

## ***The Power of Pathology***

*Animal health can have a direct bearing on the accuracy and interpretation of your experimental data; use the power of pathology to help guide your research programs.*

Elimination of experimental variability due to genetic and health factors is critical to the success of any animal-based research program. Accurate laboratory animal health information is essential in generating reproducible research results that are representative of the animal model itself, rather than artifacts of the genetic background and health status.

Pathology is a powerful tool for understanding and appreciating not only colony health status so treatment can be determined, but also for discovering genetically induced differences in animal models of disease. A full range of pathology services has been developed for application within a whole health surveillance program. A comprehensive pathology program can be used to monitor the health of laboratory animal colonies, to investigate unexpected research results, to support research studies, and to complement phenotypic characterization of genetically modified animals.

### ***Diagnostic Pathology***

Because many infections are sub-clinical, comprehensive health monitoring is a necessary part of good colony maintenance. Genetically modified animals infected with adventitious organisms may develop an alternate phenotypic characteristic. Some examples include the chronic inflammatory bowel disease induced from *Helicobacter* infection and wasting syndrome caused by MHV and *Pneumocystis*.

A diagnostic evaluation is the fundamental component of all pathology-based procedures for it can determine the cause of clinical disease or death in animals. A thorough diagnostic evaluation includes clinical observation, complete morbidity and mortality records, a complete postmortem examination and histopathological interpretation of animals that die spontaneously.<sup>[1]</sup>

### **Gross Necropsy**

The necropsy examination, including tissue collection and preservation, represents one of the most important phases in the pathological evaluation of animals.

There are two components that constitute any standard gross necropsy exam - the antemortem initial assessment and the postmortem gross exam. In the antemortem, animals are externally assessed, noting condition, behavior and movement of the animal. In the postmortem, the body condition is examined for skin and coat abnormalities, artificial manipulations, implants, or surgical scarring. Finally, all external orifices are examined.

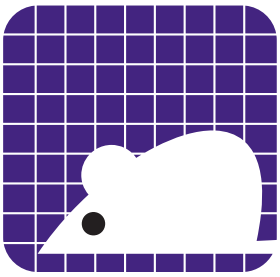
The internal component of a gross exam consists of the evaluation of all organs and musculoskeletal structure for abnormalities, noting any color changes, enlargements, absences, or misplacements.

### **Histopathology**

Most standard histopathology analysis includes complete tissue processing and slide preparation using routine and special staining techniques, as well as evaluation by a board certified pathologist. Microscopic assessments of tissues for abnormalities are important in evaluating the health status of an animal. Often, lesions that are induced by a particular viral pathogen can develop before seroconversion occurs. Histopathology of the sample can help to identify the infection early.

Most animal cells are transparent and lack natural pigment. Stains are used to provide contrast, making the components of tissues more prominent and easily identifiable. A range of stains are available that selectively bind to particular tissue components. When stains are used in combination, a more thorough and extensive evaluation of a tissue sample is

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permitted. The most basic or routine histology procedure uses the stain combination of hematoxylin and eosin (H&E stain). This form of special staining allows for the examination of both internal and external cellular structures.

### ***Phenotyping Pathology***

The scope of pathological evaluations can be expanded to encompass more complex custom design programs such as the study of gene function and its impact on phenotype. This strategy is often employed in the assessment of phenotypic expression in transgenic and knockout mice.

Phenotyping studies typically involve employing customized developmental, histological, immunohistochemical, and molecular-based tools to characterize gross and microscopic morphology, cell proliferation and apoptosis, as well as gene expression in embryos and fetuses from genetically altered mice.

When developing a phenotype characterization study, mutant models (transgenic, knockout, etc.) are selected according to the age at which the phenotype should be fully expressed. The recommended components for a basic phenotype screen include the measurement of body weights, performance of a gross necropsy in which all organs are evaluated, and collection of a complete set of tissues for histopathology analysis. A basic histopathology screen should include the collection of brain, heart, thymus, lung, liver, kidney, spleen, gastrointestinal tract, and gonad tissue. Any anticipated target organs should also be included, as should organs of interest in a particular study. It is also recommended that serum and whole blood be collected for a standard clinical chemistry panel as well as a complete blood count analysis. A Board Certified Veterinary Pathologist with expertise in laboratory animals should perform the microscopic evaluation.

Certain methods employing only gross and routine histological techniques can be used for screening atypical morphology in fetal transgenic mice quickly, and in a standardized format. The histological tissue samples collected can be further analyzed with additional pathology-based tools such as histomorphology,

immunohistochemistry, and *in situ* hybridization. In this way, specific functions governed by the transgene can be evaluated through the detection of changes in organ or tissue morphology, cell kinetics, evaluation of novel proteins or defective levels of protein products, and the assessment of messenger RNA *in vivo*.

***Please contact Charles River's Technical Assistance Department at 1.800.338.9680 with any questions on utilizing pathology for disease detection, mutant mouse phenotyping and other related services.***

### ***Reference***

1. "A Laboratory Animal Health Monitoring Program: Rationale and Development", *Technical Bulletin*, 1990.



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