

## **Report to the President year ended June 30, 2024, Division of Comparative Medicine and the Committee on 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, DAACLAM since July 2021, when founding director Dr. James Fox, DVM, MS, DAACLAM stepped down after 46 years of service. Dr. Fox remains emeritus faculty within Biological Engineering.

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 was chaired by Dr. Howard Heller, MD, MPH, faculty in the Harvard-MIT Health Sciences and Technology program, from March 2019 until he stepped down in April 2024; at the VPR's request, Dr. Metcalf Pate has served as interim while a search for a new chair is ongoing.

Both DCM and the CAC report independently to the VPR in the VPR's capacity of Institutional Official.

### **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 produces rigorous scientific results while preserving animal welfare. 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 research 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.

A top priority for both DCM and the CAC in FY24 was preparation for MIT's triennial Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) site visit, which

occurred in November 2023 and resulted in *continued full accreditation* for MIT's animal research program. AAALAC is a private nonprofit organization that provides 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. Careful coordination between DCM and the CAC, alongside MIT VPR leadership, EHS, Occupational Health, and Facilities, was essential for the successful continued accreditation of the program.

DCM and the CAC continue to evolve to accommodate growing and increasingly complex animal research support needs, and, towards that end, DCM is in the final stages of completing a comprehensive review of their available services and fee for service structure, 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 and veterinary technician students and veterinarians interested in research careers through our training programs for comparative medicine scientists. These include National Institutes of Health (NIH) T35-funded summer research opportunities for veterinary students, in addition to new partnerships with Tufts Cummings School of Veterinary Medicine and Massasoit Community College that facilitate the pursuit of a PhD for veterinarians and exposure to a research support career for veterinary technician students. To further build opportunities for training in comparative medicine, DCM hopes to successfully pursue reinstatement of DCM's NIH T32 grant in academic year 2024, 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 141 MIT and WI faculty across 18 DLCs, ultimately underpinning \$350.5 million in sponsored research dollars received in FY24 (34% of total sponsored research funding awarded to MIT). 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 76,000 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) that received its first animals in 2015 remains robust at 288 animals in FY24, and continues to successfully produce transgenic marmosets. Similarly, a hamster colony started at the end of FY22 is now populated by 169 hamsters (a 113% increase from FY23), and a collaboration between the faculty member and the DCM transgenic core facility has resulted in the generation of transgenic hamsters. Facility renovations in E25 that were anticipated to 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, have been slow due to unexpected problems with the new housing enclosures; we have identified a new supplier for the enclosures and expect to resolve these issues in FY25. The arrival of a new researcher at MIT will necessitate the establishment of a colony of temperate frog species in DCM facilities in FY25. Rodent populations are beginning to recover from the decline observed during the pandemic, and are now 9% higher than they were in FY23 (at 84% of pre-pandemic norms); the population of DCM's main rodent breeding facility similarly increased by 8% in the past year, portending further growth throughout the program. Continued underutilization of one of the two mouse facilities focused on supporting rodent models for neuroscience (census has further decreased by 10% over the past year to 47% of pre-pandemic norms) has been identified as a barrier to further growth for the rodent program. In FY25, DCM plans to work with the researcher community to assess space needs and to use that data to redefine the zones of work within rodent facilities towards optimizing the availability of usable space for researcher needs.

Additional DCM accomplishments include:

- DCM successfully hosted an AAALAC site visit in November 2023, resulting in continued full accreditation for the animal research program (see above).
- DCM initiated the formation of a Compassion Fatigue Committee composed of DCM staff and non-DCM staff who work with animals. This committee is tasked with identifying sources of and ways to combat compassion fatigue in those who work with animals at MIT. The formation of this committee was inspired by the recommendations of a Compassion Fatigue specialist who DCM hosted 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 278 active protocols, which undergo full rewrites once every 3 years.
- Twice yearly inspections of 75 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 in April 2023, with the first protocol submitted through the system approved in May the same year. The migration of protocols into CAC Connect is ongoing, with expected completion in 2026.

