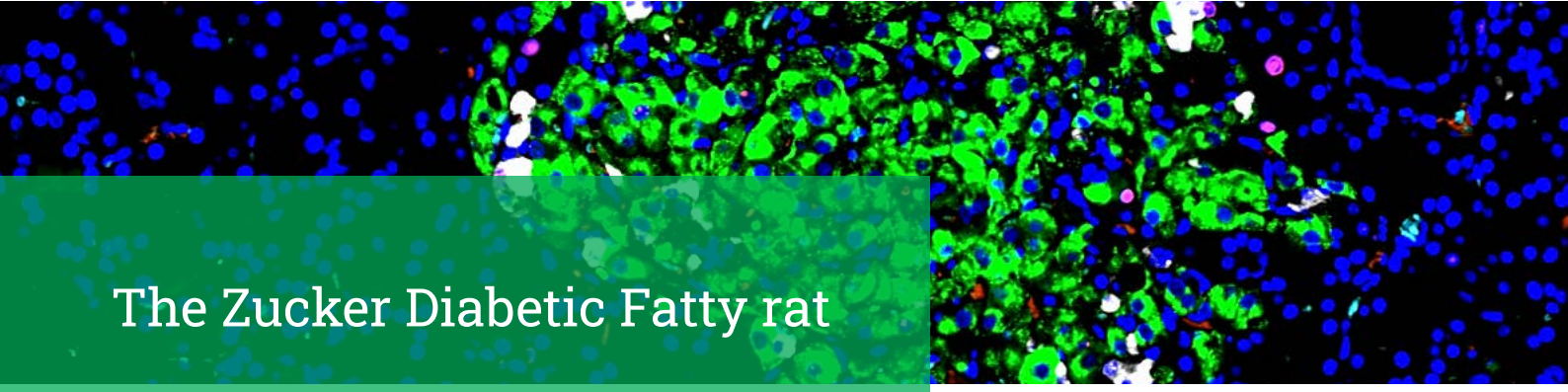


The Zucker Diabetic Fatty rat

Benchmark therapeutic drug effects in a gold standard rat model of type 2 diabetes.

A model of progressive obesity and type 2 diabetes

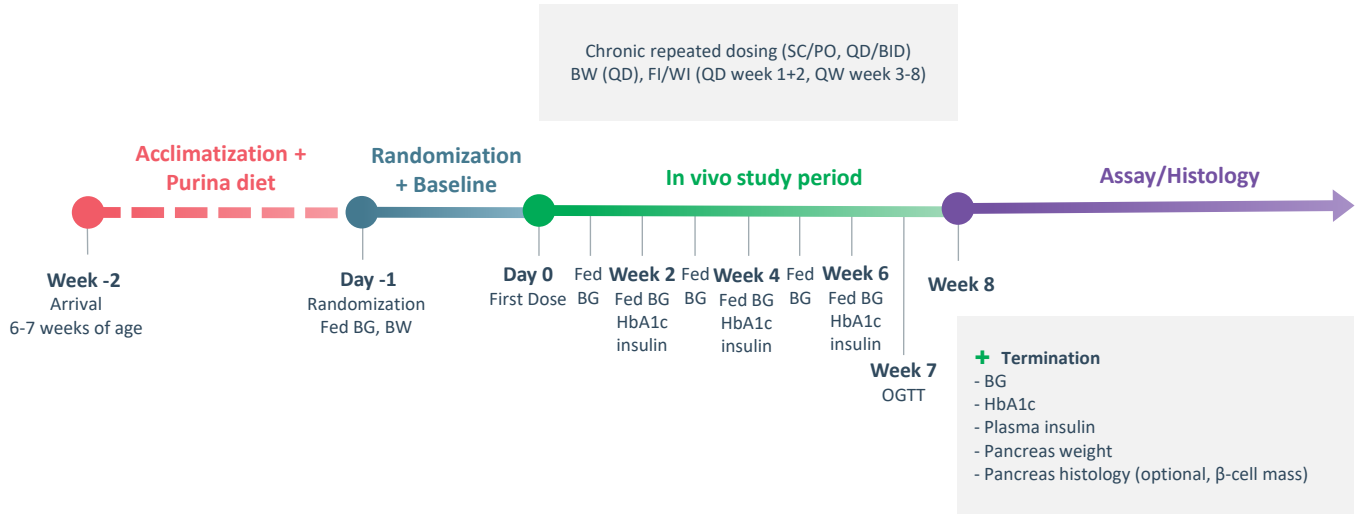
The Zucker Diabetic Fatty (ZDF) rat carries an inactivating mutation in the leptin receptor gene which causes hyperphagia, severe obesity, lipidemia, glucose intolerance and sustained hyperglycemia. The model is widely applied for characterizing metabolic and histological effects of anti-diabetic drugs in various phases of type 2 diabetes.

Key model traits

- Morbid obesity and impaired glucose tolerance.
- Early phenotype of type 2 diabetes.
- Diet-induced timing of hyperglycemia.
- Well-defined progression in islet pathology.
- Treatment efficacy across a wide range of anti-diabetic drug classes.

