



# CMHD Pathology Report



## CMHD Pathology Core

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2013  
Pathologist: Dr. H. Adissu

## Mouse Genetics Project

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

CMHD LabID: N13-575

## Relevant History:

Phenotype:

abnormal head morphology  
decreased body weight  
decreased leukocyte cell number  
increased mean corpuscular volume  
increased mean corpuscular hemoglobin  
increased T cell number  
increased CD4-positive T cell number  
abnormal cranium morphology  
abnormal parietal bone morphology  
decreased survivor rate

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**AnimalID: M00638488 (Male)**

## Histopathology Findings:

### brain (MA:0000168)

#### Histopath Description:

The brain is small and dorsoventrally flattened but architecturally normal (microencephaly). The lateral ventricles are mildly dilated.

#### Morphological Diagnosis:

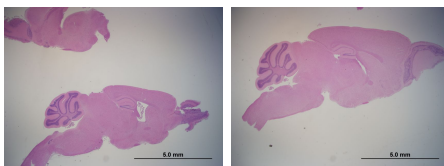
**Distribution:** diffuse; **Severity:** moderate;

#### Definitive Diagnosis:

Microencephaly

#### Histopathology Comments:

The lesion is consistent with the abnormal cranium morphology reported.



Brain,  
microencephaly,  
1.25x, HE

Brain, WT, normal,  
1.25x, HE

## testis (MA:0000411)

#### Histopath Description:

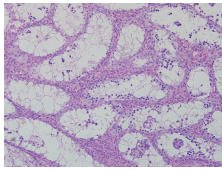
There is extensive atrophy and vacuolation of the seminiferous tubule affecting the entire testicular parenchyma. There is no evidence of spermatids and sperm cells. The interstitial tissue is prominent with marked hyperplasia of the leydig cells.

#### Morphological Diagnosis:

**Distribution:** diffuse; **Severity:** extreme;

#### Definitive Diagnosis:

Testicular vacuolation and hypoplasia; Leydig cell hyperplasia



Testis, vacuolation and atrophy, Leydig cell hyperplasia, 20x, HE

#### epididymal duct (MA:0001735)

##### Histopath Description:

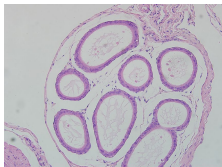
The epididymis is devoid of spermatocytes and contains cellular debris and proteinaceous fluid.

##### Morphological Diagnosis:

**Severity:** extreme;

##### Definitive Diagnosis:

Epididymal aspermia



Epididymis, aspermia, 20x, HE

#### liver (MA:0000358)

##### Histopath Description:

diffuse lipidosis

##### Morphological Diagnosis:

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

##### Definitive Diagnosis:

hepatic steatosis

#### 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

#### 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.

#### salivary gland (MA:0000346)

##### Histopath Description:

There are multifocal perivascular mononuclear inflammatory cell aggregates.

##### Morphological Diagnosis:

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

**Definitive Diagnosis:**

Interstitial inflammatory aggregates

**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: M00638498 (Male)****Histopathology Findings:****brain (MA:0000168)****Histopath Description:**

The brain is small and dorsoventrally flattened but architecturally normal (microencephaly). The lateral ventricles are mildly dilated.

**Morphological Diagnosis:**

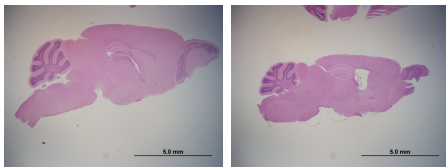
**Distribution:** diffuse; **Severity:** moderate;

**Definitive Diagnosis:**

Microencephaly

**Histopathology Comments:**

The lesion is consistent with the abnormal cranium morphology reported.



Brain, WT, normal,  
1.25x, HE

Brain,  
microencephaly,  
1.25x, HE

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

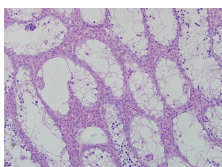
There is extensive atrophy and vacuolation of the seminiferous tubule affecting the entire testicular parenchyma. There is no evidence of spermatids and sperm cells. The interstitial tissue is prominent with marked hyperplasia of the leydig cells.

**Morphological Diagnosis:**

**Distribution:** diffuse; **Severity:** extreme;

**Definitive Diagnosis:**

Testicular vacuolation and hypoplasia; Leydig cell hyperplasia



Testis, vacuolation  
and atrophy, Leydig  
cell hyperplasia,  
20x, HE

**epididymal duct (MA:0001735)****Histopath Description:**

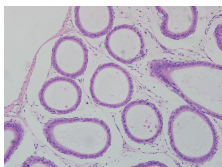
The epididymis is devoid of spermatocytes and contains cellular debris and proteinaceous fluid.