### **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 with expected completion in fall 2024. To streamline the service request process for the research community, DCM 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 started in FY23 has resulted in refinement of procedures so as to better target training to researcher needs and new training courses for those who work with non-rodent animals. 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 capital equipment. Upgrades to cagewash equipment have been approved in two DCM facilities for FY25, and will be essential to maintain the high health status of our animal populations and to stay in compliance with federal regulations. An ongoing challenge within the facilities is the corrosion of equipment that requires steam and hot water to function secondary. In FY24, DCM completed a review of the procedures for upkeep of these expensive pieces of equipment to make sure that we are optimizing their performance and longevity, and determined that Cambridge water quality played a primary role in their demise. In an attempt to slow the damage, DCM shifted to new reagents for use in these systems with chemistry that should better complement the water quality, and one of the upgraded cagewash systems will pilot the use of cold water washes in conjunction with dry heat sterilization.

The renovation of DCM's main multi-species / flex animal facility that was initiated in 2019 was completed in 2021, with repopulation of that facility in 2021. All space within that newly renovated facility remains spoken for as of the end of FY24, 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.

### **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 FY24, DCM started a comprehensive rate setting exercise to ensure that DCM is meeting that goal; these rates will be rolled out in FY25.

In FY24, 4 staff veterinarians within DCM in addition to faculty members Dr. Metcalf Pate and Dr. Fox held PI status, attracting \$2.7 million in sponsored research funding from federal and private foundation funds. These funds included 2 NIH grants, 2 DOD grants, and 2 private foundation grants.

Additionally, DCM's summer research training program for veterinary students continued to benefit from sponsored funding for the third 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, 2023 and 2024.

### **Personnel Information**

To support the activities outlined above, DCM employs 177 personnel and the CAC employs 4 staff members. DCM staff include 7 clinical veterinarians, 1 comparative pathologist, 6 veterinarian postdoctoral fellows, 6 veterinary technician managers / supervisors, 20 veterinary technicians, 13

animal resources managers / supervisors, 87 animal care technicians, 2 behavior management program staff, 3 transgenic core staff, 2 maintenance workers, 7 diagnostic / pathology laboratory staff, 10 business office staff, and 2 education professionals, as well as 5 research staff and 1 graduate student to support ongoing sponsored research efforts. A new Assistant Director for Large Animal Medicine and Surgery joined the DCM veterinarian team in December 2023 after an 18-month vacancy, an Assistant Director for Nonhuman Primate Medicine joined in February 2024 after an 8-month vacancy, and DCM eagerly anticipates welcoming three additional veterinarians to MIT in fall 2024 to fill the remaining clinical veterinarian vacancies. The role of Associate Director for Research remains open following the incumbent's FY23 retirement, and recruitment is ongoing in anticipation of the retirement of DCM's Assistant Director for Rodent Medicine in fall 2024. Though DCM ends FY24 well-staffed in most sectors (90-100%), the competitive market has made it increasingly difficult to recruit and retain qualified veterinarians and veterinary technical professionals to fill MIT's research needs. As in prior years, DCM plans to continue to work with Human Resources to build an advancement structure and robust management team in FY25 to better encourage retention within these unique staff groups in the future.

DCM staff received recognition for the incredible dedication that they show in supporting work with animals at MIT in the form of three Infinite Mile Awards in FY24:

- Keith Kun, Director for Administration and Finance;
- Erin Mathieu, Manager for Animal Resources; and
- Wontaek Chung, Advanced Veterinary Technical Specialist.

Additionally, in FY24 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, was 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. This Committee's recommendations were accepted by the NIH in February 2024, and contributed to the development of the ongoing NIH Complement Animal Research in Experimentation (Complement-ARIE) research program.
- Dr. Metcalf Pate presented on behalf of the NAS State of the Science and Future Needs for Nonhuman Primate Model Systems ad hoc committee at multiple national conferences, including at the Association of Primate Veterinarians (APV) in October 2023, the American Association of Laboratory Animal Sciences (AALAS) in October 2023, and the Society of Toxicology in March 2024.
- Dr. Metcalf Pate was an invited speaker on maintaining rigor in animal research, and on implementing refinements in preclinical research at the Public Responsibility in Medicine and Research (PRIM&R) conference in December 2023.
- Dr. Metcalf Pate concluded her term as Chair for the American Association of Laboratory Animal Sciences (AALAS) Scientific Advisory Committee in October 2023, and joined the Program Planning Committee for the 2024 National Veterinary Scholars Symposium. She serves on the advisory boards for the Massachusetts Society of Medical Research (MSMR) and the Center for Alternatives to Animal Testing (CAAT).
- Dr. James Fox, DVM, MS, DACLAM, Founding Director of DCM and Emeritus Faculty, was elected an Honorary Diplomate of the American College of Veterinary Pathologists (ACVP) in November 2023, and received the Nathan Brewer Award for Lifetime Achievement at the American College of Laboratory Animal Medicine (ACLAM) Forum in April 2024.
- 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.

