Division of Comparative Medicine and the Committee for Animal Care

The Division of Comparative Medicine (DCM) has a primary mission to support MIT's research and education objectives through the provision of excellent quality support for all research involving animals at MIT including the Whitehead Institute (WI). Since its official inception in 1974, DCM has evolved into an internationally recognized comparative medicine program that provides a full range of veterinary and surgical support, while supporting independent research for veterinarian-scientists and training postdoctoral and predoctoral students in comparative medicine and biomedical research. The excellence of DCM's animal resources program is reflected in the fact that it has maintained continued full accreditation from AAALAC International since 1972. DCM has been led by Dr. Kelly Metcalf Pate, DVM, PhD, DACLAM since July 2021 when founding director Dr. James Fox, DVM, MS, DACLAM stepped down after 46 years of service.

The Committee for Animal Care (CAC) is the federally mandated compliance oversight body for animal research at MIT and WI, also known as MIT's Institutional Animal Care and Use Committee (IACUC). The CAC is a separate entity from DCM, but works closely with DCM to assure regulatory compliance for all animal work at MIT and WI. The CAC is chaired by Dr. Howard Heller, MD, MPH.

Both DCM and the CAC report independently to the VPR.

Current Goals, Objectives, and Priorities

DCM's mission centers around Comparative Medicine and is inherently linked to MIT's tripartite focus in service, research and education. Comparative Medicine is the study of the similarities and differences between animals and humans, and how we can apply what we learn about health and disease states in different species to advance knowledge and medicine across species. Central to Comparative Medicine is the practice of modeling human disease in animals. DCM is home to expert practitioner-scientists who work closely with MIT/WI's community to ensure that they work with animal models in a way that preserves animal welfare while producing rigorous scientific results. Thus, DCM's goals continue to be to: 1) Provide excellent care to all animals; 2) Maintain a high level of service to research investigators; 3) Foster a collaborative team environment within DCM and the community that works with animals at MIT/WI; 4) Lead in, and expand, comparative medicine and translational research; and 5) Train the next generation of comparative medicine scientists.

The CAC's mission complements DCM's in that it ensures that all research and teaching with animals at MIT and WI occurs in compliance with all relevant regulations and guidelines. The CAC's goals are to 1) Review all animal work prior to its start and periodically thereafter to ensure it is occurring in compliance with relevant regulations and guidelines; 2) Receive and promptly address any animal welfare concerns; and 3) Provide excellent service to research investigators as they plan their research.

As we reach the end of FY23, the top priority for both DCM and the CAC is preparation for MIT's triennial Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) site visit, to be scheduled in fall 2023. AAALAC is a private

nonprofit organization that offers accreditation to institutions that work with vertebrate animals in research and teaching. AAALAC reviews the animal care program, including tours of the facilities and interviews with personnel, and provides an independent assessment of the program's quality and compliance compared to current guidelines. The status of "full accreditation" is a stamp of approval that indicates that a program meets or exceeds contemporary performance standards for the field, and confers the program ease of collaboration with other institutions and streamlines the reporting pathway to federal agencies. Preparation for this visit requires careful coordination between DCM and the CAC, alongside MIT VPR leadership, EHS, Occupational Health, and Facilities.

DCM and the CAC continue to evolve to accommodate growing and increasingly complex animal research support needs, and, towards that end, DCM will be conducting a comprehensive review of their available services and fee for service structure in FY24, with an eye towards anticipating and preparing for future areas of growth. Ideally, both DCM and the CAC would have appropriate resources in place in advance of evolving research needs.

MIT provides a unique environment for research training of comparative medicine professionals, allowing them to work with cutting edge animal models as well as alternatives to animal models in highly translational research. DCM continues to provide and improve upon learning opportunities for veterinary students and veterinarians interested in research careers through our training programs for comparative medicine scientists. DCM hopes to successfully pursue reinstatement of DCM's National Institutes of Health (NIH) T32 grant in academic year 2023, which was lost in 2017 after 30 continuous years of funding.

