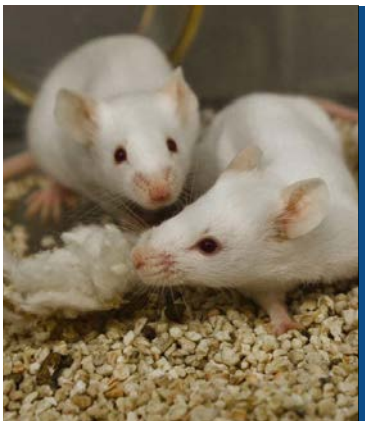
UC DAVIS Mouse Biology Program

ANNUAL STAKEHOLDER REPORT 2020-2021

INSIDE THIS ISSUE

Fiscal Year Overview

This past year (2020-2021) marks 22 years since the UC Davis Mouse Biology Program (MBP) began serving the mouse modeling needs of the campus community. Now entering its 23rd year, the MBP remains the only one-stop in-house resource of unique expertise, services, and training in the creation, testing, and application of mouse models used for the study of human biology and disease. Our mission, "*to enable and facilitate in vivo functional modeling at the frontiers of knowledge in support of accelerating human and animal health through discovery, technology, and mentoring*", is fully aligned with Chancellor May's "To Boldly Go" Strategic Vision for the future of UC Davis.



OUR VISION

For several years, our vision has been to be an essential resource for the campus community using mouse models in biomedical research. We continually seek to cultivate an innovative environment that pursues breakthrough discoveries, exciting partnerships, and strategic collaborations.

UPDATE: Gnotobiotics and Microbiome

MBP operates and manages the campus' only mouse gnotobiotic core, funded in part by an NIH G20 grant. With validation of breeding colonies and transferring animals between isolators completed, MBP has begun providing services to users with projects requiring multiple isolators. We have now begun offering microbiology surveillance testing services and validation of mice maintained in our new Tecniplast IsoCage Biocontainment system. The GMRC continues to expand its repertoire of capabilities and services for all your axenic, gut microbiome, immunocompromised, and other mouse project needs!

UPDATE: PDX Models

Heterotopic and orthotopic patient-derived xenograft (PDX) mice are a mainstay of cancer research. The MBP PDX program grew leaps and bounds over the past year, establishing tumor models from dozens of patients not only from our own Comprehensive Cancer Center but by overnight shipment of tumors from hospitals across the state. In December 2020 we implanted our 200th tumor and provided mice and tissues to several cancer researchers.

UPDATE: PET/MRI & EchoMRI

In collaboration with the Center for Molecular and Genomic Imaging (CMGI), the new PET/MRI, purchased using funds awarded from an NIH S10 "SIFAR" grant, is now fully operational in our SPF mouse vivarium on Second Street. MBP is now making brain and body cavity scans available as a service to the research community. Also, in association with the NIH Mouse Metabolic Phenotyping Center (MMPC), another S10 grant was awarded to procure and operate a home-cage metabolic caging system and an EchoMRI with the capacity for rapidly quantifying body composition data on awake (not anesthetized) mice for researchers upon request.

UPDATE: Knock Out Mouse Production

We continue to improve the efficiency of CRISPR/Cas9 genome editing in mice, producing hundreds of indel, exon deletion, conditional, and other alleles over the past year. We have expanded these services to include SNP (single nucleotide polymorphism) alleles. When made to recapitulate specific genomic variations observed in human patients, these mouse models can provide significant and informative insight into the disease-causing nature of variants of unknown significance and inform diagnostics and clinical decision-making. One of our biggest clients for knockout mouse production services is the NIH Knockout Mouse Phenotyping Project (KOMP2).

UPDATE: Conditional Mouse Models

Advances in making conditional models are in development at MBP. For example, adoption and optimization of a new electroporation procedure that shows promise to significantly decrease time and animal use for generating conditional alleles is currently under development. Preliminary data is promising. We are validating and optimizing our methods which we hope will also reduce costs.

