

## 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 a postdoctoral training program 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). The division has 169 individuals, including 87 animal technicians, 22 veterinary technical staff, five diagnostic laboratory personnel, five research personnel, 12 veterinary professional staff, seven postdoctoral trainees, 24 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 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 3.7% during FY2019 through March 2020. Due to the ramp-down in research caused by the pandemic, there was a 23% decrease in the average daily census of laboratory rodents for the final three months of the fiscal year. 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 such as 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 that started three years ago to reduce work-related injuries to our animal care staff by analyzing work methods. Despite the pandemic, DCM's veterinary care staff has worked on a regular basis to ensure animals are being well maintained.

For the past five years the division has worked closely with faculty in the McGovern Institute for Brain Research to establish a successful marmoset colony and to construct transgenic marmoset models. Marmosets are now occupying considerable space in DCM facilities located in Buildings 46 and E25.

DCM 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 providing 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 International), 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.” We are anticipating an onsite AAALAC review in November 2020.

### **Staff Changes**

Dr. Robert Marini, the division’s long-time chief of surgery resources, retired this past fiscal year. Dr. Jenny Haupt—who is board certified in veterinary surgery and who has been on the DCM staff since 2012—has been promoted to that position. Dr. Alexis Garcia rejoined DCM as a clinical/research veterinarian in August 2019. He had been a postdoctoral fellow and a research scientist in DCM from 2000 until 2015. Bruce Brown, the division’s administrative officer for 32 years, retired and has been succeeded by Keith Kun, who was previously manager of DCM’s animal resource program and has been on staff for nine years. Finally, Dr. James Fox, DCM’s director since 1974, announced his retirement and the search for his replacement is under way.

### **Research Activities**

In FY2020, DCM faculty and scientific staff had five NIH-funded grants supporting a range of studies:

- The role of *Helicobacter* as a tumor promoter in gastric cancer and the mechanisms by which it contributes to the malignant process

- An examination of the microenvironment associated with Barrett's esophagus
- 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
- An examination of how toxic environmental agents perturb biological systems and to determine how such perturbations may affect human health
- Development of a robust rodent model with phenotyping tools as a foundation for tractable microbial strategies for obesity and public health

Other studies include:

- Examining the role of the microbiome in chronic inflammation in the intestine of marmosets, to include severe cases of ulceration and stricture of the duodenum (funded by the McGovern Institute)
- Obtaining pharmacokinetic and safety data regarding the use of meloxicam in zebra finches (*Taeniopygia guttata*), a species that is often used in neuroscience research (funded by the American Association for Laboratory Animal Medicine [AALAS] Foundation)
- Developing a rodent model and phenotyping tools as a foundation for tractable microbial strategies to counteract environmental toxins for human public health (funded by a private donation)
- Testing perinatal probiotic strategies to boost oxytocin for mother-infant bonding and a societal trajectory of improved impulse control, empathy, and altruism (funded by the Templeton Foundation)

Total research expenditures were \$700,000 in FY2020.

The division was awarded second place for a poster presented at the annual AALAS convention. The award went to Dr. Melissa Stair (postdoctoral fellow), Dr. Sebastian Carrasco (comparative pathologist), Dr. Damodaran Annamalai (DCM veterinarian), Niora Fabian (postdoctoral fellow), Dr. Anthony Mannion (postdoctoral associate), Dr. Suresh Muthupalani (DCM chief pathologist), and Yan Feng (research scientist) for their poster *Diarrhea and associated bacteremia during and following antibiotic treatment in NSG mice*. Another DCM poster, *Gastric colonization with non-*H. pylori* urease positive bacteria and their effects on *H. pylori* pathogenesis*, received the Best Poster Presentation Award 2019 from the European Helicobacter and Microbiota Study Group at the XXXIInd International Workshop. The poster was authored by Zeli Shen, Joann Dzink-Fox, Keith T. Wilson, Yan Feng, Alex Sheh, Mark T. Whary, Suresh Muthupalani, Anthony J. Mannion, Dylan A. Puglisi, Blanca Maria Pizuelo, L. E. Bravo, Sebastian Suerbaum, C. Josenhans, and James G. Fox.

Importantly, DCM's supervisors of vivaria—Sarah Ambrose, Randy Curry, Corey Gallo, Brian Legace, Erin Mathieu, Suzette Morales, Stephen Plouff, Gladys Valeriano, Andrea Vargas, Lidia Vasconcelos, and Tsetan Wangchuck—received the Infinite Mile Award for the outstanding service they have provided for the MIT research community.

The Division of Comparative Medicine has been involved in postdoctoral training in comparative medicine since 1982, and this training program was supported by NIH for 30 years. Since that time, 65 doctors of veterinary medicine (DVMs) have successfully completed the program, and 47 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 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 graduates are in directorial positions, research roles, or hold positions in federal or state public health departments. Six past fellows are full professors at medical schools, five are associate professors, seven 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 comparative medicine. During FY2020, DCM had seven short-term trainees for periods ranging from eight to 10 weeks. For the past 20 years, the division has hosted seven to eight veterinary students each summer, but the pandemic prohibited this for the summer of 2020. However, the division did host 10 veterinary students for two- to four-week externships at DCM during the pre-pandemic school year.

### **Academic Activities**

DCM faculty and staff published 17 peer-reviewed papers in 2019 and presented numerous research papers at national and international meetings.

James Fox stepped down as a member of the executive committee of the Institute for Laboratory Animal Research/National Academies of Science roundtable, but continues to serve on the boards 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. Dr. Fox is also a member of the National Academy of Sciences Global Forum on Innovations in Health Professional Education and a member of the National Academy of Medicine. Dr. Susan Erdman, assistant director of DCM and principal research scientist, serves on an ad hoc review committee for NIH, as does Dr. Suresh Muthupalani, chief of comparative pathology. Dr. Robert Marini received the American College of Laboratory Animal Medicine Outstanding Mentor Award in 2019.

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 conducting wet labs for courses taught by Professor Roger Mark, 6.522(J) Quantitative Systems Physiology: Organ Transport Systems and by Professor Elazer Edelman: HST.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 also use the Collaborative Institutional Training Initiative's 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 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, CAC provides protocol review for investigators at the Whitehead Institute and for Broad Institute investigators who house animals at MIT. Dr. Howard Heller, a physician, continues as the chair of MIT's CAC.

**James G. Fox**  
**Director**  
**Professor of Biological Engineering**