



# CMHD Pathology Report



## CMHD Pathology Core

Toronto Centre for  
Phenogenomics  
25 Orde St. 3rd fl.  
Toronto, Ont. M5T 3H7  
Tel.(416) 586-8375  
Fax (416) 586-5993

contact: Dr. Susan  
Newbigging  
email:  
[newbigging@lunenfeld.ca](mailto:newbigging@lunenfeld.ca)

## Principle Investigator: Dr. Colin McKerlie ICSIG

Institute: Sick Kids  
Address:

ReportID: Report Date: November 23,  
2011  
Pathologist: H. Adissu

## Mouse Genetics Project

Wellcome Trust Sanger  
Institute  
Wellcome Trust Genome  
Campus  
Hinxton, Cambridge  
CB10 1SA  
UK

email:  
[MGPenquiries@sanger.ac.uk](mailto:MGPenquiries@sanger.ac.uk)  
[Mouse Portal](#)  
[Europhenome](#)

CMHD LabID: N11-185

## Relevant History:

(Viability at postnatal day 14; Body Weight Curves; Indirect Calorimetry; Body Composition (DEXA); Eye Morphology; Peripheral Blood Lymphocytes) Decreased body weight/length, increased T cell number, decreased BMD/BMC, decreased respiratory quotient, hydrocephaly/partial post-natal lethality, abnormal cornea and corneal opacity

## AnimalID: M00391655 Prmt het

### Tissue Preservation and Staining:

There is artifactual separation of the dermis and hypodermis. A small piece of the adrenal gland is present in section. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

### Histopathology Findings:

#### liver (MA:0000358)

#### Histopath Description:

The overall hepatic lobular architecture is normal. Diffusely, hepatocytes contain intracytoplasmic clear vacuoles (lipid). The lipid vacuoles within the midzonal and periacinar regions are small (2-3 um in diameter) and surround a central nucleus (interpreted as microvesicular lipid). The lipid vacuoles within the portal areas are large (8-12 um in diameter) and displace the nucleus to the margin (macrovesicular lipid). There are rare perivascular mononuclear inflammatory cells.

#### Morphological Diagnosis:

**Distribution:** Diffuse; **Severity:** moderate; **MPATH Diagnosis:** lipid deposition MPATH:42

#### Definitive Diagnosis:

Hepatic lipidosi

#### Histopathology Comments:

Hepatocellular vacuolar change of variable degree suggestive of lipidosi is present in all mice from WTSI, consistent with high lipid diet.

#### mesenteric lymph node (MA:0002829)

#### Histopath Description:

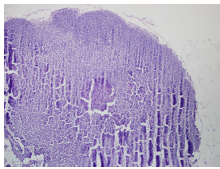
The mesenteric lymph node is enlarged upto 4x normal and the paracortex, cortex, and subcapsular sinuses are replaced by a diffuse sheet of round cells. The neoplastic cells have generally a scant amount of eosinophilic cytoplasm and deeply hyperchromatic nucleus. Mitotic figures are rare (1/ per high power field (400x)). The tissue has marked processing artifact.

#### Morphological Diagnosis:

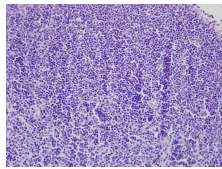
**Severity:** moderate; **MPATH Diagnosis:** lymphoma [obsolete use MPATH:516 or 535]  
MPATH:343

#### Definitive Diagnosis:

Lymphoma



Mesenteric lymph node, lymphoma, 20x, HE



Mesenteric lymph node, lymphoma, 40x, HE.

### brain (MA:0000168)

#### Histopath Description:

There is a mild enlargement of the lateral ventricle.

#### Morphological Diagnosis:

**Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

#### Definitive Diagnosis:

hydrocephalus, lateral ventricle

#### Histopathology Comments:

Variable degree of hydrocephalus is observed in a proportion of wild type C57 Black 6 mice.

### AnimalID: M00391653 Prmt het

#### Tissue Preservation and Staining:

Only one lobe of the thyroid gland is present. The parathyroid gland is not present in the section. Only one adrenal gland is present. There is artifactual separation of the dermis and hypodermis. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

#### Histopathology Findings:

##### heart (MA:0000072)

#### Histopath Description:

There is a small focus of poorly defined mineralized cartilaginous tissue at the base of the aorta.

