Lipoprotein Related Models: NPC1 knock outs and ApoB-100 Mice

Genetic defects in the lipid / cholesterol metabolism may result in such severe diseases as Niemann-Pick C1 (NPC1 mutation) or familial hypercholesterolemia (among others ApoB-100 mutations). Two characterized models offered by QPS will provide novel insights in understanding cholesterol metabolism or in evaluating the efficacy of developmental compounds against Niemann-Pick disease, familial hyper-cholesterolemia or life style diseases as atherosclerosis or coronary heart disease.

NPC1 knock out Mice

Defects in Niemann-Pick C1 (NPC1) gene cause a devastating inherited lysosomal storage disease, the Niemann-Pick disease.

NPC1 knock out (ko) mice are characterized by typical pathological features of Niemann-Pick disease:

- accumulation of cholesterol (liver, hippocampus,…)
- early ataxia
- fast neuronal loss
- neuroinflammation
- altered APP expression

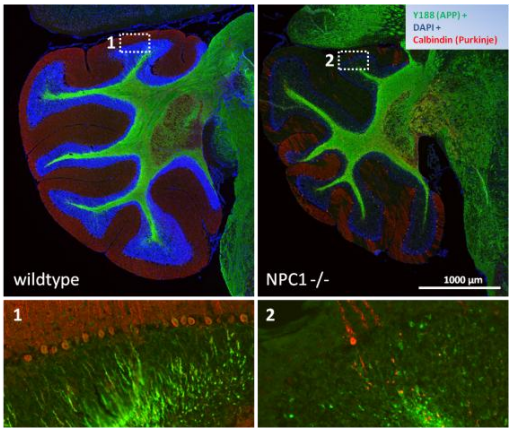

Fig. 1: NPC1 ko mice show fast neuronal loss in the cerebellum, especially affected the Purkinje network (lower panel, magnification).

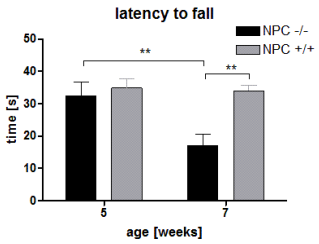

Fig. 2: Motor coordination (RotaRod) declines over age in NPC1 knock out mice.

NPC1 ko animals are a suitable model to elucidate the underlying mechanisms of this fatal, autosomal recessive disorder.

ApoB-100 Mice

ApoB-100 animals, overexpressing the entire apolipoprotein B-100 (ApoB-100) gene were originally designed as a model for hyperlipidemia and atherosclerosis. Increasing evidence also suggests that hypercholesterolemia and other vascular factors contribute to late onset Alzheimer's Disease (LOAD).

ApoB-100 mice are affected by:

- atherosclerotic lesions (high fat diet)
- severe cerebral oxidative stress (Fig. 3)
- learning deficits (Fig. 4) and
- elevated Aβ levels at higher ages

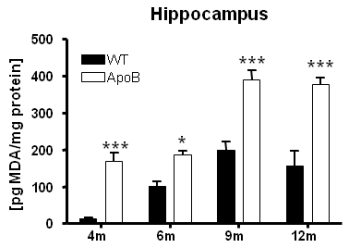

Fig. 3: Increased cerebral lipid peroxidation in hippocampus of ApoB100

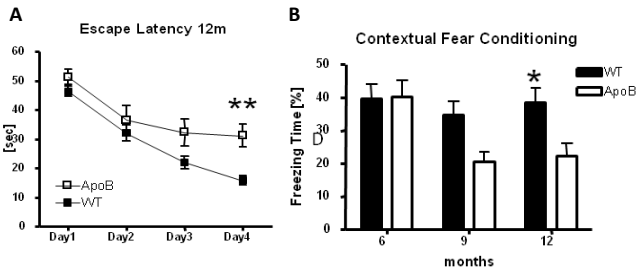

Fig. 4: Learning deficits in ApoB100 mice over age assessed by MWM (A) and Contextual Fear Conditioning (B)

ApoB-100 mice are an unique tool to screen developmental compounds interfering with lipid metabolism, oxidative stress or cognition.

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