

Phenotyping Services

We know that genetic manipulation in mice can present you with unique phenotypes. At Charles River, our Discovery and Imaging Services group provides phenotyping screens that offer a comprehensive, multi-step characterization of the anatomical, physiological, and behavioral changes in your newly created genetically engineered models. An important aspect of the drug discovery process is developing novel rodent models that accurately mimic a specific disease and its pathophysiologic processes. As novel compounds are developed to treat human diseases, it is important to precisely evaluate compound efficacy in fully characterized models.

Comprehensive phenotypic assessment is commonly used when researchers do not know the function of a gene. To aid in balancing the value of comprehensive characterization with the cost of extensive testing, the screening process may be divided into two tiers. The first tier consists of an initial phenotypic characterization that can guide the more thorough, targeted second tier phenotypic assessments in various therapeutic areas. Alternatively, if the function of a gene is known or if there is an interest in a specific phenotype, targeted phenotyping may be the primary approach to characterize a genetically engineered model.

Charles River can breed and maintain your genetically engineered colonies and readily transfer the offspring to our phenotyping program or we can receive animals for phenotyping directly from your facility. In parallel to your phenotyping studies, Charles River Discovery and Imaging Services can assist in your non-GLP pharmacology, pharmacokinetic, and lead optimization toxicology screening.

Areas of Expertise

- Initial phenotypic characterization
- Metabolic diseases
- Cardiovascular diseases
- Central nervous system disorders
- Respiratory diseases
- Inflammatory diseases
- Small animal imaging services
- Reproduction
- Pathology and biomarker services
- Molecular phenotyping

INITIAL PHENOTYPIC CHARACTERIZATION

PhenoFirst® Panel

Clinical observations
Primary neurobehavioral observations
Gross necropsy and histopathology (H&E staining) of major organs
Clinical pathology including complete blood count, clinical chemistry, and urinalysis

METABOLIC DISEASES

Body Weight and Body Condition Scoring

Body weight is monitored, and body condition is scored from 1 to 5 based on the appearance and palpable prominence of the vertebral column and pelvic bones.

Food/Water Consumption; Urine/Feces Production

Twenty-four hour measurement of food and water intake and urine and feces production

Glucose/Insulin Tolerance Test

The glucose tolerance test measures the animal's ability to clear an administered (oral or intraperitoneal) glucose load. Insulin tolerance testing (ITT) is to measure insulin resistance based on the rate of blood glucose decline after intraperitoneal injection of insulin.

Dual Energy X-Ray Absorptiometry (DEXA)

A DEXA scan is a non-invasive imaging modality that provides assessment of the fat vs. lean tissue ratio and bone mineral density.

Energy Expenditure

Energy expenditure or indirect calorimetry enables the assessment of metabolic rate by measuring oxygen consumption and carbon dioxide production.

Renal Function

Renal function includes the assessment of daily fluid intake and urine production, endogenous creatinine clearance, proteinuria, glucosuria, and urinalysis with examination of sediment.

Body Temperature

Subcutaneous transponders or rectal thermometers

CARDIOVASCULAR DISEASES

High-Resolution Ultrasound

Assessment of cardiac function and left ventricular mass (M-mode), cardiac outflow and valvular function (pulsed-wave Doppler), and atherosclerotic plaque dimensions

Indirect Blood Pressure

Non-invasive measurement of systolic, diastolic and mean blood pressure, and heart rate using tail-cuff blood pressure meter

Electrocardiogram (ECG)

Conscious recording of cardiac electrical activity via the animal's paws (lead II) is used to interpret heart rate; heart rate variability; and P, Q, R, S, and T wave intervals. Heart rate variability upon isoproterenol challenge is also available.

