

Division of Comparative Medicine

The [Division of Comparative Medicine \(DCM\)](#) has a mission to support MIT's research and education efforts through providing excellent quality animal husbandry and clinical care for all research animals on the MIT campus, including animals housed at the Whitehead Institute for Biomedical Research. DCM provides a high level of service and training to research investigators who work with animals at MIT and the Whitehead Institute, serves as an international leader in comparative medicine research, and trains the next generation of comparative medicine scientists. Since its inception in 1974, DCM has evolved into a comprehensive 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 division's research program is funded by grants from the National Institutes of Health (NIH) and private foundations, and its predoctoral training program is newly supported by an NIH T35 grant starting in summer 2022.

DCM has 172 personnel, including 84 animal care technicians, 17 veterinary technical staff, five diagnostic laboratory personnel, six research personnel, nine veterinary professional staff, 11 postdoctoral trainees, 31 administrative and supervisory staff, four support staff, one visiting graduate student, and four visiting scientists. DCM's administrative headquarters along with its diagnostic and research laboratories are located on the eighth floor of Buildings 16 and 56. The division encompasses approximately 190,000 gross square feet in seven buildings devoted to animal research activities on the MIT campus. The newly renovated E17/18 facility began the process of repopulation in FY2022. DCM's animal facilities continue to be fully accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) and in compliance with all federal and local regulations and guidelines.

Facility Management and Animal Care

DCM's average daily census of laboratory animals continues to recover from its 2020 pandemic nadir of 27% below average. Mice and rats remain the primary species on campus, and rodent census numbers remain at 16% below pre-pandemic census levels. Researchers working with rodent species continue to benefit from a high level of service across DCM's six rodent facilities. The division has two core facilities to support transgenic and gene "knockout" in vivo experiments and performs a range of transgenic services, including in vivo embryo transfer for rederivation of mice with endemic disease that have been imported to MIT from laboratories worldwide, in vitro fertilization, and genotyping of mice. The transgenic core also provides genetically engineered mice to the research community at MIT. DCM technical staff provide colony management of mouse models for researchers. The division recently recruited an additional veterinary technical services supervisor (Wontaek Chung, formerly a veterinary technician at Brigham and Women's Hospital) to spearhead expansion of these services to include more advanced technical offerings such as surgical support, technical services (e.g., gavage and injections), and samples from rodent species.

The demand for space and support for large animal species continues to steadily increase relative to pre-pandemic numbers, while rodent census numbers remain decreased. DCM operates two fully functional surgery suites (in Buildings E25 and 46) and three animal housing facilities in support of these large animal species. For the past seven years, the division has worked closely with faculty in the McGovern Institute for Brain Research to establish a successful marmoset breeding colony and to construct transgenic marmoset models. The colony has grown from zero animals at the beginning of FY2015 to 229 adult and 32 infant marmosets at the end of FY2022, with more than 120 additional animals currently housed at the Broad Institute due to lack of space on MIT's campus. This initiative is space and personnel intensive; marmosets are now occupying considerable space in DCM facilities located in Buildings 46 and E25, and plans are in place to expand into E17/18 in FY2023 to accommodate on-site growth of the colony to up to 300 animals over time to meet growing researcher needs. To further facilitate work with this unique resource, DCM is currently in the process of renegotiating the contract with the Broad Institute to allow for more seamless coordination across the two marmoset colony management programs.

Similarly, DCM is working to increase capacity for swine research in FY2023 to accommodate anticipated future needs that will arise following the inception of the K. Lisa Yang Center for Bionics (for which Media Lab faculty member Hugh Herr will serve as principal investigator [PI]) while continuing to meet the needs of existing researchers who work with swine (Mechanical Engineering faculty member Gio Traverso and Chemical Engineering faculty member Bob Langer). Additional anticipated non-rodent needs include a tree shrew (small, nonhuman primate species) breeding colony (to support Brain and Cognitive Sciences faculty member Michael Halassa), the capability to support hibernating hamsters (newly recruited Whitehead Institute faculty member Sinisa Hrvatin), and the ability to support biocontainment studies with chickens (Whitehead Institute faculty member Sebastian Lourido). To ensure that the practices in caring for these diverse large animal species remain in compliance with all federal and local regulations, to guarantee their welfare, and to facilitate translational science, DCM recruited a veterinary behaviorist, Rachele McAndrew from the Tulane National Primate Research Center, to start in June 2022, and a behavior technician, Olivia Fiske from the California National Primate Research Center, who started in winter 2021. McAndrew and Fiske will establish a behavior management program as recommended by AAALAC in its October 2020 site visit.

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. The diagnostic laboratory is equipped and staffed to provide these services at the high standards of a reference or medical laboratory. MIT was fortunate to recruit veterinary pathologist Nicola Parry to lead this service center as assistant director for comparative pathology starting in June 2022, following the recruitment of DCM's former pathologist, Dr. Suresh Muthupalani, to industry in winter 2022. A fellowship in comparative pathology for veterinarians is being established under Dr. Parry's guidance, and it currently has its first two trainees (Yao Lee from Michigan State University and Claire Lyons from the Johns Hopkins School of Medicine); this fellowship will help to train comparative pathology specialists toward decreasing the shortage of such individuals throughout the field in parallel to the clinical and research training provided to veterinarian postdoctoral fellows in the long-standing existing program.