UPDATE: CRISPR/Cas9 Genome Editing

The MBP refined and improved CRISPR/Cas9 genome editing technologies directly in mouse embryos to create knockout and knockin mice at lower cost and in significantly less time than conventional approaches using homologous recombination in mouse embryonic stem (ES) cells. Although large knockins, humanizations, and other genetic manipulations are still challenging using CRISPR, it does help us overcome the hurdles of selection cassettes, high percentage chimeric males, and germline transmission associated with mice made using ES cells.

UPDATE: Sperm Motility & Morphology Assessments

MBP now offers a first-of-its-kind comprehensive mouse sperm assessment as a fertility test for male mice. This service package uses computer assisted sperm analysis to quantify cauda epididymal sperm count, and total, rapid, and progressive sperm motility. We also determine sperm morphology and the percent of sperm with atypical heads, tails, and other abnormal shapes and types.

External Collaborations

In Spring of 2021, MBP announced an agreement with GemPharmatech to distribute thousands of mouse lines from their new conditional mutant mouse line collection. All of their lines are now here at MBP as frozen germplasm which can be shipped to you or cryorecovered to live mice at your request. As part of this agreement, MBP also can provide genotyping, breeding, and phenotyping on these mice to clients across North America. Go to https:/gempharmatech.us/ and click "Search" to browse the catalog of lines available today for almost half the mouse genome and place your order.

"I am delighted to announce this Service Agreement, as I have worked with the Mouse Biology Program in various other roles for over 20 years," said Dr. Moore, President and CEO of GemPharmatech LLC, a US subsidiary of GemPharmatech Co., Ltd. *"This arrangement in California with a world class facility gives us easy access to many top research institutions on the west coast and the ability to ship anywhere in the US easily,"* continued Dr. Moore.

GemPharmatech CEO Dr. Mark Moore

The MBP is also honored to continue working with other commercial start-ups Ravata, Verndari, and BCD Biosciences.

Mouse Biology Program Division Updates

Laboratory Operations

...includes four science and service laboratories that conduct gene targeting and genome editing in embryonic stem (ES) cells and mouse zygotes, artificial reproductive technologies (e.g., IVF, ICSI), embryo manipulation, genotyping, cryopreservation and recovery, rederivation, and other procedures. The Division offers a complete and comprehensive set of fundamental services needed to design, plan, and execute a research project involving mutant mice. Users are free to select *a la carte* from services necessary to pursue their research objectives. Over the past year, this Division delivered ~55,000 services to 99 investigators.

Vivaria and Veterinary Care

...operates and oversees four vivaria — a high containment shower-in barrier (M3), a restricted access specific-pathogen free (SPF) vivarium, quarantine rooms (M1), and the gnotobiotic mouse resource facility (GMRC). Over the past year the Division provided enterprise-level husbandry and care for 87,990 mice and fulfilled 355 mouse orders and 4,155 requests for services including colony management, complex breeding projects, PDX mice generation, vaccine efficacy/kinetic studies, and more for 308 researchers. Our biosurveillance procedures detected the presence of some unwanted pathogens in two of our vivaria which was attributed to inadequate sterilization of cages. After several intense weeks of depopulation, cleaning, disinfection, and restocking (in addition to ensuring all cages are properly sterilized) our vivaria are again clean and back to normal operations. Melinda Zmerzlikar was appointed Assistant Director of all vivaria management, operations, and personnel, sharing responsibility with Associate Director Dr. Kristin Grimsrud who will continue oversight of animal health, pathogen biosecurity, import/export services, and research.