Accomplishments

DCM continues to strive to provide a high standard of animal care, veterinary clinical, and research technical support for all research involving animals across MIT and WI. The scope of this support spans the animal research needs of 140 MIT and WI faculty across 16 DLCs, ultimately underpinning $323.9 million in research expenditures in FY22 (financial data unavailable for FY23 at this time). To support the most rigorous research, DCM holds itself and the Institute to the highest of standards. DCM provides expert support to research investigators in animal model selection and procurement through DCM's business office. DCM's mouse facilities maintain the highest of health standards, with in-house core breeding facilities and transgenic animal production facilities managed by DCM supporting MIT's / WI's requirement to rederive in all rodent lines from nonapproved vendors, as well as supporting the production of genetically modified mouse lines for faculty research. A germ-free mouse core facility and DCM-managed medical microbiology laboratory supports microbiome research initiatives campus-wide, while in-facility behavior spaces support neuroscience aims, and in-facility irradiators and a state-of-the art imaging core support cancer research. Large animal neuroscience and device development / drug delivery research is facilitated by the presence of two operating suites managed by DCM with associated imaging equipment and in facility transgenic and behavior space for researcher use. DCM additionally provides comparative pathology, clinical pathology, histology, and microbiology laboratory services as part of the veterinary care program and in support of research needs. Highly specialized veterinarian, veterinary behaviorist, veterinary technician, and teaching staff provide expert guidance to research investigators as they design their studies, and are available to provide technical assistance for accomplishing study aims.

This work ultimately involves the care of over 75,000 animals daily. DCM continues to adapt to changes in the nature of the animal models and the work that needs to be done with animals since the pandemic. Though fish and mice remain overrepresented in DCM's census, the needs for large animal research models has continued to grow significantly in the past year, especially in neuroscience and device development research. The common marmoset colony for neuroscience research (supported by NIH and philanthropic funds for faculty within the MIT Department of Brain and Cognitive Sciences, McGovern and Picower) has grown to 309 animals in FY23, an 18.4% increase from the prior year and especially notable for a colony that received its first animals in 2015. Similarly, a hamster colony started at the end of FY22 is now populated by 79 hamsters (to support a new WI faculty member), and facility renovations in E25 will soon allow the population of swine to increase by 25% in FY23 to accommodate new emerging lines of device development research within The Media Lab funded by the new K. Lisa Yang Center for Bionics, while continuing to meet the needs of existing Mechanical Engineering and Chemical Engineering researchers who work with swine. Rodent populations remain down by approximately 25% from their pre-pandemic norms; however, the population of DCM's main rodent breeding facility has increased by 25% in the past year which portends growth throughout the program, with the sustenance of the decreased numbers originating mainly from underutilization of one of the two mouse facilities focused on supporting rodent models for neuroscience (census has remained at 43% of pre-pandemic norms for the past two years).

Additional DCM accomplishments include:

- DCM hosted the annual D. E. Schauer Lecture in collaboration with BE in September 2022. This lecture honors Dr. David Schauer, a former BE / DCM faculty member who passed away. Dr. Vincent B. Young, MD, PhD, Professor of Internal Medicine at University of Michigan Medical School spoke on "Host-microbe interactions in the gut" for the first in person instance of this lecture since the COVID-19 pandemic.

- DCM Director Kelly Metcalf Pate, DVM, PhD, DACLAM, led tours of DCM facilities for the VPR's MIT Visiting Committee in October 2022. This was the first time that tours of the animal facilities were featured in such a visit.

- DCM hosted a Compassion Fatigue specialist in April 2023 to educate DCM staff and the MIT community about the dangers of compassion fatigue in an animal research setting, to conduct an assessment of the level of compassion fatigue experienced by the animal research community at MIT/WI, and to begin to work with DCM to build a compassion fatigue support program for the MIT/WI community.

- DCM partnered with Americans for Medical Progress (AMP), Massachusetts Society for Medical Research (MSMR), and Novartis to host a short course on "Communicating About Animal Research" in July 2023. This course attracted participants from throughout MIT/WI, including members of the research community and those who play roles in media relations for the VPR and other DLCs, as well as participants from 15 other local institutions representing both industry and academia.

