



CMHD Pathology Report



CMHD Pathology Core

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ReportID: Report Date: April 12, 2013
Pathologist: H. Adissu

Mouse Genetics Project

Wellcome Trust Sanger
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Campus
Hinxton, Cambridge
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UK

CMHD LabID: N13-235

Relevant History:

increased susceptibility to bacterial infection
decreased bone mineral density
decreased body length
decreased body weight
decreased lean body mass
decreased bone mineral content
abnormal tooth morphology
decreased body weight
hypoalbuminemia
decreased circulating total protein level
decreased bone mineral content
decreased bone strength
decreased bone trabecula number

AnimalID: M00540324 (Male)

Tissue Preservation and Staining:

poorly preserved and processed skin

Histopathology Findings:

thymus (MA:0000142)

Histopath Description:

There is a 150 um diameter epithelial cyst.

Morphological Diagnosis:

Distribution: focal; **MPATH Diagnosis:** cyst MPATH:62

Definitive Diagnosis:

Epithelial cyst

Histopathology Comments:

This is a developmental abnormality commonly seen in mice.

lymph node (MA:0000139)

Histopath Description:

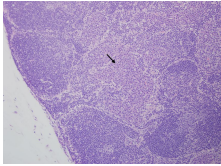
The lymph node contains moderately prominent lymphoid nodules with prominent germinal centers. Occasional apoptotic bodies are present within germinal center freely or within the cytoplasm of macrophages. There are numerous mature lymphocytes within medullary sinuses.

Morphological Diagnosis:

Distribution: multifocal; **Severity:** mild; **MPATH Diagnosis:** hyperplasia MPATH:134

Definitive Diagnosis:

Lymphoid hyperplasia with sinus plasmacytosis



Lymph node,
hyperplasia with
sinus
plasmacytosis, 20x,
HE

liver (MA:0000358)

Histopath Description:

No lipidosis observed

Definitive Diagnosis:

No hepatic lipidosis

heart (MA:0000072)

Histopath Description:

There are black pigments in the endothelial cells and stromal cells in cardiac valve.

Morphological Diagnosis:

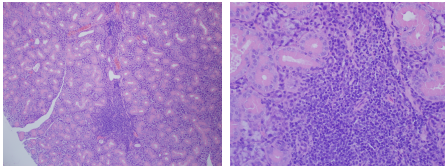
Duration: chronic; **Distribution:** multifocal; **Severity:** moderate;

Definitive Diagnosis:

Valvular melanosis

Histopathology Comments:

Melanin deposition in multiple organs are common in C57BL6 mice.



Salivary gland,
inflammatory cell
infiltrate, 10x, HE

Salivary gland,
inflammatory cell
infiltrate, 10x, HE

salivary gland (MA:0000346)

Histopath Description:

In the submandibular gland, there is a focal aggregate of lymphocytes and macrophages that have infiltrated between serous acini. The mucous acini are replaced by the inflammatory cells.

Morphological Diagnosis:

Duration: acute; **Distribution:** focal; **Severity:** mild;

Definitive Diagnosis:

Submandibular acute focal sialadenitis

testis (MA:0000411)

Histopath Description:

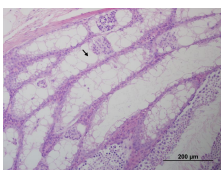
There are multifocal vacuolar degeneration and atrophy of the seminiferous tubules affecting 10% of the testicular parenchyma.

Morphological Diagnosis:

Distribution: multifocal; **Severity:** moderate;

Definitive Diagnosis:

Testicular degeneration and atrophy



Testis,
degeneration and
testis, 20x, HE

retina (MA:0000276)

Histopath Description:

Involving one eye, there are clusters of external nuclear structures within the internal plexiform layer.

Morphological Diagnosis:

Distribution: Focal; **Severity:** mild;

Definitive Diagnosis:

Retinal dysplasia

kidney (MA:0000368)

Histopath Description:

Focally contingent tubules have large basophilic tubular cells.

