

PHENOTYPING

An important aspect of the drug discovery process is developing novel rodent models that accurately mimic a specific disease and its physiologic processes. Additionally, as novel compounds are developed to treat human diseases, it is important to precisely evaluate compound efficacy in fully-characterized models. To aid researchers in evaluating their models and compounds, Charles River Laboratories offers Phenotyping Services. Phenotyping Services is a comprehensive program designed to characterize genetically-modified and/or treated rodent models. All services are carried out under the direction of our board-certified veterinarians and PhDs. This high level of scientific expertise is essential to accurately evaluate and interpret the study design and results of these valuable experiments.

Approaches to Phenotyping

Charles River Laboratories can approach model characterization in two unique ways. Our animal-based screens can characterize a genetically-engineered, mutant, or preconditioned rodent model. Alternatively, our compound-based screens can evaluate compounds in a characterized or treated rodent model. Together, these approaches provide researchers with a broad spectrum of capabilities to assess animal models of human disease and corresponding targeted therapeutic approaches.

Phenotyping Services' animal-based screens can be used for a variety of purposes. As novel genetically-modified animals are created, characterization of these models is important to validate the targeted mutation. By characterizing lines early, researchers select the models that best fit a particular therapeutic area, and save valuable time and resources. Our animal-based screens can also characterize a genetically-modified animal outside of its primary targeted therapeutic area. This approach can fully examine a rodent model and/or reveal new biology in support of target validation.

Phenotyping Services' compound-based screens evaluate the effects of novel compounds in rodent models. Models used for assessing compound efficacy can include genetically-modified rodents, commercially available inbred models, or treated rodent models designed to mimic disease conditions. Compounds can be administered to the animals via parenteral injection, oral gavage, or by infusion pump for constant dosing.

Phenotyping Panels

To assist researchers with their study design, Charles River has developed an assortment of phenotyping panels based on various therapeutic areas and specific disease entities. The most commonly used panels fall into five areas: metabolism, neuroscience, immunology, cardiovascular physiology, and oncology. Each panel recommends basic characterization screens and also provides

PhenoFirstSM

The PhenoFirstSM panel was developed by Charles River Laboratories to provide a high throughput, cost effective screen of novel animal models to determine overt phenotypes. The panel includes an *in vivo* evaluation consisting of clinical and behavioral observations, basic pathology, and basic clinical pathology. The primary behavioral assessment is based on a modified SHIRPA protocol. The basic pathology component includes a gross external and internal examination, digital images of gross necropsy findings, major organ weights and collection, and a histological examination of H&E stained slides by a board-certified veterinary pathologist. Basic clinical pathology includes a CBC, standard clinical chemistry profile, and urinalysis. Charles River recommends performing PhenoFirstSM on at least 3 gene carriers and 3 wild types of each strain that are matched for age, sex, health status, and genetic background. Animals to be evaluated by the PhenoFirstSM panel can be shipped directly from the client's institution or bred at Charles River.

Visit www.criver.com/info/quotes for project estimates.



suggestions for more advanced characterization. In addition to the therapeutic areas listed above, Phenotyping Services has extensive experience working with models that have reproductive difficulties or lethality, and a reproduction panel is available to determine the cause of any reproductive impediment. Extensive maintenance and rescue options are also available for models that face reproductive challenges. Further, a panel is available to define embryonic or perinatal lethality and determine the stage of development at which lethality occurs. All of the assays listed in the phenotyping panels can also be ordered a la carte. Please see the table below for a complete listing* of the available screens. As with all of Phenotyping Services, each panel is 100% customizable by the client.

*Listing is current as of print date. For the most up-to-date list, please visit www.criver.com/info/pheno.

In vivo Phenotypic Screens

Acoustic Startle Reflex Pre-Pulse Inhibition	Activity Level – Open Field System	Analgesic Testing
Blood Pressure	Body Temperature	Characterization of Potential Embryonic Lethal KO Model
Primary Behavioral Observation	Cognitive Analysis: Holeboard System and Barnes Maze	Clinical Observation
Electrocardiogram	Food and/or Water Consumption	DEXA Scan
Glucose Tolerance Test	Grip Strength Measurement	Gait Analysis – Footprint Pattern
High-resolution Ultrasound Imaging	Insulin Tolerance Test	Growth Curve
Metabolism Measurements	Motor Coordination and Balance: Rotarod	Meal Tolerance Test
Porsolt Forced Swim Test	Radiography	Radial Arm Maze
Reproductive Diagnostics	Reproductive Performance	Respiratory Functions

Experimental Design

Phenotyping Services is a fully customizable array of model characterization tools. Prior to initiating any project, our senior scientific staff works closely with each researcher to construct and optimize an experimental design to characterize each model's target. Factors such as genetic background, age, zygosity, health status, and environmental conditions are carefully considered for each project. Appropriate sample sizes are determined depending on the specific assays comprising a study. During the study protocol design phase, go/no-go decision points and milestones for evaluation are established and incorporated into the final protocol. This provides researchers the opportunity to determine whether to proceed with the remainder of the study, modify the active protocol, or stop the study based on results obtained to date. Additional milestones such as start and end dates, transfer of raw data, and delivery of a final study report are also included in all study protocols. This information ensures that each study is carried out in the most efficient and cost effective manner. Upon study completion, clients receive a final report including the study protocol, all raw data, complete statistical analyses with graphs, and a summary of findings in both hard copy and electronic format.


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