DCM continues to support the highest quality in animal care and research in compliance with all federal and local regulations and guidelines. An annual inspection by the US Department of Agriculture in August 2021 revealed no deficiencies in the program. The facility remains fully AAALAC accredited, and the next AAALAC site visit is anticipated in fall 2023.

Staff Changes

In addition to DCM's success in recruiting a staff veterinarian pathologist and a veterinary behaviorist in FY2021, DCM welcomed two clinical veterinarians who have advanced training in nonhuman primate medicine and are diplomates in the American College of Laboratory Animal Medicine (ACLAM), Dr. Alexis Mackiewicz in July 2021 and Dr. Martina Jackson in August 2021; these veterinarians filled the roles previously occupied by Dr. Mary Patterson, who retired in October 2020 after more than 20 years of service to DCM, and Dr. Monika Burns, who left MIT after three and a half years of service for an industry job just prior to the pandemic. DCM furthermore looks forward to welcoming Dr. Abigail Needleman, a specialist in exotic and large animal medicine and surgery, to the team in September 2022 to fill the clinical veterinarian role vacated by Dr. Damodaran Annamalai, who was recruited to an industry job in winter 2022 after five years at MIT.

DCM continues to recruit for a new assistant director for large animal medicine and surgery, a role that was vacated in spring 2022 by Dr. Jennifer Haupt, a boarded specialist in veterinary surgery and laboratory animal medicine who was recruited to an industry job after eight years at MIT. DCM looks forward to adding an associate director/attending veterinarian to its ranks in FY2023 to lead the veterinary clinical service center alongside DCM's director, Dr. Kelly Metcalf Pate; the attending veterinarian role was vacated by Dr. Mark Whary when he retired prior to the pandemic, never filled, and only recently approved to post. The competitive market makes it increasingly difficult to recruit and retain qualified veterinary and veterinary technical professionals to fill MIT's research needs. DCM plans to work with Human Resources to build an advancement structure and robust management team in FY2023 to better encourage retention within these staff groups in the future.

Research Activities

In FY2022, five DCM faculty and scientific staff held PI status. Five NIH-funded grants supported a range of studies, as follows:

1. An assessment of the role of *Helicobacter* as a tumor promoter in gastric cancer and the mechanisms by which it contributes to the malignant process (James Fox, founding director and emeritus professor)
2. An examination of the microenvironment associated with Barrett's esophagus (Fox)
3. Exploration of 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)

4. Development of a robust rodent model with phenotyping tools as a foundation for tractable microbial strategies for obesity and public health (Susan Erdman, assistant director and senior research scientist)
5. Establishment and characterization of a mouse model for studying the effect of the microbiome on latent viral reservoirs in HIV (Metcalf Pate).

Dr. Scooter Holcombe, associate director and clinical/research veterinarian, will serve an important role as an expert in the development of rodent models to study the physiological efficacy of acupuncture within the newly formed K. Lisa Yan Brain-Body Center. In addition, veterinarian postdoctoral trainee India Napier is partially funded by a Deshpande Foundation grant (with Biological Engineering faculty member Linda Griffith as PI) to validate a novel in vitro fertilization method using a murine model and DCM's established transgenic facilities.

Comparative medicine research to increase the translational value of animal models of human disease continues to be a unique strength within DCM. A new ACLAM Foundation grant (with Dr. Holcombe as PI) will allow for the definition of the effect of the common opportunistic pathogen *Corynebacterium bovis* on cancer research in mouse models, whereas a new American Association for Laboratory Animal Science (AALAS) Grants for Laboratory Animal Science (GLAS) program grant (with new staff veterinarian Niora Fabian as PI) will facilitate determination of the effect of LED lighting on behavior, stress, and reproductive success in zebra finch models of communication and learning. Continued funding from a GLAS grant (again with Fabian as PI) supports an examination of the pharmacokinetic properties of the analgesic agent buprenorphine in marmoset monkeys. Templeton Foundation funds support research to test perinatal probiotic strategies to boost oxytocin for mother-infant bonding and a societal trajectory of improved impulse control, empathy, and altruism (with Susan Erdman as PI). Total research expenditures were \$821,470 in FY2022.

The Division of Comparative Medicine has been involved in postdoctoral training in comparative medicine since 1982. Since that time, 71 Doctors of Veterinary Medicine (DVMs) have successfully completed the program and 50 have become diplomates of the American College of Laboratory Animal Medicine. An additional 22 DVMs, PhDs, or MDs have completed postdoctoral fellowships sponsored by individual R01 or program project grants. Thirty of our graduates are in comparative medicine positions in academic institutions with sizable NIH-supported biomedical research programs, and 21 of our fellows are directors or associate directors of laboratory animal medicine programs at universities or medical centers. The remaining graduates and fellows are in director's positions or research roles in pharmaceutical or biotech firms or hold positions in federal or state public health departments. Six past fellows are full professors at medical schools, five are associate professors, six are assistant professors, and five are at the instructor level.

