

From the Jackson Laboratory

Prize4Life and The Jackson Laboratory Team up to Fight ALS

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Today, there is no cure or significant treatment for amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease), but that may change in the very near future. A partnership between The Jackson Laboratory and Prize4Life (an organization dedicated to finding a cure for ALS), million-dollar prizes, and a unique mouse model are sowing seeds of hope for people with ALS.

Prize4Life Attracts Researchers with \$1 Million Prizes

In 2004, Avi Kremer, a 29-year old Harvard Business School student, was diagnosed with ALS. Avi's doctors told him there was nothing that modern medicine could do for him. In response, he and fellow students founded Prize4Life, Inc. (www.prize4life.org), a non-profit organization dedicated to accelerating research for treating and curing ALS by using the leverage of large inducement prizes. In 2006, Prize4Life opened the "ALS Biomarker Challenge", offering a \$1 million prize to a researcher who could find a biomarker that would reliably measure disease progress in ALS patients. A year ago, it established the "Avi Kremer ALS Treatment Prize", a \$1 million award for finding a treatment candidate that reliably and significantly increases the lifespan of ALS mouse models. Competing teams are actively pursuing several approaches, including therapies to replace damaged cells, protein-based therapeutics, and small molecule drugs that interfere with ALS-implicated pathways. Competition for both prizes is open to all interested researchers. Both prizes have attracted research teams from industry and academia from around the world.

The SOD1 Mouse

Three percent of ALS cases are associated with mutations in the antioxidant enzyme superoxide dismutase-1 (SOD1) gene, the first gene associated with ALS. With so little known about the genetics of ALS, research so far has concentrated on the pathogenesis of SOD1 mutations in laboratory mice. To provide researchers with the most widely used ALS mouse models available for preclinical drug testing, Prize4Life has partnered with The Jackson Laboratory (JAX). The models, popularly known as SOD1 mice, are distributed from dedicated supply colonies maintained by JAX® Breeding Services. JAX currently distributes 12 different SOD1 models - with different forms of the SOD1 mutation and on different genetic backgrounds. Among the most widely used of these models is JAX® Mice strain B6SJL-Tg(SOD1*G93A)1Gur/J (002726). Like several other SOD1 models, this one has a high copy number of the mutant human superoxide dismutase 1 (SOD1) transgene, which contains the Gly93-->Ala (G93A) substitution. The mutation underlies the most studied form of inherited ALS in humans. The mice lose motor neurons in the spinal cord, become paralyzed in one or more limbs, and die by four to five months. These phenotypes closely model those of human ALS (Gurney et al. 1994). As noted by Dr. Tom Maniatis, Chair of Columbia University's Biochemistry &

Molecular Biophysics Program, a prominent ALS researcher, and a member of Prize4Life's Scientific Advisory Board, "An effective treatment for ALS is desperately needed, and the existing [SOD1] mouse model is the primary gateway to clinical trials" (CheckOrphan 2009).

SOD1 Mice Need Special Care

Many of the initial studies conducted with Tg(SOD1*G93A)1Gur/J mice have provided a wealth of information and insight on how to best use them in preclinical trials. However, like other highly expressed transgenes, the G93A transgene can spontaneously lose copy number, which can greatly confound experimental results. Therefore, the mice need to be handled carefully. When Prize4Life approached JAX to establish a dedicated supply for their researchers, Dr. Melanie Leitner (Chief Operating Officer and Chief Scientific Officer for Prize4Life), Dr. A. Sheila Menzies (Scientific Program Officer for Prize4Life), and Dr. Cathleen Lutz (Associate Director for Genetic Resource Science at JAX) produced a companion set of informational materials entitled "Working with ALS Mice". The materials are available at www.jax.org/jaxmice/literature/factsheet/working_with_ALS_mice.pdf. "Prize4Life spearheaded this effort," say Lutz. "It's really targeted to those investigators who are new to the field of ALS and who are working with the SOD1 mice and designing their preclinical trials. The scientific community has learned a great deal about how to work with these mice over the years. It's important to make that information more widely known so that valuable time and resources aren't wasted by repeating past mistakes."

If Prize4life succeeds in its goal of bridging the critical steps between academic discovery and therapy in the clinic, it could have major implications for ALS patients and for any group trying to solve a biomedical problem. Interested researchers can learn more at www.prize4life.org.