#### Morphological Diagnosis:

**Distribution:** Focal; **Severity:** no lesions;

#### Definitive Diagnosis:

osteocartilaginous metaplasia of base of aorta

#### Histopathology Comments:

Foci of cartilage or bone can be found within the base of the aorta in the mouse.

### brain (MA:0000168)

#### Histopath Description:

There is a mild enlargement of the lateral ventricle. There is mild rarefaction (edema) of the periventricular neuropil caudal to the hippocampus.

#### Morphological Diagnosis:

**Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

#### Definitive Diagnosis:

hydrocephalus, lateral ventricle

#### Histopathology Comments:

Variable degree of hydrocephalus is observed in a proportion of wild type C57 Black 6 mice.

### liver (MA:0000358)

#### Histopath Description:

The overall hepatic lobular architecture is normal. Diffusely, hepatocytes contain intracytoplasmic clear vacuoles (lipid). The lipid vacuoles within the midzonal and periportal regions are small (2-3 um in diameter) and surround a central nucleus (interpreted as microvesicular lipid). The lipid vacuoles within the portal areas are large (8-12 um in diameter) and displace the nucleus to the margin (macrovesicular lipid). There are rare perivascular mononuclear inflammatory cells.

#### Morphological Diagnosis:

**Distribution:** Diffuse; **Severity:** moderate; **MPATH Diagnosis:** lipid deposition MPATH:42

#### Definitive Diagnosis:

Hepatic lipidosi

#### Histopathology Comments:

Hepatocellular vacuolar change of variable degree suggestive of lipodosis is present in all mice from WTSI, consistent with high lipid diet.

#### salivary gland (MA:0000346)

##### Histopath Description:

There are occasional interstitial aggregate of histiocytes and lymphocytes.

##### Morphological Diagnosis:

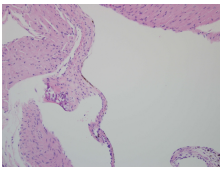
**Duration:** Chronic; **Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212

##### Definitive Diagnosis:

Interstitial histiocytic and lymphocytic sialadenitis

##### Histopathology Comments:

This is a common and insignificant incidental finding in mice.



Base of aorta,  
osteocartilaginous  
metaplasia, 20x,  
HE.

---

#### AnimalID: M00391658 Prmt het

##### Tissue Preservation and Staining:

There is artifactual separation of the dermis and hypodermis. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

##### Histopathology Findings:

#### brown fat (MA:0000057)

##### Histopath Description:

There are multifocal aggregates of mononuclear inflammatory cells within the cervical subcutaneous brown fat. There is central nuclear rowing within few myocytes in the underlying muscle.

##### Morphological Diagnosis:

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

##### Definitive Diagnosis:

Steatitis

##### Histopathology Comments:

The lesion is likely secondary to a non specific traumatic lesion or extension from non specific dermatitis.

#### adrenal gland (MA:0000116)

##### Histopath Description:

In one of the adrenal glands there is a focally extensive stream of subcapsular spindle cell proliferation that segmentally displaces the superficial cortical layer. Embedded within the peri-adrenal fat is a 50 um diameter adrenocortical tissue.

##### Morphological Diagnosis:

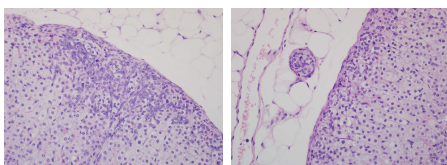
**Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** hyperplasia MPATH:134

##### Definitive Diagnosis:

Spindle cell hyperplasia; extra-adrenal cortical tissue

##### Histopathology Comments:

Proliferation of subcortical spindle cells, with displacement of the cortex, is common in mice of all ages. The function of these cells is not known. Extra-adrenal cortical tissue is occasionally seen in wild type mice.



Adrenal gland, spindle cell hyperplasia, 40x, HE	Adrenal gland, extra-adrenal tissue, 40x, HE.
--	---

### lymph node (MA:0000139)

#### Histopath Description:

The sinuses of the of the superficial cervical lymph nodes are expanded by large numbers of histiocytes.

