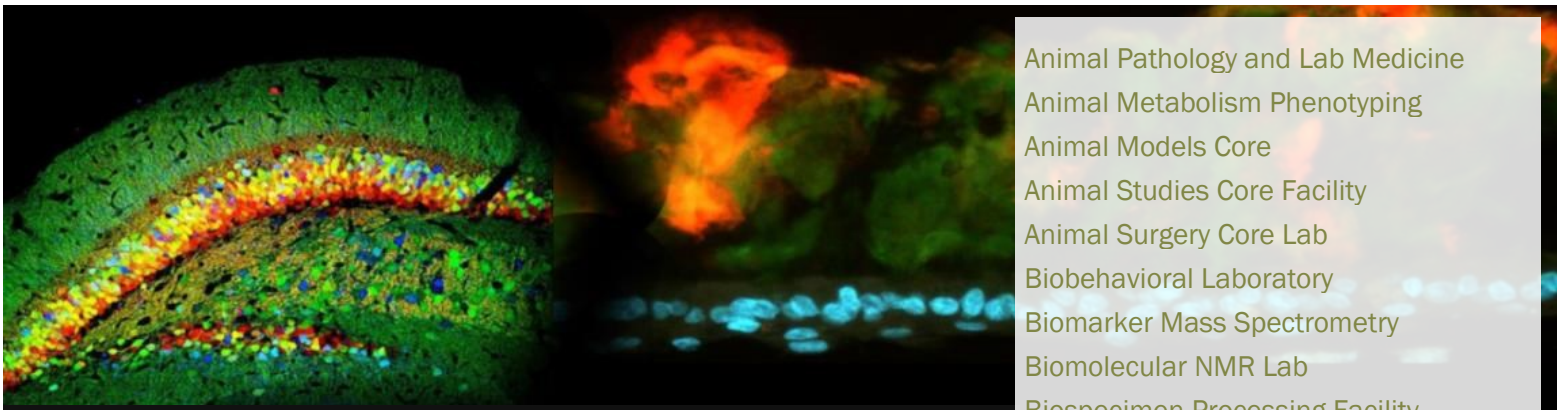

CORE FACILITIES at UNC *Summer | 2018*

Research Cores Newsletter

FROM THE OFFICE OF RESEARCH TECHNOLOGIES

Creating a Culture of Collaboration and Excellence

Many factors drive scientific progress, including constant advances in technology and team-oriented science that requires pooling of knowledge and resources. Democratization of the research support infrastructure through core facilities enhances access to sophisticated and expensive equipment that would otherwise be cost-prohibitive to individual laboratories or departments. UNC cores have a strong reputation for technical expertise, useful service offerings and collaboration, and the Office of Research Technologies (ORT) and the Core Facilities Advocacy Committee (CFAC) are focused on supporting the cores and ensuring growth into the future.

To this end, ORT and CFAC would like to encourage core users to partner with core directors and managers to develop new methods and services that can be offered to all investigators. This fall and spring, pilot project funds will be made available from CFAC through an RFA mechanism, specifically targeted to fund projects submitted by user/core partnerships, and may include new equipment if required for method development.

As we work to ensure that our research core facilities are technologically-advanced, we depend on our user base to partner with our core staff and leaders to drive scientific progress. Thanks for your continued utilization of UNC core labs and please contact ORT with feedback or ideas for new core services.

UNC SCHOOL OF MEDICINE

UNC THE NORTH CAROLINA TRANSLATIONAL & CLINICAL SCIENCES INSTITUTE

Visit the Core Facilities website

Office of Research Technologies
corefacilities@med.unc.edu

For more information on UNC Cores and the Office of Research Technologies, please visit:
www.med.unc.edu/corefacilities

Animal Pathology and Lab Medicine
Animal Metabolism Phenotyping
Animal Models Core
Animal Studies Core Facility
Animal Surgery Core Lab
Biobehavioral Laboratory
Biomarker Mass Spectrometry
Biomolecular NMR Lab
Biospecimen Processing Facility
BRIC Human Imaging
BRIC Small Animal Imaging
Center for BioInformatics
CFAR HIV/STD Laboratory
CGIBD Advanced Analytics
CH Analytical & Nanofabrication Lab
Chemistry Mass Spectrometry
Neuroscience Ctr. Microscopy Core
Cytokine Analysis Facility
Flow Cytometry Core Facility
Functional Genomics Core
High Throughput Genomic Sequencing
High Throughput Peptide Library Arrays
Histology Research Core Facility
Hooker Imaging Core
Human Pluripotent Stem Cell Fac.
Lenti-shRNA Core Facility
Macromolecular Crystallography
Macromolecular Interactions Fac.
Mammalian Genotyping Core
MH Proteomics Center
Microscopy Services Laboratory
Mouse Behavioral Phenotyping
Nanomedicines Characterization
RL Juliano Structural BioInformatics
Systems Genetics Core
Tissue Culture Facility
Tissue Procurement Facility
Translational Pathology Lab.
UNC CFAR Clinical Pharmacology
UNC Microbiome Core Facility
UNC RNAi Screening Fac
Vector Core
Vironomics Core
Zebrafish Aquaculture Core

