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Introduction

Current Topics in Research, Care, and Welfare of Common Marmosets

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Abstract

Although the common marmoset (*Callithrix jacchus*) has been maintained in captivity in biomedical research settings for decades, interest and use of the species as an animal model for a diverse array of purposes has increased in the 21st century. Unfortunately, the development of validated animal care standards such as nutrition, husbandry, and clinical care has not expanded with the same rapidity as the use of the species in research. The goal of this themed issue of the ILAR Journal is to review current literature relevant to topics that impact marmoset health, welfare, and use in research. As the population of captive marmosets increases worldwide, the editors urge scientists, veterinary clinicians, and colony managers to continue conducting and publishing robust studies to develop evidence-based standards related to marmoset care and use. The editors also encourage IACUCs and other institutional review bodies to seek training on topics relevant to marmoset welfare and develop related policies prior to acquiring animals as a novel species.

Key words: analgesia, anesthesia, assisted reproduction, imaging, marmoset, neurodevelopment, neuroscience, transgenics, welfare

INTRODUCTION

Nonhuman primates (NHPs) serve as critical animal models for basic and preclinical biomedical research. Due to the intrinsic characteristics of NHPs as well as their phylogenetic proximity to humans, the use of these species as research models warrants special consideration and scrutiny. Whereas basic husbandry practices, veterinary procedures, and experimental techniques are relatively well-defined in Old World primate species such as rhesus and cynomolgus macaques, such consensus is lacking for New World primate species.[1] In recent years, the common marmoset has been selected with increasing frequency for use in NHP studies, particularly in the areas of neuroscience research and for transgenic models. Ultimately, a greater consensus and development of guidelines on best practices related both to research and animal care for New World primates would improve both animal welfare and study outcomes. This issue of the ILAR Journal focuses on the common marmoset from 2 distinct vantage points: (1) marmosets as models in biomedical research, and (2) pressing clinical topics.

Although multiples species of macaques are used commonly in biomedical research, there has long been interest in the use of common marmosets as an alternative NHP model. For example, marmosets have been used as the species of choice for the Brain/MINDS initiative in Japan.[2,3] The small size of the species, high fecundity, short timeline to reproductive maturity, relatively lower occupational health risk, and other reasons justify interest in the species as animal models for biomedical research. However, along with the advantages outlined above there are significant limitations and challenges to use of marmosets as animal models of human disease.[4]

Although *Callithrix jacchus* is the most used marmoset species in biomedical research, there are multiple marmoset species

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endemic to Brazil, including *Callithrix aurita*, *Callithrix flaviceps*, *Callithrix geoffroyi*, *Callithrix kuhlii*, and *Callithrix penincillata*. Malukiewicz et al provides an overview of the characteristics and differences between species in the *Callithrix* genus from an evolutionary and genomic perspective.[5] The authors review hybridization that occurs naturally between *Callithrix* species and highlight the characteristics unique to each species. Chimerism and effect on research is discussed in this article, and individual variation within the species is acknowledged. A review of pertinent genomics and genetics topics is provided, and the authors conclude that more accurate and (largely) complete reference genome sequences for marmosets are opening tremendous opportunities for novel research. Other topics addressed in this review include marmoset cognition, viruses of import to *Callithrix* species, the marmoset virome, and arboviruses and their impact on the species. Saravanan et al provide a thorough review of background pathology in the NHP species most used in biomedical research. In addition to compiling relevant literature related to pathological changes commonly seen, the authors provide a concise historical overview of the use of each species in biomedical research.[6]

Colman et al provide historical context to the use of marmosets in research as well as a review of ethical considerations that must be followed when designing and approving studies involving marmosets.[7] Current areas of research that often employ marmosets as animal models include neuroscience, transgenics, obesity and metabolism, infectious disease, autoimmune disease, and aging. Each of these areas of research come with their own unique ethical considerations for animals enrolled in these projects. This article reviews the diverse regulations governing marmoset care and use in research. The editors encourage IACUCs and other regulatory bodies to preemptively seek appropriate training and experienced employees to provide adequate ethical oversight of the use of marmosets in biomedical research. All institutions should strive for continuous improvement and use of evidence-based practices, with ongoing review of the literature serving as a cornerstone of the program. The development of the Marmoset Working Group initiative has provided a key forum for collaboration and training for both experienced and new marmoset users.