CENTRAL NERVOUS SYSTEM DISORDERS

Open Field Activity System

Evaluation of spontaneous locomotor activity and exploratory behavior in Huntington's disease, attention deficit and hyperactivity disorder, or depression, as well as in compound efficacy/toxicity testing

Rotarod System

Measurement of locomotor coordination and balance utilizing the fear-of-falling motivation in neurodegenerative diseases (especially cerebellar dysfunction) and in compound efficacy/toxicity testing

Gait Analysis

Quantification of gait abnormalities from footprint pattern to characterize locomotor and balance phenotypes in neurodegenerative diseases such as Huntington's disease, Parkinson's disease, or amyotrophic lateral sclerosis (ALS)

Grip Strength

Measurement of muscular strength of forelimbs or combined fore- and hind limbs in neuromuscular disorders

RESPIRATORY DISEASES

Respiratory Function	Unrestrained whole body plethysmography system permits the analysis of pulmonary resistance and compliance in conscious mice.
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INFLAMMATORY DISEASES

Experimental Allergic Encephalitis	Autoimmune disease of the central nervous system mimicking multiple sclerosis
TNP-OVA Immunization	Evaluation of T-cell-dependent antibody response (IgM and IgG response)
Thioglycollate-Induced Peritonitis	Assessment of inflammatory cell recruitment in peritoneal lavage after intraperitoneal injection of thioglycollate
LPS-Induced Cytokine Release	Pro-inflammatory cytokine response to acute lipopolysaccharide challenge
Delayed-Type Hypersensitivity	Carrageenan-induced footpad edema and DNFB-induced ear edema
Collagen-Induced Arthritis	Rheumatoid arthritis induced by immunization with type II collagen, collagen antibody (LPS synchronized), or adjuvant

SMALL ANIMAL IMAGING SERVICES

Magnetic Resonance Imaging (MRI)	Anatomical and diffusion MRI of tumors Dynamic contrast-enhanced (DCE) MRI for quantification of anti-angiogenesis therapy ¹⁹ F MRI of macrophages in chronic inflammation
Computed Tomography (CT)	Soft tissue and bone imaging (e.g., rheumatoid arthritis) Evaluation of primary and metastatic tumor burden Imaging of blood flow and perfusion
Positron Emission Tomography (PET)	Applications in tumor, cardiovascular, neurological, and inflammatory diseases Glucose metabolism by ¹⁸ FDG PET Cellular proliferation by ¹⁸ FLT PET
Bioluminescence and Fluorescence Imaging	Visualization of luciferase-expressing orthotopic and metastatic tumor models and biodistribution of fluorescent-labeled test articles
High-Resolution Ultrasound	Assessment of embryonic viability, cardiac function and left ventricular mass (M-mode), cardiac outflow and valvular function (pulsed-wave Doppler), and atherosclerotic plaque dimensions
Dual Energy X-Ray Absorptiometry (DEXA)	A DEXA scan is a non-invasive imaging modality that provides assessment of the fat vs. lean tissue ratio and bone mineral density.
Digital X-Ray	Assessment of organ size, bone density, and skeletal malformations

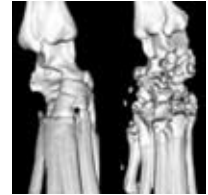
REPRODUCTION

Embryonic Lethality	Timed matings are established to harvest, culture, genotype, and pathologically assess embryos.
Reproductive Performance	Analysis of breeding records and genotype results to assess fertility, average litter size born and weaned, male to female ratio, and expected Mendelian ratio



PATHOLOGY AND BIOMARKER SERVICES

Necropsy	Gross necropsy, organ collections, and gross photographs
Histopathology	Routine H&E staining of tissues
Specialty Pathology, Tissue Biomarkers	Histomorphometry, immunohistochemistry, and in situ hybridization can be used to assess functional changes governed by the transgene.
Clinical Pathology	Clinical chemistry, complete blood count (CBC) with differential, and urinalysis
Plasma Biomarkers	Multi-analyte profiles (MAPs) are comprehensive panels used to evaluate multiple markers of infectious diseases, autoimmunity, metabolic and renal function, and cardiovascular risk, as well as hormones, cytokines/chemokines, and acute phase reactants in 50 μ L of plasma (offered through Rules-Based Medicine).



MOLECULAR PHENOTYPING

Quantitative PCR Analysis	Q-PCR determines transgene copy number and expression levels within genetically engineered models.
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Phenotyping services are a fully customizable array of model characterization tools. Prior to initiating any project, our scientific staff works closely with you 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. This methodology provides researchers the opportunity to determine whether to proceed with the remainder of the study, modify the active protocol, or terminate the study based on results obtained to date. Upon study completion, you 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.