Zucker diabetic fatty (ZDF) rats

**Model advantages:**
The Zucker Diabetic Fatty (ZDF) rat fed a lipid-rich diet, closely mimics human adult onset of type II diabetes and its related complications. In time, ZDF rats evolve from a model of metabolic syndrome to a type II diabetic rat based on impaired glucose tolerance caused by the inherited obesity gene mutation which leads to insulin resistance.

**Pathophysiological features:**

**Metabolic features**
- Age-dependent evolution from insulin resistance to type II Diabetes mellitus (figure 1)
- Variable hyperinsulinemia
- Hyperglycemia
- Hypertriglyceridemia / Hypercholesterolemia

![Figure 1: Age-dependent evolution of glucose metabolism in ZDF rats](image)

**Cardiovascular features**
- Vascular endothelial dysfunction (aorta, superior mesenteric artery, …) from 20 weeks of age (figure 2)

![Figure 2: Comparison of endothelium dependent relaxations in ZDF and in their control (Lean) obtained in in vitro experiments performed in aortic and superior mesenteric artery rings. (2-way ANOVA, ***P<0.001) (Pelvipharm, internal data).](image)

**Other pathophysiological features**
- Nephropathy
- Neuropathy
- Blindness
- Impaired wound healing

**Summarized methodology:**
- ZDF: homozygous for non-functional leptin receptors (ZDF/Gmi fa/fa)
- Lean controls: homozygous for normal receptors remain lean and normoglycaemic (ZDF/Gmi +/?)

**Related Pelvipharm bibliography:**
Non disclosable information for confidentiality reasons

**Links to applicable experimental skills:**
- Administration routes / regimen
- Plasma / urine / tissue collection
- In vivo experiments – conscious animals
  - Telemetry
  - Urine collection - Metabolic cages
  - Tail cuff
- Organ bath studies (EFS / Pharmacological studies)
  - Animal tissues
- Biochemistry (Plasma / Urine / Tissue)
  - Spectrophotometric assays
  - Protein expression and activity
- Histology
  - Histomorphology
  - Histomorphometry
  - Oxidative fluorescence
- Immunohistology / Confocal microscopy
  - Protein expression – immunohistochemistry / immunofluorescence
  - Confocal microscopy