CMHD Pathology Report

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ReportID: Report Date: November 23, 2011
Pathologist: H. Adissu

Mouse Genetics Project
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Mouse Portal
Europhenome

CMHD LabID: N11-187

Relevant History:
(Body Weight Curves; Grip Strength; Body Composition (DEXA); X-ray Imaging) Abnormal joint morphology, decreased grip strength, abnormal tooth and patellar morphology, decreased body weight/length, abnormal joint morphology

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AnimalID: M00326676 Rhobtb3 hom

Tissue Preservation and Staining:
Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

Histopathology Findings:

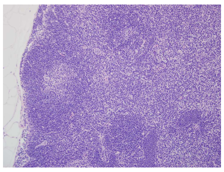
lymph node (MA:0000139)

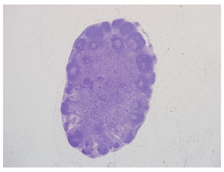
Histopath Description:
The mesenteric lymph node is enlarged (greater than three-fold). There are multiple follicles with large germinal centers. The sinuses contain large numbers of mature lymphocytes.

Morphological Diagnosis:
Duration: Sub-acute; **Distribution:** Diffuse; **Severity:** moderate; **MPATH Diagnosis:** 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.


Mesenteric lymph node, hyperplasia, 20x, HE.


Mesenteric lymph node, hyperplasia, 4x, HE.

spleen (MA:0000141)

Histopath Description:
There are multiple follicles with germinal centers.

Morphological Diagnosis:
Duration: Chronic-active; **Distribution:** Multifocal; **Severity:** mild; **MPATH Diagnosis:** hyperplasia MPATH:134

Definitive Diagnosis:
Multifocal germinal centers

Histopathology Comments:
This change indicates antigenic stimulation.

liver (MA:0000358)

Histopath Description:
The overall hepatic lobular architecture is normal. Nearly 50 of hepatocytes notably within the midzonal region contain large (8-12 um in diameter) intracytoplasmic clear vacuoles (macrovesicular lipid). Rare small clusters of lymphocytes are present.

Morphological Diagnosis:
Distribution: Multifocal; **Severity:** mild; **MPATH Diagnosis:** lipid deposition MPATH:42

Definitive Diagnosis:
Hepatic lipidosis; multifocal inflammatory foci

Histopathology Comments:
Hepatocellular vacuolar change of variable degree suggestive of lipidosis is present in all mice from WTSI, consistent with high lipid diet. The changes in this mouse are less severe.

AnimalID: M00317716 Rhobtb3 hom

Tissue Preservation and Staining:
There is artifactual separation of the dermis and hypodermis. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

Histopathology Findings:

thyroid gland (MA:0000129)

Histopath Description:
The thyroid interstitium is infiltrated by large round cells with high nuclear: cytoplasm ratio (lymphocytes). Occasional mitotic figures are present. There is a focal atrophy of thyroid follicles with occasional cellular debris.

Morphological Diagnosis:
Distribution: Multifocal to coalescing; **Severity:** mild; **MPATH Diagnosis:** lymphoma [obsolete use MPATH:516 or 535] MPATH:343

Definitive Diagnosis:
Lymphoma (tentative)

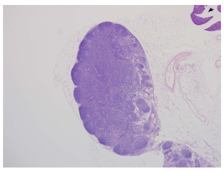
lymph node (MA:0000139)

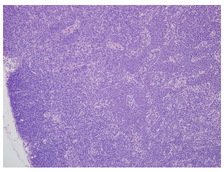
Histopath Description:
The mesenteric lymph node is enlarged (greater than three-fold). There are multiple follicles with large germinal centers. The sinuses contain large numbers of mature lymphocytes.

Morphological Diagnosis:
Duration: Sub-acute; **Distribution:** Diffuse; **Severity:** moderate; **MPATH Diagnosis:** 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.


Mesenteric lymph node, hyperplasia, 4x, HE.


Mesenteric lymph node, hyperplasia, 20x, HE.

liver (MA:0000358)

Histopath Description:
The overall hepatic lobular architecture is normal. Nearly 50 of hepatocytes notably within the midzonal region contain large (8-12 um in diameter) intracytoplasmic clear vacuoles (macrovesicular lipid). Rare small clusters of lymphocytes are present.

Morphological Diagnosis:
Distribution: Multifocal; **Severity:** mild; **MPATH Diagnosis:** lipid deposition MPATH:42

Definitive Diagnosis:
Hepatic lipidosis; multifocal inflammatory foci

Histopathology Comments:

Hepatocellular vacuolar change of variable degree suggestive of lipidosis is present in all mice from WTSI, consistent with high lipid diet. The changes in this mouse are less severe.

pancreas (MA:0000120)

Histopath Description:
There is a focal mononuclear inflammatory infiltrate and rare cellular debris within the pancreatic interstitium.

Morphological Diagnosis:
Distribution: Focal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212

Definitive Diagnosis:
Focal inflammatory aggregate.

stomach (MA:0000353)

Histopath Description:
There is a focal aggregate of neutrophils and mononuclear cells within the non-glandular region at the limiting ridge.

Morphological Diagnosis:
Duration: Sub-acute; **Distribution:** Multifocal; **Severity:** moderate; **MPATH Diagnosis:** inflammation MPATH:212

Definitive Diagnosis:
Gastritis, suppurative

Histopathology Comments:
This lesion is most commonly associated with Helicobacter infection. Further investigation is suggested using histochemistry (Silver stain) or colony fecal PCR.

