



# CMHD Pathology Report



## CMHD Pathology Core

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ReportID: Report Date: July 11, 2013  
Pathologist: Dr. H. Adissu

## Mouse Genetics Project

Wellcome Trust Sanger  
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Hinxton, Cambridge  
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UK

CMHD LabID: N13-472

## Relevant History:

Phenotypes:

hyperalbuminemia  
increased circulating total protein level  
impaired glucose tolerance  
increased body weight  
increased percent body fat  
increased total body fat amount  
increased body weight  
increased susceptibility to bacterial infection  
decreased mature B cell number  
increased circulating insulin level

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## AnimalID: M00663345 (Male)

### Histopathology Findings:

#### lymph node (MA:0000139)

##### Histopath Description:

The mesenteric lymph node is markedly enlarged (greater than five-fold). The medulla is expanded by chords and sheets of plasmotoid cells.

##### Morphological Diagnosis:

**Distribution:** Diffuse; **Severity:** extreme; **MPATH Diagnosis:** hyperplasia MPATH:134

##### Definitive Diagnosis:

Lymphoid hyperplasia with medullary plasmacytosis.

##### 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.

#### liver (MA:0000358)

##### Histopath Description:

extreme and diffuse lipidosis

##### Morphological Diagnosis:

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

##### Definitive Diagnosis:

Hepatic lipidosis

##### Histopathology Comments:

The degree of hepatic lipidosis is extreme in this mouse

#### spleen (MA:0000141)

##### Histopath Description:

moderate erythroid hyperplasia

##### Morphological Diagnosis:

**Distribution:** multifocal; **Severity:** moderate; **MPATH Diagnosis:** extramedullary hemopoiesis

MPATH:595

**Definitive Diagnosis:**

Splenic erythroid hyperplasia

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

mild neutrophilic gastritis; there is also mild epithelial proteinosis

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

Mild neutrophilic gastritis with epithelial proteinosis

**eye (MA:0000261)****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:**

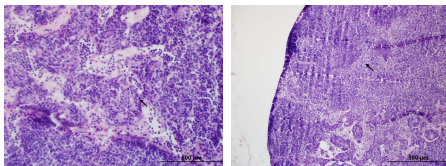
Retinal dysplasia

**brown fat (MA:0000057)****Histopath Description:**

There is focally extensive hyperplasia of brown fat infiltrated with low numbers of inflammatory cells (lymphocytes, macrophages and rare neutrophils)

**Morphological Diagnosis:****Duration:** Chronic-active; **Distribution:** Focal; **Severity:** mild; **MPATH Diagnosis:** steatitis MPATH:636**Definitive Diagnosis:**

Steatitis with 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, testis, epididymis, seminal vesicle, and prostate.

**AnimalID: M00527045 (Male)****Histopathology Findings:****liver (MA:0000358)****Histopath Description:**

diffuse lipidosis

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

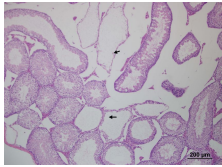
Hepatic lipidosis

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

There are occasional foci of vacuolar degeneration and atrophy of the seminiferous tubules. These seminiferous tubules lack maturing spermatids and spermatocytes.

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

Testicular degeneration and atrophy

**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: M00506744 (Female)****Histopathology Findings:****lymph node (MA:0000139)****Histopath Description:**

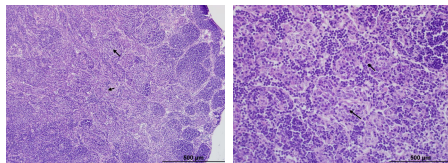
The mesenteric lymph node is markedly enlarged (greater than five-fold). The medulla is expanded by chords and sheets of plasmacytoid cells.

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

Lymphoid hyperplasia with medullary plasmacytosis.

**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.



Lymph node, lymphoid hyperplasia with medullary plasmacytosis, 10x, HE.

Lymph node, lymphoid hyperplasia with medullary plasmacytosis, 40x, HE.

