488, 543, 633, 748nm laser and a Weather Station cell incubation system.

#### **Revenue/Expenses**

#### FY16 Expenses: Total \$368,462

#### FY16 Revenue: Total \$373,618

- VP of Health Sciences Support for normal operating expenses: \$146,000
- VP of Research (RIF): \$83,200
- FY16 revenue generated from services: \$144,418





#### Advisory Board Committee

Last meeting date: June 16th, 2015.

- Kristen Kwan, Assistant Professor, Human Genetics
- Gabrielle Kardon, Associate Professor, Human Genetics
- Jody Rosenblatt, Assistant Professor, Oncological Sciences
- Josh Bonkowsky, Associate Professor, Neurobiology and Anatomy
- Adam Douglass, Assistant Professor, Neurobiology and Anatomy
- Jason Shepherd, Assistant Professor, Neurobiology and Anatomy
- Matt Wachowiak, Associate Professor, Neurobiology and Anatomy

#### Addendum

Faculty Oversight Committee Guidelines: <u>http://www.cores.utah.edu/?page\_id=3725.</u>

#### **FY16 Scientific Impact**

**Research Support** Revenue Generated (see charts following):







#### **Top Users**

1	Li, Dean	NIH, Advanced Heart Failure
2	Bonkowsky, Josh	NIH
3	Rutter, Jared	Treadwell Foundation, NIH,HHMI
4	Rosenblatt, Jody	NIH
5	Yost, Joseph	NIH
6	Phadnis, Nitin	NIH, National MS Society
7	Lane, Thomas	NIH, Department
8	Bhaskara, Srividya	NIH
9	Thummel, Carl	NIH
10	Shaw, Janet	NIH, HHMI



#### Publications

- 1. Xing, L., *et al.* A Serotonin Circuit Acts as an Environmental Sensor to Mediate Midline Axon Crossing through EphrinB2. *Journal of Neuroscience* **35**, 14794–14808 (2015).
- 2. Son, J.-H., *et al.* Transgenic FingRs for Live Mapping of Synaptic Dynamics in Genetically-Defined Neurons. *Sci. Rep. Scientific Reports* **6**, 18734 (2016).



## Centralized Zebrafish Animal Resource Facility

#### Overview

The CZAR Core Facility provides state-of-the-art systems for housing, breeding, and doing experiments with zebrafish, an emerging vertebrate model system. The CZAR underwent a major renovation/expansion in FY2016 with the goal of increasing its capacity from 5000 to 8000 fish tanks maintained on 5 independent recirculating water systems. Throughout FY2016 the CZAR staff spent much time (in addition to their regular responsibilities) in advising the design and execution of the renovation/expansion project. The communal laboratory space also increased, providing additional areas for Zebrafish mating, embryo microinjection, and afternoon embryo production in an Alternate Light Cycle room. The design encourages intellectual and experimental synergism among research groups, facilitating 1) large genetic screens carried out as collaborations between multiple laboratories; 2) collaborative research projects that require shared use of specific genetically marked or mutagenized animals; 3) development and distribution of resources and new technologies that advance the research efforts of all laboratories on campus; 4) a teaching environment in which the newest technologies and resources are disseminated quickly; and 5) training and experimental support for laboratories wishing to try pilot zebrafish experiments. The expanded facility will house approximately 135,000-170,000 fish, including a large number of wildtype and mutant fish strains. Currently it is used by 10 laboratories that have large-scale commitments to zebrafish research and ten additional small-scale user groups.

The CZAR staff is constantly conducting experiments to improve and optimize husbandry. Over the years this has involved introducing new methods for caring for larvae and young Zebrafish fry. The staff constantly monitors and troubleshoots health issues raised by individual labs, and provide pathology screening for the facility. They also conducted the experiments necessary to demonstrate that the new wing of the facility can support fish maintenance and healthy breeding conditions.

#### Services

The CZAR Core Facility is responsible for the daily care and maintenance of the fish and aquatic systems. The facility provides the following services:

- Housing and maintaining zebrafish, monitoring their health, and providing specialized nursery care and diets resulting in high survival rates of young fry.
- Establishing practices and providing oversight to ensure the safety and health of the animals in compliance with IACUC standards and regulations.
- Propagating wildtype lines and providing animals from these lines to investigators
- Providing laboratory bench space and supplies to perform experiments
- Providing and maintaining shared-use equipment including 7-8 microinjection stations with bright field stereomicroscopes, and 3 fluorescence stereomicroscopes.
- Providing education and training to investigators and students on an individual basis
- Providing specialized centralized services performed by the permanent staff, such as *in vitro* fertilization, sperm cryopreservation and storage
- Providing Quarantine facilities to house fish from outside sources to generate clean lines to import into the facility.
- Monitoring husbandry success through mating success data and nursery survival rates.
- Propagating individual lab WT or transgenic lines for a nominal fee. This service can now be requested through the Cores web site.



• Offering a "Fish School" course for new users to learn best practices in handling and caring for their fish, as well as how to tell male and female fish apart.

#### Equipment

- M205 FA Leica Fluorescence Microscope
- Zeiss Fluorescence Microscope with LED light source
- Olympus Fluorescence Microscope
- 7 microinjection stations with bright field stereomicroscopes
- Analog camera and monitor to facilitate teaching microinjection in real time
- Temperature sensors throughout facility to help monitor the quality of temperature control, and record deviations that could affect fish health.

#### Personnel

- Maurine Hobbs, PhD, Director
- Sharon Johnson, Senior Laboratory Specialist Zebrafish Husbandry and WT line maintenance
- Talmage Long, Technician Dedicated Nursery Manager

#### 2016 Annual Update

#### **New Equipment**

- June 2015, Construction began on the \$1.13 M expansion of the CZAR. The expansion will increase the capacity by nearly 3,000 additional tanks holding 40,000 - 60,000 more fish. The expansion will include additional experimental procedure space, increased nursery capacity, and an off-cycle room for increased egg production.
- June 2016, Began moving wild-type fish into the new wing of the facility at the rate of 50 tanks per week. These fish help establish the biofilter required to support housing research fish starting in mid-September, 2016.

#### **New Services**

No new services for FY16.

#### **Revenue/Expenses**

#### FY16 Expenses: Total \$416,200

#### FY16 Revenue: Total \$362,337

- VP of Health Sciences Support: \$105,000
- Total FY16 Revenue Generated from Services: \$257,337





#### **Advisory Board Committee**

Last meeting date: 3/18/15.

- David Jonah Grunwald, Professor, Human Genetics
- Joshua Bonkowsky, Associate Professor, Neurobiology and Anatomy and Pediatrics
- Richard Dorsky, Associate Professor, Neurobiology and Anatomy
- Kristen Kwan, Assistant Professor, Human Genetics
- Amnon Schlegel, Assistant Professor, Internal Medicine
- Rodney Stewart, Assistant Professor, Oncological Sciences
- Jack Taylor, Director, Office of Comparative Medicine
- H. Joseph Yost, Professor, Neurobiology and Anatomy and Pediatrics

#### Addendum

Faculty Oversight Committee Guidelines: <u>http://www.cores.utah.edu/?page\_id=3725</u>

#### FY16 Scientific Impact Research Support

- Grunwald, Title: Expansion of a Zebrafish Research Core Facility, Grunwald, 1G20OD018369-01, NIH, \$500,000, 06/01/2014 – 05/31/2015.
- Grants supported by this facility, as of July 2016, are listed on pages 23-25.





#### Publications

- 1. Barber, A. E., *et al.* Strengths and Limitations of Model Systems for the Study of Urinary Tract Infections and Related Pathologies. *Microbiology and Molecular Biology Reviews Microbiol. Mol. Biol. Rev.* **80**, 351–367 (2016). doi:10.1128/mmbr.00067-15.
- Barber, A. E *et al.* Similarly Lethal Strains of Extraintestinal PathogenicEscherichia coliTrigger Markedly Diverse Host Responses in a Zebrafish Model of Sepsis. *mSphere* 1, (2016). doi:10.1128/msphere.00062-16
- 3. Bryan, C. D., *et al.* Loss of laminin alpha 1 results in multiple structural defects and divergent effects on adhesion during vertebrate optic cup morphogenesis. *Developmental Biology* **416**, 324–337 (2016). doi:10.1016/j.ydbio.2016.06.025.
- 4. Cox, A. G. *et al.* Yap reprograms glutamine metabolism to increase nucleotide biosynthesis and enable liver growth. *Nature Cell Biology Nat Cell Biol* **18**, 886–896 (2016).
- 5. Dukes, A. A. *et al.* Live imaging of mitochondrial dynamics in CNS dopaminergic neurons in vivo demonstrates early reversal of mitochondrial transport following MPP exposure. *Neurobiology of Disease* **95**, 238–249 (2016). doi:10.1016/j.nbd.2016.07.020.
- 6. Duncan, R. N. *et al.* Hypothalamic radial glia function as self-renewing neural progenitors in the absence of Wnt/ -catenin signaling. *Development* **143**, 45–53 (2015).
- 7. Eisenhoffer, G. T. *et al.* A toolbox to study epidermal cell types in zebrafish. *Journal of Cell Science J Cell Sci* (2016). doi:10.1242/jcs.184341
- 8. Gu, Y. *et al.* Defective apical extrusion signaling contributes to aggressive tumor hallmarks. *eLife* 4, (2015). doi:10.7554/elife.04069.
- 9. Hendrickson, P. G. & Cairns, B. R. Tet proteins enhance the developmental hourglass. *Nature Genetics Nat Genet* **48**, 345–347 (2016). doi:10.1038/ng.3533.
- 10. Hoshijima, K., Jurynec, *et al.* Precise Editing of the Zebrafish Genome Made Simple and Efficient. *Developmental Cell* **36**, 654–667 (2016). doi:10.1016/j.devcel.2016.02.015.
- Hoshijima, K., et al. Precise genome editing by homologous recombination. Methods in Cell Biology The Zebrafish - Genetics, Genomics, and Transcriptomics 121–147 (2016). doi:10.1016/bs.mcb.2016.04.008
- 12. Karanth, S., Zinkhan, *et al.* FOXN3 Regulates Hepatic Glucose Utilization. *Cell Reports* **15**, 2745–2755 (2016). doi:10.1016/j.celrep.2016.05.056.
- 13. May, M. *et al.* ZC4H2 , an XLID gene, is required for the generation of a specific subset of CNS interneurons. *Hum. Mol. Genet. Human Molecular Genetics* **24**, 4848–4861 (2015).
- Mcpherson, A. D. *et al.* Motor Behavior Mediated by Continuously Generated Dopaminergic Neurons in the Zebrafish Hypothalamus Recovers after Cell Ablation. *Current Biology* 26, 263–269 (2016). doi:10.1016/j.cub.2015.11.064.
- 15. Milash, B. *et al.* Temporal Dysynchrony in brain connectivity gene expression following hypoxia. *BMC Genomics* **17**, (2016). doi: 10.1186/s12864-016-2638-x.
- Murphy, P. & Cairns, B. Genome-wide DNA methylation profiling in zebrafish. *Methods in Cell Biology The Zebrafish Genetics, Genomics, and Transcriptomics* 345–359 (2016). doi:10.1016/bs.mcb.2016.05.002
- Percival, S. M. *et al.* Variations in dysfunction of sister chromatid cohesion in esco2 mutant zebrafish reflect the phenotypic diversity of Roberts syndrome. *Disease Models* & *Mechanisms* 8, 941–955 (2015). doi:10.1242/dmm.019059.
- 18. Poulain, F. E. & Yost, H. J. Heparan sulfate proteoglycans: a sugar code for vertebrate development? *Development* **142**, 3456–3467 (2015). doi:10.1242/dev.098178.
- 19. Russell, C. W. & Mulvey, M. A. The Extraintestinal Pathogenic Escherichia coli Factor RqII Constrains the Genotoxic Effects of the RecQ-Like Helicase RqIH. *PLoS Pathog PLOS Pathogens* **11**, (2015).



- Safavi-Hemami, H., et al. Specialized insulin is used for chemical warfare by fish-hunting cone snails. Proceedings of the National Academy of Sciences Proc Natl Acad Sci USA 112, 1743–1748 (2015). doi:10.1073/pnas.1423857112
- 21. Schlegel, A. Metyrapone stimulation test to diagnose central adrenal insufficiency. *The Lancet Diabetes & Endocrinology* **3**, 407 (2015). doi: 10.1016/s2213-8587(15)00130-8.
- Son, J.-H., *et al.* Transgenic FingRs for Live Mapping of Synaptic Dynamics in Genetically-Defined Neurons. *Sci. Rep. Scientific Reports* 6, 18734 (2016). doi: 10.1038/srep18734
- Yabe, T., *et al.* Quadruple zebrafish mutant reveals different roles of Mesp genes in somite segmentation between mouse and zebrafish. *Development* 143, 2842–2852 (2016). doi:10.1242/dev.133173.