AnimalID: M00308143 Rhobtb3 hom

Tissue Preservation and Staining:
Thyroid gland is not present in the section. There is artifactual separation of the dermis and hypodermis. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

Histopathology Findings:

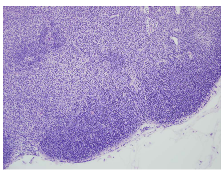
lymph node (MA:0000139)

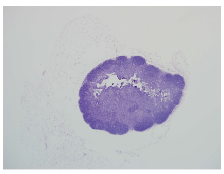
Histopath Description:
The mesenteric lymph node is enlarged (greater than three-fold). There are multiple follicles with large germinal centers. The sinuses contain large numbers of mature lymphocytes.

Morphological Diagnosis:
Duration: Sub-acute; **Distribution:** Diffuse; **Severity:** moderate; **MPATH Diagnosis:** 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.


Mesenteric lymph node, hyperplasia, 20x, HE.


Mesenteric lymph node, hyperplasia, 4x, HE.

pancreas (MA:0000120)

Histopath Description:
There is a focal lobular atrophy of exocrine glands with occasional apoptotic figures and low number of interstitial mononuclear inflammatory cells.

Morphological Diagnosis:
Duration: Chronic; **Distribution:** Focal; **Severity:** mild; **MPATH Diagnosis:** atrophy MPATH:127

Definitive Diagnosis:
lobular pancreatic atrophy

retina (MA:0000276)

Histopath Description:
There is a focal retinal disorganization characterized by retinal folding and blending of the internal and external layer.

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

Definitive Diagnosis:
Retinal dysplasia

AnimalID: M00308142 Rhobtb3 hom

Tissue Preservation and Staining:
The thyroid gland is not present in section. There is artifactual separation of the dermis and hypodermis. Mesenteric lymph nodes are not present in the section. Tissues not present in submission: Calvarium, ears, tongue, Harderian gland, zymbal gland, nasal sinuses, teeth, gall bladder.

Histopathology Findings:

heart (MA:0000072)

Histopath Description:
There are two small (40x50 and 20x40 um) foci of mineralization of the left ventricle.

Morphological Diagnosis:
Distribution: Multifocal; **Severity:** mild; **MPATH Diagnosis:** mineralisation MPATH:555

Definitive Diagnosis:
Myocardial mineralization

urinary bladder (MA:0000380)

Histopath Description:
There is a focal subserosal mineralization.

Morphological Diagnosis:
Distribution: Focal; **Severity:** mild; **MPATH Diagnosis:** mineralisation MPATH:555

Definitive Diagnosis:
Subserosal focal mineralization pf the bladder.

liver (MA:0000358)

Histopath Description:
There are rare small aggregates of inflammatory cells.

Morphological Diagnosis:
Distribution: Multifocal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212

Definitive Diagnosis:
Inflammatory cell aggregates

brain (MA:0000168)

Histopath Description:
There is a mild enlargement of the lateral ventricle.

Morphological Diagnosis:
Severity: mild; **MPATH Diagnosis:** hydrocephalus MPATH:639

Definitive Diagnosis:
hydrocephalus, third ventricle

Histopathology Comments:
Variable degree of hydrocephalus is observed in a proportion of wild type C57 Black 6 mice.

patella (MA:0001374)

Histopath Description:

The patella is markedly enlarged (2x normal) and displaced proximally by a nodular, 1 mm diameter, osteocartilaginous expansion at the distal aspect the patella

Morphological Diagnosis:

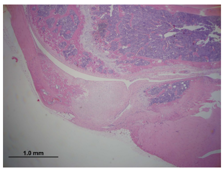
Distribution: Diffuse; **Severity:** severe; **MPATH Diagnosis:** developmental and structural abnormality MPATH:55

Definitive Diagnosis:

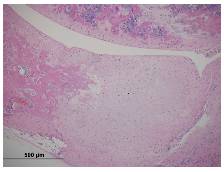
Patellar dysplasia

Histopathology Comments:

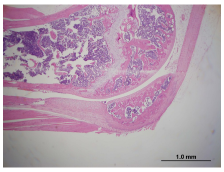
This is uncommon lesion in mice. It is unceratin whether it is of genetic or traumatic in origin. The absence of accompanied degenerative changes in the knee joint and absence of fibrous adhesions suggest this is a a developmental abnormality. The lesion may be consistent with the observed abnormal patellar morphology on X-ray imaging.



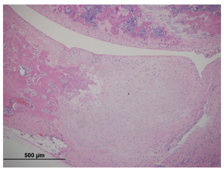
Patella, dysplasia, 4x



Patella, dysplasia, 10x



Patella, normal from WT control, 4x



Patella, normal from WT control, 10x

Summary:

Hyperplastic and early neoplastic changes are present within the mesenteric lymph nodes in 3 of the four mice in this line. The mesenteric lymph nodes can be dramatically variable within an animal and between animals due to the constant exposure of various antigenic substances in the intestinal lumen. For this reason, comparison of nodes between the mutant lines and a cohort wild type control is required to identify genotype effect.

One mouse from this line has patellar dysplasia consistent with patellar morphological abnormality observed by x-ray imaging.

Report Summary and Recommendation:

Patellar dysplasia was observed in one mouse consistent with abnormal patellar morphology on X-ray imaging in this line. Hyperplastic and early neoplastic changes are present within the mesenteric lymph nodes in 3 of the four mice in this line. The mesenteric lymph nodes can be dramatically variable within an animal and between animals due to the constant exposure of various antigenic substances in the intestinal lumen. For this reason, comparison of nodes between the mutant lines and a cohort wild type control is required to identify genotype effect.

Lymph node: precursor b cell neoplasms MPATH:517
Patella: dysplasia MPATH:64