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 animals housed at the Whitehead Institute for Biomedical Research. 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 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 now has 170 personnel, including 89 animal technicians, 22 veterinary technical staff, five diagnostic laboratory personnel, six research personnel, 12 veterinary professional staff, eight postdoctoral trainees, 19 administrative and supervisory staff, and eight support staff. DCM's administrative headquarters and 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 seventh edition of the updated *Laboratory Animals Users' Handbook* continues to be available online. The average daily census of laboratory animals decreased by 1% during FY2018. 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 encompass 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 provide colony management of mouse models for investigators using mice in their studies. They advise investigators on breeding paradigms and tracking systems to optimize the efficiency of production colonies, as well as providing hands-on services for routine mating, weaning, and genotyping. The division continued an initiative to reduce work-related injuries among our animal care staff. A consultant and employee teams have analyzed work methods to determine ways to minimize injuries due to work-related activities.

The division continues to work closely with faculty in the McGovern Institute for Brain Research to establish a successful marmoset colony and to construct transgenic marmoset models.

DCM also operates two surgery suites, one in Building 46 and the other in E25, along with providing 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, mycoplasmology, chlamydiology, 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.

The division had its triennial three-day site visit from the Association for the Assessment and Accreditation of Laboratory Animal care (AAALAC International) this past November. We were 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 homogenously 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 FY2018, DCM faculty and scientific staff had NIH-funded grants (six in total) supporting a range of studies in areas such as the role of *Helicobacter* as a tumor promoter in gastric cancer and the mechanisms by which it contributes to the malignant process, the microenvironment associated with Barrett's esophagus, the role of *Helicobacter pylori* as a tumor initiator in gastric cancer, *Helicobacter*-associated colitis and colon cancer, and modulation of systemic immune responses and the Th1/Th2 gastric cytokine profile due to *H. pylori* infection and concurrent infection from parasites. In addition, division faculty and staff conducted studies investigating the means by which toxic environmental agents perturb biological systems and how such perturbations may affect human health, the way in which pathogenic gastrointestinal tract microbes trigger extra-intestinal cancers in tissues such as those of the breast, and microbial reprogramming to counteract xenobiotic-induced cancer. Funding has also been secured to study nosocomial *Enterococcus fecalis* in non-human primates. Dr. Galit Frydman has used a grant from the Deshpande Center for Technological Innovation to develop a newly patented device for the detection of anticoagulants in plasma and whole blood. Her poster presentation at the annual meeting of the International Society of Thrombosis and Haemostasis in Dublin received a first-place award. Dr. Steve Artim, a postdoctoral fellow in DCM, also received a first-place award for his poster on myocarditis presented

at the national convention of the American Association for Laboratory Animal Medicine. Total DCM research expenditures were $1.3 million in FY2018.

FY2018 was the 30th and final year of the division's NIH postdoctoral training grant. Our NIH sponsored postdoctoral program was completed by 64 trainees; 47 have become diplomates of the American College of Laboratory Animal Medicine. An additional 22 DVMs, PhDs, or MDs completed postdoctoral fellowships sponsored by individual R01 or program project grants. Two postdoctoral DVMs, Galit Frydman and Mia Lieberman, matriculated in the Department of Biological Engineering graduate program and received their PhDs in AY2018. Many former trainees hold leadership positions in academia as well as pharmaceutical and biotechnology companies.

Staff Changes and Academic Activities

Dr. Sebastian Carrasco joined the division as a veterinary pathologist to replace Dr. Vasudevan Bakthavatchalu, who left in June 2017.

Dr. Mark Whary retired this June after 23 years as the associate director of DCM. Dr. Robert Marini, assistant director and chief of surgical resources, has retired as well but is present during the three summer months.

On a national level, previous fellows have been elected to fill the presidency of three national organizations: Dr. Steve Niemi (director of animal resources at Harvard University) at the American College of Laboratory Animal Medicine, Dr. Scott Perkins (director of the Division of Laboratory Animal Medicine at the Tufts-New England Medical Center) at the American Association of Laboratory Animal Science, and Dr. Kim Saunders (director of the Department of Comparative Medicine at Oregon Health and Science University), also at the American Association of Laboratory Animal Science. Dr. Susan Erdman, a former DCM postdoctoral fellow and currently the division's assistant director, is past president of the American Committee on Laboratory Animal Diseases.

The division continues to provide short-term training opportunities for veterinary students interested in careers in comparative medicine. During FY2018, DCM had five short-term trainees for periods ranging from eight to 10 weeks. Many of the students taking part in these training opportunities have, upon graduation, entered careers in biomedical research. One hundred twenty veterinary students sponsored through NIH training grants have participated in the summer training program during the past 20 years. Also, the division hosted eight veterinary students who elected to spend two- to four-week externships at DCM during the school year.

DCM faculty and staff published 35 peer-reviewed papers during the past year and presented numerous research papers at national and international meetings. Dr. Marini and Dr. James Fox are editing a text on the biology and use of marmosets that is due for publication later this year.

Dr. Fox continues to serve on the boards of directors of national associations and on editorial boards of scientific journals. He most recently served on the Physician Scientist Workforce Committee commissioned by the director of NIH. Dr. Fox also serves on ad

hoc review committees for NIH and is a member of the National Academy of Sciences Global Forum on Innovations in Health Professional Education. Dr. Whary is a member of the editorial boards of *Comparative Medicine* and the *Journal of the American Association of Laboratory Animal Science*. He currently serves on the council for AAALAC. Dr. Erdman, assistant director of DCM and principal research scientist, serves on an ad hoc review committee for NIH. Dr. Suresh Muthupalani, DCM chief of comparative pathology, also serves on an NIH ad hoc review committee.

DCM faculty and staff teach 20.202 In vivo Models: Principles and Practices, a graduate course in the Department of Biological Engineering. Dr. Marini serves as a lecturer for teaching labs in the Institute for Medical Engineering and Science.

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 materials, 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'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 also offered on a regular basis. CAC, DCM, and MIT Medical coordinate an occupational health program for animal-related occupational health issues. In addition to its work on the MIT campus, CAC provides protocol reviews for the Whitehead Institute for Biomedical Research and the Broad Institute. Dr. Bobbi O'Prey, the long-time chair of CAC, retired this past year but is continuing on as chair until a replacement is named.

James G. Fox
Director
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