Active Grant Support of Zebrafish Research Associated with the UofU CZAR Core Facility 2015						
Zebrafish Investigator	Grant Title	PD/PI	Grant Award Number	Funding Source	Annual Amount of Direct Cost Funding	Start Dates (& End Dates)
Bonkowsky	Trans-Cellular Activation Of Transcription To Analyze Dopaminergic Axon Reorganization	Bonkowsky	1DP2 MH100008	NIH/NIM H	\$300,000	09/30/12  09/29/17
Bonkowsky	Characterization Of Genetic Pathways Regulating Connectivity Disruption In Hypoxic Injury	Bonkowsky	1FY13425	March Of Dimes	\$88,000	06/01/13 - 05/31/16
Cairns	Howard Hughes Medical Institute	Cairns	N/A	ННМІ	\$619,981	07/01/00 - 08/31/15
Dorsky	Regulation Of Hypothalamic Radial Glia By Wnt Signaling	Dorsky	5R01NS08 2645-03	NIH/NIN KS	\$250,000	03/01/13 - 02/29/16
Grunwald	Expansion of a Zebrafish Research Core Facility	Grunwald	1G20OD01 8369-01	NIH OFFICE OF THE DIRECT OR	\$500,000	06/01/14 - 05/31/16
Grunwald	Gene targeting in zebrafish: building models to assay disease genes	Grunwald	5R21OD01 8323-02	NIH NTNL INST CHILD	\$182,525	4/01/15 - 3/31/16



Zebrafish Investigator	Grant Title	PD/PI	Grant Award Number	Funding Source	Annual Amount of Direct Cost Funding	Start Dates (& End Dates)
Grunwald	A toolkit for gene- targeting in zebrafish	Grunwald	5R01HD08 1950-03	NIH NTNL INST CHILD	\$383,170	7/01/14 - 4/30/19
Kwan	Hedgehog Signaling and Cilia in Choroid Fissure Morphogenesis and Coloboma	Kwan	1R01EY02 5378-01	NIH NTNL EYE INSTITU TE	\$335,250	7/01/15 - 8/31/19
Li	Endothelial Toll- Like Receptor Signaling and Inflammation	Li	5R01HL07 7671-10		\$366,912	1/30/15 -
Mulvey	Bacterial Invasion And Trafficking Within The Bladder	Mulvey	5R01Al095 647-05	NIH/NIAI DIABETE	\$250,000	05/01/11 - 04/30/16
Rosenblatt	The Role Of Extrusion In Controlling Epithelial Homeostasis	Rosenblatt	5R01GM10 2169-04	NIH/NIG MED	\$207,475	08/01/12 - 04/30/17
Rosenblatt	The Role Of Extrusion In Controlling Epithelial Homeostasis	Rosenblatt	5R01GM10 2169- 02S1(Supp lement)	NIH/NIG MED	\$75,000	08/01/12 - 04/30/17
Schlegel	Molecular Genetics Of Lipid Metabolism	Schlegel	5R01DK09 6710-04	NIH/NID DIABETE	\$209,888	07/01/12 - 06/30/17
Stewart	Foxd3- Dependent Pathways In Neural Crest Migration And Metastasis	Stewart	RSG13025 01CSM	American Cancer Society	\$150,000	01/01/13 - 12/31/16
Tavtigian	Classifying DNA Mismatch Repair Gene Variants of Unknown Significance	Tavtigian	4R01CA16 4944-04	NCI	\$520,565	3/01/16 - 2/28/17
Tristani- Firouzi	"Zebrafish Model Organism Core For The Cardiovascular	Tristani- Firouzi	5U01 HL098188	NIH	\$164,000	06/01/11 - 2/29/16



Zebrafish Investigator	Grant Title	PD/PI	Grant Award Number	Funding Source	Annual Amount of Direct Cost Funding	Start Dates (& End Dates)
Yost	Genome-Wide Analysis Of Cardiac Development In Zebrafish	Yost	5U01HL09 8160	NIH/NHL BI	\$1,570,415	09/30/09  08/31/15
Yost	Developmental Biology Training Grant	Yost	2T32HD00 7491-16	NIH/NIC HD	\$253,526	09/29/95 - 03/31/17
Total Current Grants, Annual Direct Costs: \$7,130,167						



## **DNA Peptide Facility**

#### Overview

The DNA Peptide Facility provides researchers with chemical synthesis of custom oligonucleotides and oligopeptides. The facility synthesizes standard DNA/RNA oligos and peptides with multiple purity options, ranging from crude to HPLC. This Core has the ability to incorporate a wide array of specialty modifications, including fluorophore-labeling and functional group derivatization via amino-, thiol-, and modifications compatible with click chemistry. The goal of the facility is to provide quality service with speedy turnaround times.

#### Services

- Routine and custom DNA synthesis
- Routine and custom RNA synthesis
- Routine and custom Peptide synthesis
- Peptide Purification
- Amino Acid Analysis

#### Equipment

- Dr. Oligo 192 DNA Synthesizer
- ABI 3900 DNA Synthesizer
- ABI 394 DNA Synthesizer (2)
- ABI 433 Peptide Synthesizer
- ABI 433 Peptide Synthesizer
- Beckman Coulter System Gold 125P HPLC System
- Beckman Coulter System Gold 126 HPLC System
- Hewlett Packard Series 1100 HPLC system (2)
- Beckman Coulter DU800 Spectrophotometer
- BioTek Epoch Plate Reader Spectrophotometer

#### Personnel

- Mike Hanson, Ph.D., Director
- Scott Endicott, Research Associate
- Karen Freedman, Lab Specialist
- Jan Mees, Lab Aide
- Sheyenne Shamsa, Lab Aide
- Amanda Jarvis, Lab Aide

#### 2016 Annual Update

#### New Equipment

- The DNA Peptide Facility obtained a Dr. Oligo 192 DNA synthesizer through the University of Utah RIF program.
- The DNA Peptide Facility now offers Amino Acid Analysis services.











Тор	Users	
1	BioFire Diagnostics	Off Campus
2	Burrows, Cynthia	NIH, NSF, DHHS,
3	Sundquist, Wesley I	Department, NIH, DHHS
4	Heemstra, Jennifer	Department, Arizona State University
5	Wittwer, Carl	Department, BioFire, US Life Sciences
6	Dahlem, Timothy	HSC Cores
7	Rutter, Jared	Department, Treadwell Foundation, HHMI
8	Bass, Brenda	NIH, DHHS, Department
9	UC Davis	Off Campus
10	Yost, Christian	Department

#### **Publications**

- 1. An, N., *et al.* Human Telomere G-Quadruplexes with Five Repeats Accommodate 8-Oxo-7,8-dihydroguanine by Looping out the DNA Damage. *ACS Chem. Biol. ACS Chemical Biology* **11**, 500–507 (2016).
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- Ding, Y., *et al.* Unfolding Kinetics of the Human Telomere i-Motif Under a 10 pN Force Imposed by the α-Hemolysin Nanopore Identify Transient Folded-State Lifetimes at Physiological pH. *J. Am. Chem. Soc. Journal of the American Chemical Society* **137**, 9053–9060 (2015).
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- Perera, R. T. *et al.* Unzipping of A-Form DNA-RNA, A-Form DNA-PNA, and B-Form DNA-DNA in the α-Hemolysin Nanopore. *Biophysical Journal* **110**, 306–314 (2016). doi:10.1016/j.bpj.2015.11.020.
- 7. Riedl, J *et al.* Sequencing of DNA Lesions Facilitated by Site-Specific Excision via Base Excision Repair DNA Glycosylases Yielding Ligatable Gaps. *J. Am. Chem. Soc. Journal of the American Chemical Society* **138**, 491–494 (2016).
- Robinson, G., et al. In vitro visualization and characterization of wild type and mutant IDH homo- and heterodimers using Bimolecular Fluorescence Complementation. Cancer Res Front Cancer Research Frontiers 2, 311–329 (2016).
- 9. Zhu, J., Fleming, A. M., Orendt, A. M. & Burrows, C. J. pH-Dependent Equilibrium between 5-Guanidinohydantoin and Iminoallantoin Affects Nucleotide Insertion Opposite the DNA Lesion. *The Journal of Organic Chemistry J. Org. Chem.* **81**, 351–359 (2016).



## **DNA Sequencing Facility**

#### Overview

The DNA Sequencing Facility provides DNA sequencing services and employs the latest technologies to generate high quality data with the goal of rapid sample turnaround at competitive prices. DNA sequencing is accomplished with the use of state-of-the-art DNA sequencers and lab robotics such as the Ion Torrent PGM and Proton, the Qiagen Q24 Pyrosequencer, and the Biomek FX for liquid handling needs. Data from standard DNA sequencing services are typically reported to customers the same day as they are run. Sample information can be submitted online and sequencing data files are also available online for download using a simple and secure interface.

#### Services

#### **DNA Sequencing**

- Standard Sanger DNA sequencing
- Primer walking on clones
- Mutation detection and resequencing custom projects
- Ion Torrent NGS sequencing
- Pyrosequencing

#### Robotics

• Biomek FX with Span-8 and 96 head

#### **Other Services**

- Lab consumables for sample submission
- Life Technologies freezer program

#### Equipment

#### Sequencers

- Ion Torrent PGM
- Ion Torrent Proton
- Qiagen Q24 Pyrosequencer
- Applied Biosystems 3730xl

#### Liquid Handlers

• 2 Biomek FX programmable liquid sample dispensers

#### Personnel

- Derek Warner, Director
- Michael Powers, Senior Laboratory Specialist
- Jinlan Wang, Lab Specialist

#### 2016 Annual Update

#### New Equipment

No new instrumentation this year.

#### New Services

No new services this year.










Top Users		
1	Blaschke, Anne Jeannette	Thrasher Research, Department
2	Olivera, Baldomero	HHMI, NIH
3	Parkinson, John	NIH
4	Phillips, John	NIH
5	Yost, Joseph	NIH
6	Pulst, Stefan	Department
7	Schiffman, Joshua	NIH, HCI
8	VanBrocklin, Matthew	Gift, American Cancer Society
9	Hill, Christopher	NIH
10	Sundquist, Wesley I	NIH, Department, DHHS

- Allen-Brady, K., *et al.* Evidence for pelvic organ prolapse predisposition genes on chromosomes 10 and 17. *American Journal of Obstetrics and Gynecology* **212**, (2015). PMID: 25557205.
- Andrade, D. *et al.* SUMOylation Regulates Growth Factor Independence 1 in Transcriptional Control and Hematopoiesis. *Molecular and Cellular Biology Mol. Cell. Biol.* 36, 1438–1450 (2016).
- 3. Ronquillo, C. C. *et al.* Ciliopathy-associated IQCB1/NPHP5 protein is required for mouse photoreceptor outer segment formation. *The FASEB Journal* (2016). doi:10.1096/fj.201600511r.
- 4. Bonthuis, P. J. *et al.* Noncanonical Genomic Imprinting Effects in Offspring. *Cell Reports* **12**, 979–991 (2015). doi: 10.1016/j.celrep.2015.07.017.
- 5. Domyan, E. T. *et al.* Molecular shifts in limb identity underlie development of feathered feet in two domestic avian species. *eLife* **5**, (2016).. doi: 10.7554/elife.12115.
- 6. Hanke-Gogokhia, *et al.* (2015, December 02). The Function of Arf-like Proteins ARL2 and ARL3 in Photoreceptors. *Retinal Degenerative Diseases Advances in Experimental Medicine and Biology*, 655-661. doi:10.1007/978-3-319-17121-0\_87.
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- Hanke-Gogokhia, C. *et al.* Arf-like Protein 3 (ARL3) Regulates Protein Trafficking and Ciliogenesis in Mouse Photoreceptors. *Journal of Biological Chemistry J. Biol. Chem.* 291, 7142–7155 (2016). PMID: 26814127. PMCID: PMC4807295.
- Jiang, L. *et al.* Heterotrimeric Kinesin-2 (KIF3) Mediates Transition Zone and Axoneme Formation of Mouse Photoreceptors. *Journal of Biological Chemistry J. Biol. Chem.* 290, 12765–12778 (2015).PMCID: PMC443229.3
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- Kalbfleisch, T. *et al.* Characterization of an APC Promoter 1B deletion in a Patient Diagnosed with Familial Adenomatous Polyposis via Whole Genome Shotgun Sequencing. *F1000Research F1000Res* (2015). doi:10.12688/f1000research.6636.1. eCollection 2015. PMID: 26213617. Free PMC Article.



- Karanth, S., *et al.* FOXN3 Regulates Hepatic Glucose Utilization. *Cell Reports* 15, 2745–2755 (2016). doi: 10.1016/j.celrep.2016.05.056. Epub 2016 Jun 9. PMID: 27292639. PMCID: PMC4917433.
- Mcknight, R. A. *et al.* Intrauterine growth restriction inhibits expression of eukaryotic elongation factor 2 kinase, a regulator of protein translation. *Physiol. Genomics Physiological Genomics* **48**, 616–625 (2016). doi: 10.1152/physiolgenomics.00045.2016. PMID: 27317589 [PubMed - in process].
- 14. Mcknight, R. A. *et al.* Intrauterine growth restriction perturbs nucleosome depletion at a growth hormone responsive element in the mouse IGF-1 gene. Physiol. Genomics Physiological Genomics (2015). doi:10.1152/physiolgenomics.00082.2015. PMID: 26487705.
- Rainy, N. *et al.* Knockdown of unc119c results in visual impairment and early-onset retinal dystrophy in zebrafish. *Biochemical and Biophysical Research Communications* 473, 1211–1217 (2016). PMID: 27079236.
- 16. Rao, K. N *et al.* (2016, June 02). Ciliopathy-associated protein CEP290 modifies the severity of retinal degeneration due to loss of RPGR. *Hum. Mol. Genet. Human Molecular Genetics,* in Press. doi:10.1093/hmg/ddw075. PMID:26936822.
- 17. Ying, G. *et al.* Small GTPases Rab8a and Rab11a Are Dispensable for Rhodopsin Transport in Mouse Photoreceptors. *PLOS ONE PLoS ONE* **11**, (2016).