The CAC is a committee of Institutional Official (IO)-appointed MIT/WI researchers, CAC, DCM and EHS staff, and unaffiliated representatives who serve as the federally required Institutional Animal Care and Use Committee (IACUC) for MIT and The Whitehead Institute. As such, it has a complex charge of providing regulatory oversight for the whole of MIT's animal research enterprise. This includes:

- Timely review of all new proposals for animal research, and any significant proposed changes to ongoing animal research, similar to the process undertaken by an Institutional Review Board for human subjects research.
- Annual review of 290 active protocols, which undergo full rewrites once every 3 years.
- Twice yearly inspections of 140 research spaces and 190,000 gross square feet of animal facility space.
- Serving as the primary point of contact for the regulatory agencies with oversight of animal research, including the United States Department of Agriculture (USDA), NIH Office of Laboratory Animal Welfare (OLAW), the Cambridge Commissioner office, and AAALAC International. This involves at a minimum preparing annual reports for all, as well as conducting and documenting noncompliance investigations as necessary.

In an ongoing effort to improve the quality and timeliness of their service to researchers at MIT/WI, the CAC has been working with VPR to develop an online protocol submission system since January 2020. This "CAC Connect" system officially went live this year in April, with the first protocol submitted through the system approved in May 2023.

Administrative Initiatives

A primary objective for DCM and the CAC remains continual improvement of their service to the research community. Prior iterations of both websites were not user friendly nor mobile compatible. Ongoing efforts to improve the visibility of and accessibility to services have led to VPR-funded website updates for both entities, with the new CAC website going live in February 2023, and development of a new DCM website started in May 2023. To streamline the service request process for the research community, DCM has rolled out standardized forms and online submission platforms for multiple services in FY23, including new systems for Large Animal Surgery scheduling requests and Pathology case submissions; similarly, DCM has centralized the process of adopting out and retiring research animals that are no longer needed for study in an effort to make these options more readily accessible for eligible animals and to ensure that such animals go to suitable homes. An updated paper records system for large animal species has been lauded by USDA inspectors as an improvement in clinical care, and the adoption of online large animal rounds sheets have allowed for improved communication about active clinical cases among staff while simultaneously streamlining operations, to free up staff for more research support activities. A thorough review of training requirements for research investigators is underway, and has resulted in refinement of procedures so as to better target training to researcher needs. For instances in which researchers would rather contract with skilled professionals instead of learning the skills themselves, DCM continues to build a team of veterinary technicians with advanced skills to directly aid researchers in accomplishing their study aims.

DCM and the CAC continues to strive to maintain and strengthen relations with academic units throughout MIT/WI, as well as our partners in service. DCM and the CAC continue to coordinate closely with DLC Directors for Administration and Finance to connect with new faculty during the negotiations phase to ensure both DCM and CAC are able to provide the highest quality and timeliest support to their new animal research programs. Similarly, efforts continue to strengthen ties across DCM, the CAC, EHS, Occupational Health, and Facilities, as effective coordination among these groups is essential to the optimal functioning of the animal care program.

The quality of service in part depends on the quality of equipment within DCM facilities. DCM has historically benefited from strong institutional investments in upgrades of aging equipment, with the FY23 replacement of an autoclave within one of DCM's two surgical facilities allowing for continued support of aseptic surgeries within this space. Upgrades to cagewash equipment have been approved in two DCM facilities for FY24, and will be essential to maintain the high health status of our animal populations and to stay in compliance with federal regulations. DCM is currently undertaking a review of the procedures for upkeep of these expensive pieces of equipment to make sure that we are optimizing their performance and longevity for years to come.

