# CMHD Pathology Report

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ReportID: Report Date: March 12, 2013
Pathologist: H. Adissu

**CMHD LabID: N12-1512**

**Relevant History:**
Phenotypes:

preweaning lethality
embryonic lethality

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**AnimalID: M00183831 (Male)**

**Histopathology Findings:**

**liver (MA:0000358)**

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

**Definitive Diagnosis:**
Hepatic lipidosis, severe

**retina (MA:0000276)**

**Histopath Description:**
Involving one eye, there are clusters of external nuclear structures within the internal plexiform layer.

**Morphological Diagnosis:**
**Distribution:** Focal; **Severity:** mild; **MPATH Diagnosis:** developmental and structural abnormality MPATH:55

**Definitive Diagnosis:**
Retinal dysplasia

**fat (MA:0000056)**

**Histopath Description:**
A fat pad is adjacent to a section of pancreas. The adipose tissue has multifocal hemorrhage and inflammation throughout. There is evidence of chronic hemorrhage due to erythrophagocytosis and brown pigment (hemosiderin), and inflammatory cells consisting mainly of lymphocytes with the scattered neutrophil.

**Morphological Diagnosis:**
**Duration:** Chronic; **Distribution:** Multifocal; **Severity:** moderate; **MPATH Diagnosis:** inflammation MPATH:212

**Definitive Diagnosis:**
steatitis

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**AnimalID: M00183837 (Male)**

**Histopathology Findings:**

**liver (MA:0000358)**

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

**Definitive Diagnosis:**
Hepatic lipidosis, severe

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**AnimalID: M00184545 (Female)**

**Histopathology Findings:**

**liver (MA:0000358)**

**Histopath Description:**
Multifocal macrovesicular lipid deposition in hepatocytes

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

**Definitive Diagnosis:**
Moderate hepatic steatosis

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**AnimalID: M00183840 (Female)**

**Histopathology Findings:**

**liver (MA:0000358)**

**Histopath Description:**
Multifocal macrovesicular lipid deposition in hepatocytes

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

**Definitive Diagnosis:**
Moderate hepatic steatosis

**retina (MA:0000276)**

**Histopath Description:**
Involving both eyes, there are clusters of external nuclear structures within the internal plexiform layer.

**Morphological Diagnosis:**
**Distribution:** Focal; **Severity:** mild;

**Definitive Diagnosis:**
Retinal dysplasia

**lymph node (MA:0000139)**

**Histopath Description:**
The mesenteric lymph node is enlarged 3x than normal). There are multiple follicles with large germinal centers. The sinuses contain large numbers of mature lymphocytes.

**Morphological Diagnosis:**
**Duration:** Sub-acute; **Distribution:** Diffuse; **Severity:** moderate; **MPATH Diagnosis:** lymphoid hyperplasia MPATH:147

**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.

**Report Summary and Recommendation:**
Incidental lesions attributable to diet or strain background are observed in this line. Note that this gene is

implicated in familial dysautonomia (FD) in humans. A mouse model of FD has been created by conditional inactivation of the Ikbkap gene specifically in neuronal cells (Dietrich et al., 2012). This mouse model recapitulates various features of FD including abnormalities in dorsal root ganglia and absence of fungiform papillae on the tongue. On the other hand Ikbkap flox/+ mice were normal and fertile (Dietrich et al., 20121) similar to the WTSI line analyzed here. We did not observe any morphological abnormalities in nervous tissues (brain, spinal cord, trigeminal and dorsal root ganglia, and peripheral nerves). The tongue was not available for analysis.

**References:**

Dietrich P et al. (2012). IKAP expression levels modulate disease severity in a mouse model of familial dysautonomia. Human Molecular Genetics, 23 5078-5090