UNIVERSITY OF UTAH HEALTH SCIENCES



# **Drug Discovery Facility**

#### Overview

The Drug Discovery Facility provides compound collections for screening. The facility delivers low-cost and efficient access to chemical libraries for screening, to equipment for automation, and to synthetic chemistry support for the characterization and validation of compounds for potential use as therapeutics, diagnostics and biological tools.

#### Uniqueness

The University of Utah possesses the scientific and medical talent, innovation research culture, and state-of-the-art research facilities to contribute substantially to the discovery of small molecule drugs. However, significant challenges still remain in translation of basic scientific discoveries into potential human therapeutics. The uniqueness of the Drug Discovery Facility is it coordinates the cooperative efforts of individual research groups in a wide variety of different drug discovery stuides, ultimately leading to discover novel chemical probes and new pharmaceutical lead compounds.

The most valuable assets at the facility are the private/proprietary chemical collections that could result in new intellectual property. These unique molecules of therapeutic potential offer the facility to assist in the translation of fundamental discoveries in biology into novel therapeutics and commercial opportunities. It's anticipated that the discovery of candidate lead compounds from the facility will stimulate interest in commercial development of technology at the University of Utah through licensing agreements with pharmaceutical industry partners and the production of new start-up biotechnology companies.

#### Services

- High-throughput screening
- Small molecule chemical libraries
- Pooled CRISPR-Cas9 libraries
- Assay development
- Consultation on target identification/validation, hit to lead optimization, PK/PD/Efficacy
- Chemical support for drug discovery

# Equipment/Compound Collection

# Automated Liquid Handling Stations:

- Tecan EVO100/MCA96 Liquid Handler with sterile bio-hoods
- Tecan EVO100/MCA384 Liquid Handler with sterile bio-hoods
- CyBio(Matrix) 96/384 Liquid Handler
- Matrix PlateMate Plus 384 Liquid Handler
- HP D300 Digital Dispenser
- Bio-tek Plate Washer with stacker

#### Automated Detection Systems:

- Molecular Devices ImageXpress XLS Automated High-Content System
- Bio-tek Plate Neo 2 Plate Reader with stacker



#### **CRISPR Libraries:**

- The genome-scale CRISPR-Cas9 knockout (GeCKO) v2 library
- Subset CRISPR libraries: a) human Lentiviral sgRNA library-kinases, and b) human Lentiviral sgRNA library-nuclear proteins

#### **Commercial Compound Libraries:**

- Chembridge Diverset EXP(50K) and CL (50K)
- Microsource Spectrum Collection
- NIH Clinical Collection
- Epigenetics Screening Library
- Kinase Inhibitor Library
- NCI Diversity Set IV
- Natural Products Set II
- Enamine 3D Diversity Set (50K)

# **Private/Proprietary Chemical Collections:**

- UUPCC University of Utah Private Chemical Collection
- Dept. of Chemistry Library
- Ireland Natural Product Collection

#### Personnel

• Bai Luo, Ph.D., Director

# 2016 Annual Update

# New Equipment:

**Bioteq Synergy Neo 2 Multi-Mode Microplate Reader** ----- It combines the features expected on a traditional HTS reader (dual PMT read head, ultra-fast stacker, excellent performance) with unique features to make it more adaptable to today's screening requirements, like the hybrid filter/monochromator optical system, a powerful 100mW laser-based excitation source for Alpha assays, and orbital/linear shaking.

# New Compound Collection:

**Enamine 3D Diversity Set:** 50240 compounds were selected from the drug-like portion of Enamine HTS collection (1.3 million compounds) by application of conformational analysis and shape clustering algorithms.

# Location update:

The core is in the process of moving from its current facility on Colorow Drive to renovated space in the original Skaggs Pharmacy building, 3<sup>rd</sup> floor. The move will be completed in early FY17.









#### Top Users

1	Recursion Pharmaceuticals Inc.	Off Campus Commercial
2	Li, Dean	NIH, Advanced Heart Failure
3	Vettore Bio	Off Campus
4	Bild, Andrea	Off Campus, Boston University, NIH
5	University of Georgia	DHHS
6	Swaminathan,Sankar	Department
7	Planelles, Vicente	NIH
8	Deininger, Michael	NIH
9	Hill, Christopher	Off Campus
10	Phillips, John	NIH

# Goals for FY17

#### **Expand Capabilities**

- Start CRISPR Screening
- Enhance Utility of UUPCC Library
- Make a selective/proprietary UUPCC library (300-400 compounds)

#### **Expand Business**

- Move to HSC campus
- Explore the possibility of institutional seed funding for screening

- 1. Gibson, C. C. *et al.* Dietary Vitamin D and Its Metabolites Non-Genomically Stabilize the Endothelium. *PLOS ONE PLoS ONE* **10**, (2015).
- 2. Yoo, J. H. *et al.* ARF6 Is an Actionable Node that Orchestrates Oncogenic GNAQ Signaling in Uveal Melanoma. *Cancer Cell* **29**, 889–904 (2016).



# **Electron Microscopy**

#### Overview

The Electron Microscopy (EM) Facility utilizes transmission electron microscopy (TEM) and scanning electron microscopy (SEM) imaging to determine cellular structures, the morphology of biological macromolecules, the three-dimensional structures of biological macromolecules, and the size and structure of nanoparticles and other small particles. The EM Facility also prepares specimens for the microscope. The EM facility has four spatially distinct locations to serve the needs of the clinical and research groups. The main facility is in SMBB, and two TEMs are located there. Each of the following buildings house one TEM: RB LAB, BIOL, and ASB. Experiments requiring SEM technology are done in collaboration with the microscopes owned by the Surface Analysis Laboratory.

#### Services

#### **Clinical Services:**

Thin-section electron microscopy of tissue biopsies (technical component of clinical EM)

#### Research Services:

- Training on the TEMs, microtomes, sample preparation, and 3D image reconstruction
- Sections ("thick" and "thin") cut on microtome and ultramicrotome
- Record images on transmission or scanning electron microscopes
- Procedures for observing tissues and cellular specimens including embedding, drying, osmification, and storage
- Procedures for observing particulate and macromolecular samples including staining, metal coating, drying, and cryogenic TEM

#### Equipment

- FEI Tecnai 12, transmission electron microscope
- JEOL JEM-1400 Plus, transmission electron microscope
- Two Hitachi 7100, transmission electron microscopes
- FEI Tecnai F20, transmission electron microscope
- Leica (UC7, UC6, and UCT) and Reichert (Ultracut E), ultramicrotomes
- Leica JUNG RM2055, microtome
- Two FEI Vitrobots, vitrification robots
- Gatan K2 Summit, direct electron detector (mounted on FEI Tecnai F20)
- Two automatic tissue processors
- Two laboratory microwave ovens
- Sputter coater
- Glow discharger
- High-pressure freezer
- Freeze substitution machine
- Critical-point dryer
- High-performance computing nodes (CHPC)



# Personnel

- David Belnap, Ph.D., Director
- Nancy Chandler, Senior Laboratory Specialist
- Linda Nikolova, Senior Laboratory Specialist
- Megan Kent, Laboratory Technician
- Guilherme Cordovil, Laboratory Specialist
- Kalavathy Ramachandran, Laboratory Technician
- Taylor Gemperline, Laboratory Technician
- Alexander Wheeler, Undergraduate Clinical Assistant

# 2016 Annual Update

# **New Equipment**

- FEI Vitrobot, installed June 2016.
- Two high-performance computing nodes (CHPC), installed June 2016

# New Services

No new services for FY16.

# **Revenue/Expenses**

# FY16 Expenses: Total \$683,677

# FY16 Revenue: Total \$727,908

- VP of Research Support: \$50,000 (Service Contracts)
- VPof Research Support (RIF): \$40,000
  - FY16 revenue generated from services: \$638,127



\* Legend displays total annual revenue by year earned.

# **Advisory Board Committee**

Last meeting date: October 2, 2013.

- Erik Jorgensen, Distinguished Professor, Department of Biology
- Mary Bronner, Professor, Department of Pathology

# Addendum

Faculty Oversight Committee Guidelines can be found for all cores at the following link: <u>http://cores.utah.edu/wp-content/uploads/2015/09/Faculty-Advisory-Committee-Responsibilities-2.pdf</u>











Top Users		
1	ARUP	Off Campus
2	Scripps	Off Campus
3	TriCore	Off Campus
4	Primary Children's Medical Center	Off Campus
5	Sundquist, Wesley I	NIH, Department, DHHS
6	Jorgensen, Erik	HHMI
7	Hill, Christopher	NIH
8	St. John's	Off Campus
9	Utah State University	Off Campus
10	Bass, Brenda	HHMI

# Goals for FY17

- Obtain high-quality TEM data with FEI Tecnai F20 and Gatan K2 Summit camera
- Maintain high-quality clinical services
- Improve clinical services by establishing remote capability
- Establish tomography as a frequently used method
- Plan for new facility on main campus (Crocker Service Center)
- Increase usage of main-campus microscopes

- 1. Mccullough, J. *et al.* Structure and membrane remodeling activity of ESCRT-III helical polymers. *Science* **350**, 1548–1551 (2015). PMCID: PMC4684769.
- 2. Li, Y.-L. *et al.* Primate TRIM5 proteins form hexagonal nets on HIV-1 capsids. *eLife* **5**, (2016). PMCID: PMC4936896.

UNIVERSITY OF UTAH HEALTH SCIENCES



# **Flow Cytometry Facility**

#### Overview

The Flow Cytometry Facility offers quantitative, multiparameter fluorescence analysis, and cell sorting services that assists over 90 investigators including a subset of industry clients. The expertise and instrumentation to perform most flow cytometric assays that have been described in the literature are available within the expertise of the collective personnel and the physical resources of the Flow Cytometry Facility. The facility offers investigators the entire spectrum of cytometric experiment management, if desired, all the way from initial design consultation to the creation of graphics for publication.

#### Uniqueness

The Flow Cytometry facility is recognized for the most part as instrumentation based service lab. However, we believe that education is a crucial component for the growth and sustainability of the facility. First of all, facility staffs are encouraged to maintain state of the art knowledge in order to pass this information along to the users. Secondly, we believe that education in the field of flow cytometry for users will lead to more successful experimental outcomes which will in turn increase overall usage. To this end, we provide multiple levels of education from one on one consultation to routine seminars covering a variety of topics. Although this may not be absolutely unique when compared to other Core facilities, it is a noticeable quality of our services when compared to other non-centralized instrumentation on campus.

# Services

The assays offered by the facility range from routine cell cycle analysis and immunophenotyping to complex multi-laser applications and high speed cell sorting. Examples of the assays available include, but are not limited to the following:

- DNA content/cell cycle measurement
- Immunofluorescence analyses
- Characterization of cell populations based on scattered light intensity measurements and autofluorescence
- Cell sorting including viable, sterile cell sorting
- Intracellular calcium flux
- A range of apoptosis assays
- Fluorescence Resonance Energy Transfer (FRET)
- Nanoparticle characterization
- Bivariate and univariate chromosome analysis
- Receptor-ligand interactions
- Cell proliferation studies including BrdU incorporation and CFSE tracking
- Viability assays (membrane exclusion and metabolic viability)
- Various function assays including oxidative metabolism, neutrophil function (oxidative burst, phagocytosis) cytoplasmic pH, membrane potential
- Kinetic analyses
- Signal transduction pathway analyses (simultaneous assessment of multiple intracellular phosphorylated epitopes combined in complex multi-color assays)
- Sample preparation and staining



Consultation and training is provided in order to define projects in the early stages of development to make optimal and efficient use of flow cytometry. The staff will prepare samples including staining, data collection, quality control, data analysis/interpretation, and creation of graphics. Alternatively, if the investigator chooses, the facility can provide consultation only on any of the above services so that the research is entirely in the hands of the investigator.

# Equipment

#### Sorters

- BD FACSAria-5 laser
- Propel Labs Avalon-2 laser
- BD FACSAria-2 laser

# Analyzers

- BD FACSCanto
- BD LSRFortessa
- BD Celesta
- Cytek DxP
- BD FACScan

# Personnel

- James Marvin, Director
- Chris Leukel, Sr. Laboratory Specialist

# FY16 Annual Update

#### **New Equipment**

The Flow Facility nearly doubled the available instrumentation in FY16! First of all a new cell sorter was acquired from ARUP laboratories. This instrument saw incredibly limited usage while located at ARUP. For this reason the flow core pursued a transfer agreement that was finalized in April of 2016. Although this instrument is more limited in capabilities than our other cell sorter, it can be upgraded, and immediately alleviated some of the capacity issues with cell sorting in the core. Next, with funds from the VP office, HCI, and the flow core, we purchased a state of the art BD LSRFortessa. This expanded our current analytical capabilities from a maximum of 8 colors to 16. This instrument is housed within HCI as a satellite facility. Finally, Paul, Sigala, a new investigator in the Biochemistry department gave the flow lab \$150,000 towards the purchase of a BD Celesta analyzer that is located in EEJ Medical Research Building. This will also operate as a satellite facility.