CORE HIGHLIGHT

HPSSC: Developing Organoids for Basic and Translational Research

The Human Pluripotent Stem Cell Core (HPSSC) was awarded a method development grant from the Core Facilities Advocacy Committee (CFAC) to generate and standardize organoid methods using stem cells. Organoids offer unbounded potential in the study of both human normal development and disease, especially when combined with gene editing technologies.

Organoids form when stem cells undergo differentiation and self-organize into complex tissue structures that closely resemble *in vivo* organs. These systems, which allow the patient's own cells to be used for disease modeling, efficiently create structures displaying key features mimicking human organ complexity. Accordingly, organoids provide a framework for the study of cell behavior during a diverse range of biological processes or environmental changes. Potential applications include the study of human development, the modeling of disease progression, and drug screening.

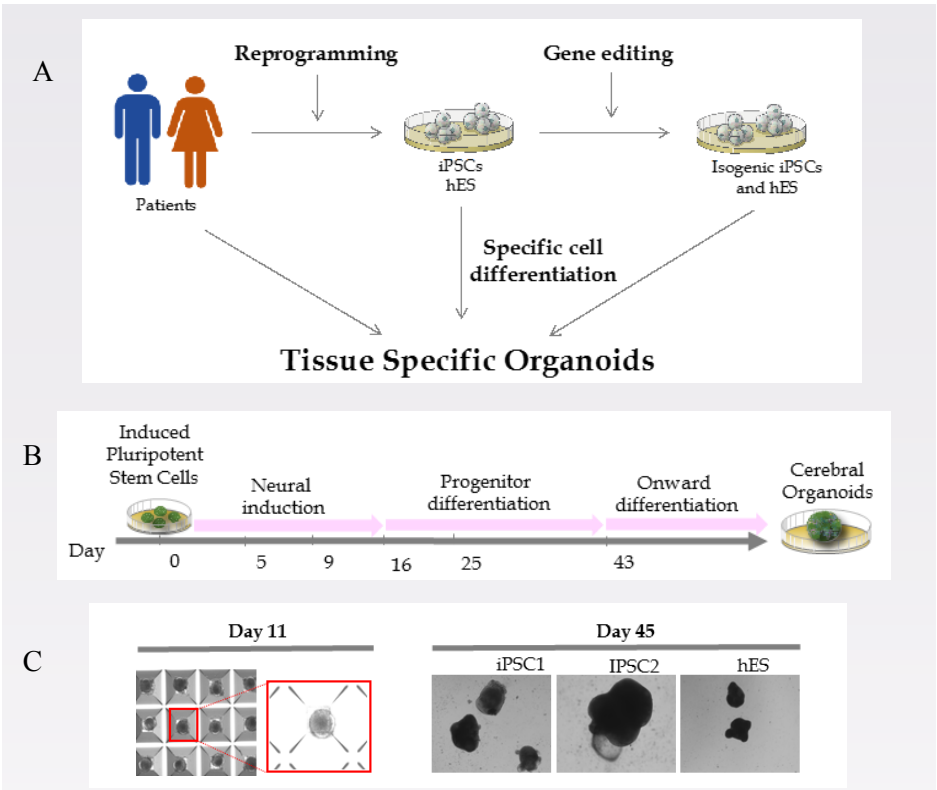

Figure 1. Tissue-specific organoids derived from stem cells.
A) Illustration of cell sources used to derived tissue specific organoids.
B) Illustration of a time line for the differentiation of embryonic stem cells (hES) and induced pluripotent stem cells (iPSC) into brain organoids.
C) Images of brain organoids grown in Aggrewell for 11 days or in suspension for 45 days.

The HPSSC will be adapting and standardizing published methods to generate brain, kidney, lung, liver, retinal and breast organoids. The HPSSC goal is to provide a complete workflow including iPSC generation, genetic modification, cell differentiation and organoid production to support and advance translational research.
The HPSSC is currently offering brain and breast organoids, while lung and kidney organoids are currently under development and expected to be available as a core service later this year, while liver and retinal organoids are expected to be available early next year.