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

moderate lipidosis

**Morphological Diagnosis:****Distribution:** multifocal; **Severity:** moderate; **MPATH Diagnosis:** steatosis MPATH:622**Definitive Diagnosis:**

Hepatic lipidosis

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

moderate erythroid hyperplasia

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

Splenic erythroid hyperplasia

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

moderate neutrophilic gastritis; there is also mild epithelial proteinosis

**Morphological Diagnosis:**

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

**Definitive Diagnosis:**

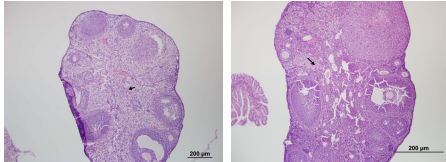
Moderate neutrophilic gastritis with epithelial proteinosis

**ovary (MA:0000384)****Histopath Description:**

There is stromal hyperplasia with cystic focus on the fallopian tube

**Definitive Diagnosis:**

Ovarian stromal hyperplasia



Ovary, stromal hyperplasia, 10x, HE

Ovary, WT, normal (note minimal stroma, arrow), 10x, 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. 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. 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: M00506746 (Female)****Histopathology Findings:****liver (MA:0000358)****Histopath Description:**

moderate lipidosis

**Morphological Diagnosis:**

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

**Definitive Diagnosis:**

Hepatic lipidosis

**brown fat (MA:0000057)****Histopath Description:**

There is focally extensive hyperplasia of brown fat infiltrated with low numbers of inflammatory cells (lymphocytes, macrophages and rare neutrophils)

**Morphological Diagnosis:**

**Duration:** Chronic-active; **Distribution:** Focal; **Severity:** mild; **MPATH Diagnosis:** steatitis MPATH:636

**Definitive Diagnosis:**

Steatitis with hyperplasia

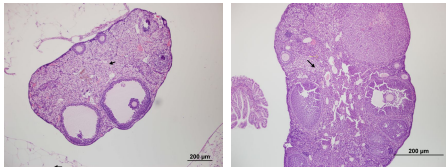


**ovary (MA:0000384)****Histopath Description:**

There is stromal hyperplasia with cystic focus on the fallopian tube

**Definitive Diagnosis:**

Ovarian stromal hyperplasia



Ovary, stromal hyperplasia, 10x, HE

Ovary, WT, normal (note minimal stroma, arrow), 10x, 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).

**pancreas (MA:0000120)****Histopath Description:**

Pancreatic islets in the examined sections are enlarged (compare to WT).

**Morphological Diagnosis:**

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

**Definitive Diagnosis:**

Islet cell hyperplasia

**Histopathology Comments:**

The majority of the islets examined are found along the pancreatic artery and its branches (where larger size islets are normally seen); hence this finding must be interpreted with caution.

**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:**

Main findings in this line are ovarian stromal hyperplasia (2/2) and lymphoid hyperplasia with marked plasmacytosis (2/2). The ovarian stromal proliferative lesion may explain the obesity and impaired glucose tolerance in females. Human patients with ovarian stromal proliferative lesions may display obesity and abnormal glucose tolerance. Most of the stromal hyperplastic lesions are hormonally active and most produce testosterone. In two mice there is lymphoid hyperplasia with marked plasmacytosis. These changes are suggestive of robust of humeral immunity; we are not certain how this relates to the immune phenotypes documented in this line.

Line summary: Ovarian stromal hyperplasia (2/2); Lymphoid hyperplasia with sinus plasmacytosis (2/4)

**References:**

1: Oler A, Singh M, Ural SH. Bilateral ovarian stromal hyperplasia concealing a nonhilar, pure stromal-Leydig cell tumor. A case report. J Reprod Med. 1999, 44):563-6. 2: Tuffnell DJ. Virilizing nodular ovarian stromal hyperthecosis, diabetes mellitus and insulin resistance in a postmenopausal woman. Br J Obstet Gynaecol. 1990 Jan;97(1):89. PubMed PMID: 2306435.