# Staffing

In June of 2016, Chris Leukel, a long- time employee of the flow lab decided to leave and pursue another career path. His replacement, Tessa Galland, was hired as a lab technician and she began working in the lab on July 11<sup>th</sup>.





\* Total annual revenue displayed in legend.

# **Advisory Board Committee**

Last meeting date: July 2016

- Ryan O'Connell, Assistant Professor, Pathology
- Thomas O'Hare, Associate Professor, Hematology
- Daniel Leung, Assistant Professor, Internal Medicine (NEW in FY16)
- Matthew Williams, Assistant Professor, Pathology

# Addendum

Faculty Oversight Committee Guidelines can be found for all cores at the following link: <u>http://cores.utah.edu/wp-content/uploads/2015/09/Faculty-Advisory-Committee-Responsibilities-2.pdf</u>













Top Users		
1	ARUP	Off Campus
2	Camp, Nicola	Department, NIH
3	Williams, Matthew	Department
4	Deininger, Michael	NIH, Leukemia & Lymphoma Society, MPN Research Foundation, V Foundation
5	Atanackovic, Djordje	Department, HCI
6	Rutter, Jared	Treadwell Foundation, NIH,HHMI
7	Cazalla, Demian	Am. Foundation for Aids, UNC, NIH
8	Planelles, Vicente	HHMI, Akers Private Foundation
9	Snyder, Eric	NIH, Department
10	Kardon, Gabrielle	NIH, Department, March of Dimes

# Goals for FY17

As noted above, a very large push in FY16 was made to increase instrumentation capabilities and capacity within the core facility. Now that this has been accomplished, a main focus will be on training new staff to provide the most efficient and best quality of service. With 11 instruments under our management, we will also be implementing an enhanced instrument quality assurance program that will involve sensitivity testing along with cross instrument comparisons.

- 1. Abegglen, L. M. *et al.* Potential Mechanisms for Cancer Resistance in Elephants and Comparative Cellular Response to DNA Damage in Humans. *Jama* **314**, 1850 (2015).
- Chamberlain, L. M., Holt-Casper, D., Gonzalez-Juarrero, M. & Grainger, D. W. Extended culture of macrophages from different sources and maturation results in a common M2 phenotype. *Journal of Biomedical Materials Research Part A J. Biomed. Mater. Res.* 103, 2864–2874 (2015).
- 3. Gupta, S. *et al.* Reversible lysine-specific demethylase 1 antagonist HCI-2509 inhibits growth and decreases c-MYC in castration- and docetaxel-resistant prostate cancer cells. *Prostate Cancer Prostatic Dis Prostate Cancer and Prostatic Diseases* (2016). doi:10.1038/pcan.2016.21
- 4. Hughes, A. L., *et al.* Selective sorting and destruction of mitochondrial membrane proteins in aged yeast. *eLife* **5**, (2016).
- 5. Lewis, A., *et al.* Histone Deacetylase 6 Regulates Bladder Architecture and Host Susceptibility to Uropathogenic Escherichia coli. *Pathogens* **5**, 20 (2016).
- 6. Mason, C. C. *et al.* Age-related mutations and chronic myelomonocytic leukemia. *Leukemia* **30**, 906–913 (2015).
- 7. Rowley, J. W. *et al.* Dicer1-mediated miRNA processing shapes the mRNA profile and function of murine platelets. *Blood* **127**, 1743–1751 (2016).
- 8. Shakya, A. *et al.* Oct1 and OCA-B are selectively required for CD4 memory T cell function. *J Cell Biol The Journal of Cell Biology* **211**, (2015).



# **Genomics Facility**

#### Overview

The Genomics Facility offers a variety of genetic analysis services including full service genotyping, from PCR setup through analysis, and assistance to researchers performing genotyping projects. The facility has commercial and custom sets of fluorescently labeled microsatellite markers that can be used for whole genome linkage studies and fine mapping projects. Researchers can select genes or regions of interest and the facility designs and optimizes the PCR primers, performs the initial PCR, runs the sequencing reactions, and analyzes the data using SoftGenetics Mutation Surveyor software.

#### Services

# **Fragment Analysis**

- Full service genotyping from PCR setup through analysis
- Capillary Runs
- Microsatellite Instability
- Loss of Heterozygosity
- Multiplex Ligation Dependent Amplification

# **SNP** Genotyping

- Taqman SNP Genotyping
- Illumina GoldenGate SNP Genotyping
- Whole-Genome Genotyping and Copy Number Variation Analysis
- Methylation Analysis
- Open Array Genotyping

# DNA Sequencing

Mutation Detection

# Real Time PCR

• Gene Expression

#### Equipment

- One AB 7900HT system
- Illumina iScan
- Quantstudio 12k Flex Real-Time PCR System

#### Personnel

- Derek Warner, Director
- Michael Klein, Manager

# 2016 Annual Update

New Equipment

No new instrumentation for FY16.

#### New Services

No new services for FY16.





\* Legend displays total annual billed revenue by year.

# **Advisory Board Committee**

Last meeting date: July 20, 2015

- Gerald Krueger, Professor, Dermatology
- Deborah Neklason, Research Associate Professor, Huntsman Cancer Institute
- Nicola Camp, Professor, Genetic Epidemiology

#### Addendum

Faculty Oversight Committee Guidelines can be found for all cores at the following link: <u>http://cores.utah.edu/wp-content/uploads/2015/09/Faculty-Advisory-Committee-Responsibilities-2.pdf.</u>













Тор	Top Users		
1	Pulst, Stefan	Department	
2	Weiss, Robert B.	Department, NIH, EMMES Corporation, DHHS	
3	DeAngelis, Margaret	Department, Alsam Foundation, LJ&Mary C. Skaggs Foundation	
4	Tulane University	Off Campus Academic	
5	Carrell, Douglas	Department	
6	Bush, Sarah	NSF, Ecology & Environmental Biology	
7	Coon, Hilary	NIH	
8	Taylor, Jack	Department	
9	Leppert, Mark	Department, Lewy Medical Research Institute	
10	Boston University	Off Campus Academic	

- 1. Allen-Brady, K., *et al.*, *Evidence for pelvic organ prolapse predisposition genes on chromosomes 10 and 17.* Am J Obstet Gynecol, 2015. **212**(6): p. 771 e1-7.
- Andrade, D. *et al.* SUMOylation Regulates Growth Factor Independence 1 in Transcriptional Control and Hematopoiesis. *Molecular and Cellular Biology Mol. Cell. Biol.* 36, 1438–1450 (2016).
- 3. Aston, K. I. *et al.* Aberrant sperm DNA methylation predicts male fertility status and embryo quality. *Fertility and Sterility* **104**, (2015). 1388-97.
- 4. Bonthuis, P. J. *et al.* Noncanonical Genomic Imprinting Effects in Offspring. *Cell Reports* **12**, 979–991 (2015).
- 5. Cho, J. H. *et al.* AKT1 Activation Promotes Development of Melanoma Metastases. *Cell Reports* **13**, 898–905 (2015).
- 6. Chuong, E. B., Elde, N. C. & Feschotte, C. Regulatory evolution of innate immunity through co-option of endogenous retroviruses. *Science* **351**, 1083–1087 (2016).
- 7. Cirulli, E.T., et al., Exome sequencing in amyotrophic lateral sclerosis identifies risk genes and pathways. Science, 2015. **347**(6229): p. 1436-41.
- 8. Dansithong, W. *et al.* Ataxin-2 Regulates RGS8 Translation in a New BAC-SCA2 Transgenic Mouse Model. *PLoS Genet PLOS Genetics* **11**, (2015).
- 9. Domyan, E. T. *et al.* Molecular shifts in limb identity underlie development of feathered feet in two domestic avian species. *eLife* **5**, (2016).
- 10. Flygare, S. *et al.* Taxonomer: an interactive metagenomics analysis portal for universal pathogen detection and host mRNA expression profiling. *Genome Biol Genome Biology* **17**, (2016).
- 11. Green, Y. S., Kwon, S. & Christian, J. L. Expression pattern of bcar3, a downstream target of Gata2, and its binding partner, bcar1, during Xenopus development. *Gene Expression Patterns* **20**, 55–62 (2016).
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- 36. Ying, G. *et al.* Small GTPases Rab8a and Rab11a Are Dispensable for Rhodopsin Transport in Mouse Photoreceptors. *PLOS ONE PLoS ONE* **11**, (2016).
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# Machine Shop

#### Overview

The Machine Shop Facility is equipped with a full complement of lathes, drills, mills, welders, grinders, and CNC systems, staffed by experienced machinists and engineers capable of turning an idea into reality. The Shop Staff provide consultation to assist with the design process for products ranging from precise surgical instruments to large-scale testing equipment. They also fabricate as well as repair devices and parts made from carbon-steel, stainless steel, brass, copper, plastics, and other materials depending upon the requirements of design specifications.

#### Services

- Device Design/Engineering from basic concept to finished product
- Milling
- Turning
- Drilling
- Grinding
- Soldering
- Welding of steel, aluminum, and other types of fabrication
- Sawing
- Repair and Maintenance
- The Machine Shop Facility continues to supply fast plastic fabrication using technology developed in our shop.

# Equipment

- CNC Mills
- Traditional Mills
- Manual Lathes and CNC Lathe
- Grinders
- MIG, TIG, Gas, Arc, and Spot welders
- Wood Working Equipment
- Band & Table Saws
- Sharpening Equipment
- Polishing Equipment

#### Personnel

- Barry Evans, Engineer, Director
- Kim Slusser, Machinist, Surgical Tool Expert
- Mike Sanches, Machine Operator, Research Specialist, Graphic Artist

# 2016 Annual Update

# **New Equipment**

State of the art CNC Tormach Lathe 15L Slant Pro





\* Legend displays total annual revenue by year generated.

# **Advisory Board Committee**

- Perry Renshaw, Professor, Psychiatry
- Michelle Ford, Materials Management Facilitator, Facilities Engineering
- Kyle Thomson, Researcher, Add Program

# Addendum

Faculty Oversight Committee Guidelines can be found for all cores at the following link: <u>http://cores.utah.edu/wp-content/uploads/2015/09/Faculty-Advisory-Committee-Responsibilities-2.pdf</u>







Top Users		
1	White, H.	University Hospital Surgical Services
2	Myriad Genetics	Off Campus
3	Ford, Michelle	University Hospital Surgical Services
4	Meisner, Steve	Radiation Oncology
5	Peacock, Darren	University Hospital Operating Room
6	Primary Children's Medical Center	Off Campus
7	Clausing, Alishia	University Hospital Operating Room
8	Wilcox, Karen	Department, NIH
9	Rodesch, Chris	HSC Cell Imaging Core
10	Rajamani, Raj	Metallurgical Engineering

# Publications

No publications acknowledged this facility in FY16.



# **Mass Spectrometry & Proteomics**

#### Overview

The Mass Spectrometry & Proteomics Facility is geared toward supporting proteomics research as well as providing basic mass spectrometry (MS) support for a broad range of research and sample types, such as polymers, natural products, small synthetic molecules, peptides, large intact proteins, and nucleic acids. The facility is equipped with several high-performance mass spectrometers, including a state-of-the-art FTMS instrument (LTQ-FT; ThermoElectron) with nano-LC and nano-ESI ionization, and a state-of-the-art Maldi/ToF/ToF instrument (UltrafleXtreme; Bruker Daltonics) with tissue-imaging capabilities. LC/MS/MS instruments in the lab are equipped with nano-LC for ultimate sensitivity and chromatographic performance. The mission of this facility is to provide the highest quality mass spectrometry analyses for protein and other biomolecule investigations.