**Morphological Diagnosis:**

**Severity:** extreme;

**Definitive Diagnosis:**

Epididymal aspermia



Epididymis,  
aspermia, 20x, HE

#### **liver (MA:0000358)**

##### **Histopath Description:**

diffuse lipidosis

##### **Morphological Diagnosis:**

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

##### **Definitive Diagnosis:**

hepatic steatosis

#### **sternum (MA:0001331)**

##### **Histopath Description:**

There is a partial sternal fracture between the 4th and 5th sternal bodies. The chondroid tissue along the fracture is markedly degenerate. There is a nodular cartilagenous proliferation at the perichondrial margins at the outer aspect of the body wall (reactive reparative chondroid hyperplasia)

##### **Morphological Diagnosis:**

**Duration:** chronic; **Distribution:** focally extensive;

##### **Definitive Diagnosis:**

Sternal osteoarthritis with fracture and reactive and reparative chondroid hyperplasia ('calus')

#### **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: M00609660 (Female)**

##### **Histopathology Findings:**

##### **brain (MA:0000168)**

##### **Histopath Description:**

The brain is small and dorsoventrally flattened but architecturally normal (microencephaly).

##### **Morphological Diagnosis:**

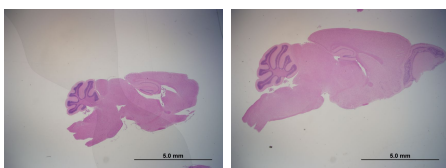
**Distribution:** diffuse; **Severity:** moderate;

##### **Definitive Diagnosis:**

Microencephaly

##### **Histopathology Comments:**

The lesion is consistent with the abnormal cranium morphology reported.



Brain,  
microencephaly,  
1.25x, HE

Brain, WT, normal,  
1.25x, HE

#### **liver (MA:0000358)**

##### **Histopath Description:**

diffuse lipidosis

##### **Morphological Diagnosis:**

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

##### **Definitive Diagnosis:**

hepatic steatosis

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

Mild erythropoiesis

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

Mild erythropoiesis

**bone marrow (MA:0000134)****Histopath Description:**

Erythroid to myeloid ratio is 1:2 (compared to the average 1:4 ratio in WT mice).

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

Erythroid hyperplasia

**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.

**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: M00606656 (Female)****Histopathology Findings:****brain (MA:0000168)****Histopath Description:**

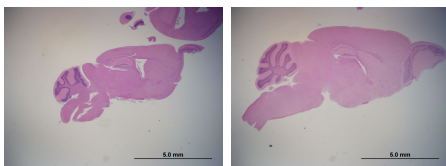
The brain is small and dorsoventrally flattened but architecturally normal (microencephaly).

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

Microencephaly

**Histopathology Comments:**

The lesion is consistent with the abnormal cranium morphology reported.



Brain,  
microencephaly,  
1.25x, HE

Brain, WT, normal,  
1.25x

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

Moderate lipidosis

**Morphological Diagnosis:**

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

**Definitive Diagnosis:**

hepatic steatosis

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

Mild erythropoiesis

**Morphological Diagnosis:**

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

**Definitive Diagnosis:**

Mild erythropoiesis

**bone marrow (MA:0000134)****Histopath Description:**

Erythroid to myeloid ratio is 1:2 (compared to the average 1:4 ratio in WT mice).

**Morphological Diagnosis:**

**Severity:** mild;

**Definitive Diagnosis:**

Erythroid hyperplasia

**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 distinct lesions are noted in this lines.

Microencephaly and dorsolaterally flattened brain in all mice is consistent with abnormal cranium morphology. Note that the orthologous gene in humans is associated with microcephaly OMIM #604804 (MICROCEPHALY 3, PRIMARY, AUTOSOMAL RECESSIVE; MCPH3).

In both males, there is diffuse seminiferous atrophy and degeneration with absence of sperm storage in the epididymis. This lesion is expected to cause infertility, a phenotype not documented in this line. The histological features in the testis are remarkably similar to those observed in Pik3cb line (line 50).

Three mice from these line also have mild splenic erythroid hyperplasia; the lesion may explain the increased mean corpuscular volume (a feature of erythroid regeneration).

**Line summary:**

Microencephaly (4/4);

Testis - Seminiferous tubule degeneration and atrophy (diffuse) with Interstitial (Leydig) cell hyperplasia and epididymal aspermia (2/2 males);

Spleen: Erythroid hyperplasia (3/4).