Mouse Phenotyping 101: Necropsy and Tissue Trimming

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Overview

- Diagnostic pathology vs. phenotyping
- Describing lesions
- The mouse necropsy
  - Necropsy procedure
  - Gross anatomy
  - Examples of lesions
- Tissue fixation and trimming
- Mouse specific histology
- Resources

Diagnostic Pathology vs. Phenotyping

<table>
<thead>
<tr>
<th></th>
<th>Diagnostic Pathology</th>
<th>Phenotyping</th>
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<tbody>
<tr>
<td>Number of animals</td>
<td>Usually 1</td>
<td>2 or more (wildtype, mutant, male, female)</td>
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<tr>
<td>Manner of death</td>
<td>Natural or euthanasia because of disease</td>
<td>Euthanasia (animals may appear completely normal)</td>
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<tr>
<td>Goal</td>
<td>Determine cause of death or disease</td>
<td>Determine differences between wildtype and mutant animals</td>
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<tr>
<td>Strategy</td>
<td>Gross necropsy, histopathology of lesions and standard tissue set</td>
<td>Gross necropsy, histopathology of all organs/tissues, comparison to wildtype</td>
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<td>Challenges</td>
<td>Autolysis, lack of a control animal (need to know what is normal)</td>
<td>Changes may be subtle, novel, difficult to name or characterize</td>
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Describing Gross Lesions

- Location:
  - Organ
    - Sublocation (capsular surface, medial lobe, left/right)
- Distribution:
  - Focal
  - Locally extensive
  - Multifocal
  - Multifocal to coalescing
  - Diffuse
- Color
- Size:
  - Measure 3 dimensions, when possible
- Consistency:
  - Soft
  - Firm
  - Hard
**The Mouse Necropsy**

**What You Need**
- Mouse
- 10% Neutral Buffered Formalin Fixatives
- Digital Camera
- Cassettes
- Paper Towels
- Gloves
- Euthanasia Equipment
- Cutting Board
- Ruler
- Syringes
- Blood Collection Tube
- Forceps
- Scissors
- Scale

**Step 1: External Examination**
- Collect blood via cardiocentesis
- Weigh mouse
- Confirm gender
- Note coat and eye color
- Check teeth, ears, eyes, fur, external genitalia, perianal region
- Collect tail snip for genotyping


http://www.theodora.com/rodent_laboratory/general_procedures.html
Post-Mortem Change

Lumps, Bumps and Deformities

Skin/Fur

Corynebacterium bovis hyperkeratosis

Ulcerative Dermatitis

Fight Wounds

Barbering

www.bidl.missouri.edu/info/dora/Dora.htm

Front End
Step 2: Remove the Skin (Optional)
Subcutaneous Hemorrhage

Subcutaneous Abscess

Alternate Step 2: Midline Skin Incision

Hyperkeratosis
Mammary Glands

Diagram A
1. Mammary Gland-Left Cervical
2. Mammary Gland-Left Thoracic
3. Mammary Gland-Left Abdominal

Diagram B
1. Mammary Gland-Left Cervical
2. Mammary Gland-Left Thoracic
3. Mammary Gland-Left Abdominal
4. Mammary Gland-Left Inguinal
5. Mammary Gland-Right Cervical
6. Mammary Gland-Right Thoracic
7. Mammary Gland-Right Abdominal
8. Mammary Gland-Right Inguinal

Mammary Adenocarcinoma

Lymph Nodes

1. Superficial cervical nodes
2. Deep cervical nodes
3. Mediastinal nodes
4. Axillary node
5. Brachial node
6. Pancreatic node
7. Renal nodes
8. Mesenteric node
9. Inguinal node
10. Lumbar nodes
11. Sacral Node
12. Sciatic node
Step 3: Removal of the Salivary Glands

Step 4: Open the Abdomen
Step 5: Inject the GI Tract with Formalin

Step 6: Collect the Sternum
Step 7: Open the Thorax

Hemothorax

Step 8: Inflate the Lungs

Step 9: Split the Mandible
Step 10: Remove the Pluck

Step 11: Separate and Examine the Organs

Heart

Gastrointestinal Tract

Thymus

Liver

Adrenal Glands

Kidneys

Pancreas

Reproductive Tract, Bladder

Tongue, Thyroid, Trachea

Lungs

Spleen

http://icg.eprcolumbia.edu/catserv/Protocols/HemorrhageTrehogy.pdf
Distrophic Cardiac Calcinosis

Kidneys and Adrenals

Renal Cysts

Hydronephrosis

http://www.informatics.jax.org/ relevanceSearch/WIFetch?page=imageDetail&key=73360


Enlarged Renal Lymph Nodes

Gastrointestinal Tract

Distended GI Tract

Fecal Impaction
Lungs

- Larynx
- Trachea
- Thyroid Glands
- Apical Lobe
- Azygos Lobe
- Diaphragmatic Lobe

Left Lobe Pneumonia

Left Lobe Nodule

Liver

- Median Lobe
- Left Lobe
- Right Lobe
- Caudate Lobe
Hepatomegaly, Splenomegaly

Multifocal to Coalescing Cellular Infiltrate

Median Lobe, Multiple White Foci

Female Reproductive Tract

Scrotal Fat Necrosis

Enlarged Seminal Vesicles

Step 12: Fix the Tissues

Step 13: Remove Head and Leg +/- Spinal Cord
Remove Brain (Optional)

Step 14: Fix/Decal For 24 Hours

Step 15: Trim the Remaining Tissues

Cassette 1
Slide 1: Heart, Tongue, Thymus

Slide 2: Lungs, Trachea, Esophagus, Thyroid Glands

Cassette 2: Trachea, Esophagus, Thyroid

Cassette 3: Left and Right
Slide 3: Kidneys and Adrenal Glands

Glomerular Dimorphism

Subcapsular Cell Hyperplasia

Cassette 4

Salivary Glands, Exorbital Lacrimal Glands, Lymph Nodes
Slide 4: Salivary glands, exorbital lacrimal glands, lymph nodes
Slide 5: Pancreas and mesenteric lymph nodes
Slide 6: GI Tract

Alternative: Swiss Roll

Segmented Filamentous Bacteria

Flagellates
Entamoeba

Photos courtesy of Dr. Brayton

Cassette 7

Slide 7: Liver and Spleen

Spleen and Liver
Extramedullary Hematopoiesis

Hepatitis

Anisokaryosis

Cytoplasmic Invagination (Pseudoinclusion)
Cassette 8

Slide 8: Reproductive Tract and Bladder

Male Repro
“Not Amyloid”
Books

Web Sites

- Virtual Mouse Necropsy
  - http://tvmouse.compmed.ucdavis.edu/virtualnecropsy/
- Guide for organ sampling and trimming
  - http://www.item.fraunhofer.de/reni/trimming/
- Additional information