Morphological Diagnosis:

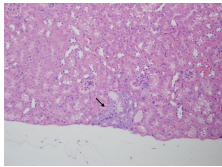
Distribution: focally extensive; **Severity:** mild;

Definitive Diagnosis:

Tubular hyperplasia

Histopathology Comments:

This change is consistent with regenerative hyperplasia. This is a typical regenerative response following a tubular damage. The cause is not evident in the sections examined.



Kidney, tubules,
hyperplasia, 20x,
HE

salivary gland (MA:0000346)

Histopath Description:

There are multifocal interstitial mononuclear inflammatory aggregates.

Morphological Diagnosis:

Distribution: Multifocal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212

Definitive Diagnosis:

Interstitial mononuclear inflammatory infiltrate

Organ/Tissue Analyzed:

Brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, esophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, testis, epididymis, seminal vesicle, and prostate.

AnimalID: M00227843 (Male)

Tissue Preservation and Staining:

poorly preserved and processed skin

Histopathology Findings:

heart (MA:0000072)

Histopath Description:

There are black pigments in the endothelial cells and stromal cells in cardiac valve.

Morphological Diagnosis:

Distribution: multifocal; **Severity:** moderate;

Definitive Diagnosis:

Valvular melanosis

Histopathology Comments:

Melanin deposition in multiple organs are common in C57BL6 mice.

liver (MA:0000358)

Histopath Description:

Minimal lipidosis

Morphological Diagnosis:

Distribution: multifocal; **Severity:** mild;

Definitive Diagnosis:

Hepatic lipidosis

Histopathology Comments:

Hepatic lipidosis is minimal despite high-fat diet.

thymus (MA:0000142)**Histopath Description:**

There is a 100 um diameter epithelial cyst.

Morphological Diagnosis:**Distribution:** focal; **MPATH Diagnosis:** cyst MPATH:62**Definitive Diagnosis:**

Epithelial cyst

Histopathology Comments:

This is a developmental abnormality commonly seen in mice.

spleen (MA:0000141)**Histopath Description:**

mild erythroid hyperplasia

Morphological Diagnosis:**Distribution:** multifocal; **Severity:** mild; **MPATH Diagnosis:** extramedullary hemopoiesis MPATH:595**Definitive Diagnosis:**

Splenic erythroid hyperplasia

stomach (MA:0000353)**Histopath Description:**

moderate neutrophilic gastritis

Morphological Diagnosis:**Distribution:** multifocal to coalescing; **Severity:** moderate;**Definitive Diagnosis:**

Gastritis, neutrophilic

eye (MA:0000261)**Histopath Description:**

The uvea and the retinal epithelium are non pigmented

Morphological Diagnosis:**Distribution:** diffuse;**Definitive Diagnosis:**

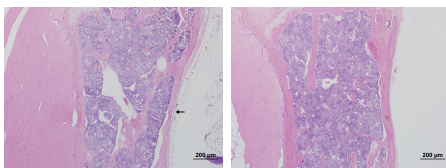
absence of uveal and retinal melanin pigmentation

sternum (MA:0001331)**Histopath Description:**

The thickness of the cortical bone of the sternum is slightly decreased in some segments (compared to WT)

Morphological Diagnosis:**Distribution:** segmental; **Severity:** mild; **MPATH Diagnosis:** osteopenia MPATH:53**Definitive Diagnosis:**

Cortical osteopenia



Sternum,
osteopenia, 10x,
WT

Sternum, normal,
10x, WT

testis (MA:0000411)**Histopath Description:**

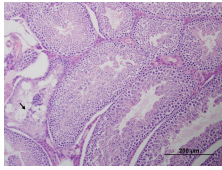
There are multifocal vacuolar degeneration and atrophy of rare seminiferous tubules.

Morphological Diagnosis:

Distribution: multifocal; **Severity:** mild;

Definitive Diagnosis:

Testicular degeneration and atrophy



Testis,
degeneration and
atrophy, 20x, WT

Organ/Tissue Analyzed:

Brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, esophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, testis, epididymis, seminal vesicle, and prostate.

AnimalID: M00227829 (Female)

Histopathology Findings:

liver (MA:0000358)

Histopath Description:

Minimal lipidosis

Morphological Diagnosis:

Distribution: multifocal; **Severity:** mild;

Definitive Diagnosis:

Hepatic lipidosis

Histopathology Comments:

Hepatic lipidosis is minimal despite high-fat diet.

heart (MA:0000072)

Histopath Description:

There are black pigments in the endothelial cells and stromal cells in cardiac valve.