# Services

A range of proteomics, FTMS, and general and tissue-imaging MS services are available. In addition, the facility periodically participates in an international proteomics proficiency evaluation conducted by the Association of Bimolecular Resource Facilities (ABRF) to ensure the competency of the facility compared with other leading proteomics laboratories for the structural analysis of proteins and peptides. The following services are provided to investigators:

# **Proteomics Services:**

- Protein ID from SDS Gel
- Protein ID from Solution
- Protein ID from Complex Isolates in Solution and IP Pull-down Experiments
- Identification of Protein Modifications/Post-translational Modifications
- Intact Protein MW Analysis
- Peptide Screening with MS/MS (FTMS) and accurate mass de novo sequencing
- Disulfide Linkage Characterization
- Identification of Sulfur-containing peptides
- "Top-Down" and "Bottom-Up" Proteomics
- Protein Expression/Quantification Analysis
- Custom Database Searching
- FTMS Services
- Accurate mass measurement-external calibration (Positive Ion)
- Accurate mass measurement-internal calibration (Positive Ion)
- Accurate mass measurement (Negative Ion)
- Peptide Sequencing with MS/MS and accurate mass de novo sequencing
- Identification of Sulfur-containing peptides
- High-resolution mass spectrometry (HR-MS) analysis



#### General MS Services

- ESI/MS
- ESI/MS/MS
- Nucleic Acids
- LC/MS
- LC/MS/MS
- Maldi/ToF/ToF
- Special Project/Method Development

# **Tissue-Imaging MS Services**

- Cryostat Tissue Sectioning and Maldi Plate Setup
- Tissue Section Preparation and Setup
- Maldi/ToF Imaging of Tissue Sections
- Software Data Processing and Image Generation
- Software Data Processing and Image Generation-by User

# Equipment

- Mass Spectrometers
  - Thermo LTQ-FT
  - Bruker UltrafleXtreme
  - Waters Q-ToF-2
  - Bruker Maxis II HD for high mass accuracy intact protein analysis.
  - Thermo Orbitrap XL

# **HPLC Systems**

- Two Eksigent 1D nanoLC systems
- One Eksigent 2D-Ultra system
- One Shimadzu 10AD system
- One Leica CM1950 cryostat system

# Personnel

- James Cox, Ph.D., Director
- Krishna Parsawar, Ph.D., Assistant Director
- Spencer Thompson, Technician

# **Advisory Board Committee**

- Darrell Davis, Professor, Medicinal Chemistry
- Wes Sundquist, Professor, Biochemistry
- Guy Zimmerman, Professor, Human Genetics
- Michael Kay, Professor, Biochemistry









Тор	Top Users 2016		
1	Yu, Michael	NIH	
2	Baldomero, Olivera	HHMI, NIH,	
3	Hamidreza, Ghandehari	Department, NIH	
4	Vankayalapati, Hari	Taylor Endowment Cancer Research	
5	Hill, Christopher	NIH	
6	NuSkin	Off Campus Commercial	
7	Hung-Chieh, Chou	USTAR, Juvenile Diabetes Research	
8	University of Phillipines	Off Campus	
9	Hanson, Mike	HSC Cores DNA Peptide	
10	Yost, Christian	Department	



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- 2. Fletcher, A. J. *et al.* TRIM5 requires Ube2W to anchor Lys63-linked ubiquitin chains and restrict reverse transcription. *The EMBO Journal* **34**, 2078–2095 (2015).
- 3. Han, H. *et al.* Binding of Substrates to the Central Pore of the Vps4 ATPase Is Autoinhibited by the Microtubule Interacting and Trafficking (MIT) Domain and Activated by MIT Interacting Motifs (MIMs). *Journal of Biological Chemistry J. Biol. Chem.* **290**, 13490–13499 (2015).
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- Neti, S. S. & Poulter, C. D. Site-Selective Synthesis of 15 N- and 13 C-Enriched Flavin Mononucleotide Coenzyme Isotopologues. *The Journal of Organic Chemistry J. Org. Chem.* 81, 5087–5092 (2016).
- 6. Shen, P. S. *et al.* Rqc2p and 60S ribosomal subunits mediate mRNA-independent elongation of nascent chains. *Science* **347**, 75–78 (2015).
- 7. Vanderlinden, R. T. *et al.* Structural Basis for the Activation and Inhibition of the UCH37 Deubiquitylase. *Molecular Cell* **61**, 487 (2016).
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# **Metabolic Phenotyping**

# Overview

The Metabolic Phenotyping Facility offers several services to help investigators evaluate metabolic phenotypes in multiple model organisms. Services include mitochondrial bioenergetics (respirometry for tissue and isolated mitochondria, Seahorse XF24 and Seahorse XFe96 for cells, isolated mitochondria and tissue slices), determination of whole animal energy expenditure using the Columbus Instruments Oxymax Lab Animal Monitoring System, determination of body composition by NMR and determination of circulating metabolite and hormone concentrations using the multiplexing technology (MAGPIX and Luminex 200). The facility also offers services on more complex projects that require detailed in vivo metabolic phenotyping such as glucose and insulin tolerance tests and glucose clamps. In addition, the facility offers protocol consultation and data analysis as needed.

# Services

- Mitochondrial Bioenergetics
- Metabolic chambers
- NMR
- Biomarker quantification with the Luminex MAGPIX and Luminex 200
- Multiplex assays
- Glucose and insulin tolerance tests
- Euglycemic-hyperinsulinemic clamps

# Equipment

- Seahorse Flux Analyzer XF24
- Seahorse Flux Analyzer XF<sup>e</sup>96
- Eight Columbus Instruments metabolic chambers equipped with temperature-controlled enclosure.
- NMR
- Luminex MAGPIX
- Luminex 200 System

## Personnel

- Sihem Boudina, Ph.D., Interim Director
- Yonghwan Han, Ph.D., Research Associate
- Adriana Vieira de Abreu, Ph.D., Lab. Specialist

# 2016 Annual Update

## Equipment

• Seahorse XF<sup>e</sup>96 that can analyze up to 92 samples.

## **New Services**

- 96 well Seahorse energy metabolism experiments
- Glucose clamps on mice



# Revenue/Expenses

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FY16 Expenses: Total \$146,096

FY16 Revenue: Total \$226,567

- VP of Health Sciences Support: \$75,000
  - VP of Research Support (RIF): \$99,250 (for Seahorse system)
- FY16 revenue generated from services: \$52,317



\* Legend displays total annual revenue by year earned.

# **Advisory Board Committee**

Last meeting date: January, 2016.

- Jared Rutter, Professor, Biochemistry
- Carl Thummel, Professor, Human Genetics
- Simon J. Fisher, Professor, Internal Medicine
- Timothy E. Graham, Associate Professor, Internal Medicine

# Addendum

Faculty Oversight Committee Guidelines can be found for all cores at the following link: <u>http://cores.utah.edu/wp-content/uploads/2015/09/Faculty-Advisory-Committee-Responsibilities-2.pdf</u>







Top Users				
1	Thunder, Jalili	Albion Laboratories		
2	Drummond, Micah	NIH, Orthopaedic Trauma Association		
3	Rutter, Jared	Department, HHMI, Treadway Foundation		
4	Boudina, Sihem	NIH		
5	Villanueva, Claudio	NSF, Department, NIH		
6	Kardon, Gabrielle	NIH, Department, March of Dimes		
7	Grossman, Douglas	Department		
8	Tantin, Dean	NIH, Department		
9	Donato, Anthony	NIH		
10	Symons, John	NIH, Center on Aging, Washington University St. Louis		

# **Publications**

- 1. Haller, J. M. *et al.* Intraarticular Matrix Metalloproteinases and Aggrecan Degradation Are Elevated After Articular Fracture. *Clinical Orthopaedics and Related Research® Clin Orthop Relat Res* **473**, 3280–3288 (2015).
- 2. Han, Y. H. *et al.* Adipocyte-Specific Deletion of Manganese Superoxide Dismutase Protects From Diet-Induced Obesity Through Increased Mitochondrial Uncoupling and Biogenesis. *Diabetes* **65**, 2639–2651 (2016).
- 3. Koepke, S. J., Watkins, J. J. & Minteer, S. D. Understanding the Role of Mitochondrial Health in the Mechanism of Mitochondrial Bioelectrocatalysis. *Journal of The Electrochemical Society J. Electrochem. Soc.* **163**, 292-298 (2016).



# **Metabolomics Facility**

## Overview

The Metabolomics facility provides analysis of metabolites found within a tissue, biological fluid, whole organism, culture, or other biological source. Currently metabolomics is a comparative science; the facility usually analyzes the differences found between biological samples that have been subjected to a treatment. This can be a genetic mutation, drug treatment, etc. Most analyses are relative; therefore the facility can only make judgments on individual metabolites such as comparing the relative amounts of succinate between a mutant and a wild type but not compare the levels of succinate and fumarate within the same group or between groups. No one method is fully capable of completely profiling the metabolome. To maximize the number of metabolites observed, the facility is equipped with three chemical analysis platforms, GC-MS, LC-MS, and NMR.

# Services

The primary mission of the facility is the metabolomics profiling of biological samples including serum, urine, tissues, *Drosophila*, *C. elegans*, yeast, and bacteria. The following metabolites can be analyzed from many biochemical pathways:

- Amino acids
- TCA cycle intermediates
- Organic acids including lactic acid and pyruvate
- Carbohydrates
- Nucleotides
- Lipids including sterols
- Di and tri peptides including glutathione
- Full lipid profiling by LC-MS
- Stable isotope label flux analysis by GC-MS

The facility processes every sample using two distinct but overlapping procedures, a targeted analysis and a non-targeted analysis. The targeted analysis is used to search every chromatogram for known metabolites. The non-targeted analysis uses data mining software to detect chromatographic peaks that are altered in two different conditions. This procedure is done with Principle Components Analysis (PCA) and Partial Least Squares-Discriminate Analysis (PLS-DA).

# Equipment

# **Chemical Analysis Platforms**

- Waters GCT Premier gas chromatograph-mass spectrometer (GC-MS)
- Agilent 5973 gas chromatograph-quadrupole mass spectrometer (GC-MS)
- Agilent 6530 Ultrapressure liquid chromatograph-quadrupole time of flight massspectrometer (UPLC-QTOF-MS)
- Agilent 6550 Ultrapressure liquid chromatograph-quadrupole time of flight massspectrometer (UPLC-QTOF-MS)
- Agilent 6490 Triple quadrupole UPLC-MS for the targeted quantification of metabolites, lipids and peptides.
- Varian 500 MHz NMR with data processed by the Chenomx software suite



# **New Equipment**

- New! Agilent 7200 gas chromatograph-quadrupole time of flight mass spectrometer (GC-QTOF) purchased through a NIH S10 (J. Cox, PI).
- New! Agilent 7900 inductively coupled plasma mass spectrometer (ICP-MS) for the quantification of metals.

# Personnel

- James Cox, Ph.D., Director
- Ren Miao, Ph.D., Laboratory Technician
- Alan Maschek, Ph.D., Research Associate

# 2016 Annual Update

# New Satellite Laboratory

 A satellite core has been opened in the Eccles Institute of Human Genetics room 2400. This facility houses the Agilent 6490 QQQ-UPLC-MS, the Agilent 7200 GC-QTOF, and the Agilent 7200 ICP-MS.

# Revenue/Expenses

# FY16 Expenses: Total \$332,681

FY16 Revenue: Total \$373,742

- VP of Health Sciences Support : \$240,000
- FY16 revenue generated from services: \$133,742



\* Legend displays total annual revenue by year earned.

# **Advisory Board Committee**

Last meeting date: February 03, 2015.

- Dennis Winge, Professor, Hematology
- Carl Thummel, Professor, Department of Human Genetics
- Eric Schmidt, Professor, Medicinal Chemistry
- Jared Rutter, Professor, Biochemistry







Top Users				
1	University of South Florida	Off Campus Academic		
2	Rutter, Jared	Department, HHMI, Treadway Foundation		
3	Villanueva, Claudio	NSF, Department, NIH		
4	Utah State University	Off Campus Academic		
5	Hughes, Adam	Department		
6	Weyrich, Andy	NIH		
7	Drummond, Micah	NIH, Orthopaedic Trauma Assoc.		
8	Winter, Jaclyn	Department, University of Washington		
9	University of Iowa	Off Campus Academic		
10	Brigham Young University	Off Campus Academic		

# **Publications**

- Gray, L. R. *et al.* Hepatic Mitochondrial Pyruvate Carrier 1 Is Required for Efficient Regulation of Gluconeogenesis and Whole-Body Glucose Homeostasis. *Cell Metabolism* 22, 669–681 (2015). NIHMSID: NIHMS713478. PMCID: PMC475467.
- Hibbs, J. B., Vavrin, Z. & Cox, J. E. Complex coordinated extracellular metabolism: Acid phosphatases activate diluted human leukocyte proteins to generate energy flow as NADPH from purine nucleotide ribose. *Redox Biology* 8, 271–284 (2016). PMCID: PMC4761651.
- Nam, H. *et al.* Synergistic Inhibitory Effects of Hypoxia and Iron Deficiency on Hepatic Glucose Response in Mouse Liver. *Diabetes* 65, 1521–1533 (2016). PMCID: PMC4878425.
- Tianero, M. D. *et al.* Metabolic model for diversity-generating biosynthesis. *Proceedings* of the National Academy of Sciences Proc Natl Acad Sci USA **113**, 1772–1777 (2016). PMCID: PMC4763782.



# Mutation Generation & Detection Facility

# Overview

The Mutation Generation & Detection (MGD) Core Facility specializes in providing customized Engineered DNA Nucleases in either the TALEN or CRISPR-Cas9 formats. These DNA Nucleases are cutting edge technologies used to perform targeted genomic engineering that modifies a specific genomic region of interest. The system works in multiple model systems, including *D. rerio*, *D. melanogaster*, *C. elegans*, *P. falciparum*, *S. cerevisiae*, *T. castaneum*, mammalian cell lines, *A. aegypti*, and *M. Musculus*. The MGD Core also offers services to identify induced genomic modification using High Resolution Melt Analysis (HRMA). Our support includes hardware, reagents, and expert advice for optimizing and performing HRMA. Beyond these two main services the MGD Core has a partnership with the Mouse Transgenic Facility to create engineered mouse models using CRISPR DNA Nucleases, provides custom HRMA genotyping services, custom CRISPR validation services, and custom donor molecule services. To date the MGD Core has helped further the research of over 100 different laboratories around the world by providing more than 525 unique TALEN and CRISPR reagents.

