MOLECULAR PATHOLOGY AND IMAGING CORE

The Molecular Pathology and Imaging Core (MPIC) is excited about the upcoming year and being able to continue working with the labs of Penn. Please feel free to stop by and see if there is anything we can do to help you. Additionally, we continue to maintain an average turn around of 5 working days for orders, which gets you results quicker.

A human GI Cancer tissue bank is maintained by MPIC, which paraffin embedded samples. The bank is a service that is provided by the MPIC and can be used at no additional charge to sectioning. The majority of tissues also have a pathology report.

If you are interested in seeing what is available please contact Adam Bedenbaugh, blakebe@mail.med.upenn.edu, for more information.

CENTER SYMPOSIUM

Save the date
September 22, 2016
for our
2016 17th Annual NIH Center for Molecular Studies in Digestive and Liver Diseases Symposium
“3D organoids in the GI tract, liver and pancreas”
to be held at the National Constitution Center in Philadelphia.

Please remember to cite the Center (NIH-P30-DK050306) and its core facilities (Molecular Pathology and Imaging Core, Molecular Biology/Gene Expression Core, Transgenic and Chimeric Mouse Core, and Cell Culture Core) in your publications.
TECHNIQUES IN MOLECULAR BIOLOGY COURSE 2015

Sarah Andres, PhD

This summer the NIH/NIDDK Center for Molecular Studies in Digestive and Liver Diseases and GI Division re-launched its wildly successful course, Techniques in Molecular Biology, created and directed by Sarah Andres, a post-doc in Dr. Anil Rustgi’s lab. The NIH/NIDDK Center for Molecular Studies in Digestive and Liver Diseases, the GI Division, and the Abramson Cancer Center sponsored this 8-week course geared toward laboratory technicians and GI fellows with limited or no lab experience. Twenty-six students enrolled to learn from a team of post-docs and junior faculty. The students attended class sessions twice weekly where they learned the theory behind common molecular biology techniques such as gel electrophoresis, PCR, western blotting, or cloning and were introduced to RNA sequencing, genetic mouse models, and immunostaining, just to name a few. The students engaged in problem-solving and critical thinking exercises throughout the summer. At the conclusion of the course students worked in small groups designing a series of experiments to answer a scientific question. This activity required both the ability to understand and synthesize the course material. Overall, the course received rave reviews from the students who found it immediately applicable to their day-to-day work and highly recommended it to colleagues.

Student knowledge was assessed by a self-evaluation taken before and after the course. The students showed highly significant improvements in their knowledge of all subject areas covered, further emphasizing course success. This course is unique to the medical school. Drs. Andres and Rustgi plan to offer it again next summer, but open enrollment to other departments across Penn’s campus as well.

UNDERGRADUATE STUDENT SCHOLARS PROGRAM 2015

This summer, the Center hosted 14 exceptional undergraduate students for 10-weeks through the Undergraduate Student Scholars Program (USSP), an organized program of summer lectures and presentations combined with an intensive research experience with an expert investigator. At the end of the summer program, the students will present their research at the USSP Symposium, with a keynote address by Dr. Michael S. Parmacek, who joined the students for lunch prior to the symposium. We are always delighted to have our Center investigators serve as mentors for this unique undergraduate training program.

This year’s students and mentors:
Anna Briker in Dr. Klaus Kaestner’s Lab
Rocky Giwa in Dr. Rebecca Well’s Lab
Simran Handa in Dr. Serge Fuchs’ Lab
Venkata Jonnakuti in Dr. Doris Stoffer’s Lab
Jonathan Kluger in Dr. Hiroshi Nakagawa’s Lab
Maxwell Lee in Dr. Patrick Seale’s Lab
Abigail Loneker in Dr. Rebecca Well’s Lab
Jenna Marinock in Dr. John Lynch’s Lab
Heather Mentch in Dr. Robert Heuckeroth’s Lab
Edmund Qiao in Dr. Anil Rustgi’s Lab
Divya Rao in Dr. Jonathan Katz’s Lab
Medha Sharma in Dr. Hiroshi Nakagawa’s Lab
Samip Sheth in Dr. Kiran Musunuru’s Lab
Daniel Stadtmauer in Dr. Sarah Tishkoff’s Lab

Additional information on the USSP is available at https://www.med.upenn.edu/molecular/undergrad.shtml

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Several years ago the University of Pennsylvania School of Medicine funded the creation of a dedicated mouse embryo cryopreservation storage facility. This facility is located in a secured room in the Anatomy-Chemistry Bldg and is overseen by the Core. The facility currently contains 9 liquid N\textsubscript{2} storage tanks (plus a working tank in the microinjection room) with alarms and a source tank for liquid N\textsubscript{2} refills. The Core bears responsibility for maintaining the integrity of the N\textsubscript{2} dewars, and maintaining up-to-date, computerized storage records that can be accessed in real time by P.I.s. There is a modest per line yearly charge to Core users for this cryostorage service ($24/line/yr for center members). The fee will be collected quarterly through our database according to the account number that the user provides. Users can monitor their inventories and arrange with the Core to have samples sent to collaborators. The user needs only to provide the contact info for the recipient and the name of the line to be sent and the Core will take care of the shipping process.

The Transgenic and Chimeric Mouse Facility began providing direct genome editing services using the CRISPR-cas9 technology two years ago. CRISPRs (clustered regularly interspersed short palindromic repeats) encode RNAs (guide RNA) target a CRISPR-associated protein (Cas9) to cleave a DNA sequence in a site-specific manner. Following the double-stranded break, non-homologous end joining generates targeted deletions of random size. The DNA cleavage can also be used to enhance high-fidelity homologous recombination using a co-injected single stranded or double stranded DNA template. These CRISPR/Cas9-based methodologies significantly reduce the time and resources involved in generating genetically modified mouse lines.

The direct genome modification service based on CRISPR-Cas9 was integrated into the Core services in 2014 and has rapidly increased in its utilization. The overwhelming majority of the projects use an injection mix of Cas9 RNA and sgRNA either with or without template DNAs. The mix is injected into the cytoplasm of fertilized mouse oocytes of the strain of choice requested by the user. Similar to the DNA injection service, injected eggs are cultured O/N and the embryos are surgically transferred into pseudopregnant females and allowed to go to term. For ‘knock-in’ and targeted sequence modification projects, the eggs are cultured O/N in the presence of 50 uM SCR7, an inhibitor of Ligase IV to enhance homologous recombination (vs. non-homologous end-joining) events. The success rate for the KO projects ranges from 5%-50% of the live-born with frequent occurrence of bi-allelic mutations. KI projects based on homologous recombination remain less successful (3-10%) and the success frequency varies tremendously based on multiple variable in the project (base substitution, LoxP or tag insertion, large segment insertion). The Core continues to monitor the outcome of all projects and collect data that would help improve the efficiency of this technology.

Recent Publications from Center Members

Li N, Yousefi M, Nakauka-Ddamba A, Tobias JW, Jensen ST, Morrissey EE, Lengner CJ.
Heterogeneity in readouts of canonical Wnt pathway activity within intestinal crypts.

Merrell AJ, Stanger BZ.
Adult cell plasticity in vivo: de-differentiation and transdifferentiation are back in style.

Esophageal Expression of Active IKK Kinase-β in Mice Up-Regulates Tumor Necrosis Factor and Granulocyte-Macrophage Colony-Stimulating Factor, Promoting Inflammation and Angiogenesis.

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