Morphological Diagnosis:

Distribution: multifocal; **Severity:** mild;

Definitive Diagnosis:

Valvular melanosis

Histopathology Comments:

Melanin deposition in multiple organs are common in C57BL6 mice.

brain (MA:0000168)

Histopath Description:

There is mild dilation of the lateral ventricles

Morphological Diagnosis:

Distribution: bilateral; **Severity:** mild;

Definitive Diagnosis:

Dilation of the brain ventricles

Histopathology Comments:

Mild dilation of the lateral ventricles is a background condition in mice of C57BL/6N background (Brayton et al., 2004).

lymph node (MA:0000139)

Histopath Description:

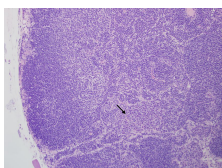
The lymph node contains moderately prominent lymphoid nodules with prominent germinal centers. Occasional apoptotic bodies are present within germinal center freely or within the cytoplasm of macrophages. There are numerous mature lymphocytes within medullary sinuses.

Morphological Diagnosis:

Distribution: multifocal; **Severity:** mild; **MPATH Diagnosis:** hyperplasia MPATH:134

Definitive Diagnosis:

Lymphoid hyperplasia with sinus plasmacytosis



Lymph node,
hyperplasia with
sinus
plasmacytosis, 20x,
HE

kidney (MA:000368)**Histopath Description:**

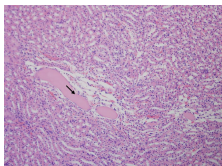
Rare tubules contain protein casts

Morphological Diagnosis:**Distribution:** multifocal; **Severity:** mild;**Definitive Diagnosis:**

Tubular protein casts

Histopathology Comments:

This change is consistent with low grade glomerulopathy (although affected glomeruli are not seen in the field examined). The change is minimal to explain low blood protein level detected in this line. Glomerulopathy and subsequent tubular protein loss is seen as mice age.



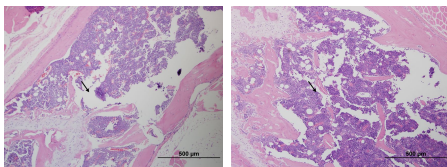
Kidney, tubules,
intraluminal protein,
20x, HE

femur (MA:0001359)**Histopath Description:**

Trabecular bones are rare and of smaller size in the femoral diaphysis compared to the other mice in this line and that of the controls

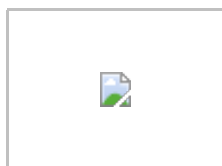
Morphological Diagnosis:**Severity:** mild; **MPATH Diagnosis:** osteopenia MPATH:53**Definitive Diagnosis:**

Trabecular osteopenia

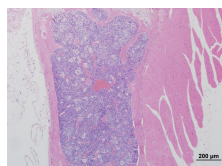


Femur, trabecular
osteopenia (note
fewer trabecular
bone), 10x, HE

Femur, normal, 10x,
HE



bone



Sternum, normal

Organ/Tissue Analyzed:

Brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, esophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, uterus, oviduct, ovary, and mammary gland.

AnimalID: M00227845 (Female)**Histopathology Findings:****heart (MA:0000072)****Histopath Description:**

There are black pigments in the endothelial cells and stromal cells in cardiac valve.

Morphological Diagnosis:

Distribution: multifocal; **Severity:** mild;

Definitive Diagnosis:

Valvular melanosis

Histopathology Comments:

Melanin deposition in multiple organs are common in C57BL6 mice.

liver (MA:0000358)**Histopath Description:**

Moderate lipidosis

Morphological Diagnosis:

Distribution: multifocal to coalescing; **Severity:** moderate; **MPATH Diagnosis:** steatosis
MPATH:622

Definitive Diagnosis:

Hepatic lipidosis

Histopathology Comments:

Hepatic lipidosis is due to high-fat diet.

spleen (MA:0000141)**Histopath Description:**

Lymphoid follicles are enlarged and most contain germinal centers

Morphological Diagnosis:

Distribution: multifocal; **Severity:** moderate; **MPATH Diagnosis:** lymphoid hyperplasia
MPATH:147

Definitive Diagnosis:

Lymphoid hyperplasia

eye (MA:0000261)**Histopath Description:**

One of the eyes is 1.5x smaller than normal. The lens occupies all the ocular chambers with little vitreous chamber visible.