# Main Services

# **TALEN Services**

- TALEN plasmid pair design and construction
- 2X TALEN plasmid pair design and construction (same gene)
- 0.5X TALEN effector plasmid design and construction
- Different Destination Vector

# **Crispr Services**

- 1X CRISPR design and construction
- 2X CRISPR design and construction (same gene)

# **High Resolution Melt Analysis**

- BioFire LightScanner Access Fee
- HRMA PCR plates (10 pack)
- HRMA PCR sealing film (10 pack)
- BioFire LightScanner MasterMix 100 rxns
- BioFire LightScanner MasterMix 500 rxns
- Mineral Oil (500ml bottle)
- HRMA Training
- Help with optimization and analysis of HRMA assays
- Custom Mutation Detection upon request

# Additional Services

- Mouse Transgenic Injection (partnership with Mouse Transgenic Facility)
- Blastocyst Validation of CRISPR reagents (partnership with Mouse Transgenic Facility)
- ssDNA donor design and production
- dsDNA donor design and production
- Custom HRMA genotyping in D. rerio, D. melanogaster, and mouse embryos
- Production of transgenic *D. rerio* using CRISPR reagents



# Equipment

- BioFire LightScanner
- 3X Eppendorf Mastercycler ProS
- Eppendorf Centrifuge 5430
- 27" Apple iMac Desktop with QWC Mercury Elite-Al Pro External Hard drive
- Illumina Eco
- Innova 43 bacterial Shaker
- Innova 42 bacterial Shaker
- Frigidaire -20°C Freezer
- 2X Eppendorf 5424 Microcentrifuges
  - Lonza 4D Nucleofector system:
  - 4D-Nucleofector Core Unit
    - 4D-Nucleofector X Unit
  - 4D-Nucleofector Y Unit
  - 4D-Nucleofector 96-well Shuttle
  - CCI Biological Safety Cabinet

# Personnel

• Timothy Dahlem, Ph.D., Director

# 2016 Annual Update

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# **New Equipment**

- Lonza 4D Nucleofector system
  - 4D-Nucleofector Core Unit
  - 4D-Nucleofector X Unit
  - 4D-Nucleofector Y Unit
  - 4D-Nucleofector 96-well Shuttle
- CCI Biological Safety Cabinet

# **New Services**

The MGD Core has not developed any entirely new services, but has instead expanded the functionality of its current services by constructing unique Crispr expression constructs.



# Revenue/Expenses

FY16 Expenses: Total \$160,609

FY16 Revenue: **Total \$191,674** 

- VP of Health Sciences Support: \$15,000
- VP of Research Support (RIF): \$40,321
- FY16 revenue generated from services: \$136,353



\* Legend displays total annual revenue by year earned.

# **Advisory Board Committee**

Last meeting date: July 23, 2014.

- David Grunwald, Department of Human Genetics (Senior Faculty Advisor)
- Dana Carroll, Department of Biochemistry
- Ryan O'Connell, Department of Pathology
- Lewis Charles Murtaugh, Department of Human Genetics

## Addendum

Faculty Oversight Committee Guidelines can be found for all cores at the following link: http://cores.utah.edu/wp-content/uploads/2015/09/Faculty-Advisory-Committee-Responsibilities-2.pdf

# FY16 Scientific Impact

**Research Support** Revenue Generated (see charts following):







# **Top Users**

1	Kundra Transgenics	Off Campus Commercial
2	Tristani-Firouzi, Martin	Treadwell Foundation, New England Research Inst., NIH
3	Science Exchange	Off Campus Commercial
4	Grunwald, David J.	Department, NIH
5	Weizmann Institute of Science	Off Campus Academic
6	Cairns, Bradley	HHMI,Department, NIH
7	Bonkowsky, Josh	NIH, Department
8	Evason, Kimberley	HCI, NIH
9	Balagurunathan, Kuberan	Virginia Commonwealth University, DHHS
10	Kardon, Gabrielle	NIH, Department, March of Dimes



# **Collaboration and Support of Other HSC and University Facilities**

The MGD Core has partnered directly with Dr. Ryan O'Connell on the production of custom Crispr reagents for his lab. As part of this collaboration Dr. O'Connell has covered 10% of the Core's salary requirements for the first six months of FY'16 and 5% of the Core's salary requirements for the last six months of FY'16

# **DNA Sequencing Facility**

The MGD Core spent \$6,557.00 with the DNA Sequencing Core in FY15.

# **DNA Peptide Facility**

The MGD Core spent \$12,062.82 with the DNA/Peptide Synthesis Core in FY15. The MGD Core has also partnered with the DNA Peptide Facility in helping to test the quality control of new services the DNA Peptide Facility was developing in FY'16

# Mouse Transgenic Facility

The MGD Core's partnership with the Mouse Transgenic Facility to produce transgenic mouse models has directly brought in 41 different projects to the Mouse Transgenic Facility totaling at least \$103,300 in chargebacks for that facility. All of these projects were initiated in the MGD Facility.

Total charge back impact of the MGD Core on other University facilities: \$121,919.82

# Non-billable Invoice Hours

One of the central purposes of the MGD Facility is to be a resource of education for researchers on the University of Utah campus. The MGD Core achieves this aim in official ways such as seminars given directly to different departments on campus. However, the central avenue of education by the facility is informal one-on-one, in person communication with researchers. In the past the MGD Core has tracked these interactions, but due to the number and randomness of these interactions for FY'16 the MGD Core stopped tracking them. Based on previous numbers the MGD Core estimates that it spends around 250 hours per year in direct interaction with researchers.

# **Grant Applications**

Known awarded, submitted, or in preparation grant applications mentioning MGD Facility as a crucial resource:

# 1. Grant type: K08

PD/PI: Dr. Russell Butterfield Grant Title: Genetic control of phenotypic variability in collagen VI related muscular dystrophies Funding Source: NIH Grant Award Number: 1K08NS097631-01 Total Project Period: 5 years Total Amount: \$972,810.00 *Funded* 

# 2. Grant type: K99/R00

PD/PI: Dr. Paul Bonthuis Grant Title: Genomic imprinting in circuits for social behavior Funding Source: NIH/NIMH



## Grant Award Number: KMH111912A Total Project Period: 9/01/2016-8/31/2021 Total Amount: \$919,897 *Scored*

# 3. Grant type: RO1

PD/PI: Dr. Julie Hollien Grant Title: Lysosome regulation by the unfolded protein response Funding Source: NIH Grant Award Number: R01GM123004 Total Project Period: 5 years Total Amount: \$1,217,250 *Under Review* 

# 4. Grant type: R01

PD/PI: Dr. Dean Tantin Grant Title: Developmental gene poising by Oct transcription factors Funding Source: NIH/NIGMS Grant Award Number: 1R01GM122778-01 Total Project Period: 12/2016-11/2021 Total Amount: \$1,125,000 Under Review

# 5. Grant type: R21

PD/PI: Dr. Robby Bowles Grant Title: Genetically Engineered Cell/Biomaterial Systems Using CRISPR Gene Editing and SELP Recombinant Polymers for Treatment of Intervertebral Disc Pathology Funding Source: NIH Grant Award Number: DUNS 009095365 Total Project Period: 04/01/2016-03/31/2018 Amount: \$409,750.00 *Not granted* 

# 6. Grant type: RO1

PD/PI: Corrine Welt Grant Title: The Genetics of Polycystic Ovary Syndrome Funding Source: NIH/NICKD Grant Award Number: 2 R01 HD065029-06A1 *Not granted* 

# 7. Grant type: R01

PD/PI: Dr. Josh Bonkowsky Grant Title: Mechanisms of Dopamine in Neuromotor Development Funding Source: NIH Grant Award Number: review pending Total Project Period: 04/01/17-03/31/22 Total Amount: \$1,902,816.00 *Review pending* 



8. Grant type:	1 R43 OD023027-01 PD/PI: Dr. Raheel Samuel and Dr. Josh Bonkowsky Grant Title: Microfluidic devices for early (less than 48 hpf), non-destructive zebrafish genotyping Funding Source: NIH/NCATS Grant Award Number: funded- grant award number expected mid-July Total Project Period: 08/01/16-02/28/17 Total Amount: \$225,000 <i>Funded</i>
9. Grant type:	IOS EDGE track PD/PI: Dr. Colleen Farmer Grant Title: Transgressive Interrogation of Reptilian Genomes/Phenomes using CRISPR-Cas9 Funding Source: NSF Grant Award Number: DUNs 009095365 Total Project Period: 01/01/17-01/01/20 Total Amount: \$1,440,064 Submitted
10. Grant type:	Cooperative Hematology Specialized Core Centers PD/PI: Dr. John Phillips Grant Title: Center for Iron and Heme Disorders (CIHD) Funding Source: NIH/ NIDDK Grant Award Number: 1 U54 DK110858-01 Total Project Period: 07/01/2016-06/30/21 Total Amount: \$4,115,741 <i>Funded</i>
11. Grant type:	PD/PI: Dr. Esther Betran and Dr. Cedric Freschotte Grant Title: Collaborative Research: Domesticated transposons as a source of new regulatory proteins in Drosophila Funding Source: NSF-MCB- GENES AND GENOMES SYSTEMS Grant Award Number: Pending final decision after submitting subproject breakdown Total Project Period: 07/01/2016-06/30/2019 Total Amount: \$946,250 <b>Submitted</b>
Letters of Support Written and pro 1. LOS for Dr. J Developmen 2. LOS for Dr. F "Microfluidic 3. LOS for Dr. F 4. LOS for Dr. F	ovided to faculty for support of grant applications: Josh Bonkowsky RO1 proposal "Mechanisms of Dopamine in Neuromotor t" Raheel Samuel, Dr. Bruce Gale and Dr. Josh Bonkowsky's proposal devices for early (less than 48 hpf), non-destructive zebrafish genotyping" Paul Bonthuis proposal "Genomic imprinting in circuits of social behavior" Robby Bowles R21 proposal "Genetically Engineered Cell/Biomaterial

Systems Using CRISPR Gene Editing and SELP Recombinant Polymers for Treatment of Intervertebral Disc Pathology"



- 5. LOS for Dr. Russell Butterfield's KO8 proposal "Geneticcontrol of phenotypic variability in collagen VI related muscular dystrophies"
- LOS for Dr. Esther Betran and Dr. Cedric Freschotte's proposal "Collaborative Research: Domesticated transposons as a source of new regulatory proteins in Drosophila"
- 7. Two LOS for the company Progenitor's SBI application
- 8. LOS for Dr. Doug Grossman's R21 proposal "p16 mechanisms in melanoma"
- 9. LOS for Dr. Julie Hollien's RO1 proposal "Lysosome regulation by the unfolded protein response."
- 10. LOS for Dr. Matt Mulvey's RO1 proposal
- 11. LOS for Dr. Francis Miller's proposal "Regulation of the Nox1 NADPH Oxidase in Vascular Smooth Muscle Cells"
- 12. LOS for Dr. Ellen Pritham's NSF proposal "Transposable elements and regulatory innovation"
- 13. LOS for Dr. Dean Tantin's R01 application "Developmental gene poising by Oct transcription factors."
- 14. LOS for Dr. Corrine Welt's RO1 proposal "The Genetics of Polycystic Ovary Syndrome"
- 15. LOS for Dr. Young-Wook Won's BCRP application: "Genome Editing to Express HER2 in Triple Negative Breast Cancer using CRISPR/Cas9".

# **Publications**

- 1. Hoshijima, Kazuyuki *et al.* Precise Editing of the Zebrafish Genome Made Simple and Efficient. *Developmental Cell* **36**, 654-667 (2016).
- Isaacman-Beck, J., Schneider, V., Franzini-Armstrong, C. & Granato, M. The Ih3 Glycosyltransferase Directs Target-Selective Peripheral Nerve Regeneration. *Neuron* 88, 691–703 (2015).
- 3. Rahn, J. J., Bestman, J. E., Stackley, K. D. & Chan, S. S. Zebrafish lacking functional DNA polymerase gamma survive to juvenile stage, despite rapid and sustained mitochondrial DNA depletion, altered energetics and growth. *Nucleic Acids Res Nucleic Acids Research* (2015). doi:10.1093/nar/gkv1139.
- Remédio, L. *et al.* Diverging roles for Lrp4 and Wnt signaling in neuromuscular synapse development during evolution. *Genes & Development Genes Dev.* **30**, 1058–1069 (2016). doi:10.1101/gad.279745.116.
- 5. Wallace, J. *et al.* Genome-Wide CRISPR-Cas9 Screen Identifies MicroRNAs That Regulate Myeloid Leukemia Cell Growth. *PLOS ONE PLoS ONE* **11**, (2016). doi:10.1371/journal.pone.0153689.



# Nuclear Magnetic Resonance Core Facility

# Overview

This NMR core facility offers services, expertise, and collaboration for the research community at the University of Utah, other Utah academic institutions, and for-profit companies. Our staff is extremely helpful and has significant experience in characterizing small molecules, natural products, nucleic acids, carbohydrates, and proteins using NMR. Our preferred business model is for users to become skilled and independent users of the NMR facility. We train new users, or help experienced but out-of-practice users to brush up their skills, with the goal of user independence. On a limited basis, we will also record and analyze NMR data for a staff service charge.

We provide convenient access to five high field NMR spectrometers (400, 500, 600, 800, and 900 MHz instruments; see Equipment below) located on the University of Utah Health Sciences campus and the University of Colorado-Boulder and -Denver campuses. The 600, 800, and 900 instruments are equipped with state-of-art cryogenic HCN probes that provide maximum sensitivity. The 800 and 900 are state-of-art NMR consoles while the 400, 500, and 600 are older but still fully capable for all NMR requirements. The facility has several Linux workstations and a considerable number of implemented NMR software programs (member of SBGrid; www.sbgrid.org) for data processing, data analysis, and structure calculation.

