

Division of Comparative Medicine

The [Division of Comparative Medicine \(DCM\)](#) provides animal husbandry and clinical care for all research animals on the MIT campus, including the Whitehead Institute. Since its inception in 1974, DCM has evolved into a comprehensive laboratory animal program that provides a full range of veterinary and surgical support. Additionally, DCM continues to maintain postdoctoral training to prepare veterinarians for careers in biomedical research. The division also has an active research program funded by several grants from the National Institutes of Health (NIH). DCM's total personnel comprises 170 individuals. The personnel of the division for this past year included 89 animal technicians, 24 veterinary technical staff, five diagnostic laboratory personnel, five research personnel, 12 veterinary professional staff, eight postdoctoral trainees, 20 administrative and supervisory staff, and seven support staff. DCM's administrative headquarters, along with its diagnostic and research laboratories, are located on the eighth floor of Buildings 16 and 56. The division now encompasses approximately 190,000 gross square feet in seven buildings devoted to animal research activities on the MIT campus.

Facility Management and Animal Care

The March 2019 edition of the Laboratory Animals Users' Handbook continues to be available online. The average daily census of laboratory animals decreased 1% during fiscal year 2019. Mice remain the primary species used by MIT investigators and represent more than 98% of DCM's animal population. 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. Services include a full range of cryogenic services including laser-assisted in vitro fertilization and freezing and retrieval of sperm and embryos. The transgenic core also provides genetically engineered mice to the investigative community at MIT. DCM staff provides colony management of mouse models for investigators using mice in their studies. They advise investigators on breeding paradigms and tracking systems to optimize efficiency of production colonies, as well as providing hands-on services for routine mating, weaning, and genotyping. The division continued an initiative, which started two years ago, to reduce work-related injuries to our animal care staff. A consultant and employee teams continue to analyze their work methods to determine ways to minimize injuries due to work-related activities.

For the past four years the division has worked closely with faculty in the McGovern Center to establish a successful marmoset colony and to construct transgenic marmoset models. This initiative is space intensive; marmosets are now occupying considerable space in vivaria located in Buildings 46 and E25.

DCM also operates two surgery suites, one in Building 46, the other in Building E25. DCM provides diagnostic laboratory services in support of the veterinary care, surveillance, and quarantine programs. The diagnostic laboratory is equipped and staffed to provide technical services in microbiology, mycology, mycoplasma, chlamydia, virology, serology, hematology, parasitology, clinical chemistry, urinalysis, and pathology. A fully equipped and staffed histology laboratory also supports DCM research and diagnostic efforts as well as technical support for the MIT investigative community.

Following the last site visit from the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC), the division was granted full accreditation for another three years as noted in the follow-up letter from AAALAC: "The council commends you and the staff for providing and maintaining an exemplary program of laboratory animal care and use. Especially noteworthy were the organization and extensive elaboration of the animal user training program, including web-based e-courses, all implemented with pedagogical acuity; the similarly based training program focusing on ergonomics for animal husbandry personnel, emphasizing personnel participation; the designation of animal laboratory representatives as contact persons in each laboratory using animals and their monthly meetings with Division of Comparative Medicine and Institutional Animal Care and Use Committee (IACUC) staff; the yearly training of physical plant personnel on the animal care program; the administrative support for the upgraded and well-maintained animal housing and use facilities, including excellent health and well-being of the animals; the very knowledgeable personnel in critical areas, including husbandry, veterinary, and research fields and their highly cohesive team approach to the execution of the animal care and use program homogeneously applied to all buildings in the Institution; the engaged IACUC, including the Environmental Health and Safety member and the new community representative, and its in-depth program reviews and facility inspections, as well as the concurring quality of documentation of IACUC activities; and the integral occupational health and safety program. The Council is pleased to inform you that the program conforms with AAALAC International standards as set forth by the *Guide for the Care and Use of Laboratory Animals*, NRC 2011. Therefore, FULL ACCREDITATION shall continue."

Research Activities

In FY2019 DCM faculty and scientific staff had five NIH-funded grants supporting a range of studies:

1. the role of *Helicobacter* as a tumor promoter in gastric cancer and examine the mechanisms by which it contributes to the malignant process;
2. an examination of the microenvironment associated with Barrett's esophagus;
3. the role of *Helicobacter pylori* as a tumor initiator in gastric cancer, and the role of *Helicobacter* associated colitis and colon cancer, modulation of systemic immune responses and the Th1/Th2 gastric cytokine profile due to *Helicobacter pylori* infection and concurrent infection from parasites;
4. how toxic environmental agents perturb biological systems and to determine how such perturbations may affect human health; and
5. develop a robust rodent model with phenotyping tools as a foundation for tractable microbial strategies for obesity and public health.

Funding has also been obtained to examine the role of the microbiome in chronic inflammation in the intestine of marmosets, to include severe cases of ulceration and stricture of the duodenum; obtain pharmacokinetic and safety data regarding the use of meloxicam in zebra finches (*Taeniopygia guttata*), a species that is often used in neuroscience research; and, develop a rodent model and phenotyping tools as a foundation for tractable microbial strategies to counteract environmental toxins for human public health. Total research expenditures were \$480,000 in FY2019.

