For understanding ALS and developing new treatments, mouse models are indispensable tools of research. Making the very best mouse models available as widely as possible is the mission of Jackson Laboratories of Bar Harbor, Maine. In a recent webinar The ALS Association sponsored, Cathleen Lutz, Ph.D., Associate Director of the Genetic Resource Science Repository at Jackson Laboratories, spoke about the Lab’s work to develop, maintain and distribute ALS mice. The full webinar is available at https://alsa.webex.com/alsa/ldr.php?AT=pb&SP=MC&rID=64409397&rKey=d77e897e75b72614.

“Dr. Lutz has made a tremendous contribution to ALS in making sure that mouse resources are distributed worldwide,” said ALS Association Chief Scientist Lucie Bruijn, Ph.D., who hosted the webinar.

“The goal is to work with the scientific community to provide rapid access of relevant mouse models to researchers to accelerate the treatment and cure of ALS,” Dr. Lutz began. “This is about strengthening the core resources for everyone involved in ALS research.”

The Jackson Laboratories, run as a non-profit enterprise, has worked for 50 years “to make most mouse models available with no strings attached” to academic researchers in many different diseases. In addition to providing the mice themselves, they assist researchers with genotyping, surgery, and other hands-on aspects of performing animal research.

In 2009, The ALS Association met with investigators and other ALS funding agencies to coordinate the creation of a national repository for ALS mouse models at the Jackson Laboratories. The goal was to promote earlier deposition of mouse models at the lab and to standardize them genetically. This has since become a central resource for researchers worldwide.

A major function of the Jackson Laboratories is to work with researchers who have begun to develop a new mouse model of the disease, Dr. Lutz explained, to accelerate their ability to make it available to others. One of the most important jobs they perform is to genetically standardize the animals they accept and provide. This assures researchers in different labs that they are working with the same model, and, therefore, can be confident in comparing their results.

For instance, one of the most common genetic models of ALS for many years has been the so-called G93A SOD1 mouse supplied by Jackson Labs. This mouse carries many copies of the mutated SOD1 gene, but on its own, that number may fluctuate from generation to generation. Since the copy number may influence survival, Jackson Laboratories constantly checks and rebreeds the animals to ensure a consistent copy number in the colony and in the animals it distributes. Without that, Dr. Lutz said, differences in survival seen in an experiment might be due to genetic differences among the mice rather than to differences in treatment.

Researchers who develop new mouse models are encouraged to deposit them with the Jackson Laboratories, which can perform much greater levels of “quality control” than most individual
scientists can. For all models, this includes breeding the mice through 20 or more generations to make a uniform strain in which all the offspring are genetically identical.

There are currently nine ALS mouse models available for distribution, including several carrying different SOD1 mutations and the newest ones with TDP43 mutations. It can take six months or more to fully develop a mouse model from the initial deposition by a researcher to making it available to others.

“2011 was the year of gene discovery in ALS,” Dr. Lutz said, with new discoveries about TDP43, FUS, ubiquilin and C9ORF72. “This opens a whole new world of mouse genetics. This gives an opportunity to find out a lot about the biology of ALS.” Jackson Laboratories is currently developing embryonic stem cell lines, in addition to mouse models, that will also be made available to ALS researchers.

Dr. Bruijn noted that when the Association funds a research project in which new models are developed, funding is contingent on the researcher agreeing to deposit the model with Jackson Laboratories in order to make it available to others. “Our goal is to maximize the benefit from every development in ALS research,” she said, “and this is an important step in that process.”