



CMHD Pathology Report



CMHD Pathology Core

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ReportID: Report Date: April 03, 2013
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Mouse Genetics Project

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CMHD LabID: N13-241

Relevant History:

increased drinking behavior

AnimalID: M00498820

Histopathology Findings:

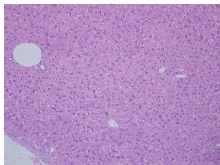
liver (MA:0000358)

Histopath Description:

no lipidosiis observed

Definitive Diagnosis:

Absence of hepatic lipidosiis



Liver, absence of
lipidosiis, 20x

pancreatic islet (MA:0000127)

Histopath Description:

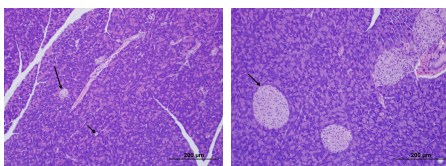
There are fewer pancreatic islets in this mouse compared to WT controls. The size of islets are also markedly small and some of these islets are composed of as few as 1-2 islet cells.

Morphological Diagnosis:

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

Definitive Diagnosis:

Pancreatic islet hypoplasia (number and size)



Pancreas, islet cell
hypoplasia (not few
and small islets),
20x

Pancreas, wildtype,
normal islets, 20x

testis (MA:0000411)

Histopath Description:

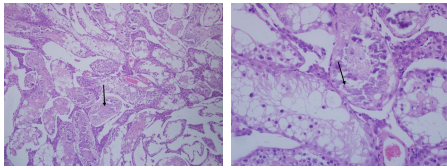
There is extensive atrophy, degeneration and mineralization of the seminiferous tubules affecting 90% of the testis. The epididymis is devoid of spermatocytes.

Morphological Diagnosis:

Distribution: multifocal to coalescing; **Severity:** severe;

Definitive Diagnosis:

Testicular degeneration, atrophy and mineralization



Testis,
degeneration,
atrophy and
mineralization, 10x

Testis,
degeneration,
atrophy and
mineralization, 40x

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).

AnimalID: M00498819**Histopathology Findings:****liver (MA:0000358)****Histopath Description:**

severe lipidosi

Morphological Diagnosis:

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

Definitive Diagnosis:

Hepatic lipidosi

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

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

There is a focally extensive retinal fold

Morphological Diagnosis:

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

Definitive Diagnosis:

Retinal dysplasia

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:

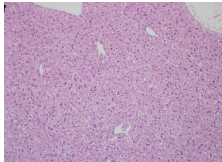
Mild dilation of the lateral ventricles is a background condition in mice of C57BL/6N background (Brayton et al., 2004).

AnimalID: M00459750**Histopathology Findings:****liver (MA:0000358)****Histopath Description:**

no lipidosis observed

Definitive Diagnosis:

Absence of hepatic lipidosis



Liver, absence of lipidosis, 20x

pancreatic islet (MA:0000127)**Histopath Description:**

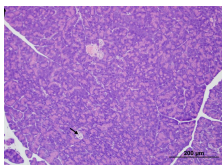
There are fewer pancreatic islets in this mouse compared to WT controls. The size of islets are also markedly small and some of these islets are composed of as few as 1-2 islet cells.

Morphological Diagnosis:

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

Definitive Diagnosis:

Pancreatic islet hypoplasia (number and size)



Pancreas, islet cell hypoplasia (not few and small islets), 20x

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

Marked erythropoiesis

Morphological Diagnosis:

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

Definitive Diagnosis:

Marked erythropoiesis

aorta (MA:0000062)**Histopath Description:**

There is a well differentiated thyroid glandular structure within the fat abutting the adventitia of the aortic base

Morphological Diagnosis:

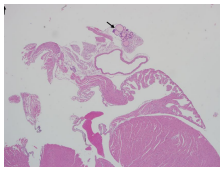
Distribution: focal; **MPATH Diagnosis:** choristoma MPATH:477

Definitive Diagnosis:

Thyroid choristoma

Histopathology Comments:

This is a rare congenital lesion of minimal clinical significance



Aorta, thyroid
choristoma,4x

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).

AnimalID: M00459753

Histopathology Findings:

liver (MA:0000358)

Histopath Description:

no lipidosis observed

Definitive Diagnosis:

Absence of hepatic lipidosis

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).

Report Summary and Recommendation:

Main finding in this line are pancreatic islet hypoplasia (decreased number and size) (2/4) and absence of hepatic lipidosis (3/4). The significance of pancreatic islet cell hypoplasia in absence of hyperglycemia is uncertain. Note that Slc5a2 (SGLT2) is implicated in familial glycosuria in humans (Yu et al., 2011) and mice (Vallon et al., 2011). SGLT2 mediates glucose reabsorption in the early proximal tubule and most of the glucose reabsorption by the kidney. We did not see any morphological abnormality in the proximal tubules except the background vacuolation noted in nearly all mice (likely associated with high lipid diet). One of the male mice have severe testicular degeneration and mineralization. Other lesions in this line are considered incidental and/or attributable to strain background.

Note: Preliminary image analysis with Visiopharm to compare islet size between this line and WT controls by Qiang Xu (CMHD pathology) confirms the histopathology observation.

References:

1. Brayton C. (2006). Spontaneous diseases in commonly used inbred mouse strains. Chapter 25. Pp 647-651. In Fox, J.G. & al. Ed's. In THE MOUSE IN BIOMEDICAL RESEARCH 2nd Ed. Vol 3. ACLAM series. Elsevier.
2. Yu L, et al. (2011). Abnormal expression and dysfunction of novel SGLT2 mutations identified in familial renal glucosuria patients. Hum Genet 129, 335-44
3. Vallon V, et al. (2011). SGLT2 mediates glucose reabsorption in the early proximal tubule. J Am Soc Nephrol 22, 104-12.