The renovation of DCM's main multi-species / flex animal facility that was initiatited in 2019 was completed in 2021, with repopulation of that facility started in that same year. All space within that newly renovated facility has been spoken for as of the end of FY23, highlighting a continued need to keep space for animal research in mind as MIT considers future construction projects, as well as the need to continue to invest in upgrades to aging HVAC and plumbing infrastructure in DCM's older facilities. Renovations of the swine housing space (underway as of June 2023) will provide enclosures that facilitate co-housing of compatible swine and a larger more enriched environment, in addition to allowing DCM to expand our capacity for swine housing as above.

Finances and Funding

DCM's animal resources, surgical center, and diagnostic laboratory enterprise operates as a service center with the goal of recouping expenses by charging for services as close to a break-even rate as possible. In FY23 – FY24, DCM plans to complete a comprehensive rate setting exercise to ensure that DCM is meeting that goal, with a review of per diem rates already underway.

In FY23, 5 staff veterinarians within DCM in addition to faculty members Dr. Metcalf Pate and Dr. Fox held PI status, attracting $2.9 million in sponsored research funding from federal and private foundation funds. These funds included 2 NIH grants, 2 DOD grants, and 3 private foundation grants.

Additionally, DCM's summer research training program for veterinary students continued to benefit from sponsored funding for the second year in a row, with funding from an NIH T35 grant and Boehringer Ingelheim allowing for summer research experiences for 6 veterinary students at MIT in summers 2022 and 2023.

Personnel Information

To support the activities outlined above, DCM employs 178 personnel and the CAC employs 3 staff members. DCM staff include 8 clinical veterinarians, 1 comparative

pathologist, 7 veterinarian postdoctoral fellows, 4 veterinary technician managers / supervisors, 19 veterinary technicians, 13 animal resources managers / supervisors, 87 animal care technicians, 2 behavior management program staff, 4 transgenic core staff, 2 maintenance workers, 6 diagnostic / pathology laboratory staff, 9 business office staff, and 2 education professionals, as well as 7 research staff to support ongoing sponsored research efforts. A new Associate Director for Clinical Services, Dr. Tiffany Borjeson, DVM, CPIA, DACLAM was hired in June 2023 following a 10-month recruitment process; Dr. Borjeson will aid the DCM Director in overseeing veterinary care throughout MIT/WI. Other notable changes to DCM's roster in FY23 include the addition of a Financial Officer and the addition of an IT systems administrator towards improving business operations within the service center, an additional veterinary technicians with advanced technical skills and two necropsy technicians to meet growing service center demands, and an additional education professional with a concentration on quality assurance and communications to facilitate regulatory compliance. FY23 saw turnover in DCM's Comparative Pathologist role, with the incumbent leaving in December 2022 and successful recruitment of a replacement in May 2023, as well as the retirement of the Associate Director for Research; the latter role remains open, as does the Assistant Director for Large Animal Medicine and Surgery role vacated in spring 2022. As in FY22, the competitive market makes it increasingly difficult to recruit and retain qualified veterinarians and veterinary technical professionals to fill MIT's research needs. DCM plans to continue to work with Human Resources to build an advancement structure and robust management team in FY24 to better encourage retention within these unique staff groups in the future.

DCM veterinary technical and facilities maintenance staff received recognition for the incredible dedication that they show in supporting work with animals at MIT in the form of two Infinite Mile Awards in FY23. Additionally, in FY23 DCM veterinarians continue to be recognized nationally as experts in comparative medicine and research:

- Dr. Kelly Metcalf Pate, DVM, PhD, DACLAM, Director of DCM and Associate Professor, participated in an NAS State of the Science and Future Needs for Nonhuman Primate Model Systems ad hoc committee in FY22 – 23, cumulating in publication of their findings in May 2023.
- Dr. Metcalf Pate has since been appointed to the NIH Advisory Committee to the Director Working Group on Catalyzing the Development and Use of Novel Alternative Methods to Advance Biomedical Research, and continues to serve as Chair for the American Association of Laboratory Animal Sciences (AALAS) Scientific Advisory Committee.
- Dr. James Fox, DVM, MS, DACLAM, Founding Director of DCM and Emeritus Faculty, chaired an NIH ORIP Workshop on Enhancing Rigor and Reproducibility in Animal Research by Managing Extrinsic Factors in September 2022.
- Dr. Fox continues to play a pivotal role in overseeing the revisions for the premier guiding document for animal care programs, the Guide for the Care and Use of Laboratory Animals, as Chairman for a standing committee within the National Academy of Sciences as part of his role as a member of the National Academy of Medicine. Furthermore, he continues to serve on the executive committee for the Massachusetts Society of Medical Research (MSMR), and

as editor-in-chief for the American College of Laboratory Animal Medicine (ACLAM) Publications Committee.