Phenotyping and Analytics

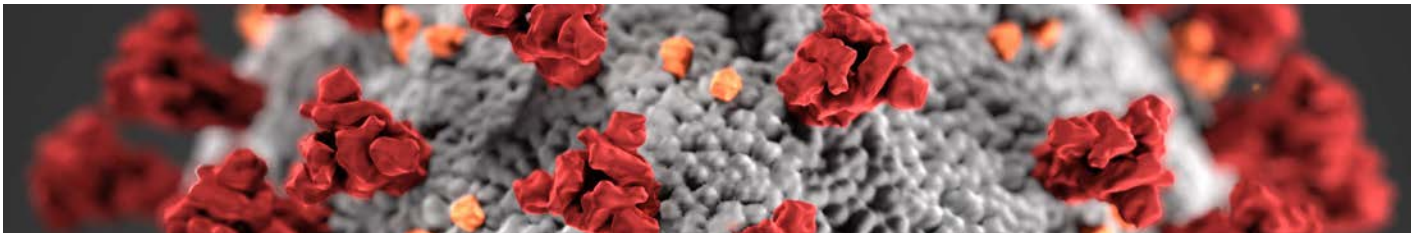
...provides a full suite of *in vivo* and *ex vivo* testing services to screen, identify and characterize the pathophysiologial consequences of gene targeting, editing and other in-life manipulations in mice. Over the past year, the Division performed over 60,000 tests and analytical services including SHIRPA, fear conditioning, grip strength, open field, nociception, auditory brain response (ABR) and acoustic startle-pre pulse inhibition (PPI), electrocardiograms, X-rays, DEXA body composition analysis, glucose tolerance, ophthalmological examinations, embryo phenotyping, complete blood counts (CBC) and chemistry panels, indirect calorimetry (CLAMS), PDX modeling and necropsies, generating millions of data points. Dr. Louise Lanoue, an expert developmental biologist and nutritionist, was newly appointed as Associate Director and will oversee and supervise "after-life" and embryo phenotyping in partnership with Assistant Director Lynette Bower who will continue to direct "in-life" phenotyping and PDX work.

Information Services

...manages all informatics, databases, cybersecurity, and data tracking services for MBP, including implementation and maintenance of custom software for the collection, analysis, mining, storing, and reporting of data. This past year, the Division worked on consolidating multiple databases for ease of management, upgrading older servers and code base, as well as hardening our existing infrastructure to meet UC IS-3 security policy requirements. Last year, the Division managed 49 terabytes of research data consisting of 8.4 million files, including 1.2 million high resolution images using 33 terabytes of storage. All services and supporting hardware are maintained within an internal, enterprise-grade data center with a robust and high-performance virtual architecture. With the significant challenges presented by the COVID-19 pandemic, providing remote access to staff and the loss of personnel, IS maintained smooth and functional operations throughout the year.

Repository and Project Management

... operates the MBP-hosted biorepositories, provides customer and technical services, performs billing and recharge for services rendered, and manages all material importation and exportation processes throughout the MBP. The Division teams processed 757 orders from 637 researchers at 311 institutions for 51,865 services and 7,729 products during the past year. Orders were down ~10% in response to the COVID-19 pandemic as well as due to a temporary reduction of operations in our vivaria while we eradicated unexpected pathogens.



Mouse Biology Program Activity During The COVID-19 Shutdown

MBP was deemed "essential" for operations during the pandemic, ensuring the health and welfare of mice in its care, protecting and preserving irreplaceable experimental data, providing emergency cryopreservation services to campus investigators to prevent catastrophic loss of their mice, and conducting SARS-CoV-2 research. Regarding the latter, MBP collaborated on a $1million NIH grant to design, develop, and validate new, genetically-humanized mouse models to study COVID-19. Human knockin/mouse knockout mouse lines for *ACE2, TMPRSS2, FURIN, DPP4, NRP1, SLC6A20,* and several other genes are in various stages of development, testing, and phenotyping as next generation mouse models for COVID-19 research.

While this work was both important and necessary to help combat the SARS-CoV-2 virus, we also had a responsibility to keep our staff informed, safe, and secure. For example, monthly "All Hands" meetings were moved entirely online and kept staff, both on-site or sheltered-in-place at home, informed about scientific goings-on and business operations. We also used the time to introduce new employees, celebrate staff birthdays, and announce SPOT awards to recognize "employees of the quarter." In addition, the MBP Director Dr. Lloyd distributed a "MBP Operations Status" update via e-mail every Sunday night, informing staff of any changes to COVID precautions, campus and site updates, and critical meetings and presentations scheduled for the coming week.

