CMHD Pathology Report

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ReportID: Report Date: November 23, 2011
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CMHD LabID: N11-87

Relevant History:
(Viability at postnatal day 14; Recessive Lethal Study (E14.5); Modified SHIRPA; Dysmorphology; Body Composition (DEXA); X-ray Imaging; Eye Morphology; Salmonella Challenge)

AnimalID: M00232927 Csrp2b -/-

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

Histopathology Findings:

kidney (MA:0000368)

Histopath Description:
There are two foci of lymphocytes and histiocytes within the medullary interstitium.

Morphological Diagnosis:
Duration: Chronic; **Distribution:** Multifocal to coalescing; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212

Definitive Diagnosis:
mononuclear inflammaory cell aggregates

Histopathology Comments:
This is a common incidental lesion of minimal significance.

Organ/Tissue Analyzed:
There were no significant findings in the following tissues: Brain, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, spleen, liver, exocrine and endocrine pancreas, esophagus, stomach, intestines, adrenal gland, reproductive organs, lymph nodes, spinal cord, bones, bone marrow, skeletal muscles, brown fat, and skin.

AnimalID: M00232929 Csrp2b -/-

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

Histopathology Findings:

liver (MA:0000358)

Histopath Description:
The overall hepatic lobular architecture is normal. Diffusely, hepatocytes contain intracytoplasmic clear vacuoles (lipid). The lipid vacuoles within the midzonal and periacinar regions are small (2-3 um in diameter) and surround a central nucleus (interpreted as microvesicular lipid). The lipid vacuoles within the portal areas are large (8-12 um in diameter) and displace the nucleus to the margin (macrovesicular lipid). There are rare perivascular mononuclear inflammatory cells.

Morphological Diagnosis:
Distribution: Diffuse; **Severity:** moderate; **MPATH Diagnosis:** lipid deposition MPATH:42

Definitive Diagnosis:

Hepatic lipidosis

Histopathology Comments:
Hepatocellular vacuolar change of variable degree suggestive of lipidosis is present in all mice from WTSI, consistent with high lipid diet.

eye (MA:0000261)

Histopath Description:
Eye sectioned at odd angle revealing only thick layers of retina and choroid.

Definitive Diagnosis:
Pending deeper section

Histopathology Comments:
deeper eye section required

Organ/Tissue Analyzed:
There were no significant findings in the following tissues: Brain, eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, spleen, exocrine and endocrine pancreas, esophagus, stomach, intestines, urinary organs and tract, adrenal gland, reproductive organs, lymph nodes, spinal cord, bones, bone marrow, skeletal muscles, brown fat, and skin.

AnimalID: M00351191 Csrp2b -/-

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

Histopathology Findings:

liver (MA:0000358)

Histopath Description:
The overall hepatic lobular architecture is normal. Nearly 30% of hepatocytes within the midzonal and periacinar regions contain large (8-12 um in diameter) intracytoplasmic clear vacuoles (macrovesicular lipid).

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

Definitive Diagnosis:
Hepatic lipidosis

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.

testis (MA:0000411)

Histopath Description:
Occasional large (100 um diameter) multinucleated cells are present within the seminiferous tubule; their nuclei are mostly located in the center surrounded by granular eosinophilic cytoplasm.

Morphological Diagnosis:
Distribution: Multifocal; **Severity:** no lesions;

Definitive Diagnosis:
Multinucleated cells within the seminiferous tubule

Histopathology Comments:
Multinucleated germ cells are often seen in the seminiferous tubules of fertile males from a number of species of rodents (Bryan, 1977). They can be present as spontaneous age associated lesions (Gordon et al., 1996), or are caused by various insults including ligation of the efferent duct (Singh and Abe, 1987), chemicals (Chinoya et al., 2005) and radiation toxicity associated with tritium (Bhatia, 1985). Increased numbers have been documented in sterile Pink-Eyed Mutant Mouse (Bryan 1977). Ultrastructural studies suggest that the giant cells are formed as a result of the fusion of spermatids due to alterations in the intercellular bridges (Singh and Abe, 1987) or from degenerate spermatocytes or spermatids (Gordon et al., 1996). The cause for their presence in nearly all ES male mice in this group is uncertain. Reference: Bhatia AL. (1985). Tritium Toxicity: Age-dependent Radiosensitivity of Mouse Testes. Bull. Environ. Contam. Toxicol. 34:803-808 Bryan JHD (1987). Spermatogenesis Revisited III. The Course of Spermatogenesis in a Male-Sterile Pink-Eyed Mutant Type in the Mouse. Cell Tiss. Res. 180, 173-186. Chinoya NJ et al. (2005). Fluoride+aluminium induced toxicity in mice testis with giant cells and its reversal by vitamin c. fluoride 38:109–114 Gordon LR, Majika JA, and Boorman GA (1996). Spontaneous Nonneoplastic and neoplastic lesions and experimentally induced neoplasms of the testes and accessory sex glands. In Pathobiology of the Aging Mouse. Mohr U et al (ed). Vol 1. ILSI, P422. Singh SK, Abe K. (1987). Light and electron microscopic observations of giant cells in the mouse testis after efferent duct ligation. Arch Histol

Jpn. 50:579-85.

