Investigation of Hypothalamic Selenoprotein M in Energy Metabolism

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Selenium and Selenoproteins

Selenium

- **Selenium (Se)** is an essential micronutrient
- Important role in maintaining human health
- Required for:
  - Normal thyroid hormone metabolism
  - Brain development
  - Immune function
- Obtained primarily through diet

Selenoproteins

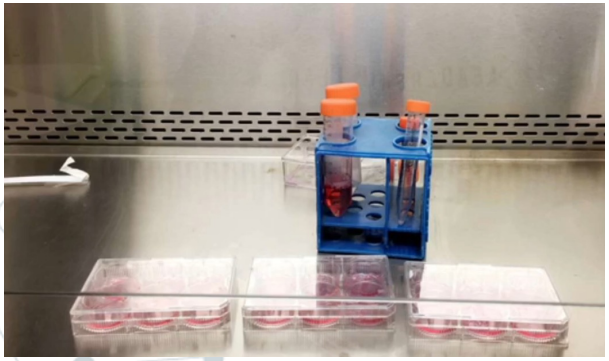
- Proteins with amino acid **Selenocysteine**
- 25 genes in humans and 24 genes in mice encode selenoproteins

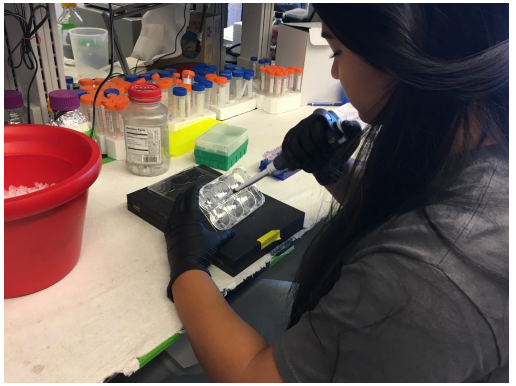
SelM

- A Thioredoxin-like protein
- Highly expressed in the brain
- Protects against oxidative stress

Last Year's Research

- **The Role of Selenium in Hypothalamic leptin signaling**
  - **Leptin**- Hormone released from fat that regulates energy homeostasis
  - **Leptin Resistance**- Failure of leptin to stimulate cell signaling pathways that promote energy metabolism
- **Hypothesis**- Selenium deficiency promotes hypothalamic leptin resistance
- **Experiment timeline**
  - Transfected cells, treated with Leptin, collected protein and analyzed by western blotting
- Results were inconclusive
  - SelM was significantly affected by the selenium treatment





Experiment

SelM KO Mice

- Lack a functional SelM gene sequence
- SelM KO Mice developed leptin resistance and obesity at 18-20 weeks old when raised on a standard diet

Mice used in Hypothalamic Microarray Study

- 10- week-old males
- Similar body weight

Experimental Design

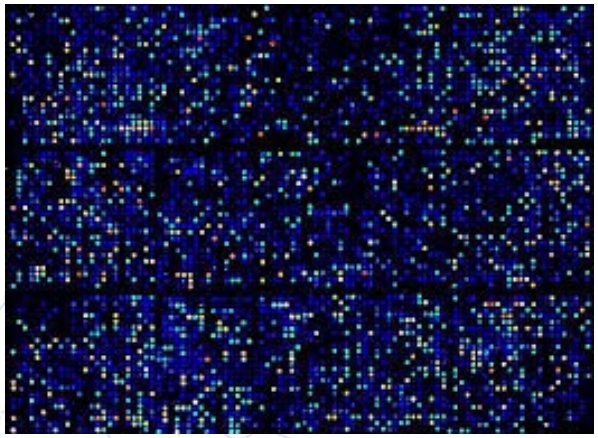
Microarray
Identify genes affected by SelM deletion