The division was awarded first, second, and third place for posters presented at the annual American Association for Laboratory Animal Medicine convention. First place went to Dr. Mia Lieberman, a postdoctoral fellow; Dr. Alex Sheh, a research scientist; and Dr. Anthony Mannion, a postdoctoral associate, for their poster, Comparison of Microbiota among Multiple Sites in Cranially-Implanted Research Macaques. Alex Sheh; Dr. Steve Artim, research scientist; and Dr. Monika Burns, chief of marmoset resources, received the second place award for their poster, Evaluating Collection Methods for Gut Microbiome Analysis in the Common Marmoset (*Callithrix jacchus*). Third place was awarded to Dr. Damodaran Annamalai, research and clinical veterinarian, for his poster, Surveillance of *Tritrichomonas muris* in mice by direct microscopic exam and polymerase chain reaction.

After 30 years, funding has ceased on our NIH-sponsored postdoctoral training program. The division uses departmental funds to continue providing postdoctoral training for veterinarians specializing in biomedical research. Our program has been completed by 64 trainees; 47 have become diplomates of the American College of Laboratory Animal Medicine. An additional 22 doctors of veterinary medicine (DVM), PhDs, or MDs have completed postdoctoral fellowships sponsored by individual R01 or program project grants. Many former trainees hold leadership positions in academia as well as pharmaceutical and biotechnology companies.

The Division of Comparative Medicine has been involved in postdoctoral training in comparative medicine since 1982. Since that time 64 DVMs have successfully completed the program and eight are currently enrolled in the program. Thirty of our graduates are in comparative medicine positions in academic institutions with sizable NIH-supported biomedical research programs, and 20 of our 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 a pharmaceutical or biotech firm, or hold positions in federal or state public health departments. Six past fellows are full professors at medical schools (Drs. Lipman, Otto, Perkins, Saunders, Versalovic, and Young); five are associate professors (Bergin, Ihrig, Nagamine, Mesina, Saiffudin); nine are assistant professors (Andrutis, Blanco, Lemke, Lertpiriyapong, Lofgren, Martin, Maurer, Poutahidis, and Swennes); and six are at the instructor level (Burns, Corning, Ellenberger, Esmail, Garibaldi, and Niemi).

Dr. Hilda Holcombe has been promoted to the position of associate director of DCM, following the retirement of Dr. Mark Whary. Bruce Brown, DCM's administrative officer for 32 years has retired.

The division continues to provide short-term training opportunities for veterinary students interested in careers in comparative medicine. During FY2019, DCM had seven short-term trainees for periods ranging from eight to 10 weeks. Many have, upon graduation, entered careers in biomedical research. For the past 20 years the division has hosted seven to eight veterinary students each summer. Also, the division hosted 10 veterinary students who elected to spend two to four week externships at DCM during the school year.

Academic Activities

DCM faculty and staff published 19 peer reviewed papers in 2018 and presented numerous research papers at national and international meetings. Drs. Marini and James Fox were editors on a 2018 published text “The Common Marmoset in Captivity and Biomedical Research.”

Dr. Fox stepped down as a member of the executive committee of Institute for Laboratory Animal Research /National Academies of Science, Engineering, and Medicine round table and continues to serve on the board of directors of national associations and editorial boards of scientific journals. He most recently served on the Physician Scientist Workforce Committee commissioned by the director of NIH. Fox is also a member of the National Academy of Sciences Global Forum on Innovations in Health Professional Education. In 2016 he was the distinguished Phi Zeta lecturer, Purdue University and in 2018 he was the American College of Laboratory Animal Medicine James Russell Lindsey Distinguished lecturer. Dr. Susan Erdman, assistant director of DCM and principal research scientist serves on an ad hoc review committee for NIH. Dr. Suresh Muthupalani, chief of comparative pathology in DCM, also participates on an NIH ad hoc review committee. Fox also serves on ad hoc review committees for NIH. Marini received the 2018 Outstanding Alumni Award from Cummings School of Veterinary Medicine.

DCM faculty and staff teach 20.202 In Vivo Models: Principles and Practices, a graduate course in the Department of Biological Engineering. DCM veterinary staff assist in the conduction of wet labs for courses taught by Professor Mark, 6.002(J)/ HTS 542 Quantitative Systems Physiology and by Professor Edelman, HST 090/091 Cardiovascular Pathophysiology.

Committee on Animal Care Activities

All students, staff, visiting scientists, and principal investigators who use 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 material, and information about CAC activities. In conjunction with CAC, DCM staff have developed an online training program and are using 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. CAC, DCM, and the MIT Medical Department coordinate an occupational health program for animal-related occupational health issues. In addition to the MIT campus the CAC provides protocol review for investigators at the Whitehead and for Broad Institute investigators who house animals at MIT. Dr. Howard Heller, an MIT physician, assumed the chair position of MIT’s CAC, following the retirement of Dr. Barbara O’Pray.

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