

Mouse model of diabetic neuropathy and nephropathy

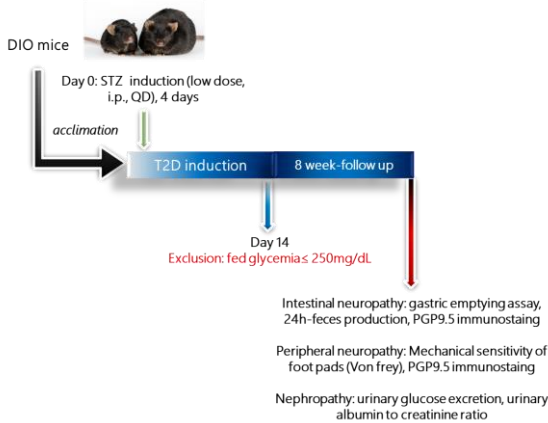
Physiogenex provides a unique mouse model of diabetic neuropathy and nephropathy to test your compounds targeting both comorbidities

Key benefits

- ✓ A tailor-made type 2 diabetic animal model that mimics human development of type 2 diabetes and associated diabetic neuropathy and nephropathy progression.
- ✓ Demonstrate the benefits of your drug on both peripheral/autonomic nervous system nerves and kidneys, an additional benefits for diabetic patients.

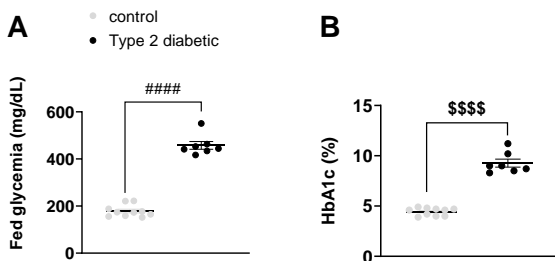
ANIMAL MODEL

- Background strain: DIO C57Bl6/J mice
- Gender/Weight: male, ~40-45g
- 60% High Fat Diet
- Time on diet: from 6 weeks to 22 weeks of age, 16 weeks under HFD
- Type 2 diabetes induction : streptozotocin (STZ), low dose, QD, 4 days



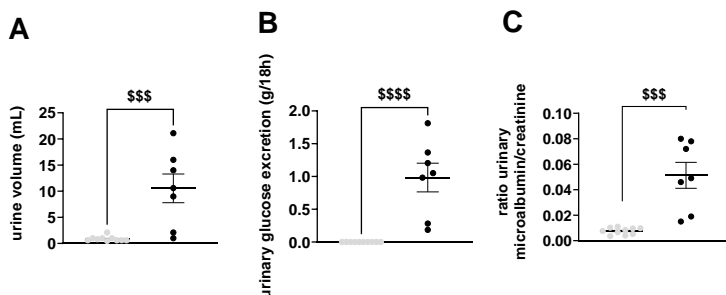
Diabetic neuropathy and nephropathy characterisation

1 – DIO+STZ MICE ARE STRONGLY HYPERGLYCEMIC



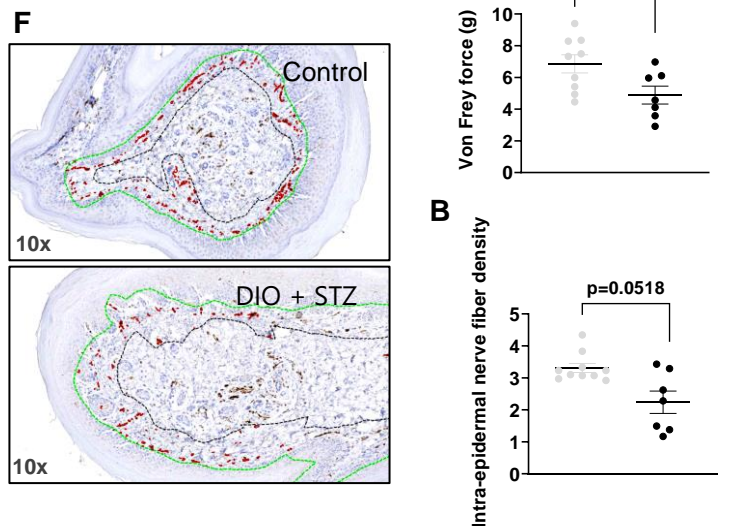
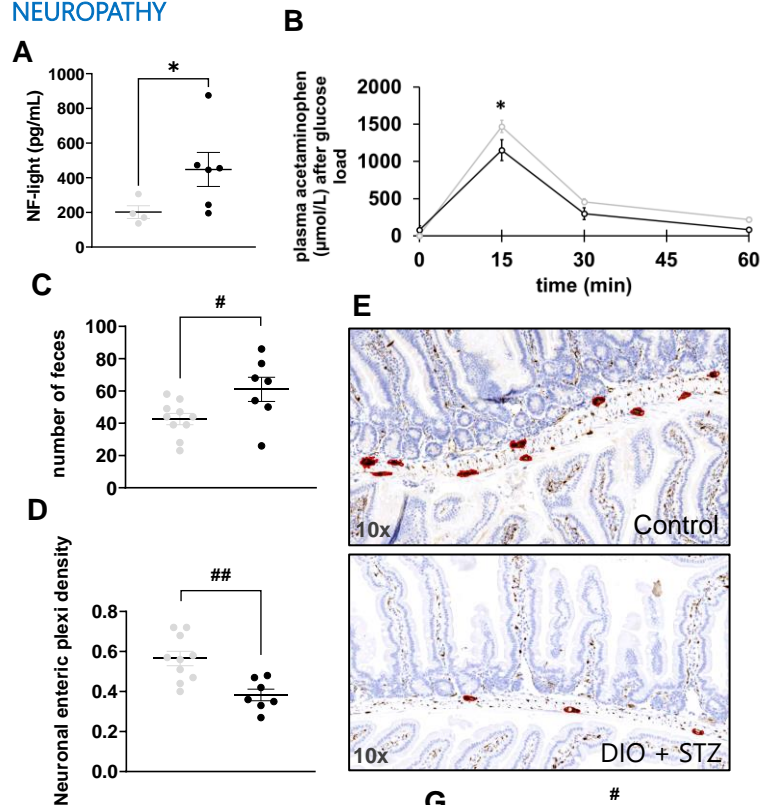
(A) Fed glycemia, (B) blood HbA1c level at the end of follow-up period. #### p < 0.0001

2 –DIO+STZ MICE SHOW DIABETIC NEPHROPATHY



(A) Urine volume, (B) urinary glucose excretion and (C) ratio urinary microalbumin and creatinine after 18 hours of urine collection, at the end of follow-up period \$\$\$ p < 0.001; #### p < 0.0001

2 – DIO+STZ MICE HAVE BOTH INTESTINAL AND PERIPHERAL NEUROPATHY



(A) Plasma neurofilament light chain levels. (B) Gastric emptying assay by oral gavage of acetaminophen and measurement of plasma acetaminophen. (C) Feces production over 18 hours. Immunohistochemistry of neuronal marker PGP9.5 in small intestine, (D) representative images (magnification: 10x, red dots: PGP9.5 positive area corresponding to neuronal enteric plexi) and (E) quantification. (F) Mechanical sensitivity assay using VonFrey test. Immunohistochemistry of neuronal marker PGP9.5 in foot pad, (G) quantification and (H) representative images (magnification: 10x, red square: PGP9.5 positive area corresponding to neuronal fiber crossing epiderma of foot pads). #, * p < 0.05; ## p < 0.01