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).

DCM's total personnel comprises 158 individuals; the personnel of the Division for this past year included 85 animal technicians, 15 veterinary technical staff, four diagnostic laboratory personnel, nine research personnel, eight veterinary professional staff, 10 postdoctoral trainees, 23 administrative and supervisory staff, and four 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 October 2020 edition of the *Laboratory Animals Users' Handbook* is now available online. The average daily census of laboratory animals decreased 3.7% cumulatively during fiscal year 2020 through March. Due to the ramp down in research caused by the pandemic, there was an additional 23% decrease in the average daily census of laboratory rodents over the final three months of the fiscal year. In July 2021, the rodent census remains 13% below the pre-pandemic census levels. Mice remain the primary species used by MIT investigators and represent more than 98% of DCM's animal population, and 18.5% of laboratories at a June 2021 town hall for the MIT research community projected that their mouse census would double or triple over the coming year.

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 provide colony management of mouse models for investigators using mice in their studies. In addition to providing hands-on services for routine mating, weaning, and genotyping, they advise investigators on breeding paradigms and tracking systems to optimize efficiency of production colonies.

The division continued an initiative, which started three years ago, to reduce work-related injuries to our animal care staff. Consultant and employee teams continue to analyze their work methods to determine ways to minimize injuries due to work related activities. Throughout the pandemic, DCM's veterinary care staff has worked on a regular basis to ensure animals are being well-maintained.

For the past six years, the division has worked closely with faculty in the McGovern Center to establish a successful marmoset colony and to construct transgenic marmoset models. The colony has grown from zero animals at the beginning of FY2015 to 236 at the end of FY2021, with more than 100 additional animals currently housed at the Broad Institute. This initiative is space intensive; marmosets are now occupying considerable space in DCM facilities located in Buildings 46 and E25.

DCM also operates two surgery suites, one in Building 46 and 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, 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 technical support for the MIT investigative community.

Following the recent site visit from the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) International in 2020, the division was granted full accreditation for another three years as noted in the follow-up letter from AAALAC International:

> "The council commends you and the staff for providing and maintaining an excellent program of laboratory animal care and use. Especially noteworthy were the excellent administrative support, evidenced in part by the well maintained facilities and the extensive facility upgrades to the cage wash areas in several buildings; the elaborate and complete training program for all Division of Comparative Medicine staff, research staff and physical plant personnel that included emphasis on ergonomic concerns; the well constituted and engaged Institutional Animal Care and Use Committee (IACUC); the very detailed IACUC protocols; the dedicated and extremely qualified veterinary staff, facility managers, supervisors and animal care staff, evidenced in part by the appearance of healthy animals; the detailed and effective post-approval monitoring program; and the state-of-the-art rodent imaging facility. 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."

Staff Changes

DCM recently recruited Dr. Alexis Mackiewicz and Dr. Martina Jackson, two clinical veterinarians who have advanced training in nonhuman primate medicine and are American College of Laboratory Animal Medicine (ACLAM) Diplomates, or DACLAM; these veterinarians will fill the roles previously occupied by Dr. Mary Patterson, who retired in October 2020 after more than 20 years of service to DCM, and by Dr. Monika Burns, who left MIT after three and a half years of service just prior to the pandemic. Bruce Brown, who was the division's administrative officer for 32 years, retired and has been succeeded by Keith Kun. Kun was previously manager of DCM's animal resource program and has been on the DCM staff for nine years. Finally, Dr. James. G. Fox, DCM's director since 1974, retired effective March 2021 after 46 years directing DCM.

Dr. Kelly Metcalf Pate assumed the director role in DCM and joined the BE faculty as a tenured associate professor in March 2021. Pate, a DACLAM, received her DVM from Purdue University, followed by a PhD in platelet biology and virology and postdoctoral training in comparative medicine at Johns Hopkins University School of Medicine.

Research Activities

In FY2021, DCM faculty and scientific staff held six 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, 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
4. How toxic environmental agents perturb biological systems and to determine how such perturbations may affect human health
5. Develop a robust rodent model with phenotyping tools as a foundation for tractable microbial strategies for obesity and public health
6. The establishment and characterization of a mouse model for studying the effect of microbiome on latent viral reservoirs in HIV

Continued funding from the McGovern Institute 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. An ACLAM Foundation grant provides support to investigate dietary interventions in marmoset diets; its influence on microbial flora and whether these microbial altercations affect inflammatory bowel disease, a common disease in captive marmosets; and both ACLAM Foundation and Grants for Laboratory Animal Science funded projects examining the pharmacokinetic properties of the analgesic agent, buprenorphine, in marmosets. A private donation is funding a project to develop a rodent model and phenotyping tools as a foundation for tractable microbial strategies to counteract environmental toxins for human public health. The Templeton Foundation funds research to test perinatal probiotic strategies to boost oxytocin for mother-infant bonding and a societal trajectory of improved impulse control, empathy, and altruism. Total research expenditures were $821,390 in FY2021.

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, 67 DVMs have successfully completed the program and 47 have become DACLAM. 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 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, Young); five are associate professors (Bergin, Swennes, Nagamine, Mesina, Saiffudin), six are assistant professors; (Andrutis, Blanco, Lemke, Lertpiriyapong, Martin, Maurer, Poutahidis), and five are at the instructor level (Corning, Ellenberger, Esmail, Garibaldi, Lieberman).

The division continues to provide short-term training opportunities for veterinary students interested in careers in comparative medicine. DCM did not offer summer fellowships in 2020 because of the COVID pandemic but reinstated them with a remote program for three students in 2021. With this exception, the division has hosted 7–8 veterinary students each summer for the past 20 years. Many have, upon graduation, entered careers in biomedical research.

Academic Activities

DCM faculty and staff published 21 peer-reviewed papers in 2020 and virtually presented numerous research papers at national and international meetings.

Fox stepped down as a member of the executive committee of the Institute for Laboratory Animal Research/National Academy of Sciences (NAS) 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 NAS Global Forum on Innovations in Health Professional Education. As a member of the National Academy of Medicine, Fox also serves on workshops and other committees for NAS. In 2021, Fox was selected to receive the AAALAC International Bennett J. Cohen Award; this award is considered AAALAC International's highest honor.

Pate serves as an ad hoc consultant for AAALAC International, and stepped down in March as chair of the Animal Welfare Advisory Board for Morris Animal Foundation after five years of service.

Dr. Susan Erdman, assistant director for rodent medicine and principal research scientist, serves on an ad hoc review committee for NIH.

Dr. Suresh Muthupalani, assistant director for comparative pathology in DCM, also participates on an NIH *ad hoc* review committee.

DCM faculty and staff teach in vivo models: 20.202 Principles and Practices, a graduate course in the BE. This course will continue in 2022 with Pate being the primary course instructor. 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 by Professor Elazer R. Edelman: HST.090/HST.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 material, and information about CAC activities. In conjunction with CAC, DCM 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. 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, a physician, continues as the chair of MIT's CAC. A newly computerized version of the CAC protocol form is being finalized for use in 2021.

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