The division continues to provide short-term training opportunities for veterinary students interested in careers in research and comparative medicine. After two years of modified programming due to the pandemic, DCM welcomed six veterinary students representing five veterinary schools to MIT for summer 2022 for a reimaged on-site program in

collaboration with the Tufts Cummings School of Veterinary Medicine. This program benefits from new NIH T35 funding (with Metcalf Pate as PI) and Boehringer Ingelheim Veterinary Scholars Program funding (with Metcalf Pate and Martina Jackson as PIs).

Academic Activities

Over the past year, DCM faculty and staff published 33 peer-reviewed papers and presented numerous research papers at virtual national and international meetings. DCM veterinarian postdoctoral trainees received awards recognizing the excellence of their work at national conferences, with India Napier and Suresh Ganasan winning poster awards at the American Association for Laboratory Animal Science meeting in 2021.

DCM staff veterinarians continue to serve in leadership positions across the comparative medicine community. Metcalf Pate was appointed as a member of the National Academies of Sciences Committee on the State of the Science and Future Needs for Nonhuman Primate Model Systems in spring 2022. She continues to serve as an ad hoc specialist for the national accrediting body for comparative medicine programs, AAALAC and is currently vice chair of the AALAS Scientific Advisory Committee in preparation for service as chair starting in October 2022. James Fox is currently playing 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 of a standing committee within the National Academy of Sciences. Also, he continues to serve on the executive committee for the Massachusetts Society of Medical Research and as editor-in-chief for the ACLAM publications committee. Fox and Pate are both serving as editors for the upcoming fourth edition of *Laboratory Animal Medicine*, the textbook for comparative medicine professionals.

Susan Erdman was appointed in April 2022 as a standing member of the NIH Scientific and Technical Review Board on Biomedical and Behavioral Research Facilities and was presented the prestigious Comparative Medicine Scientist Award by ACLAM in May 2022 in recognition of her excellence in comparative medicine research. Dr. Robin Kramer, assistant director for training and compliance and DCM staff clinical veterinarian, serves as the director of the division's ACLAM-recognized training program for laboratory animal veterinarians and as such sits on ACLAM's Training Program Director's Group. She is also a member of the American Society of Laboratory Animal Professionals development committee and represents DCM as a member of the NIH Marmoset Working Group's Veterinary Care, Welfare and Captive Care Committee. Martina Jackson is a member of the ACLAM Forum Planning Committee and the Association of Primate Veterinarians Membership Committee. Nicola Parry serves on the board of directors for the American College of Veterinary Pathologists (ACVP), as chair of the American Veterinary Medical Association Council on Education, and as a committee member of the ACVP Certifying Examination Board.

DCM faculty and staff teach 20.202 In vivo Models: Principles and Practices, a graduate course in the Department of Biological Engineering. This course will continue in 2023 with Metcalf Pate being the primary course instructor following James Fox's retirement. DCM veterinary staff assist in conducting wet labs for courses taught by Professor Roger Greenwood Mark (HST 542 Quantitative Systems Physiology: Organ Transport Systems) and Professor Elazer R. Edelman (HST 090/091 Cardiovascular Pathophysiology).

Committee on Animal Care Activities

All students, staff, visiting scientists, and principal investigators who work with animals in teaching or research must be certified by the Committee on Animal Care (CAC). To enable protocol submission and personnel training, CAC's website provides required forms, continuing education materials, and information about CAC activities. In close collaboration with the Office of the Vice President for Research, the CAC protocol submission and review system is in the process of migrating to an online platform, CAC Connect, that parallels the current Committee on the Use of Humans as Experimental Subjects system. This effort-intensive migration is anticipated to significantly streamline the process for both researchers and CAC members in the future.

In conjunction with the Committee on Animal Care, DCM education and outreach staff have developed an online training program to supplement the Collaborative Institutional Training Initiative online courses via the MIT Learning Center. These tools are combined with individual orientation and training in animal use by the veterinary staff at the Institute. Individual and group didactic training sessions for Institute personnel on topics pertaining to the care and use of laboratory animals are also offered on a regular basis.

DCM was successful in recruiting two new education and outreach staff to replace Elizabeth Horrigan and Taylor Carroll, longstanding staff members who resigned in the wake of the pandemic. The new additions, Paul Chamberlain (formerly the DCM manager for veterinary technicians) and David Cawston (formerly an education and outreach specialist at Boston University), reinvigorated the education and outreach team in FY2022. CAC, DCM, and MIT Medical coordinate an occupational health program for animal-related occupational health issues. Metcalf Pate has been working closely with new occupational health physician Dr. Neil Jenkins throughout his onboarding process to facilitate his orientation to MIT needs in occupational health within the animal research community. In addition to its work on the MIT campus, CAC provides protocol review for the Whitehead Institute. Dr. Howard Heller continues as the chair of CAC.

Kelly A. Metcalf Pate

Director

Dorothy W. Poitras Associate Professor of Biological Engineering