Aged mice on demand: Boosting age-related research to the next level

The Jackson Laboratory (JAX) makes aged mice available to researchers—on demand—to more easily enable studies on aging-related processes and diseases. Located in Bar Harbor, Maine, JAX is designated as a Nathan Shock Center of Excellence in the Basic Biology of Aging, and is funded by the U.S. National Institute on Aging—a division of the U.S. National Institutes of Health.

The coveted position of favorite mammalian preclinical research model belongs to the mouse. Beyond being convenient, mice play a fundamental role in a range of research projects, dating back at least to William Harvey’s circulatory studies in the 16th century. As such, there are special and important needs for aged mice in many research areas, including metabolism, neurodegenerative diseases, immunology, oncology, and many others. While there are many advantages to employing aged mice in a given study, these mice are not always easy to obtain, and generating them in-house can be expensive, time consuming, and labor intensive. JAX is making significant efforts to remove these barriers to research, making aged mice more accessible than ever before.

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BENEFITS OF THE B6J MOUSE

Scientists use the C57BL/6J, commonly known as “B6J,” more often than any other strain of lab mice. Not only is this the most widely used inbred strain, it was also the first to have its genome sequenced. It is often the strain of choice for researchers creating genetic modifications required to tease apart the mechanisms of basic biology and disease. B6J mice have many useful features, such as being resistant to audiogenic seizures, having a relatively low bone density, and developing age-related hearing loss. They are also susceptible to diet-induced obesity, type 2 diabetes, and atherosclerosis. For these reasons, JAX selected the B6J to be the first aged mouse model to be readily available. “Researchers now have access to mice between the ages of 25 and 78 weeks, equivalent to humans who are 30–56 years of age,” notes Andrew Schile, scientific advisor at JAX. He adds that the ability to obtain mice of both sexes “fulfills certain expectations of the U.S. National Institutes of Health to account for sex difference as a biological variable.” Making these mice available already aged offers other benefits. “If you want to develop successful therapies and use mice to do research that translates to humans, you want mouse models to look more like the population you are targeting,” explains Ron Korstanje, assistant professor at JAX.
NEED AGED MICE FOR YOUR NEXT PROJECT?
Prior to JAX offering aged B6J mice, researchers had to be very strategic in their study design and timing. They considered multiple factors, such as the age of mice needed for the study and the time required to reach that age, the sample size (taking into account how many animals might be unexpectedly lost during the aging process), the need for males and/or females, and much more. As Danique Wortel, husbandry director at Ichor Therapeutics, explains, “It’s so important to be able to move rapidly with new projects in this space. Historically, if you needed 18-month-old animals, you’d have to age them in-house and wait 18 months to get started. Having these animals available on demand has greatly accelerated our research, which is essential for our intramural programs and our clients.”

Wortel and her colleagues use older mice to understand age-related ailments and develop therapeutic interventions for age-associated pathways. “We conduct research that focuses on diseases and mechanisms of aging for our own intramural programs and for clients,” says Wortel. “It is our goal to begin a study as soon as we have a contract and to avoid being delayed due to mice of the required age being unavailable.” Instead of waiting a year and a half, Ichor can order as many 18-month-old mice as a study requires, and have them delivered by JAX within approximately one week.

Sample size is also important when considering aging mice. “We want to be good stewards of mice,” states JAX’s Schile, “and as such, it is important to work with study directors who are utilizing statistical methods to determine the right sample size for each unique study rather than aging more mice than necessary.” A database of phenotypic information on the aged B6J mice is available—including blood-cell counts, clinical chemistry, body composition, and more—and can be used as a baseline. “This helps to reduce the number of animals that may be needed,” Schile explains, “because you don’t need to establish the phenotypes starting from zero.” Wortel points out that “you can’t underestimate the importance of knowing exactly how many mice you will need for your aged study. In that sort of a situation, it’s quite possible too many or too few mice are produced and then not able to be used. In such a variable space as research, it’s invaluable to have an institution as reliable as JAX to work with.” Ordering the right number of mice at the right age neatly circumvents this issue.

JAX leverages its years of experience to reduce the number of mice lost due to aging. Schile attributes that success to JAX’s animal care technicians and environmental conditions, which maintain the mice at high health status throughout the aging process.

HOW ARE RESEARCHERS UTILIZING AGED MICE?
While the effect of age on neurobiology is well known, other age-related ailments, such as chronic kidney disease (CKD), are becoming more prevalent as the world’s population ages. “Kidney function declines with age,” says Korstanje, “and more people have type 2 diabetes now, which often leads to kidney disease over time.”

Despite the growing number of people with CKD, dialysis remains the standard treatment. According to the U.S. National Institute of Diabetes and Digestive and Kidney Diseases, more than 650,000 people in the United States suffer from kidney failure, most of them requiring dialysis. “There are not really any new therapies out there,” Korstanje says. “The last new one was more than 15 years ago.”

Aged mice help scientists understand how kidney function changes with time. Moreover, studying CKD can reveal information about other health problems. “It’s thought that the kidney starts aging the earliest, which makes it a good model for organ aging. Aging of the kidney also has a huge impact on other organs,” Korstanje explains. “For example, people with CKD have a higher risk of cardiovascular disease, and in hemodialysis patients the prevalence of cognitive impairment has been estimated at 30%–60%—at least twice the values observed in age-matched controls.”

To get a handle on other markers of aging, JAX scientists completed a large study of both male and female mice, collecting a plethora of metrics—including tissue histology, blood clinical chemistry, metabolite levels, neuromuscular function, gene and protein expression, and DNA methylation—at 6, 12, and 18 months of age. “We didn’t see many changes from 6 to 12 months, but observed lots between 12 and 18,” Korstanje says. The data for these metrics and many more are freely available through the Mouse Phenome Database.

WHAT’S NEXT FOR AGED MICE?
The work of Wortel and her colleagues at Ichor Therapeutics, and of Korstanje at JAX, provides a glimpse into the unique and specialized needs that aged mouse models fulfill. By providing access to a variety of mouse models, JAX supports research that aims to further our knowledge of basic biology and helps to improve patients’ quality of life. With easy access to a variety of mouse models, including healthy aged mice, researchers can embark on their studies sooner—leading to meaningful results faster.