#### Morphological Diagnosis:

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

#### Definitive Diagnosis:

Sinus histiocytosis

#### Histopathology Comments:

The lesion indicates drainage of a local chronic inflammatory lesion; this is not evident in this section.

### stomach (MA:0000353)

#### Histopath Description:

Within the glandular stomach and adjacent to the limiting ridge are few dilated glands with mineralized material in their lumina.

#### Morphological Diagnosis:

**Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** mineralisation MPATH:555

#### Definitive Diagnosis:

Gastric gland mineralization.

#### Histopathology Comments:

This lesion is an incidental lesion occasionally seen in mouse.

### brain (MA:0000168)

#### Histopath Description:

There is a mild enlargement of the lateral ventricle.

#### Morphological Diagnosis:

**Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

#### Definitive Diagnosis:

hydrocephalus, lateral ventricle

#### Histopathology Comments:

Variable degree of hydrocephalus is observed in a proportion of wild type C57 Black 6 mice.

---

### AnimalID: M00462979 Prmt hom

#### Tissue Preservation and Staining:

Thyoid gland is not present in section. There is artifactual separation of dermis and hypodermis. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

#### Histopathology Findings:

##### adrenal gland (MA:0000116)

#### Histopath Description:

In one of the adrenal glands, there is a focally extensive stream of subcapsular spindle cell proliferation that segmentally displaces the superficial cortical layer.

#### Morphological Diagnosis:

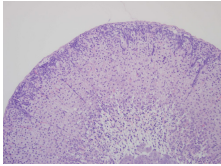
**Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** hyperplasia MPATH:134

#### Definitive Diagnosis:

Spindle cell hyperplasia.

#### Histopathology Comments:

Proliferation of subcortical spindle cells, with displacement of the cortex, is common in mice of all ages. The function of these cells is not known.



Adrenal gland,  
spindle cell  
hyperplasia (top)  
and degeneration of  
X-zone (bottom),  
20x, HE.

### adrenal gland (MA:0000116)

#### Histopath Description:

Adrenal cortical cells immediately surrounding the medulla are vacuolated and contain fine granular golden brown cytoplasmic pigment. Rare mononuclear cells are present within this zone.

#### Morphological Diagnosis:

**Distribution:** Diffuse; **Severity:** no lesions; **MPATH Diagnosis:** degenerative change MPATH:14

#### Definitive Diagnosis:

Vacuolar degeneration of X-zone of the adrenal gland with cytoplasmic ceroid accumulation (X-zone involution).

#### Histopathology Comments:

The X zone of the adrenal cortex disappears when males reach sexual maturity and females undergo their first pregnancy. The zone also disappears in virgin females, albeit gradually (Percy and Barthold, 2007).

### stomach (MA:0000353)

#### Histopath Description:

A thick band of eosinophils and few neutrophils are present within the submucosa of the glandular stomach adjacent to the limiting ridge.

#### Morphological Diagnosis:

**Distribution:** Focal; **Severity:** moderate; **MPATH Diagnosis:** inflammation MPATH:212

#### Definitive Diagnosis:

Eosinophilic submucosal gastritis.

#### Histopathology Comments:

The lesion suggests an allergic reaction (likely a reaction to a food allergen).

### stomach (MA:0000353)

#### Histopath Description:

Few glands adjacent to the limiting ridge have abundant hyalinized cytoplasm.

#### Morphological Diagnosis:

**Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** hyalinosis MPATH:40

#### Definitive Diagnosis:

Gastric epithelial hyalinosis.

#### Histopathology Comments:

This is a common incidental lesion in B6 strain.

### eye (MA:0000261)

#### Histopath Description:

The corneal epithelium is reduced in thickness and is mainly composed of a hypertrophic and disorganized and slightly vacuolated basal layer and a flattened superficial layer. There are few neutrophils within the anterior chamber adjacent to the limbus and rarely within the iris. There is a segmental sub-basilar cleft.