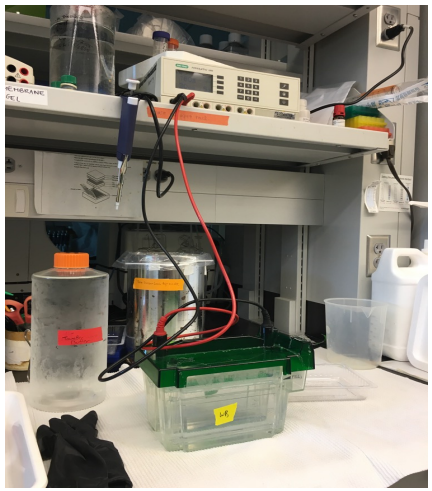
→

qPCR
Verify specific identified genes
- p21
- PGC1α
- TXNIP
- UCP2

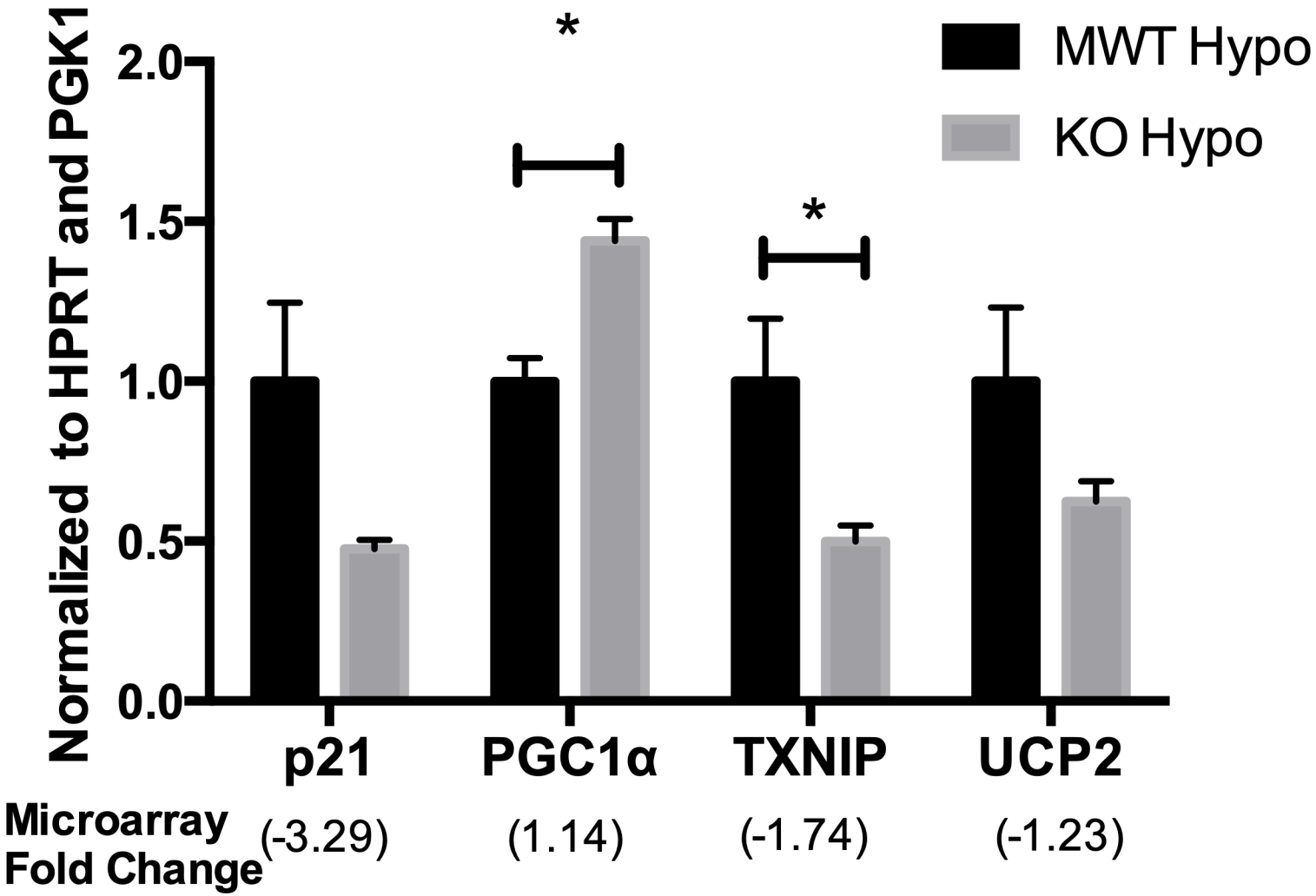
→

Western Blotting
Probe for genes verified in qPCR