- DCM Staff Veterinarian Dr. Susan Erdman, DVM, MPH, PhD, DACLAM was appointed in April 2022 as a standing member of the NIH Scientific and Technical Review Board on Biomedical and Behavioral Research Facilities.
- DCM Staff Veterinarian Dr. Robin Kramer, DVM, DACLAM serves on the American Association of Laboratory Animal Sciences (AALAS) government relations committee.
- DCM Staff Veterinarian Dr. Martina Jackson, VMD, DACLAM serves as chair of the planning committee for the American College of Laboratory Animal Medicine (ACLAM) annual conference, and as vice chair of the Association of Primate Veterinarians (APV) membership committee.
- DCM Veterinarian Postdoctoral Trainee Dr. Amanda Armijo, DVM, PhD was recipient of a highly competitive NIH Loan Repayment Program (LRP) award through NIEHS in Fall 2022, and the prestigious Karen Wetterhahn Memorial Award from NIH NIEHS Superfund Research Program in January 2023.
- Drs. Fox and Metcalf Pate both serve as editors for the upcoming 4th edition of the textbook for comparative medicine professionals, "Laboratory Animal Medicine".
- Drs. Metcalf Pate and new Associate Director Dr. Tiffany Borjeson, DVM, CPIA, DACLAM serve as ad hoc specialists for the national accrediting body for animal care programs, AAALAC.
- Staff veterinarians serve as peer reviewers for NIH, the National Aeronautics and Space Administration (NASA), USDA and private foundation grants, and numerous journals.

Teaching and Curriculum

The Division of Comparative Medicine has been involved in postdoctoral training in comparative medicine since 1982. Since that time, 75 DVMs have successfully completed the program and 53 have become diplomates of the American College of Laboratory Animal Medicine. 33 of DCM's graduates are in comparative medicine positions in academic institutions with sizable NIH-supported biomedical research programs, and 22 of DCM's fellows are Directors or Associate Directors of Laboratory Animal Medicine programs at universities or medical centers. The remaining are in a Director's position or research role in pharmaceutical or biotech firms, or hold positions in federal or state public health departments. Six past fellows are Full Professors, five are Associate Professors, eight are Assistant Professors, and five are at the Instructor level.

In FY23, DCM welcomed two new veterinarian postdoctoral trainees to its training program, and graduated four additional veterinarian postdoctoral trainees. The FY23 graduating class included two trainees with a comparative pathology focus, who went on to an Assistant Professor position at University of Michigan School of Medicine and a Digital Pathology Fellowship at Tufts Cummings School of Veterinary Medicine, and two trainees with a clinical focus, who went on to an Assistant Professor position at

Tufts Cummings School of Veterinary Medicine and a Clinical Veterinarian position at Charles River Laboratories. Three recent graduates of the program successfully passed their specialty board exam in Laboratory Animal Medicine in FY23, while the two recent graduates with a pathology focus passed the first of two phases of their specialty board exam in Veterinary Pathology.

DCM worked collaboratively with Tufts Cummings School of Veterinary Medicine in FY23 to establish a partnership that will allow veterinarian postdoctoral trainees to pursue their PhD in Biomedical Sciences through Tufts with faculty mentors at MIT. This joint program accepted its first graduate student in FY23, who will start this new program in August 2023. It is anticipated that this new program will enhance the appeal of research training at MIT to future applicants, and will increase the competitiveness of DCM's upcoming NIH T32 grant application.