#### Morphological Diagnosis:

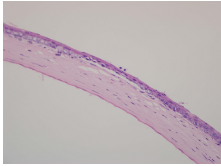
**Duration:** Chronic; **Distribution:** Diffuse; **Severity:** moderate; **MPATH Diagnosis:** inflammation MPATH:212

#### Definitive Diagnosis:

keratitis and regeneration with focal sub-basilar clefting; mild anterior neutrophilic iritis.

#### Histopathology Comments:

The lesion indicates a chronic keratitis with suboptimal regeneration. The mild inflammation within the iris might be incited by leaking lens material (lens-induced phacolytic uveitis). See lens lesion below.



Cornea,  
regeneration and  
sub-basilar clefting,  
40x, HE.

### eye (MA:0000261)

#### Histopath Description:

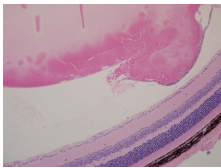
The lens is focally ruptured at the posterior aspect and there is a lenticular epithelium at this focus (posterior migration of lenticular epithelium). There is coagulation of the lens protein (Morgagnian globules) within the ruptured lens. Rare hypertrophic stromal cells are present within the lens material in this focus (migration and fibrous metaplasia of lenticular epithelium).

#### Morphological Diagnosis:

**Duration:** Chronic; **Distribution:** Focal; **Severity:** mild; **MPATH Diagnosis:** cataract MPATH:29

#### Definitive Diagnosis:

Focal lens rupture and cataract



Lens, cataract and  
focal rupture, 40x,  
HE.

### brain (MA:0000168)

#### Histopath Description:

There is a mild enlargement of the lateral ventricle.

#### Morphological Diagnosis:

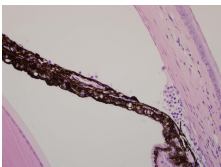
**Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

#### Definitive Diagnosis:

hydrocephalus, lateral ventricle

#### Histopathology Comments:

Variable degree of hydrocephalus is observed in a proportion of wild type C57 Black 6 mice.



Iris, neutrophilic  
iritis (mild), 40x,  
HE.

### AnimalID: M00391654 Prmt hom

#### Tissue Preservation and Staining:

Thyoid gland is not present in section. There is artifactual separation of dermis and hypodermis. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

#### Histopathology Findings:

### liver (MA:0000358)

#### Histopath Description:

The overall hepatic lobular architecture is normal. Approximately 15% of hepatocytes within the portal and midzone region contain large (8-12 um in diameter) intracytoplasmic clear vacuoles (macrovesicular lipid).

#### Morphological Diagnosis:

**Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** lipid deposition MPATH:42

#### Definitive Diagnosis:

Hepatic lipidosis

**Histopathology Comments:**

Hepatocellular vacuolar change of variable degree suggestive of lipidosis is present in all mice from WTSI, consistent with high lipid diet. The changes in this mouse are less severe.

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

There is a mild enlargement of the lateral ventricle.

**Morphological Diagnosis:**

**Severity:** mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

**Definitive Diagnosis:**

hydrocephalus, lateral ventricle

**Histopathology Comments:**

Variable degree of hydrocephalus is observed in a proportion of wild type C57 Black 6 mice.

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

One of the kidney tissues is replaced by a large multilocular cystic structure lined by cuboidal to flattened transitional epithelium and supporting scant stroma in which are present atrophic rare glomeruli. Large numbers of mononuclear inflammatory cells are present within the scant stroma.

**Morphological Diagnosis:**

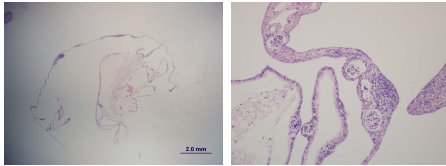
**Duration:** Chronic; **Distribution:** Unilateral; **Severity:** extreme; **MPATH Diagnosis:** degenerative change MPATH:14

**Definitive Diagnosis:**

Hydronephrosis with complete and diffuse parenchymal atrophy and chronic interstitial inflammation.

**Histopathology Comments:**

The hydronephrosis was likely caused by an ascending obstructive urinary tract infection.



