



# 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. Jacqui White

Institute: Wellcome Trust Sanger Institute  
Address: Attn: Linda Read Wellcome Trust  
Genome Campus Hinxton Cambridge CB10  
1SA, UK

ReportID: Report Date: September 25,  
2013  
Pathologist: Dr. 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: N13-577

## Relevant History:

Phenotype:

abnormal vertebral arch morphology  
preweaning lethality

## AnimalID: M00948580 (Male)

### Histopathology Findings:

#### brain (MA:0000168)

##### Histopath Description:

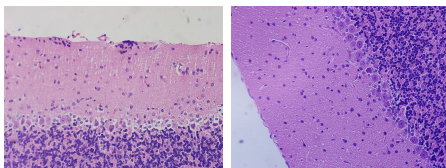
There are three foci of aggregates of granular cells in the within the outer aspect of the molecular layer.

##### Morphological Diagnosis:

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

##### Definitive Diagnosis:

Cerebellar granular cell heterotopia



Cerebellum,  
heterotopic granular  
cells, 40x, HE

Cerebellum, WT,  
normal, 40x, HE

#### 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).

#### liver (MA:0000358)

##### Histopath Description:

diffuse lipidosis

##### Morphological Diagnosis:

**Distribution:** diffuse; **Severity:** extreme; **MPATH Diagnosis:** steatosis MPATH:622

##### Definitive Diagnosis:

hepatic steatosis

### thymus (MA:0000142)

#### Histopath Description:

There is a 50 um diameter epithelial cyst within the medulla.

#### Morphological Diagnosis:

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

#### Definitive Diagnosis:

Epithelial cyst

#### Histopathology Comments:

This is a developmental abnormality commonly seen in mice.

### Organ/Tissue Analyzed:

Histopathology examination included the following organs and tissues: brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, oesophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, bone marrow, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, testis, epididymis, seminal vesicle, and prostate.

### AnimalID: M00948527 (Male)

#### Histopathology Findings:

##### liver (MA:0000358)

#### Histopath Description:

diffuse lipidosis

#### Morphological Diagnosis:

**Distribution:** diffuse; **Severity:** extreme; **MPATH Diagnosis:** steatosis MPATH:622

#### Definitive Diagnosis:

hepatic steatosis

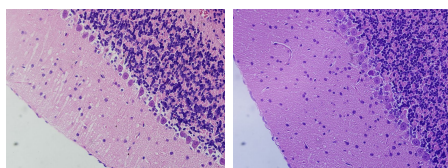
##### brain (MA:0000168)

#### Histopath Description:

Normal

#### Definitive Diagnosis:

Normal



Cerebellum, normal, 40x, HE      Cerebellum, WT, normal, 40x, HE

### Organ/Tissue Analyzed:

Histopathology examination included the following organs and tissues: brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, oesophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, bone marrow, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, testis, epididymis, seminal vesicle, and prostate.

### AnimalID: M00948558 (Female)

#### Histopathology Findings:

##### brain (MA:0000168)

#### Histopath Description:

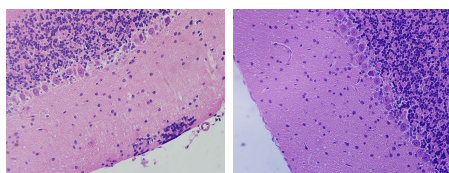
There are three foci of aggregates of granular cells in the within the outer aspect of the molecular layer.

#### Morphological Diagnosis:

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

#### Definitive Diagnosis:

## Cerebellar granular cell heterotopia



Cerebellum, heterotopic granular cells, 40x, HE  
 Cerebellum, WT, normal, 40x, HE

**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).

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

diffuse lipidosis

**Morphological Diagnosis:**

**Distribution:** diffuse; **Severity:** extreme; **MPATH Diagnosis:** steatosis MPATH:622

**Definitive Diagnosis:**

hepatic steatosis

**lung (MA:0000415)****Histopath Description:**

focal peribrochiolar lymphocyte aggregate

**Morphological Diagnosis:**

**Distribution:** focal; **Severity:** mild;

**Definitive Diagnosis:**

focal peribrochiolar lymphocyte aggregate

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

moderate erythropoiesis

**Morphological Diagnosis:**

**Distribution:** multifocal to coalescing; **Severity:** moderate; **MPATH Diagnosis:** extramedullary hemopoiesis MPATH:595