# Services

- NMR data collection and analysis with or without staff collaboration
- NMR training for individuals and groups
- Formal courses in NMR spectroscopy

# Equipment

- Varian Mercury 400 MHz NMR (University of Utah, SK H)
- Varian Inova 500 MHz NMR (University of Utah, BPRB)
- Varian Inova 600 MHz NMR with HCN cryogenic probe (University of Utah, BPRB)
- DD2 800 MHz NMR with HCN cryogenic probe (University of Colorado-Boulder)
- DD2 900 MHz NMR with HCN cryogenic probe (University of Colorado-Denver)

## Personnel

- Jack Skalicky, Ph.D., NMR Core Director and Res. Associate Professor of Biochemistry
- Dennis Edwards, RF Technician; 35+ years of NMR hardware repair
- Jay Olsen, NMR Technician; 35+ years solution state NMR experience

## 2016 Annual Update

## New Equipment

- New LINUX Centos operating system for NMR workstations; VnmrJ4A software upgrade
- Rm 50 BPRB Facility (500 and 600 room) remodeled; 10 Gigabit Ethernet install

## **New Services**

• The NMR Facility did not implement additional services in FY16





# Advisory Board Committee

Last meeting date: April 2013.

- Darrell Davis, Professor, College of Pharmacy
- Wesley Sundquist, Professor, Department of Biochemistry
- Eric Schmidt, Professor, College of Pharmacy

## Addendum

Faculty Oversight Committee Guidelines can be found for all cores at the following link: http://cores.utah.edu/wp-content/uploads/2015/09/Faculty-Advisory-Committee-Responsibilities-2.pdf







# **Top Users**

2Mitra Biotech, Inc.Off Campus Commercial3Schmidt, EricNIH, Oregon Health & Science University4Poulter, C. DaleNIH, University of Illinois Champaign5Winter, JaclynDepartment, University of Washington	
3Schmidt, EricNIH, Oregon Health & Science University4Poulter, C. DaleNIH, University of Illinois Champaign5Winter, JaclynDepartment, University of Washington	
4Poulter, C. DaleNIH, University of Illinois Champaign5Winter, JaclynDepartment, University of Washington	
5 Winter, Jaclyn Department, University of Washington	
6 VioGen Biosciences Off Campus Commercial	
7 Prestwich, Glenn DHHS, Department	
8 Wang, Xuli NIH, Utah State University	
9 Balagurunathan, Kuberan Virginia Commonwealth University, DHHS	
10 Barrios, Amy NSF	



# Publications

- 1. Ashton, N. N., Pan, H. & Stewart, R. J. Connecting caddisworm silk structure and mechanical properties: combined infrared spectroscopy and mechanical analysis. *Open Biol. Open Biology* **6**, 160067 (2016).
- 2. Bergonzo, C., Hall, K. B. & Cheatham, T. E. Divalent Ion Dependent Conformational Changes in an RNA Stem-Loop Observed by Molecular Dynamics. *J. Chem. Theory Comput. Journal of Chemical Theory and Computation* **12**, 3382–3389 (2016).
- Bergonzo, C., Henriksen, N. M., Roe, D. R. & Cheatham, T. E. Highly sampled tetranucleotide and tetraloop motifs enable evaluation of common RNA force fields. *Rna* 21, 1578–1590 (2015).
- 4. Caballe, A. *et al.* ULK3 regulates cytokinetic abscission by phosphorylating ESCRT-III proteins. (2015). doi:10.2210/pdb4wzx/pdb
- Cahoon, J. M. *et al.* Intravitreal AAV2.COMP-Ang1 Prevents Neurovascular Degeneration in a Murine Model of Diabetic Retinopathy. *Diabetes* 64, 4247–4259 (2015).
- 6. Cho, H., Lee, Y. J., Bae, Y. H. & Kang, H. C. Synthetic polynucleotides as endosomolytic agents and bioenergy sources. *Journal of Controlled Release* **216**, 30–36 (2015).
- Choi, J.-W. *et al.* pH-sensitive oncolytic adenovirus hybrid targeting acidic tumor microenvironment and angiogenesis. *Journal of Controlled Release* 205, 134–143 (2015).
- Choi, J.-W. *et al.* Tuning Surface Charge and PEGylation of Biocompatible Polymers for Efficient Delivery of Nucleic Acid or Adenoviral Vector. *Bioconjugate Chem. Bioconjugate Chemistry* 26, 1818–1829 (2015).
- Choi, J.-W. *et al.* Oncolytic Adenovirus Coated with Multidegradable Bioreducible Core-Cross-Linked Polyethylenimine for Cancer Gene Therapy. *Biomacromolecules* 16, 2132–2143 (2015).
- 10. Chow, J.-Y. *et al.* Computational-guided discovery and characterization of a sesquiterpene synthase from Streptomyces clavuligerus. *Proceedings of the National Academy of Sciences Proc Natl Acad Sci USA* **112**, 5661–5666 (2015).
- Kakule, T. B. *et al.* Native Promoter Strategy for High-Yielding Synthesis and Engineering of Fungal Secondary Metabolites. *ACS Synth. Biol. ACS Synthetic Biology* 4, 625–633 (2015).
- 12. Kakule, T. B., Zhang, S., Zhan, J. & Schmidt, E. W. Biosynthesis of the Tetramic Acids Sch210971 and Sch210972. *Org. Lett. Organic Letters* **17**, 2295–2297 (2015).
- 13. Moon, C. Y. *et al.* Dual tumor targeting with pH-sensitive and bioreducible polymercomplexed oncolytic adenovirus. *Biomaterials* **41**, 53–68 (2015).
- 14. Murph, M. M. *et al.* Vinyl sulfone analogs of lysophosphatidylcholine irreversibly inhibit autotaxin and prevent angiogenesis in melanoma. *Bioorganic & Medicinal Chemistry* 23, 5999–6013 (2015).
- 15. Nam, J.-P., Nam, K., Nah, J.-W. & Kim, S. W. Evaluation of Histidylated Arginine-Grafted Bioreducible Polymer To Enhance Transfection Efficiency for Use as a Gene Carrier. *Mol. Pharmaceutics Molecular Pharmaceutics* **12**, 2352–2364 (2015).
- Neti, S. S. & Poulter, C. D. Site-Selective Synthesis of 15 N- and 13 C-Enriched Flavin Mononucleotide Coenzyme Isotopologues. *The Journal of Organic Chemistry J. Org. Chem.* 81, 5087–5092 (2016).
- 17. Ramamoorthy, G., Phan, R. M. & Poulter, C. D. Synthesis and Enzymatic Studies of Isoprenoid Thiolo Bisubstrate Analogues. *The Journal of Organic Chemistry J. Org. Chem.* **81**, 5093–5100 (2016).
- Ramamoorthy, G. *et al.* Synthesis and Enzymatic Studies of Bisubstrate Analogues for Farnesyl Diphosphate Synthase. *The Journal of Organic Chemistry J. Org. Chem.* 80, 3902–3913 (2015).



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- 20. Sardar, D., Lin, Z. & Schmidt, E. W. Modularity of RiPP Enzymes Enables Designed Synthesis of Decorated Peptides. *Chemistry & Biology* **22**, 907–916 (2015).
- Skindersoe, M. E. *et al.* Dual Action of Lysophosphatidate-Functionalised Titanium: Interactions with Human (MG63) Osteoblasts and Methicillin Resistant Staphylococcus aureus. *PLOS ONE PLoS ONE* **10**, (2015).
- 22. Thorson, M. K. *et al.* Marine natural products as inhibitors of cystathionine beta-synthase activity. *Bioorganic & Medicinal Chemistry Letters* **25**, 1064–1066 (2015).
- 23. Tianero, M. D. B. *et al.* Species specificity of symbiosis and secondary metabolism in ascidians. *The ISME Journal ISME J* **9**, 615–628 (2014).
- 24. Tianero, M. D. *et al.* Metabolic model for diversity-generating biosynthesis. *Proceedings* of the National Academy of Sciences Proc Natl Acad Sci USA **113**, 1772–1777 (2016).
- Wang, C.-S., Pan, H., Weerasekare, G. M. & Stewart, R. J. Peroxidase-catalysed interfacial adhesion of aquatic caddisworm silk. *J. R. Soc. Interface Journal of The Royal Society Interface* 12, 20150710 (2015).
- Won, Y.-W., Ankoné, M., Engbersen, J. F. J., Feijen, J. & Kim, S. W. Poly(Amido Amine)s Containing Agmatine and Butanol Side Chains as Efficient Gene Carriers. *Macromol. Biosci. Macromolecular Bioscience* 16, 619–626 (2015).
- 27. Wu, N. *et al.* Chemical Self-Doping of Organic Nanoribbons for High Conductivity and Potential Application as Chemiresistive Sensor. *ACS Appl. Mater. Interfaces ACS Applied Materials & Interfaces* **8**, 12360–12368 (2016).
- 28. Xu, M. *et al.* Fluorescence Ratiometric Sensor for Trace Vapor Detection of Hydrogen Peroxide. ACS Appl. Mater. Interfaces ACS Applied Materials & Interfaces **6**, 8708–8714 (2014).
- 29. Yin, H., Kang, H. C., Huh, K. M. & Bae, Y. H. Effects of cholesterol incorporation on the physicochemical, colloidal, and biological characteristics of pH-sensitive AB2 miktoarm polymer-based polymersomes. *Colloids and Surfaces B: Biointerfaces* **116**, 128–137 (2014).
- 30. Zhang, L., Zhang, R., Yang, J., Wang, J. & Kopeček, J. Indium-based and iodine-based labeling of HPMA copolymer–epirubicin conjugates: Impact of structure on the in vivo fate. *Journal of Controlled Release* **235**, 306–318 (2016).

UNIVERSITY OF UTAH HEALTH SCIENCES



# **Small Animal Imaging Facility**

# Overview

The Small Animal Imaging Facility extends the benefits of modern diagnostic medical imaging systems to the studies of anatomy and physiology in small animals. The facility operates an MRI scanner, FMT scanner, and a CT/SPECT/PET scanner. The scanners are equipped with supporting and monitoring hardware that allows a wide variety of imaging experiments, including longitudinal studies, to be performed on live animals and specimens. Imaging scientists, full-time imaging personnel, and animal support technicians are available for technical consultation and experimental assistance.

# Services

The Small Animal Imaging Facility has a variety of modalities to choose from such as MRI, CT, PET, SPECT, and Fluorescence imaging. Examples of scanning capabilities include the following:

# 7 Tesla small animal MRI systems

- Diffusion-weighted and diffusion tensor imaging
- Relaxometry (T1, T2, T2\*) mapping
- Perfusion MRI
- Functional and awake-state functional MRI
- MR angiography
- Cardiac MRI
- NMR spectroscopy (localized and non-localized)
- Chemical shift imaging
- Parallel imaging techniques

## **CT Scanners**

- Automatic transition between modes and seamless coordination of CT, SPECT, and PET data
- System can be configured as an ultra-high resolution preclinical CT scanner; a highresolution, high-sensitivity preclinical SPECT scanner; or as a dual modality preclinical SPECT/CT scanner
- The Inveon 2-Head SPECT Module is designed to efficiently detect gamma rays ranging in energy from 30 keV to 250 keV, the SPECT system is ideal for use with most single photon-emitting radionuclides
- Includes two Inveon Research Workplace workstations for multimodality image review, fusion, and analysis which CT, PET, SPECT, and MR data in DICOM and Siemens Inveon CT, PET, and SPECT formats, as well as raw data import

# FMT Mouse System

- 4 channel excitation with near-infrared laser diodes at 635, 670, 745, and 785 nm, maximizing tissue penetration depth and permitting multiplexed analysis of biological pathways
- System can configured as an ultra-high resolution preclinical CT scanner; a highresolution, high-sensitivity preclinical SPECT scanner; or as a dual modality preclinical SPECT/CT scanner
- The Small Animal Imaging Facility also includes an Instrument Development Lab which primarily provides infrastructure for the construction of custom RF coils. These are often necessary to optimize the data quality for a given MRI application. The



facility also houses basic machining tools (including a Milling machine) for making experimental apparatus's such as scanning platforms and stereo taxes.

## Equipment

- 7 Tesla Bruker BioSpec MRI Scanner
- Inveon Multimodality System
- VISEN (now Perkin Elmer) FMT 2500<sup>™</sup> Fluorescence Molecular Tomography

## Personnel

- Edward Hsu, Ph.D., Director
- Osama Abdullah, M.S., Imaging Specialist
- Samer Merchant, M.S., Imaging Specialist
- Adam Schmidt, Research Student
- Boston Terry, Research Student
- Keven Wang, Research Student

# 2016 Annual Update

#### **New Equipment**

No major equipment was added in FY16

## **New Services**

No major new service was added in FY16.

## **Revenue/Expenses**

# FY16 Expenses: Total \$278,749

## FY16 Revenue: **Total \$259,246**

- VP of Health Sciences Support: \$50,000
- VP of Research Support: \$100,000
- FY16 revenue generated from services: \$109,246





# Advisory Board Committee

Last meeting date: September 21, 2015.