Diet	Chow (Purina 5008)	Develops sustained hyperglycemia from approximately 10 weeks of age. Male ZDF rats are more diabetes-prone than female ZDF rats. ZDF fa/? rats may serve as normal controls.
Strain	ZDF fa/fa	

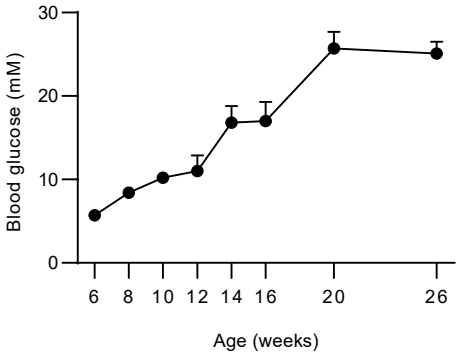
Study outline

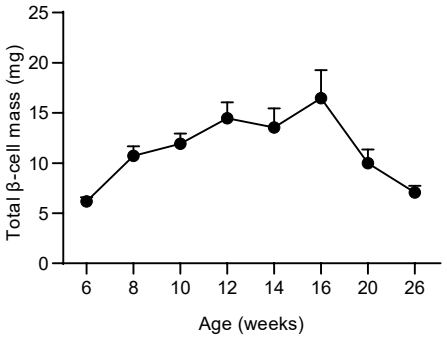


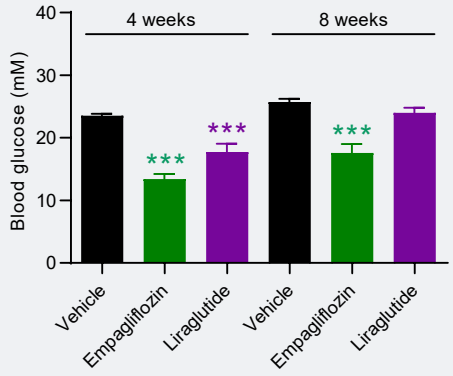
Metabolic and biochemical characteristics

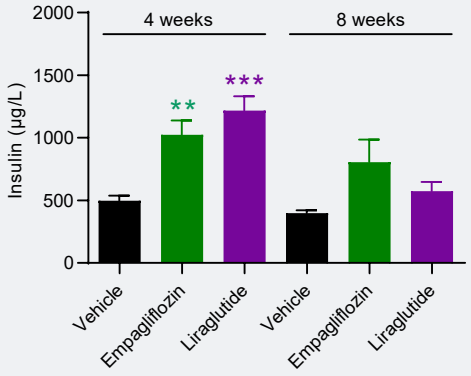
The ZDF rat exhibits overt obesity and type 2 diabetes with progressive loss of pancreatic β-cell mass. Sustained hyperglycemia is manifest after 2-3 weeks of feeding with a carbohydrate-rich diet (Purina 5008).

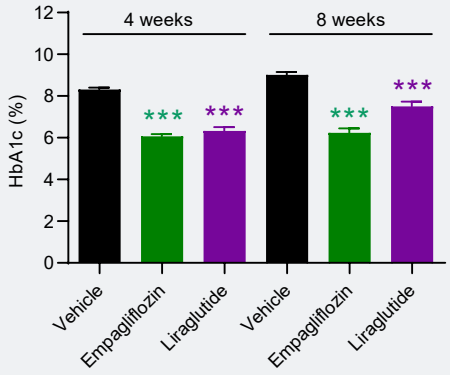
Baseline (10 weeks of age)	ZDF fa/? control	ZDF fa/fa
Body weight (g)	337 ± 3.7	362 ± 4.7
Fasted blood glucose (mM)	5.5 ± 0.1	10.2 ± 0.6
HbA1c (%)	3.9 ± 0.1	7.4 ± 0.3

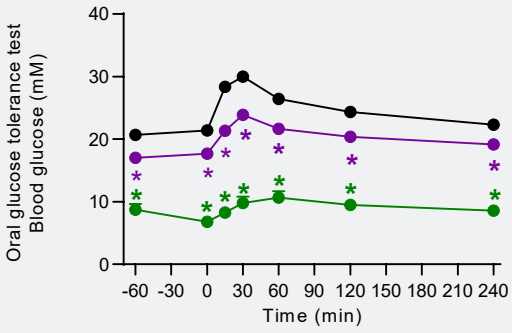












The STZ rat

A single low-dose of STZ promotes sustained and robust hyperglycemia in lean rats. STZ is weight-neutral. Test compound profiling is performed at stabile hyperglycemia (7-10 days post-STZ). Insulin and pramlintide (amylin analogue) improves glucose tolerance in STZ rats.

Pharmacological treatment: Stereological analysis of pancreatic β-cell mass

Effects of 4-8 weeks of treatment with empagliflozin (SGLT-2 inhibitor) or liraglutide (GLP-1 analogue) on pancreatic total β-cell mass.