**Definitive Diagnosis:**

Moderate erythropoiesis

**Organ/Tissue Analyzed:**

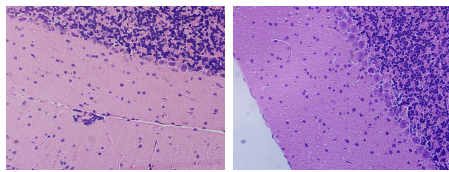
Histopathology examination included the following organs and tissues: brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, oesophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, bone marrow, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, uterus, oviduct, and ovary, and mammary gland.

**AnimalID: M00960529 (Female)****Histopathology Findings:****brain (MA:0000168)****Histopath Description:**

There are three foci of aggregates of granular cells in the within the outer aspect of the molecular layer.

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

Cerebellar granular cell heterotopia



Cerebellum, heterotopic granular cells, 40x, HE

Cerebellum, normal, 40x, HE

**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).

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

diffuse lipidosis

**Morphological Diagnosis:****Distribution:** diffuse; **Severity:** extreme; **MPATH Diagnosis:** steatosis MPATH:622**Definitive Diagnosis:**

hepatic steatosis

**lymph node (MA:0000139)****Histopath Description:**

The mesenteric lymph node is markedly enlarged (greater than four fold). The medulla is particularly expanded by chords and sheets of plasmotoid cells. There are prominent germinal centers within the medulla

**Morphological Diagnosis:****Distribution:** Diffuse; **Severity:** moderate; **MPATH Diagnosis:** hyperplasia MPATH:134**Definitive Diagnosis:**

Lymphoid hyperplasia

**Histopathology Comments:**

The changes in the mesenteric lymph node are suggestive of draining of a regional inflammatory process. However, such a process was not observed in the tissues examined. Early marginal center lymphoma is suspected.

**thyroid gland (MA:0000129)****Histopath Description:**

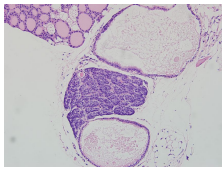
Unilaterally and adjacent to the thyroid gland and the parathyroid gland are two 75 and 100 um diameter cysts that are lined by a single squamous and a stretch of simple ciliated columnar epithelium. The cysts contain granular eosinophilic material in the lumen

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

Cystic ultimobranchial body remnants

**Histopathology Comments:**

These are branchial pouch cysts located near thyroid or occasionally within thyroid. They are very common in human neonates. They are rare in mice.



Thyroid and  
parathyroid glands,  
cystic  
ultimobranchial  
body remnants,  
40x, HE

#### **Organ/Tissue Analyzed:**

Histopathology examination included the following organs and tissues: brain, trigeminal ganglion, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, exocrine and endocrine pancreas, oesophagus, stomach, small intestine, large intestine, liver, gall bladder, spleen, kidneys, adrenal gland, lymph nodes, spinal cord, bone marrow, sternum, femur and tibia with associated skeletal muscles, brown fat, pinna, skin, uterus, oviduct, and ovary, and mammary gland.

#### **Report Summary and Recommendation:**

Three mice from these line have cerebellar granular cell heterotopia. The lesions are minimal and likely not clinically important, but its presence in 3 of the 4 mice in this line suggests genotype effect.

Other lesions in this line are incidental or attributable to diet or strain background. Histological analyses of single tissue sections is not suited to confirm vertebral dysmorphism.

There are no lesions predictive of preweaning homozygous lethality. Analysis of preweaning homozygous animals is required to determine cause of mortality. Further, such analysis may also help to assess the presence of lesions comparable to those seen humans with SEC23A gene recessive mutations. In humans homozygous missense mutation in the SEC23A gene is associated with with CRANIOLENTICULOSUTURAL DYSPLASIA; CLSD; OMIM - #607812 ).

Summary: Brain, Cerebellum: Granular cell heterotopia