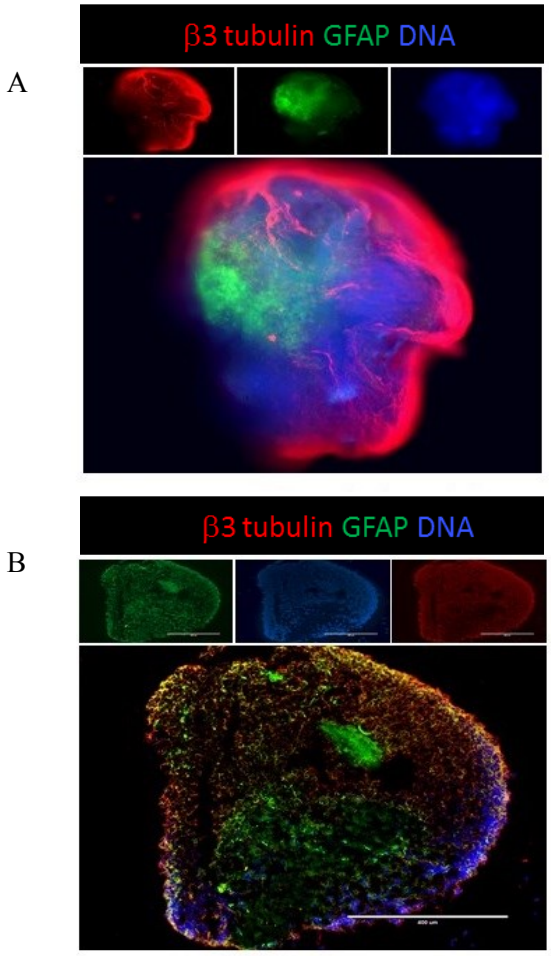

Figure 2. Brain organoids derived from iPS cells capture the complexity of the human brain.
A). Whole-mount immunofluorescent staining of a 120 day old brain organoid displaying neural projections. **B**) Immunofluorescent staining of an organoid section showing neuronal organization. Neurons are labeled with Class III β-tubulin (β3-Tubulin, in red), astrocytes with Glial Fibrillary Acidic Protein (GFAP, green) and cell's DNA with DAPI (blue). Brain organoids are been characterized in collaboration with Natasha Snider and Rachel Battaglia from the UNC Cell biology and Physiology Department.

CORE HIGHLIGHT

Quality Control Begins with the Specimen

Laboratory testing has three major phases: pre-analytical (specimen collection), analytical (specimen testing), and post-analytical (data interpretation). Often when we find ourselves faced with unexpected results, our initial thought is that there must have been an error with the instrument (analytical phase). However, it has been well established in the clinical setting that the majority of laboratory testing errors - up to 70% - arise during the pre-analytical phase.

Lessons learned from establishing practices to ensure rigor and reproducibility in the handling of patient specimens can be adapted to our research practices. The same technology that is used to run bloodwork in the clinic is employed with animal specimens in pre-clinical studies. In clinical medicine, the most common causes of pre-analytical errors in blood testing include improper specimen collection volume, tube misidentification, hemolysis, incorrect anticoagulant choice, clotted specimens, poor processing, and incorrect testing requested. While we assume that many of the same problems are common to animal bloodwork studies, data identifying common errors in the research setting is lacking.

With funding from CFAC, the Animal Studies Core and the Animal Histopathology and Laboratory Medicine Core are teaming up and conducting studies to begin to identify common errors that arise regarding blood specimen handling in the research setting. These studies are examining the effect that the extent of training in blood collection technique has on the accuracy and precision of the results. Not only will the work begin to establish a better understanding of common sources of specimen handling error in the research setting, but it will improve future training and instruction for blood specimen collection.

Excerpt from the Federation of American Societies For Experimental Biology (FASEB) report: Maximizing Shared Research Resources, Oct. 2017:

"Quality control and research rigor: Investigators recognize the importance of validating many types of stocks and reagents as well as providing more detailed information ab out experimental conditions, materials, and protocols in scientific communications [13]. As specialized providers, facilities have the capacity to achieve a high degree of consistency for each procedure, maintain detailed records of extrinsic factors that might affect results, and validate materials.

Similarly, facility personnel are able to attain a high level of excellence and competence in their work by specializing in a technology area or class of research materials. As compared with laboratory staff and trainees, facility staff reported greater confidence in their ability to determine which resources require validation or calibration [14]."