Ross et al highlight that a significant limitation to the use of marmosets in research is a lack of validated diet recommendations, nutrition, and husbandry practices.[8] As more scientists elect to use a marmoset model, development of small colonies of marmosets has increased throughout the US as well as globally. With the creation of new colonies, husbandry practices at each individual institution must be established, which leads to a need for validated guidelines to train new marmoset users. There has been a historical practice of feeding marmosets "cafeteria-style" diets, which makes it difficult to determine which food items and nutrients the animals are actually consuming. Seemingly healthy marmosets are affected by subclinical gastrointestinal (GI) disease at a high rate, which undoubtedly has impacts on overall colony health and research outcomes. It is impossible to overemphasize the negative impact that GI disease has on marmoset colony health and research around the globe. It is also striking that, although marmosets have been kept successfully in captivity for decades, no validated/standardized diet for the species has been developed. A survey performed by the authors revealed great variation in definitions of underweight/overweight marmosets. Individual assessments of propensity towards obesity and dietary preferences may be key in preventing development of obese phenotypes where not intended.

Sheh et al present a summary of recent literature involving the gastrointestinal microbiome in marmosets in health and disease.[9] Although other texts have summarized common clinical issues and pathologies previously documented in marmosets, Fitz et al provides one of the most comprehensive clinically focused summaries of spontaneous GI illness of marmosets to date.[10] It has long been known that GI disease creates a tremendous burden on the health and well-being of marmoset colonies globally.[11] This article reviews publications related to all aspects of clinical care of marmosets as it relates to identifying, preventing, and treating GI illness. Enteric diseases of bacterial origin have been discussed thoroughly in other texts.

In contrast to Old World species such as macaques, there historically have been relatively few studies conducted evaluating the efficacy and indications for commonly used anesthetic and analgesic agents in marmosets. However, this has begun to change as the species is used more often in biomedical research. Goodroe et al provide a comprehensive review of current publications related to anesthesia and analgesia topics relevant for marmoset users and clinicians.[12] Within this text, readers will also find clinically relevant advice to support optimal physiological monitoring and perioperative care. Dosages and routes of administration for commonly used drugs are provided within this article, and the authors review unique characteristics of marmoset anatomy and physiology that must be considered during pre-anesthetic planning.

Murai et al highlights the criticality of collaboration between veterinary teams and research staff in refining the use and training of marmosets in neuroscience research programs.[13] Consideration of animal health status, housing configuration, individual response to rewards and training, and the specific behavioral test to be used is crucial to successful research and welfare outcomes. The authors discuss initial training procedures, habituation programs, and specific rewards for training marmosets to participate in tasks associated with neuroscience research.

Homman-Ludiye and Bourne review aspects of marmoset brain development that make the species an excellent animal model for study of human neurodevelopmental disorders.[14] Kaas' review discusses comparative anatomical features of the marmoset brain that make the species particularly well-suited to various fields of neuroscience research.[15] The social and highly vocal nature of marmosets, along with unique anatomic features of the marmoset brain, also serve to support the species as an excellent animal model for basic neuroscience and behavioral studies.

Magnetic resonance imaging (MRI) is an important tool in comparing the anatomy of the marmoset brain with other animal and human brains. Schaeffer et al discuss the advantages of using the marmoset for MRI imaging studies.[16] These advantages include small body size that can use rodent imaging systems, a rich behavioral repertoire, and a lissencephalic cortex. The use of MRI imaging, other invasive methodologies, and the ability to generate transgenic marmoset models provide additional advantages to the use of marmosets as animal models for neuroscience research. Park and Sasaki summarize recent advances in the development of assisted reproductive and techniques of genetic manipulation in NHPs.[17]

Ultimately, although there are many characteristics of common marmosets as a species that make them an attractive NHP model for biomedical research, there are significant limitations to their utility as animal models related to lack

of validated procedures and standards for many aspects of their care and research use. Most pressing among these issues include an incomplete understanding of marmoset nutritional requirements, optimal housing and husbandry, and precise etiology of spontaneous gastrointestinal disease. With an increase in use of marmosets for basic neuroscience research and creation of transgenic models, unique welfare considerations related to this work arise.

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