The Non-Obese Diabetic mouse

A primary mouse model of type 1 diabetes in preclinical drug development.

A model of progressive obesity and type 2 diabetes

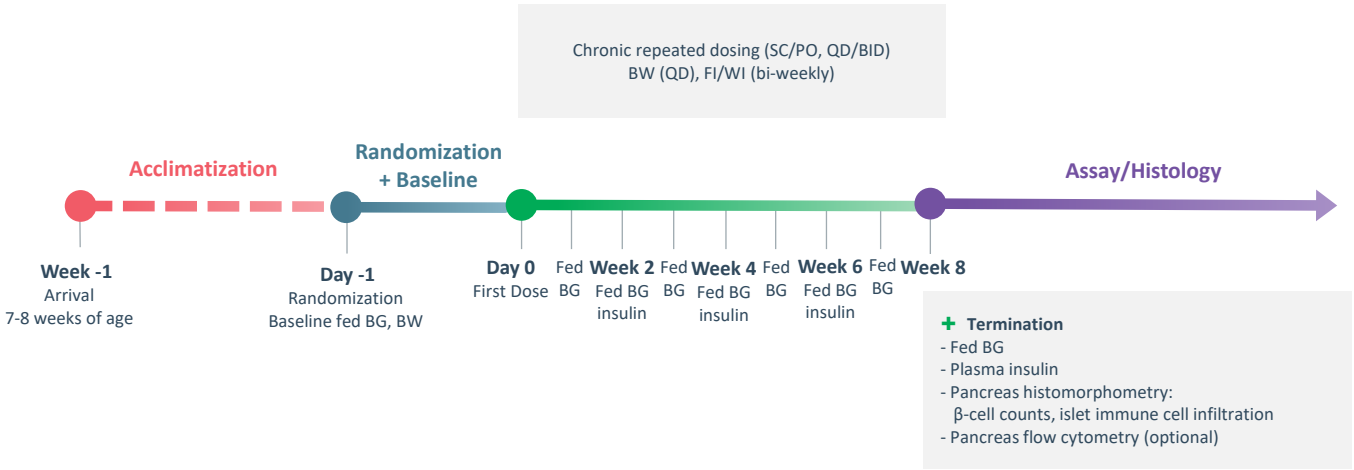
The Non-Obese Diabetic (NOD) mouse is a polygenic model of autoimmune type 1 diabetes. The NOD mice develop hyperglycemia, progressive β-cell loss and spontaneous onset of insulin-dependent diabetes attributed to pancreatic islet leukocyte infiltration.

Key model traits

- Sustained hyperglycemia from ~8 weeks of age.
- Age-dependent transition to diabetes.
- Well-defined progression in islet pathology.
- Treatment efficacy of various anti-diabetic drug classes.

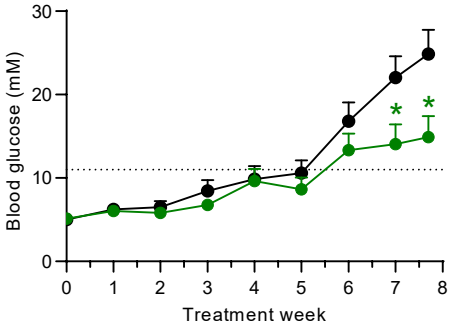
Diet	Regular chow (Altromin 1324)	Female mice show more invasive and destructive insulitis leading to earlier diabetes onset.
Strain	NOD/MrkTac	

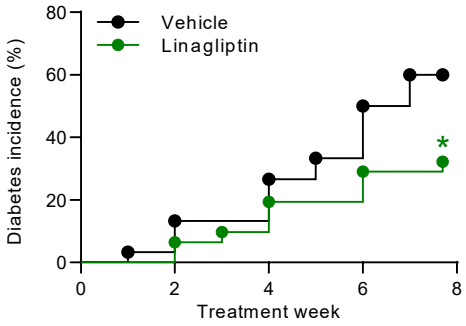
Study outline

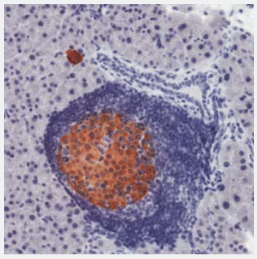


Diabetes incidence

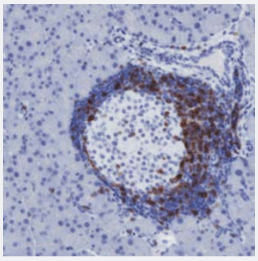
NOD mice shows diabetes incidence of approximately at 13-14 weeks of age. Linagliptin (DPP-IV inhibitor) improves glucose homeostasis and reduces diabetes incidence after 8 weeks of treatment.



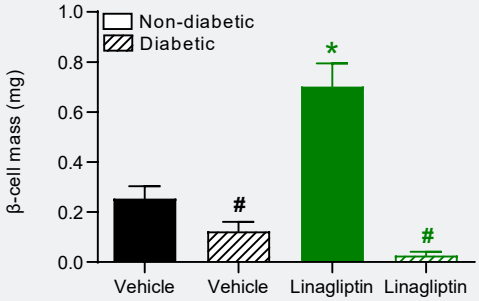


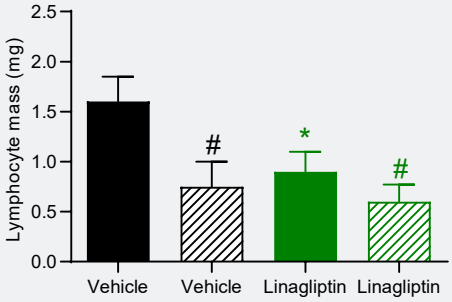


Insulin-positive islet (brown)



Peri-islet lymphocyte infiltration (CD3+ T cells, dark brown)





Pancreatic islet histology

Islet morphology in NOD mice is characterized by lymphocyte infiltration and loss of pancreatic β-cell mass. Linagliptin preserves β-cell mass and reduces lymphocyte infiltration in NOD mice.

Whole-pancreas 3D quantitative imaging of insulitis in NOD mice

Left: 3D light sheet microscopy imaging of insulin-positive pancreatic islets (red) and infiltration CD45-positive leukocytes (blue) in 14-weeks old NOD mice. Right: Whole-pancreas 3D quantitative analysis with segmentation of insulitis according to islet size.