- PGC1α
- TXNIP

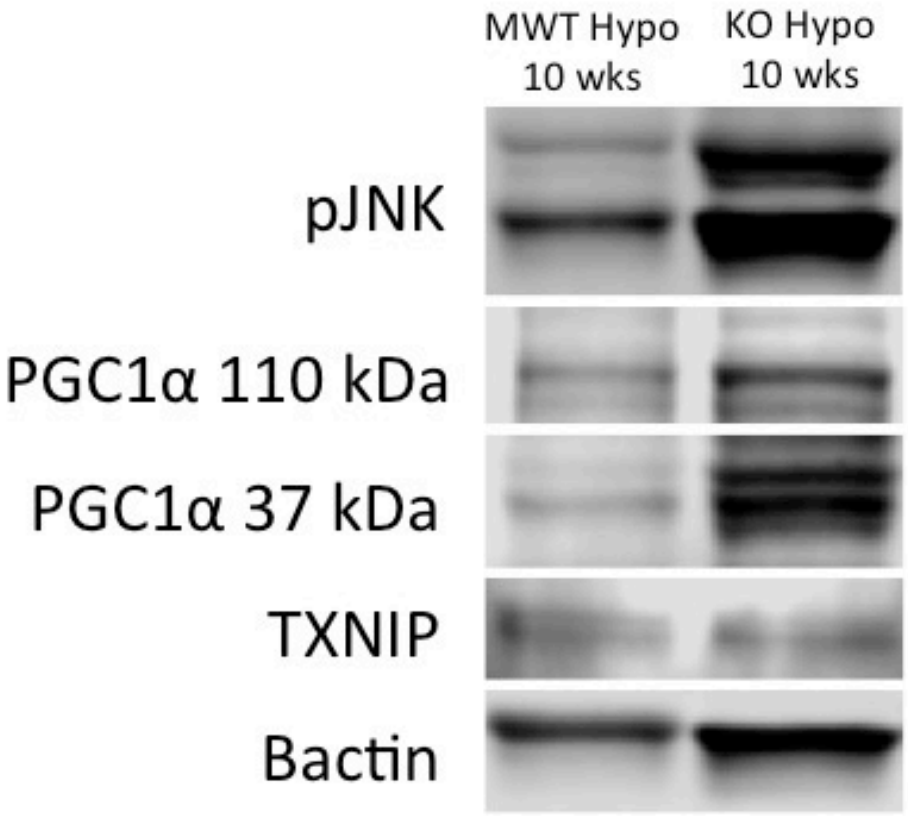


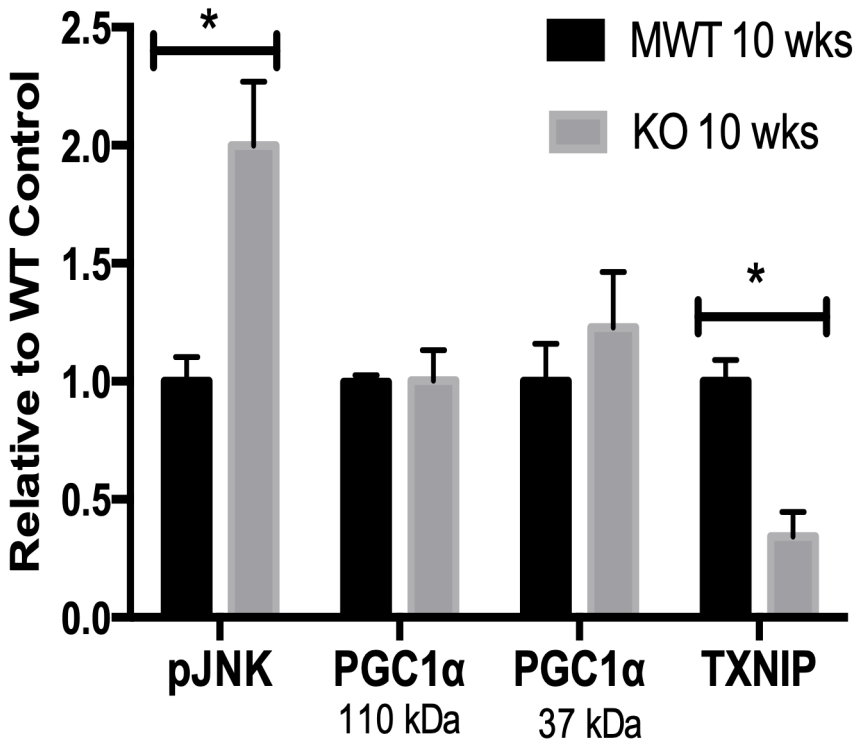


qPCR Data: Hypothalamic Tissue



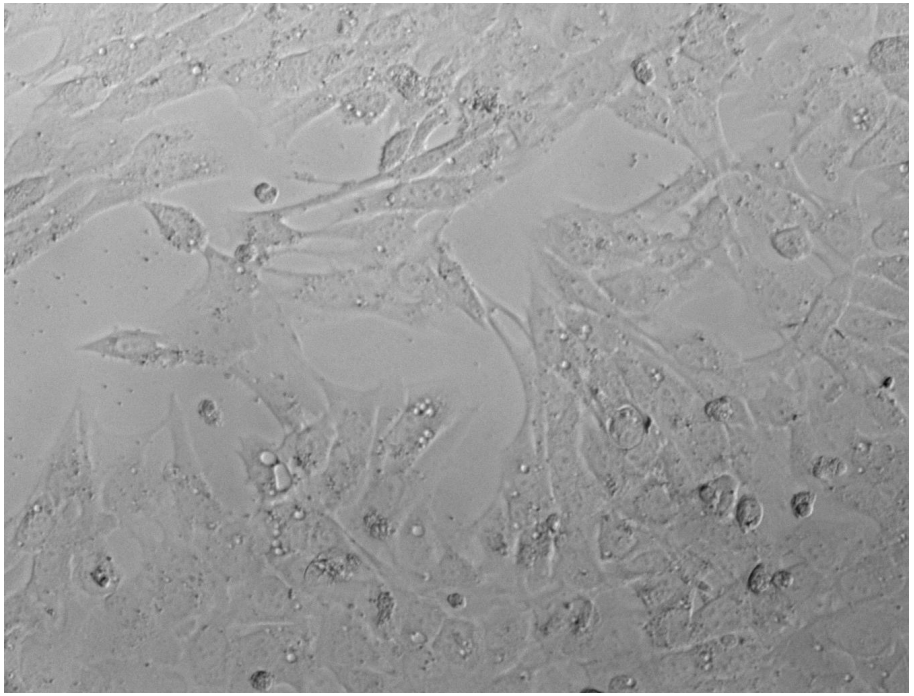
Western Blot Data: Hypothalamic Tissue