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, lateral ventricle

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

Organ/Tissue Analyzed:
There were no significant findings in the following tissues: Eyes, salivary glands, trachea, lungs, heart, thymus, thyroid gland, parathyroid gland, spleen, exocrine and endocrine pancreas, esophagus, stomach, intestines, urinary organs and tract, adrenal gland, lymph nodes, spinal cord, bones, bone marrow, skeletal muscles, brown fat, and skin.

AnimalID: M00351192 Csrp2b -/-

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

Histopathology Findings:

lung (MA:0000415)

Histopath Description:
There are rare small perivascular aggregates of mononuclear inflammatory cells in the lung.

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

Definitive Diagnosis:
Perivascular inflammatory aggregates

Histopathology Comments:
This lesion is suggestive of antigenic stimulation of hematogenous origin. It is a common and insignificant incidental finding.

kidney (MA:0000368)

Histopath Description:
There are two foci of lymphocytes and histiocytes within the medullary interstitium.

Morphological Diagnosis:
Duration: Chronic; **Distribution:** Multifocal to coalescing; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212

Definitive Diagnosis:
mononuclear inflammaory cell aggregates

Histopathology Comments:
This is a common incidental lesion of minimal significance.

liver (MA:0000358)

Histopath Description:
The overall hepatic lobular architecture is normal. Diffusely, hepatocytes contain intracytoplasmic clear vacuoles (lipid). The lipid vacuoles within the midzonal and periacinar regions are small (2-3 um in diameter) and surround a central nucleus (interpreted as microvesicular lipid). The lipid vacuoles within the portal areas are large (8-12 um in diameter) and displace the nucleus to the margin (macrovesicular lipid).

Morphological Diagnosis:
Distribution: Diffuse; **Severity:** moderate; **MPATH Diagnosis:** lipid deposition MPATH:42

Definitive Diagnosis:
Hepatic lipidosis

Histopathology Comments:
Hepatocellular vacuolar change of variable degree suggestive of lipidosis is present in all mice from WTSI, consistent with high lipid diet.

pancreas (MA:0000120)

Histopath Description:

There is a focal disorganization of acini and separation by fibroblasts and low numbers of histiocytes and lymphocytes. Occasional apoptotic pancreatic exocrine cells are present.

Morphological Diagnosis:

Duration: Chronic-active; **Distribution:** Focal; **Severity:** mild; **MPATH Diagnosis:** inflammation MPATH:212

Definitive Diagnosis:

Lymphocytic and histiocytic pancreatitis with rare single cell death

Histopathology Comments:

Aggregates of mononuclear inflammatory cells are infrequently seen within the pancreatic interstitium. This lesion is considered incidental and clinically insignificant.

testis (MA:0000411)

Histopath Description:

Occasional large (100 um diameter) multinucleated cells are present within the seminiferous tubule; their nuclei are mostly located in the center surrounded by granular eosinophilic cytoplasm.

Morphological Diagnosis:

Distribution: Multifocal; **Severity:** no lesions;

Definitive Diagnosis:

Multinucleated cells within the seminiferous tubule

Histopathology Comments:

See comment for M00351191 Csrp2b -/-

Organ/Tissue Analyzed:

There were no significant findings in the following tissues: Brain, eyes, salivary glands, trachea,heart, thymus, thyroid gland, parathyroid gland, spleen, endocrine pancreas, esophagus, stomach, intestines, adrenal gland, lymph nodes, spinal cord, bones, bone marrow, skeletal muscles, brown fat, and skin.

Summary:

Various incidental lesions were found. These lesions were also variably documented in the wild type control mice. There is no evidence of microphtalmia as indicated in in-life phenotyping. Additional section of the eye is required.

Report Summary and Recommendation:

Incidental and lesions attributable to background strain are noted in this line. These lesions were also variably documented in the wild type control mice. There is no evidence of microphtalmia as indicated in in-life phenotyping. Additional section of the eye is required.