Core Customer User Surveys

Core Customer User Surveys are important tools for evaluating core services. If you receive core satisfaction surveys, please take the time to complete these brief questionnaires.
Your feedback will assist the core facility as well as the Office of Research Technologies & CFAC in improving and strengthening core services available for your research program. *Thank you!*

Cite our Cores

If you use UNC core facilities and data generated in our cores is used in a publication, please acknowledge the core's contributions towards the research. For more information on guidelines for acknowledgment or citing a core facility in a publication, please read the ABRF Authorship Guidelines.
Core instrumentation acquired through S10 grants must also be referenced in all resulting publications. The core can provide you with the appropriate citation.

FASEB Statement on Acknowledgement, April 5, 2016 (faseb.org/sharedresources)
"By acknowledging shared resource facilities and instrumentation in publications, presentations, and other research communications, investigators play a critical role in ensuring their continued availability and future development."

WELCOME NEW CORE DIRECTORS

Stuart Parnham, PhD, has taken over leadership of the Biomolecular NMR Facility from Greg Young who retired in July. Parham served in the Royal Air Force, earned his Ph.D. in Biochemistry at the University of Leicester. and completed his post-doctoral training in HIV protein/RNA structural characterization at the Medical University of South Carolina (MUSC).
Parnham managed the NMR and Crystallography Core at MUSC as well as the NMR facility at the National Institute for Standards & Technology. He has extensive experience in protein, RNA and small molecule structure determination, protein/protein and protein/ligand interactions, dynamics and metabolomics.
The **Biomolecular NMR facility** houses four high field spectrometers: 850, 700, 600 and 500 MHz. Each spectrometer is equipped with a cryoprobe increasing the sensitivity and scope of the facility. The 700 MHz spectrometer is equipped with a Bruker SampleJet system capable of holding five 96 sample racks as well as a 95 sample open source ring thus making the 700 MHz system the ideal vehicle for high throughput screen of drug fragments and metabolomic studies.

Nathan Nicely, PhD, new Director of the Protein Expression & Purification (PEP) and Macromolecular Crystallography (MX) core facilities, joins us from Duke where he spent ten years operating a crystallography shared resource with protein production capabilities. He has extensive experience researching topics in HIV-1 structural immunology and participated in research on pathogenic metabolism, oncogenesis, structural proteins, and other scientific topics.
The UNC PEP and MX cores are cohoused in Medical Research Building B and are fully equipped to service many protein production and structural biology needs from investigators on campus and beyond.
The MX core is particularly excited to unveil a recent acquisition, the **JANSi UVEX crystal platehotel and imager.** This instrument uses an automated microscope to image miniaturized crystallization experiments in both white light and UV. Comparing pairwise images, experimenters can differentiate between spurious materials and genuine protein crystal leads, resulting in the best use of precious protein samples, streamlined workflows, and the identification of leads that may otherwise have gone overlooked.

High Throughput Sequencing Facility (HTSF) Offers New Services

HTSF is pleased to announce new technologies that are now available to the research community.

NovaSeq 6000 Sequencing System

The NovaSeq 6000 is currently the most powerful Illumina sequencing platform. Many projects will benefit from the faster turnaround time, flexible performance, and improved yield (i.e., reads per flowcell). By providing multiple flowcell types and read lengths, the NovaSeq can accommodate a variety of sequencing methods, project scales, and data needs. Run times range from ½ day for the paired end 50 cycle run on the S1 flowcell to 2 days for a paired end 150 cycle run on the S4 flowcell, cutting in half the run time on the HiSeq4000. Up to 1.6 billion reads can be produced on the S1 flowcell and up to 20 billion reads can be produced on the S4 flowcell, compared to the HiSeq 4000 that could provide a maximum of 2.5 billion reads per flowcell.

Bionano Genomics Saphyr System

The Saphyr System automates the imaging of extremely long, high-molecular-weight DNA in its native state. The proprietary technology provides structural variation sensitivity, genome assembly contiguity up to 100 times better than short-read sequencing, and accuracy that enables correction of sequencing-based assembly errors. The high-capacity Saphyr Chip is ideal for mammalian research applications and can read long molecules from 100,000bp up to megabase pairs, has a throughput of at least 640 Gbp per day for human samples for deep structural variant discovery and can complete full genome analysis in less than five days. Areas of research that will benefit include undiagnosed genetic disorders, gene discovery, cancer, genomic integrity of cell lines, selective breeding, evolutionary biology and reference genome assembly.

Please visit the HTSF website for more information or call the facility at 919.962.4395