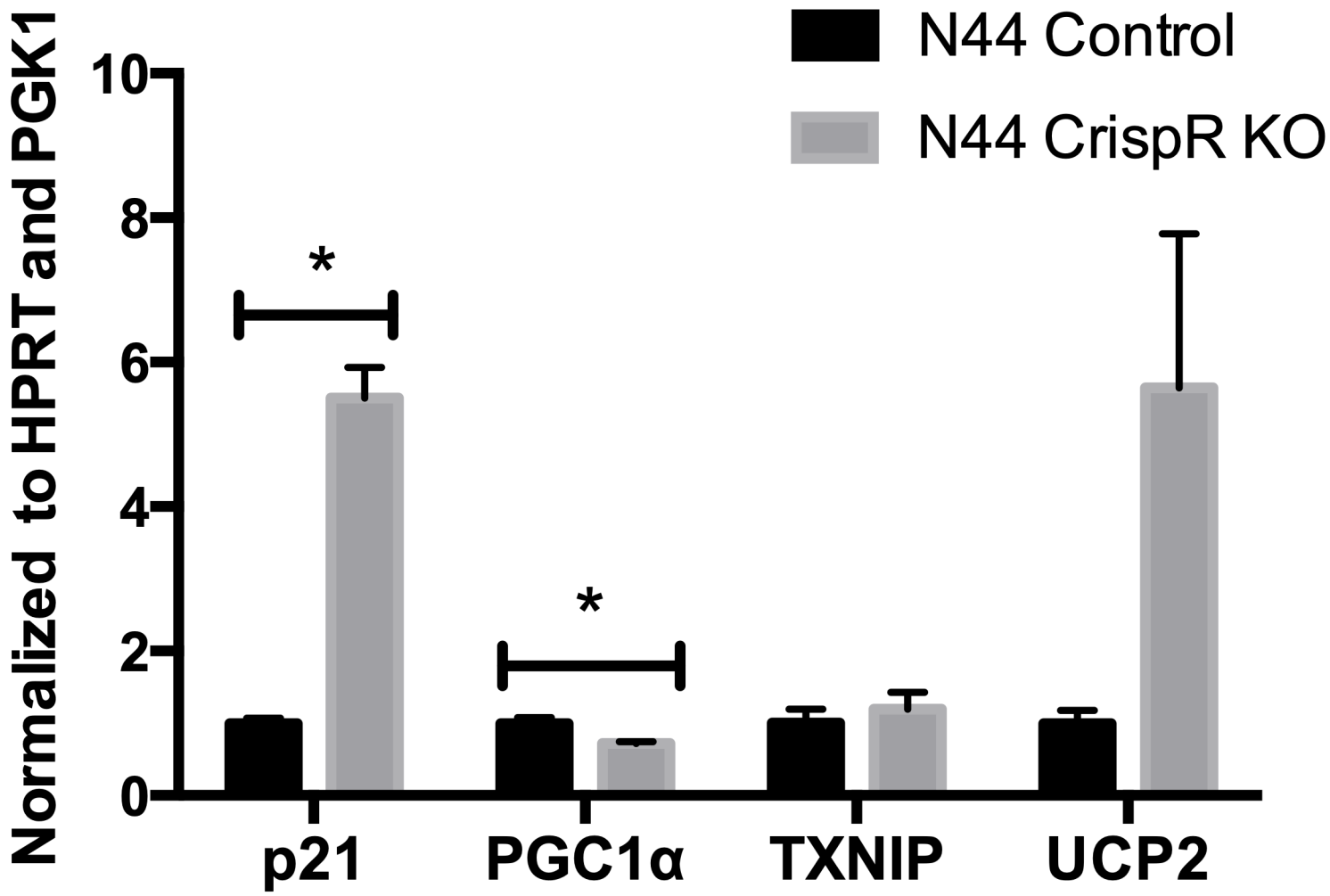


Cell line= mHypoE44

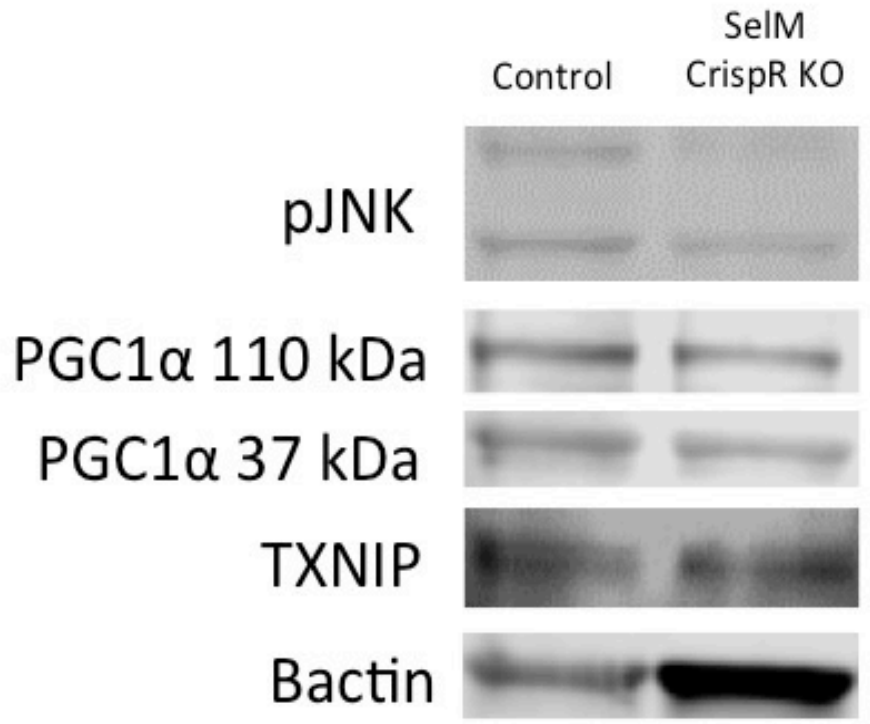
- Immortalized cell line derived from embryonic mouse hypothalamic neurons