- DCM Staff Veterinarian Dr. Susan Erdman, DVM, MPH, PhD, DACLAM continues to serve as a standing member of the NIH Scientific and Technical Review Board on Biomedical and Behavioral Research Facilities.
- 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 Staff Veterinarians Dr. Amanda Armijo, DVM, PhD and Dr. Niora Fabian, DVM, MS, DACLAM, were recipients of highly competitive NIH Loan Repayment Program (LRP) awards.
- 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, 83 DVMs have successfully completed the program and 63 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 21 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 FY24, DCM welcomed two new veterinarian postdoctoral trainees to its training program, and graduated two additional veterinarian postdoctoral trainees. The FY24 graduating class went on to an Assistant Professor position at Queens University (Toronto, Ontario, Canada) and to a Clinical Veterinarian position at Massachusetts General Hospital (Boston, MA). Three recent graduates of the program with clinical focus successfully passed their specialty board exam in Laboratory Animal Medicine in FY24, while the one recent graduate with a pathology focus passed 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, with its first graduate student starting the 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 2024 class consisted of six veterinary students conducting research onsite at MIT out of 26 total veterinary students across the Tufts and MIT sites; five veterinary schools were represented by this year's pool.

Dr. Metcalf Pate serves as professor on record for the spring semester course Biological Engineering Design (20.380), in which Visiting Scientist Dr. Galit Frydman, DVM, ScD guest lectured. 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 Engelward: Genome Stability and Engineering in the context of Diseases, Drugs, and Public Health (20.213 – Staff Veterinarian Dr. Armijo), Professor Harnett: Systems Neuroscience (9.17 – DCM Director Dr. Metcalf Pate), and by Professor Edelman: Cardiovascular Pathophysiology (HST 090/091 – Associate Director Dr. Borjeson and Staff Veterinarians Dr. Andrea Slate, DVM, DACLAM). DCM staff additionally participate in the training of medical residents who rotate through MIT's Occupational Health service.

## Research Activities

In FY24, DCM staff and trainee research activities resulted in 21 peer reviewed publications, and in presentations at multiple national conferences including the National Veterinary Scholars Symposium (NVSS) in August 2023; ExoticsCon in August 2023; Environmental Mutagenesis and Genomics Society Annual Meeting in September 2023; European Helicobacter and Microbiota Study Group (EHMSG) in September 2023; Association of Primate Veterinarians (APV) in October 2023; American Association of Laboratory Animal Sciences (AALAS) in October 2023; American College of Veterinary Pathologists (ACVP) in November 2023; the Conference on Retroviruses and Opportunistic Infections (CROI) in March 2024; and the American College of Laboratory Animal Medicine (ACLAM) Forum in April 2024.

Continued funded research aims within DCM during FY24 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 possibility of programming indigenous gut bacteria (Fox, DOD 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, NIH 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)
- Developing A deep learning-enhanced multiphysics and multiscale framework for predictive modeling of inflammation-induced thrombosis (Frydman, 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 completed in FY24 due to post-COVID-related pipeline and labor delays and aging HVAC infrastructure within the building.

July 2024 marks the 50 year anniversary of the Division of Comparative Medicine, and DCM and the CAC look forward to reflecting on their legacy and further refining their practices towards achieving further excellence in service, research and teaching in the years ahead.

**Kelly A. Metcalf Pate, DVM, PhD, DACLAM**  
**Director, Division of Comparative Medicine**  
**Interim Chair, Committee on Animal Care**  
**Associate Professor, Department of Biological Engineering**

*More information about the Division of Comparative Medicine can be found at:*  
<https://comp-med.mit.edu/>

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