To ensure everyone's safety for those coming on-site to work, MBP implemented a 3-step screening and entry process to complement the campus' system in order to directly address the specific needs of our workforce. With this thorough process in place, MBP did not experience any instances of COVID-19 within any of our facilities throughout the pandemic. And importantly, no one left their MBP job involuntarily during the pandemic: We remained and stuck together as a team through it all.

MBP Administration

Leadership and management meetings were scheduled and held regularly and virtually throughout the year without interruption. The MBP Senior Leadership Group, made up of the director, 5 division leaders, financial manager, and *ex-officio* representatives met the first Friday of the month.

In addition, financial review and oversight meetings were conducted quarterly between administrative leadership and division and laboratory leaders. This group met monthly to discuss and resolve issues related to management, safety, accounts receivables, facilities, and other activities.

As a self-supporting unit, MBP relies on income from sales of mice and other products as well as from requests for services and procedures to function and operate. It's no surprise then that business activity was severely impacted by the slowdown in research during the pandemic. Fortunately, frugal spending on our part and carry forward of a healthy reserve built up over prior years helped buffer the significant negative financial hit we took this year. As we now emerge from the pandemic, we're working to get our business back on track.



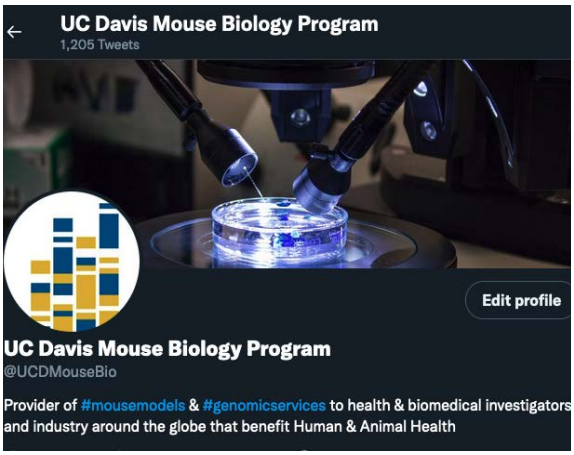


Even as the COVID-19 pandemic extended beyond June of 2021, and many institutions and organizations struggled with challenges presented by social distancing, shelter-in-place orders and supply-chain management issues, MBP strived to maintain and support delivery of excellent services and technical support to keep individuals' research projects and activities intact.

Mentoring & Outreach

Mentoring

The MBP is fully engaged in the training and education of academics, students, and staff from all backgrounds and levels, including high schoolers, undergraduate, graduate, and veterinary students, residents, fellows, and faculty. Experiential learning opportunities are highly diverse, including in genetic alteration of mice, *in vivo* phenotyping and analytics, mouse colony management, molecular construct design, embryonic stem (ES) cell gene targeting and culture, experimental design and reproducibility, and much more. Dr. Wood, Associate Director of Laboratory Operations, joined the faculty of the College of Biological Sciences and taught MIC 215 and 298 in Fall Quarter. Despite being on hiatus this year, Dr.'s Wood and Grimsrud, Associate Director of Vivaria and Animal Health, also remained mentors for the Young Scholar Program for high school students and the STAR program for veterinary students. Dr. Lanoue, Associate Director of Phenotyping and Analytics, mentored a veterinary student during his summer research internship. And Dr. Wood is working with the Western Association of Core Directors to host a series of virtual lectures in the Fall.



Outreach

MBP outreach takes many forms...through our website (*mouse.ucdavis.edu*), email blasts, presentations at scientific meetings, talks and tours to visitors and students, and more. The near total cancellation of face-to-face conferences and in-person events didn't stop MBP from getting its message out about mouse models for biomedical research. MBP focused heavily on digital platforms: Our Twitter account grew from an average of 3,000 impressions in June 2020 to over 20,000 impressions in June 2021, a seven fold increase! We also enlarged our footprint on LinkedIn by over 93%, and our Facebook engagement rose by nearly 93%, nearly doubling metrics in reach and views within a year. MBP also participated in several online campaigns, including #rarediseaseday and the European Animal Research Association's July *#BOARD21* campaign, designed to promote and educate on the benefits of animal research.