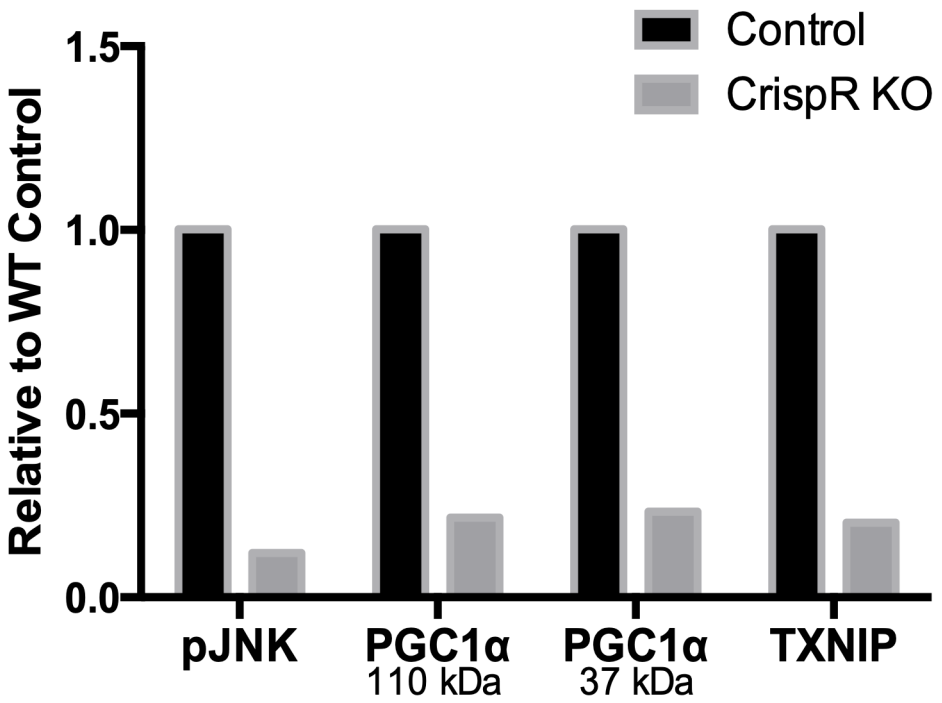


qPCR N44 Immortalized Cell Line



Western Blot Data: N44 Immortalized Cell Line





Conclusions

- SelM deletion significantly affects expression of p21, PGC1α, and TXNIP
- Increased hypothalamic ER stress (pJNK levels) precedes disturbances in energy homeostasis previously reported in SelM KO mice

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Dedicated to Dioniso Domingo 1931-2017