Goto-Kakizaki (GK) rats

Model advantages:
The Goto-Kakizaki (GK) rat model is one of the best characterized animal model of spontaneous type 2 diabetes, generated by selecting and inbreeding hyperglycemic Wistar rats (produced by Metabrain Research). This non-obese diabetic rat presents many similarities with type 2 diabetic patients in term of pancreas dysfunction such as impaired glucose stimulated insulin secretion, reduction in beta-cell mass, perturbed islets microenvironment, and multiple beta-cell functional common defects. Furthermore, it also displays both bladder and sexual dysfunctions, complications commonly associated to diabetes type 2 in patients.

Pathophysiological features:

Metabolic features:
- Hyperglycemia
- Defective insulin secretion in response to glucose (figure 1)
- Decreased β cell mass (50%)
- Hepatic and peripheral insulin resistance
- Defects in lipid metabolism (mainly cholesterol)
- Inflammation, particularly in pancreatic islets

Cardiovascular features:
- Defective cardiac function (heart hypertrophy, lower heart rate)
- Increased blood pressure

Genito-sexual features:
- Erectile dysfunction (ED)
  → only partially reversed by ED standard-of-care sildenafil (figure 2)
- Hypogonadism

![Figure 1: Plasma glucose and insulin levels in 18-weeks old GK rats and in age-matched Wistar rats before and 10, 20, 30, 60 and 120 min after oral glucose challenge (2g/kg body weight). (Pelvipharm, internal data).](image1)

![Figure 2: Erectile responses elicited by cavernous nerve stimulation at increasing stimulation frequencies in anaesthetized Wistar rats (treated with saline) and GK rats (treated with saline or with sildenafil 0.3 mg/kg i.v.) reported as intracavernosal pressure/mean arterial pressure rise (ΔICP/MAP). (Pelvipharm, internal data).](image2)
**Bladder and urinary features:**

- Diabetic bladder dysfunction (DBD) with detrusor overactivity, increased bladder capacity and micturition pressure
  → Bladder contraction parameters reversed by OAB standard-of-care solifenacin (figure 3)
- Proteinuria

**Figure 3:** Effect of i.v. solifenacin (1 mg/kg) or saline on micturition pressure parameter characterizing micturition contraction in GK rats. (Pelvipharm, internal data).

**Links to applicable experimental skills**

- **Administration routes / regimen**
- **Plasma / urine / tissue collection**
- **In vivo experiments – conscious animals**
  - Telemetry
  - metabolic cages
  - tail cuff
- **Organ bath studies**
  - Rat tissues
- **Biochemistry**
  - Spectrophotometric assays
  - Protein expression and activity
- **Histology/Morphometry**
  - Histomorphology
  - Histomorphometry
- **Immunohistologie/Immunofluorescence/Confocal microscopy**
  - Immunohistology
  - Immunofluorescence
  - Confocal microscopy