Profile Feature as seen in Nature 1st November 2018
A MODEL FOR PIONEERING NEUROBIOLOGY RESEARCH

A conversation with DR. LAURENT BOGDANIK, senior study director and lead neuroscientist of In Vivo Pharmacology Services at The Jackson Laboratory

The Jackson Laboratory is driven to empower biomedical research by accelerating advancements in the understanding and treatment of human disease. As a leader in mammalian genetics and neurobiology, we offer models that have been characterized in depth and efficacy studies that help translate to vivo findings to humans. We also help to identify the needs for new models specifically for neurobiology research, then create these models and put them through a phenotyping platform that removes the risk of preclinical drug testing. For example, new models for Friedreich’s ataxia were generated by The Jackson Laboratory using CRISPR-Cas9 or selective breeding techniques. What mouse resources are available to neurobiology researchers? We serve as a public repository for mouse models generated either at The Jackson Laboratory or donated by researchers. We have more than 10,000 colonies. Some are recent; others have been with us for 50 years or more. For every disease, we have between 1 to 20 different mouse models. Scientists worldwide can search for the most appropriate model for their neurobiology research. For instance we recently added an improved model for Duchenne muscular dystrophy that has been very successful. How do you develop knowledge about neurobiology mouse models? At The Jackson Laboratory, we are constantly conducting research that drives the development of assays, techniques, and mouse models. We utilize this knowledge to better the studies we perform on behalf of our customers. For each neurobiology model, we establish a natural history. We look at various phenotypes until we identify one that can be used as an indication of drug efficacy. We work with so many models and we’ve done this for so long that our experience is unique. For example, we are continuously benchmarking new C9ORF72- or TDP43-based ALS models with older reference models using electrophysiology to quickly identify any gain in translatability. What services and expertise do you provide? We are first and foremost scientists for many years of experience working in various neurobiology areas. So we are able to provide the research community our hands-on experience to help design the most informative study — including experimental assays best suited for each mouse model. This is complex, as many mouse models reproduce disease-causing mutations in humans but do not always present the patients’ phenotype. For example, we observed this often in models of Friedreich’s ataxia or Duchenne muscular dystrophy. This doesn’t mean that these mice are not appropriate to test drugs, but you have to be prepared to look at the right phenotype to evaluate the significance of a drug. Our familiarity with the mouse models prepares us to look at the right thing.

How do you share knowledge with the research community? All the knowledge of the mice and assays we generate while working with mouse models is publicly available. This is at the core of our non-profit mission. Through our live and on-demand courses, case studies, and on-site presentations, we highlight the latest innovations, capabilities, and tools to provide insights for better translational research. We strive to enable neurobiology researchers to reach their milestones using the most appropriate mice and efficacy studies. How are you driving innovations in personalized medicine? A lot of research at The Jackson Laboratory is driven by the observation that a single drug rarely works on all patients with a given disease. We provide and utilize mouse models to make neurobiological drug discovery more personal and to fine-tune treatments. To achieve this, we work with patients’ individual mutations in mouse genomes to hasten the understanding of the disease and allow for therapy testing. By creating these novel strains, we enable researchers to find effective treatments for ALS, neuropsychiatric, or other rare and orphan diseases. Patients are often given drugs that are not going to be most efficient for them. With new drugs you want to be right early on, and The Jackson Laboratory provides the most appropriate neurobiology mouse models and services to achieve that.