Kidney,  
hydronephrosis,  
1.25x

Kidney,  
hydronephrosis,  
20x

**AnimalID: M00398834 Prmt het****Tissue Preservation and Staining:**

Mesenteric lymph nodes are not present in section. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

**Histopathology Findings:****adrenal gland (MA:0000116)****Histopath Description:**

The adrenal glands are diffusely enlarged (about 1.5x normal). Attached to one of the adrenal gland is a 100 um, oval, encapsulated adrenocortical structure. Embedded within the peri-adrenal fat of the other adrenal gland is a similar extra-adrenal cortical tissue; the structure is similar to the above and is typical of adrenocortical tissue.

**Morphological Diagnosis:**

**Distribution:** Bilateral; **Severity:** mild; **MPATH Diagnosis:** developmental and structural abnormality MPATH:55

**Definitive Diagnosis:**

Adrenal gland hyperplasia with extra-adrenal cortical tissue

**Histopathology Comments:**

Extra-adrenal cortical tissue is occasionally seen in wild type mice.

**adrenal gland (MA:0000116)****Histopath Description:**

In both adrenal glands, there is a focally extensive stream of subcapsular spindle cell proliferation that segmentally displaces the superficial cortical layer.

**Morphological Diagnosis:**

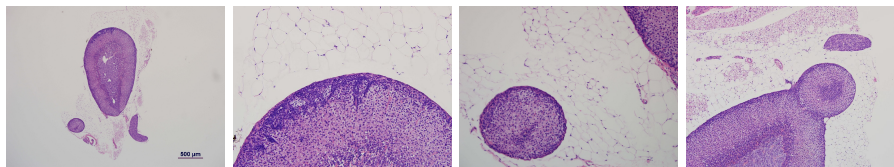
**Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** hyperplasia MPATH:134

**Definitive Diagnosis:**

Spindle cell hyperplasia.

**Histopathology Comments:**

Proliferation of subcortical spindle cells, with displacement of the cortex, is common in mice of all ages. The function of these cells is not known. Pituitary is not present in submission to assess the presence of pituitary dependent adrenocortical hyperplasia.



Adrenal gland, extra-adrenal tissue and spindle cell hyperplasia, 4x, HE.

Adrenal gland, spindle cell hyperplasia, 20x, HE.

Adrenal gland, extra-adrenal tissue, 20x, HE.

Adrenal gland, extra-adrenal tissue, 10x, HE.

**liver (MA:0000358)**

**Histopath Description:**

The overall hepatic lobular architecture is normal. Approximately 15% of hepatocytes within the portal and midzone region contain large (8-12 um in diameter) intracytoplasmic clear vacuoles (macrovesicular lipid).

**Morphological Diagnosis:**

**Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** lipid deposition MPATH:42

**Definitive Diagnosis:**

Hepatic lipidosis

**Histopathology Comments:**

Hepatocellular vacuolar change of variable degree suggestive of lipidosis is present in all mice from WTSI, consistent with high lipid diet. The changes in this mouse are less severe.

**stomach (MA:0000353)**

**Histopath Description:**

There are low numbers of neutrophils within the deep lamina propria

**Morphological Diagnosis:**

**Duration:** Sub-acute; **Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212

**Definitive Diagnosis:**

Gastritis, suppurative

**Histopathology Comments:**

This lesion is most commonly associated with Helicobacter infection. Further investigation is suggested using histochemistry (Silver stain) or colony fecal PCR.

**Summary:**

Mild hydrocephalus is present in 5 of the 6 mice in this line. Hydrocephalus is a common strain-related spontaneous condition in iC57BL/6 (B6) mice. Focal cortical hyperplasia is observed in 3 mice from this line (M00462979, M00398834, M00391658). One of the mice (M00462979) has ocular lesions that may be consistent with corneal opacity observed in some homozygotes. Hepatic lipidosis in this line is minimal compared to controls.

**Report Summary and Recommendation:**

Mild hydrocephalus is present in 5 of the 6 mice in this line. Hydrocephalus is a common strain-related spontaneous condition in iC57BL/6 (B6) mice. Focal cortical hyperplasia is observed in 3 mice from this line (M00462979, M00398834, M00391658). One of the mice (M00462979) has ocular lesions that may be consistent with corneal opacity observed in some homozygotes. Hepatic lipidosis in this line is minimal compared to controls.

Liver - lipid depletion: MPATH:52