CMHD Pathology Report

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ReportID: Report Date: October 17, 2013
Pathologist: Dr. H. Adissu

CMHD LabID: N13-700

Relevant History:
Phenotypes:
increased susceptibility to bacterial infection
Homozygous preweaning lethality
fetal edema

AnimalID: M00951745 (Male)

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: M00951746 (Male)

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: M00930155 (Female)

Histopathology Findings:

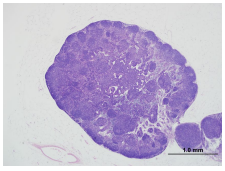
lymph node (MA:0000139)

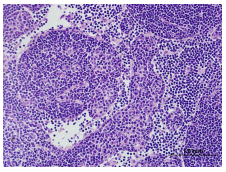
Histopath Description:
The mesenteric lymph node is markedly enlarged (greater than four fold). The medulla is particularly expanded by chords and sheets of plasmatoid cells. There are rare germinal centers within the medulla.

Morphological Diagnosis:
Distribution: Diffuse; **Severity:** moderate; **MPATH Diagnosis:** hyperplasia MPATH:134; **MPATH Process Term:** hyperplasia MPATH:134

Definitive Diagnosis:
Lymphoid hyperplasia with sinus 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. Early maginal center lymphoma is suspected.


Lymph node, lymphoid hyperplasia with sinus plasmacytosis, 4x, HE


Lymph node, lymphoid hyperplasia with sinus plasmacytosis, 40x, HE

liver (MA:0000358)

Histopath Description:
moderate lipidosis

Morphological Diagnosis:
Distribution: multifocal to coalescing; **Severity:** moderate; **MPATH Diagnosis:** steatosis MPATH:622; **MPATH Process Term:** lipid deposition MPATH:42

Definitive Diagnosis:
hepatic steatosis

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.

AnimalID: M00930157 (Female)

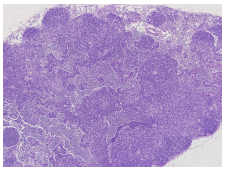
Histopathology Findings:

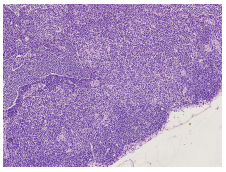
lymph node (MA:0000139)

Histopath Description:
The cortex in mesenteric lymph node is devoid of notable lymphoid nodules. The medullary sinuses contain large numbers of mature lymphocytes.

Morphological Diagnosis:
Distribution: Diffuse; **Severity:** moderate; **MPATH Diagnosis:** hyperplasia MPATH:134; **MPATH Process Term:** hypoplasia MPATH:133

Definitive Diagnosis:
Lymphoid hypoplasia


Lymph node, lymphoid hypoplasia, 40x, HE


Lymph node, lymphoid hypoplasia, 40x, HE

liver (MA:0000358)

Histopath Description:
moderate lipidosis

Morphological Diagnosis:
Distribution: multifocal to coalescing; **Severity:** moderate; **MPATH Diagnosis:** steatosis MPATH:622; **MPATH Process Term:** lipid deposition MPATH:42

Definitive Diagnosis:
hepatic steatosis

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:
The mesenteric lymph nodes in this line show one of the following changes (hyperplasia with sinus plasmacytosis 1/4; lymphoid hypoplasia, 1/4; histiocyte-associated lymphoma 1/4). The lymphoid changes are not consistent among the mice in this line. Hence it is difficult to to associate this finding with the immune phenotype abnormality in this line (increased susceptibility to bacterial infection)

In humans, mutations in RIPK4 cause the Autosomal-Recessive Form of Popliteal Pterygium Syndrome (also known as Bartsocas-Papas syndrome), a rare, but frequently lethal disorder characterized by marked popliteal pterygium associated with multiple congenital malformations (Kalay et al., 2012). Comparable pathologies were observed in RIP4 deficiency in mice including perinatal lethality associated with abnormal epidermal differentiation (Holland et al., 2002).There are no malformations in the organs and tissues analyzed in this heteterozygote line and we did not see lesions predictive of homozygous preweaning lethality and fetal edema. Analysis of preweaning homozygous mice and embryos may help to assess the presence of similar malformations and to determine the cause of mortality and fetal edema in this line.

Line summary

Mesenteric lymph node:
hyperplasia with sinus plasmacytosis 1/4;
Lymphoid hypoplasia, 1/4;
Lymphoma (histiocyte-associated lymphoma) 1/4

References:
Hao X, et al. 2010. The histopathologic and molecular basis for the diagnosis of histiocytic sarcoma and histiocyte-associated lymphoma of mice. Vet Pathol. 47(3):434-45. Holland P, et al. (2002). RIP4 is an ankyrin repeat-containing kinase essential for keratinocyte differentiation. Curr Biol. 12(16):1424-8. Kalay et al. (2012). Mutations in RIPK4 Cause the Autosomal-Recessive Form of Popliteal Pterygium Syndrome. Am J Hum Genet; 90(1): 76–85.