- John Hoffman, Professor, HCI
- John Phillips, Research Associate Professor, Hematology
- Roger VanAndel, Director, Office of Comparative Medicine
- Rob MacLeod, Professor, SCI
- Dennis Parker, Professor, Radiology Research
- Jeffrey Yap, Research Associate, HCI

# Addendum

Faculty Oversight Committee Guidelines can be found for all cores at the following link: <u>http://cores.utah.edu/wp-content/uploads/2015/09/Faculty-Advisory-Committee-Responsibilities-2.pdf</u>

# FY16 Scientific Impact

**Research Support** Revenue Generated (see charts following):







# **Top Users**

1	Hsu, Ed	U of U Research, Department,
2	Holmen, Sheri	NIH, Melanoma Research Alliance, Department
3	Shiu, Yan-Ting	NIH, Department
4	Korenberg, Julie	NIH
5	Ghandehari, Hamidreza	NIH, Department
6	Brigham Young University	Off Campus Academic
7	University of California-San Francisco	Off Campus Academic
8	Bonkowsky, Josh	NIH
9	Ekstrand, Jeffrey	NIH
10	Dudek, Ed	Mass. General Hospital, US Army Research



# Publications

- Abdullah, O. M. *et al.* Orientation dependence of microcirculation-induced diffusion signal in anisotropic tissues. *Magnetic Resonance in Medicine Magn. Reson. Med.* (2015). doi:10.1002/mrm.25980
- 2. Aojula, A. *et al.* Diffusion tensor imaging with direct cytopathological validation: characterisation of decorin treatment in experimental juvenile communicating hydrocephalus. *Fluids Barriers CNS Fluids and Barriers of the CNS* **13**, (2016).
- 3. Bogdanov, V. B. *et al.* Susceptibility of Primary Sensory Cortex to Spreading Depolarizations. *Journal of Neuroscience* **36**, 4733–4743 (2016).
- Gignac, P. M. et al. Diffusible iodine-based contrast-enhanced computed tomography (diceCT): an emerging tool for rapid, high-resolution, 3-D imaging of metazoan soft tissues. J. Anat. Journal of Anatomy 228, 889–909 (2016)..
- 5. Gomez, A. D., Bull, D. A. & Hsu, E. W. Finite-Element Extrapolation of Myocardial Structure Alterations Across the Cardiac Cycle in Rats. *Journal of Biomechanical Engineering J Biomech Eng* **137**, 101010 (2015).
- 6. Mckellar, S. H. *et al.* Animal model of reversible, right ventricular failure. *Journal of Surgical Research* **194**, 327–333 (2015)..
- 7. Merchant, S. S., Gomez, A. D., Morgan, J. L. & Hsu, E. W. Parametric Modeling of the Mouse Left Ventricular Myocardial Fiber Structure. *Annals of Biomedical Engineering Ann Biomed Eng* **44**, 2661–2673 (2016).
- Merchant, S. S., Kosaka, Y., Yost, H. J., Hsu, E. W. & Brunelli, L. Micro-Computed Tomography for the Quantitative 3-Dimensional Assessment of the Compact Myocardium in the Mouse Embryo. *Circulation Journal Circ J* 80, 1795–1803 (2016).
- Welsh, C. L., Dibella, E. V. R. & Hsu, E. W. Higher-Order Motion-Compensation for In Vivo Cardiac Diffusion Tensor Imaging in Rats. *IEEE Transactions on Medical Imaging IEEE Trans. Med. Imaging* 34, 1843–1853 (2015).
- 10. Winters, A. A. *et al.* Evaluation of Multiple Biological Therapies for Ischemic Cardiac Disease. *Cell Transplantation cell transplant* **25**, 1591–1607 (2016).
- Sun, C.-Y. *et al.* Quantitative representation and description of intravoxel fiber complexity in HARDI. *Physics in Medicine and Biology Phys. Med. Biol.* **60**, 8417–8436 (2015).
- 12. Sun, C.-Y. *et al.* Assessment of the Characteristics of Orientation Distribution Functions in HARDI Using Morphological Metrics. *PLOS ONE PLoS ONE* **11**, (2016).

UNIVERSITY OF UTAH HEALTH SCIENCES



# **Small Animal Ultrasound Facility**

# Overview

The Small Animal Ultrasound Facility has two state-of-the-art VisualSonics 2100 ultrasound machines capable of imaging mice, rats, and other animal models with excellent spatial and temporal resolution. The facility has probes that cover the spectrum from 9-70 MHz (standard human clinical ultrasound covers the spectrum from 2.5-12 MHz). These machines are capable of real-time 2D imaging as well as a full spectrum of Doppler techniques (pulsedwave, color, tissue, power). One of the two machines is also capable of 3D imaging and contrast imaging (both targeted and non-targeted). Software is available for advanced image analysis of cardiac mechanics with speckle tracking that allows analysis of strain and strain rate. These tools allow near histologic resolution imaging of live animals, and are well suited to challenging applications such as the resolving the rapid heart rates of mice, or the microscopic size and function of early and mid-gestation embryos, and everything in between. The facility has long been an extremely important tool in the practice of clinical medicine because it offers real-time imaging providing understanding of anatomy and physiology, is non-invasive, and can be repeated serially.

## Services

The facility has the capability for anesthesia and monitoring of mice and rats, and will support training laboratory personnel in the design of protocols and the use of the equipment for acquiring images. An off-line image analysis station is also available for later review and analysis of studies.

- Ultrasound imaging access
- Training in use of equipment
- Experiment design and assistance with protocol optimization
- Off-line image review and analysis

## Equipment

- Two VisualSonics 2100 ultrasound machines
- Off-line image analysis station and network storage for backing-up data files

# Personnel

- Kevin Whitehead, M.D., Director
- Kandis Carter, Laboratory Technician
- Tiehua Chen, Laboratory Technician









# **Publications**

1. Terry, C. M., *et al.* Rivaroxaban improves patency and decreases inflammation in a mouse model of catheter thrombosis. *Thrombosis Research* **144**, 106–112 (2016).

UNIVERSITY OF UTAH HEALTH SCIENCES



# Service Recharge Centers







# **Nuclear Engineering**

## Overview

UNEP provides equipment and services used for alpha, beta, gamma and neutron radiation detection, irradiation of material samples to study various effects of various types of radiation, and neutron activation analysis techniques (nondestructive technique to find a sample elemental composition). UNEP maintains a 7,500 sq. ft. nuclear engineering and radiochemistry facility, including a fully operable 100 kW TRIGA Mark-1 nuclear reactor, 3 High Purity Germanium (HPGe) gamma detectors, liquid scintillation counting, and alpha spectrometry.

# Uniqueness

The Utah Nuclear Engineering Facility is the only nuclear research reactor in the State of Utah, and one of the few in the Intermountain West area. We offer a number of unique, nondestructive testing techniques for analyzing chemical composition of a wide variety of samples. UNEP has been at the forefront of establishing safety culture and practices, already implemented at large scale commercial power plants, in a research reactor environment. UNEP also allows students from the University of Utah, as well as other local universities, to train for and obtain a Reactor Operator (RO) license from the Nuclear Regulatory Commission (NRC).

## Services

The types of services offered by UNEP include material characterization by chemical composition analysis and radiation resistance of samples placed in high radiation environments. Example services are as follows:

- Neutron Activation Analysis (NAA)
- TCA cycle intermediates
- Passive gamma spectroscopy
- Alpha spectroscopy
- Nucleotides
- Liquid scintillation counting

Because of the uniqueness and lack of familiarity that often encompasses a research reactor an important aspect of our work is consulting with researchers and PIs at the early stages of their research in order to establish an efficient and cost effective plan with utilizing our TRIGA reactor and wide variety of radiation detectors.

## Equipment

# **Radiation Detectors:**

- Canberra Alpha Analyst
- Canberra HPGe detectors
  - BEGe 3830
  - REGe 4020
  - GC 4020
- Beckman Liquid Scintillation Counter
- TRIGA Research Reactor

## Personnel

- Ryan Schow, Reactor Supervisor
- Michael Allred, Reactor Technician
- Nicholas Kanno, Laboratory Analyst/Planner




\* Legend displays total annual revenue by year earned.

# Advisory Board Committee

Last meeting date: April 22, 2016

- Jim Byrne, Reactor Safety Committee Chair
- Terry Ring, Professor, Chemical Engineering
- Greg Moffitt, Former Reactor Supervisor

# Addendum

Faculty Oversight Committee Guidelines can be found for all cores at the following link: <u>http://cores.utah.edu/wp-content/uploads/2015/09/Faculty-Advisory-Committee-Responsibilities-2.pdf</u>

# Goals for FY17

- Characterize and begin utilizing pneumatic irradiator
- Alpha spectrometry
- More consistent user base
- Reactor Operator training classes for UU and BYU students
- Possible labs/classes with outside entities

#### Publications

No known publications acknowledged this facility in FY16.



# **Scalable Analytics & Informatics**

#### Overview

The University of Utah Center for Scalable Analytics and Informatics (USAI) provides support to research and operations groups inside and outside the University of Utah. These services include Annotation and Chart Review, Natural Language Processing, EMR-driven Clinical Trial Recruitment, Analytics and Data Services, and Enterprise Architecture and Application Development.

#### Uniqueness

Utah Scalable Analytics and Informatics provides multiple services for researchers utilizing electronic medical records. EMR-driven Clinical Trial Recruitment provides the ability to identify patients during an encounter with a healthcare provider that potentially could participate in a clinical trial and could drastically reduce cost and increase recruitment. Annotation products help machines and humans mark-up data for classification. Natural Language Processing (NLP) processes test data to extract structured data to infer concepts that can be understood by machines and humans for further analysis. USAI's annotation product line focuses on easing the burden and increasing consistency of manual chart review and annotation tasks. While annotation and chart review are time consuming and expensive, they are vital to many part of the research process: data exploration, feasibility, defining study variables, identifying information in text notes, classifying information within a document, at the document level, at the encounter or patient level, and validating study results. USAI provides Enterprise Architecture and Application Development and has developed annotation tools to support Natural Language Processing, which improves outcomes in health services research and reduces the costs to the researcher. Education is also important to USAI and therefore USAI has recruited and trained computer science students.

#### Services

The following services are offered by USAI:

- Annotation and Chart Review
- Natural Language Processing
- EMR-driven Clinical Trial Recruitment
- Analytics and Data Services
- Enterprise Architecture and Application Development

Consultation is provided in order to define a projects scope and budget in the early stages of development to make optimal and efficient use of USAI's services. The staff will also handle regulatory requirements and project management if needed.

# Specialized Software

# **Chart Review**

- eHOST
- ChartReview

#### **Natural Language Processing**

- Leo
- Chex











Top Users		
1	IHC Health Services	Off Campus Commercial
2	Anolinx	Off Campus Commercial
3	Chapman, Wendy	NIH, DHHS, Northern California Institute

# Goals for FY17

USAI will continue to offer and expand its services to University and Industry members in health sciences research by providing EMR-driven patient trial recruitment, annotation and chart review, natural language processing, enterprise architecture and application development and data analysis. USAI will also continue to expand its industry members with its partnership with the Center for Hybrid Multicore Productivity and the National Science Foundation's Industry/University Cooperative Research Centers. To meet increasing demand of USAI's services, the team has brought on board several new staff members to include research health science specialists, program managers, data managers and administrative support.

# Publications

- 1. Alba PR, *et al.* Knowledge Base Acquisition For Rare Concepts Using Manual Bootstrapping. Poster session presented at *American Medical Informatics Association Annual Symposium*, San Francisco, CA. (2015).
- 2. Bress A, *et al.* Canadian Cardiovascular Society (CCS) Angina Classification Extracted from Clinical Notes by Natural Language Processing: Validation and Association with Healthcare Utilization in an Integrated Health Delivery System. *ESC Congress*, Rome, Italy, (2016).
- 3. Lynch KE, *et al.* The Impact of Formulary Changes on Corticosteroid and Long-Acting-Beta-Agonist Prescription Practices for COPD Patients within the Department of Veterans Affairs, 2007-2014. *International Conference on Pharmacoepidemiology & Therapeutic Risk Management.* Dublin Ireland, (2016).
- 4. Lynch KE, *et al.* Prevalence and Factors Associated with Prescription of Overlapping Monotherapy Inhalers of Corticosteroids and Long-Acting Beta-Agonists among US Veterans. *Conference on Pharmacoepidemiology & Therapeutic Risk Management.* Dublin, Ireland, (2016).
- 5. Nelson, R. E. *et al.* Multiple Sclerosis and Risk of Infection-Related Hospitalization and Death in US Veterans. *International Journal of MS Care* **17**, 221–230 (2015).
- 6. Patterson OV, et al. Extraction of Vital Signs from Clinical Notes. Studies in Health Technology and Informatics, **216** 1035, (2015). PMID: 26262334.
- Patterson OV, et al. Classifying the Indication for Colonoscopy Procedures: A Comparison of NLP Approaches in a Diverse National Healthcare System. Studies in Health Technology and Informatics, 216 614-8. (2015).
- 8. Patterson OV, *et al.* Building custom lexicon for a large number of related concepts using templates. Poster session presented at American Medical Informatics Association Annual Symposium, San Francisco, CA, (2015).
- Pattison, E. *et al.* Mp31-14 Leveraging Bladder Cancer Pathology Reports For Research: Gleaning Meaning Despite Widely Variable Language. *The Journal of Urology* **195**, (2016).
- 10. Schroeck, F. *et al.* Mp13-13 Surveillance For Bladder Cancer Patients Do Pathology Reports Tell Us What We Need To Know? *The Journal of Urology* **195**, (2016).