Morphological Diagnosis:

Distribution: unilateral;

Definitive Diagnosis:

Microphthalmia

Histopathology Comments:

Microphthalmia and other ocular defects are noted as incidental lesion in C57BL6/B6 mice.

brain (MA:0000168)**Histopath Description:**

There is mild dilation of the lateral ventricles

Morphological Diagnosis:

Distribution: bilateral; **Severity:** mild;

Definitive Diagnosis:

Dilation of the brain ventricles

Histopathology Comments:

Mild dilation of the lateral ventricles is a background condition in mice of C57BL/6N background (Brayton et al., 2004).

kidney (MA:0000368)**Histopath Description:**

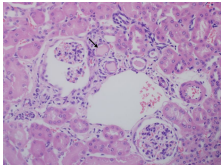
Rare glomeruli are hypercellular, cystic, or adhered to the glomerular capsule (glomerular synechiae). Few tubules abutting these glomeruli are dilated and contain protein casts. There is hypertrophy and sliding of epithelium in these tubules (regeneration).

Morphological Diagnosis:**Distribution:** multifocal; **Severity:** mild; **MPATH Diagnosis:** glomerulonephritis MPATH:197**Definitive Diagnosis:**

Tubular protein casts

Histopathology Comments:

This change is consistent with low grade glomerulopathy. The lesion is minimal to explain low blood protein level detected in this line. Glomerulopathy and subsequent tubular protein loss is seen as mice age.



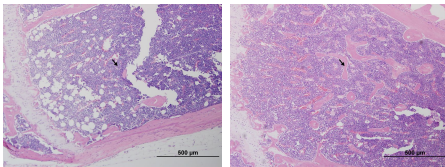
Kidney, tubules,
intraluminal protein,
20x, HE 40x

tibia (MA:0001361)**Histopath Description:**

Trabecular bones are rare and of smaller size in the tibial diaphysis compared to the other mice in this line and that of the controls

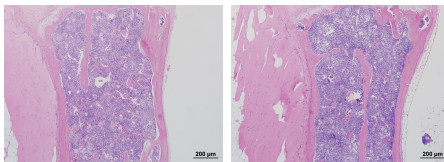
Morphological Diagnosis:**Severity:** moderate; **MPATH Diagnosis:** osteopenia MPATH:53**Definitive Diagnosis:**

Trabecular osteopenia



Tibia, trabecular
osteopenia, 10x, HE

Tibia, WT, normal,
HE 10x



Sternum, ET
control, normal,
10x, HE

Sternum, normal,
10x, HE

Organ/Tissue Analyzed:

Brain, trigeminal ganglion, eyes, salivary glands, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, esophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, uterus, oviduct, ovary, and mammary gland.

Report Summary and Recommendation:

Minimal hepatic lipidosis is observed in this line consistent with decreased body weight. Mild tubular protein loss with/without minimal glomerulopathy is observed in two mice (M00227845 and M00227829). Note that hypoproteinemia and notably hypoalbuminemia is observed in this line; however, the lesions are considered minimal to account for this blood biochemistry phenotype. Two mice (M00227829 and M00227845) have a smaller number and size of trabecular bone in the femoral/tibial diaphysis while one mouse has minimal osteopenia of the sternal cortical bone (M00227843). These lesions are consistent with the bone phenotypes documented in this line. Further analysis of multiple sections together with image analysis may be required to confirm the skeletal phenotypes. We did not observe histological evidence for increased susceptibility to bacterial infection. The mesenteric lymph nodes in two mice (M00227829 and M00540324) are hyperplastic with marked sinus plasmacytosis, suggesting a strong humoral response to an antigenic response. We speculate that the increased susceptibility to bacterial infection might be associated with hypoproteinemia. Both male mice (M00540324 and M00227843) have testicular degeneration and atrophy; the lesion is more severe in the former.