The Division continues to provide short-term summer training opportunities for veterinary students interested in careers in research and comparative medicine in collaboration with Tufts Cummings School of Veterinary Medicine, facilitated by NIH T35 and Boehringer Ingelheim Veterinary Scholars funding first procured in FY22. The summer fellowship program serves to introduce veterinary students to careers in research, and serves as an important pipeline to subsequent research training and comparative medicine careers. The summer 2023 class consisted of six veterinary students conducting research onsite at MIT out of 19 total veterinary students across the Tufts and MIT sites; five veterinary schools were represented by this year's pool.

DCM staff veterinarians continue to assist in the instruction of lectures and wet labs for courses taught to the MIT community by Professor Wilson: Responsible Conduct of Science (9.S911 – Staff Veterinarian Dr. Erdman), Professor Harnett: Systems Neuroscience (9.17 – DCM Director Dr. Metcalf Pate), by Professor Mark: Quantitative Systems Physiology: Organ Transport Systems (HST 542 – Staff Veterinarians Drs. Alison Hayward, DVM, CPIA, DACLAM and Abby Needleman, DVM), and by Professor Edelman: Cardiovascular Pathophysiology (HST 090/091 – Staff Veterinarians Drs. Niora Fabian, MS, DVM, DACLAM, Hayward, and Needleman). DCM staff additionally participate in the training of medical residents who rotate through MIT's Occupational Health service.

Research Activities

In FY23, DCM staff and trainee research activities resulted in 20 peer reviewed publications, and in presentations at multiple national conferences including the National Veterinary Scholars Symposium (NVSS) in August 2022; European Helicobacter and Microbiota Study Group (EHMSG) in September 2022; Association of Primate Veterinarians (APV) in October 2022; American Association of Laboratory Animal Sciences (AALAS) in October 2022; to the National Primate Research Collaborative Behavior Management Committee in March 2023; to the American College of Laboratory Animal Medicine (ACLAM) Forum in May 2023; at the Canadian Association of Laboratory Animal Sciences (CALAS) in June 2023; to the Society of Toxicologic Pathology (STP) in June 2023; and to the American Society of Primatologists (ASP) in June 2023 (ultimately receiving the Primate Welfare Award).

Continued funded research aims within DCM during FY23 included:

- Defining the effect of post-traumatic stress on the composition of mucin and the microbiome in the gastrointestinal system in a mouse model, and determining if a synthetic mucin may protect against the effect of stress on the microbiome (Metcalf Pate, DOD funding)
- Examining the microenvironment associated with Barrett's esophagus (Fox, NIH subaward)
- Defining the role of *Helicobacter pylori* as a tumor initiator in gastric cancer, modulation of systemic immune responses and the Th1/Th2 gastric cytokine profile due to *H. pylori* infection and concurrent infection with non-*H. pylori* gastric microbiota (Fox, DOD subaward)
- Testing perinatal probiotic strategies to boost oxytocin for mother-infant bonding and a societal trajectory of improved impulse control, empathy, and altruism (Erdman, John Templeton Foundation funding)
- Determining the effect of LED lighting on behavior, stress and reproductive success in zebra finch models of communication and learning (Fabian, Grants for Laboratory Animal Science (GLAS) foundation funding)
- Definition of the effect of the common opportunistic pathogen Corynebacterium bovis on cancer research in mouse models (now retired Associate Director for Research Dr. Scooter Holcombe, DVM, PhD, DACLAM, American College for Laboratory Animal Medicine (ACLAM) Foundation)
- Validation of a novel in vitro fertilization method using a murine model and DCM's established transgenic facilities (Erdman, and recent postdoctoral trainee graduate Dr. India Napier, DVM, PhD, Deshpande Foundation and NIH funding)

The Metcalf Pate lab renovation project, as planned at the time of Dr. Metcalf Pate's recruitment in 2021 to allow for BSL-2+ work necessary to continue her work on HIV pathogenesis, was started in November 2022 and has continued through the end of FY23 due to post-COVID-related pipeline and labor delays and aging HVAC infrastructure within the building.

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