Diversity, Equity, and Inclusion

In alignment with similar efforts on campus, MBP has made DEI among its staff a top priority for action at its recent programmatic retreat. We've also partnered with various organizations such as the National Institute on Minority Health and Health Disparities to promote communications that address diversity, equity, and inclusion with underrepresented populations within the scientific community.

Research & Innovation

As a scientifically-driven academic program, the MBP engages in research and discovery activities and technology development to advance and promote scientific rigor, reliability, and reproducibility in the use of mouse models for biomedical research. A few examples of our research efforts over the past year include...

- Enhancing Cas9 genome editing by electroporation of zygotes
- Developing new genetically humanized mouse models for COVID-19 research
- Creating mouse avatars that recapitulate specific genetic variants in human patients

MBP also assisted faculty with the preparation and submission of several NIH and other grants and peer-reviewed publications, including by researchers here at UC Davis. We are excited to report that over the course of the year the MBP was co-author, acknowledged, and/or cited in 149 scientific publications, including in Nature, Cell, JBC, and Science.

Priorities for Fiscal Year 2021-2022

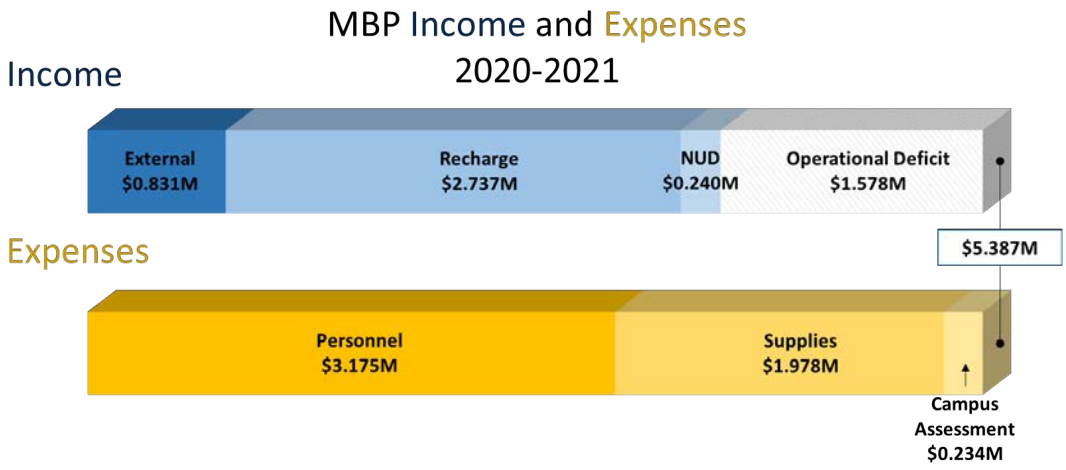
Over the next year the MBP will continue to evolve and develop both scientifically and professionally. We also will pursue financial sustainability and promote the application of laboratory mice for basic and translational research.

In particular, MBP will aim to improve responsiveness to users, expand product and service line offerings, and increase technology development activity to better meet the research and resource needs of campus faculty.

Specifically, we've set the following goals for the next fiscal year:

- Secure additional sources of funds, including from campus, to support base operations.
- Engage the new Internal Advisory Committee to guide programmatic efforts and future planning.
- Secure a Memorandum of Understanding to access and utilize the J1 ABSL3 vivarium facility.
- Assist with the competitive renewal of the NIH KOMP2-Phase3 project.

Mouse Biology Program Financial Statement



UCDAVIS
Mouse Biology Program

Contact Us

For more information about our products and services, please contact us by phone, email, or visit us on the web.

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