Apo E knockout atherosclerotic mice

Model advantages:

The Apolipoprotein E knockout mouse model is one of the most widely used experimental model of atherosclerosis. These mice rapidly develop atherosclerotic lesions that resemble human lesions evolving over time from initial fatty streaks to complex lesions.

Pathophysiological features:

Cardiovascular features:

- Apolipoprotein E deficiency directly results in the increase of plasma levels of LDL and VLDL.
- Spontaneous development of atherosclerotic lesions throughout the arterial tree appearing first in the aortic arch in young mice and progressing in the thoracic and abdominal aorta in older mice, which can be further accelerated by a lipid-rich diet or type I diabetes induction by streptozotocin (cf. Links to applicable therapeutic areas / targeted disorders: Streptozotocin-induced diabetic rats/mice (STZ) (figure 1).
- Vascular endothelial dysfunction

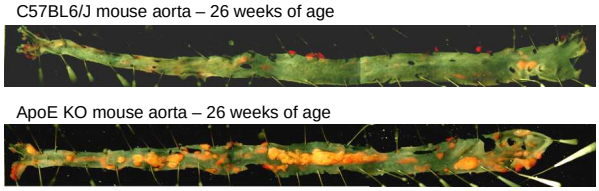

Figure 1: En face preparations of oil red O stained aortas from C57BL6/J and ApoE KO mice at 26 weeks of age (from Behr-Roussel et. Al, 2006).

Erectile function features:

- Erectile dysfunction from 26 weeks of age in ApoE KO mice fed a lipid-rich diet from 4 weeks of age (figure 2).

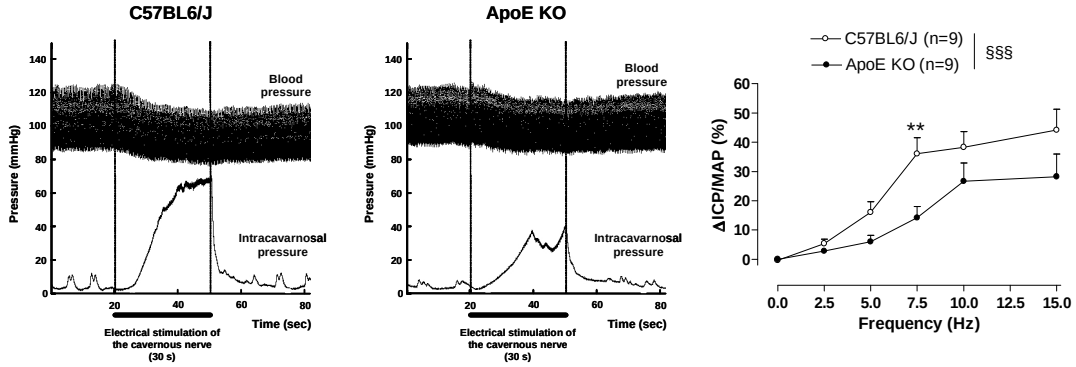

*Figure 2: Original recordings of arterial blood pressure (BP) and intracavernosal blood pressure (ICP) during one erectile response elicited by electrical stimulation of the cavernous nerve (ES CN)(6V, 7.5Hz, 0.3ms for 30s) in an anaesthetized 26 weeks-old C57BL6/J mouse (left panel) and in an age-matched ApoE KO mouse (middle panel); Frequency-response curves to ES CN (right panel) in C57BL6/J and ApoE KO mice at 26 weeks of age ($^{§§§}P<0.001$, two-way ANOVA, followed by a Bonferroni's post-test, **P<0.01. (from Behr-Roussel et. Al, 2006)*

Summarized methodology:

In ApoE KO mice, the development of atherosclerosis can be accelerated by a lipid-enriched Western-diet. Age-matched C57BL6/J mice fed with standard mouse chow are used as control mice.

Related Pelvipharm bibliography:

Behr-Roussel, D. *et al.* **J Sex Med** (2006) : 3(4):596-603

Links to applicable experimental skills:

- **Administration routes / regimen**
- **Plasma / urine / tissue collection**
- **In vivo experiments – conscious animals**
  - * Telemetry
  - * Urine collection - Metabolic cages
- **In vivo experiments – anesthetized animals**
  - * Erection elicited by pharmacological or electrical neural stimulation
- **Organ bath studies (EFS / Pharmacological studies)**
  - * Animal tissues
- **Biochemistry (Plasma / Urine / Tissue)**
  - * Spectrophotometric assays
  - * Protein expression and activity
- **Histology**
  - * Histomorphology
  - * Histomorphometry
  - * Oxydative fuorescence
- **Immunohistology / Confocal microscopy**
  - * Protein expression – immunohistochemistry / immunofluorescence
  - * Confocal microscopy