# CMHD Pathology Report

**CMHD Pathology Core**
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Europhenome

ReportID: Report Date: April 03, 2013
Pathologist: H. Adissu

**CMHD LabID: N13-241**

**Relevant History:**
increased drinking behavior

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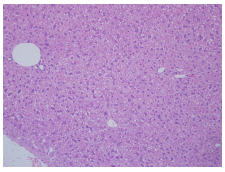
**AnimalID: M00498820**

**Histopathology Findings:**

**liver (MA:0000358)**

**Histopath Description:**
no lipidosis observed

**Definitive Diagnosis:**
Absence of hepatic lipidosis

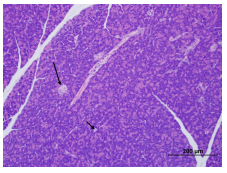

Liver, absence of lipidosis, 20x

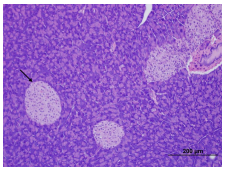
**pancreatic islet (MA:0000127)**

**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

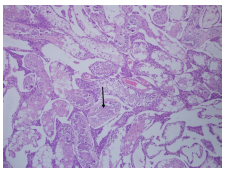

Pancreas, wildtype, normal islets, 20x

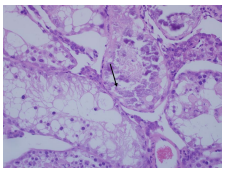
**testis (MA:0000411)**

**Histopath Description:**
There is extensive atrophy, degeneration and mineralizatiion 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).

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**AnimalID: M00498819**

**Histopathology Findings:**

**liver (MA:0000358)**

**Histopath Description:**
severe lipidosis

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

**Definitive Diagnosis:**
Hepatic lipidosis

**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).

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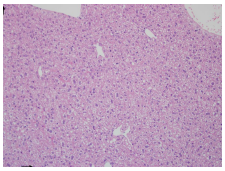
**AnimalID: M00459750**

**Histopathology Findings:**

**liver (MA:0000358)**

**Histopath Description:**
no lipidosis observed

**Definitive Diagnosis:**
Absence of hepatic lipidosis



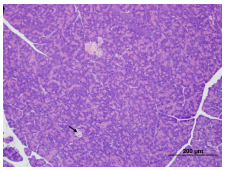
Liver, absence of lipidosis, 20x

**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

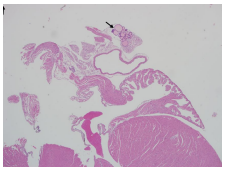
**aorta (MA:0000062)**

**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).

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**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 hyperglyecemia is unceratin. 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 neary 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 consdiered 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. Yu L, et al. (2011). Abnormal expression and dysfunction of novel SGLT2 mutations identified in familial renal glucosuria patients. Hum Genet 129, 335-44 Vallon V, et al. (2011). SGLT2 mediates glucose reabsorption in the early proximal tubule. J Am Soc Nephrol 22, 104-12.