

NEWSLETTER

SUMMER 2020



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Please remember to cite the Center (NIH-P30-DK050306) and its core facilities (MPIC, H-MARC, G-MMC, and BDSC) in your publications.

GENETICALLY-MODIFIED MOUSE CORE UPDATE

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 N₂ storage tanks (plus a working tank in the microinjection room) with alarms and a source tank for liquid N₂ refills. The Core bears responsibility for maintaining the integrity of the N₂ 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. <http://www.med.upenn.edu/genetics/tcmf/>

SAVE-THE-DATE

Save the Date for the 20th Annual Center for the Molecular Studies in Digestive and Liver Diseases Symposium

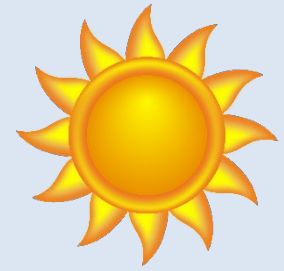
"Metabolic Control of GI Biology"

Friday, November 20, 2020

[Register Now!](#)

NEWSLETTER

SUMMER 2020 continued



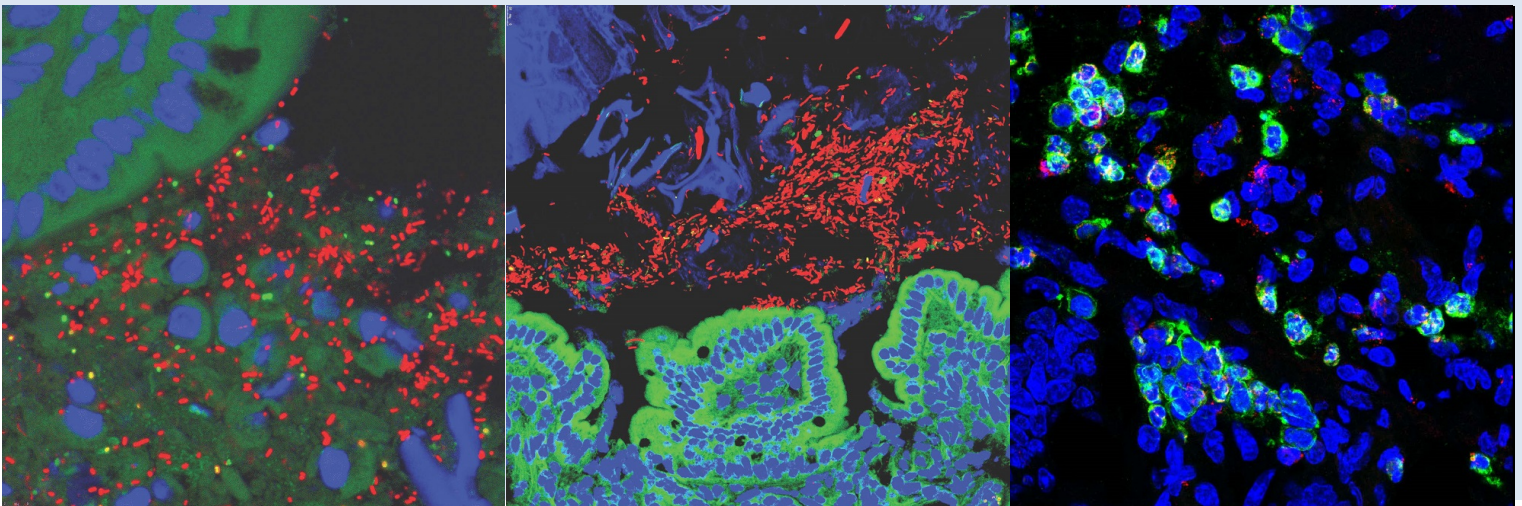
MICHAEL C. ABT, PHD, LAB UPDATE

Michael Abt is an Assistant Professor in the Department of Microbiology at the University of Pennsylvania, Perelman School of Medicine. He attended Loyola University of Maryland where he obtained a B.Sc in Biology. Michael performed his graduate studies in the Immunology Graduate Group at the University of Pennsylvania. His thesis work investigated the role of intestinal microbial communities in calibrating antiviral immunity. He joined Dr. Eric Pamer's lab at Memorial Sloan Kettering Cancer Center as a postdoctoral fellow in 2013. His research on innate immunity against enteric bacterial infections led to him being named a recipient of an Irvington Fellowship from the Cancer Research Institute and a K99/R00 NIH Pathway to Independence Award. Michael started his own lab at UPenn in January of 2018 where his lab is currently engaged in research exploring immune-microbiota interactions in the context of infectious disease, specifically studying mucosal immune defenses against enteric pathogens.

The Abt lab's research focuses on the pathogenesis of and host response to *Clostridium difficile*, a bacterium that infects the large intestine following perturbation of the intestinal microbiota. *C. difficile* represents one of the most urgent public health threats in the United States due to high recurrence rates following antibiotic treatment. The increasing failure of conventional therapy to control *C. difficile* associated disease highlights the need to identify alternative strategies to control this disease.

C. difficile is the first disease effectively treated with microbiota-based therapeutics, however implementation of this therapy as a reliable treatment option is limited due to inadequate understanding of its mechanism of action. Using a murine model of *C. difficile* infection and human clinical samples, our research investigates immune-microbiota regulation of *C. difficile* associated disease. These studies seek to reveal insights that are broadly applicable to the treatment of infectious or inflammatory diseases driven by dysbiosis of the microbiome.

Dr. Abt is a recipient of a Center Pilot Grant.



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For access to our Center website and list of current members, please visit us at www.med.upenn.edu/molecular/