THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Department of Surgery

agillis@uabmc.edu

Validation of Adversity-Linked Genes in Pancreatic Neuroendocrine Tumors

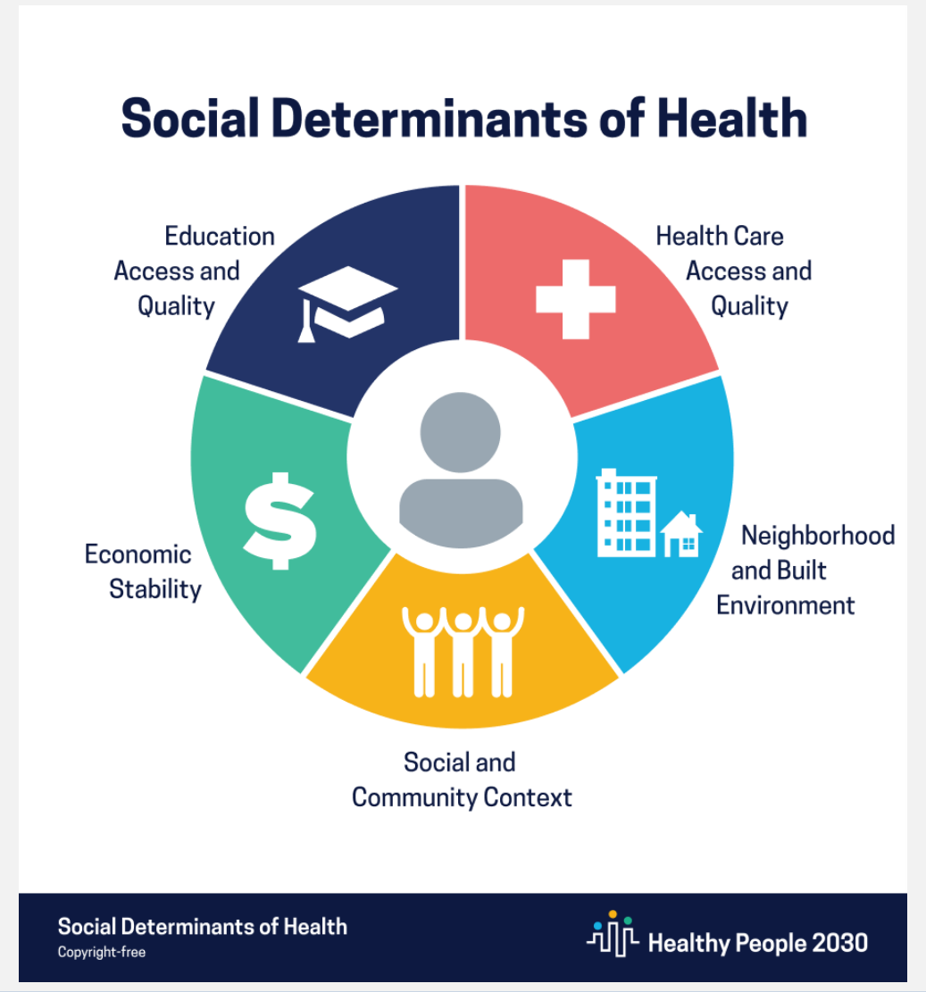
Mourad Bendjennat, Rachael Guenter, Brendon Herring, Elquis Castillo II, Stuart Phipps, Theo Hines, Doug Welsch, Changde Cheng,
Dai Chen, Isra Elhussin, Upender Manne, Herbert Chen, Clayton Yates, Smita Bhatia, J Bart Rose, Andrea Gillis

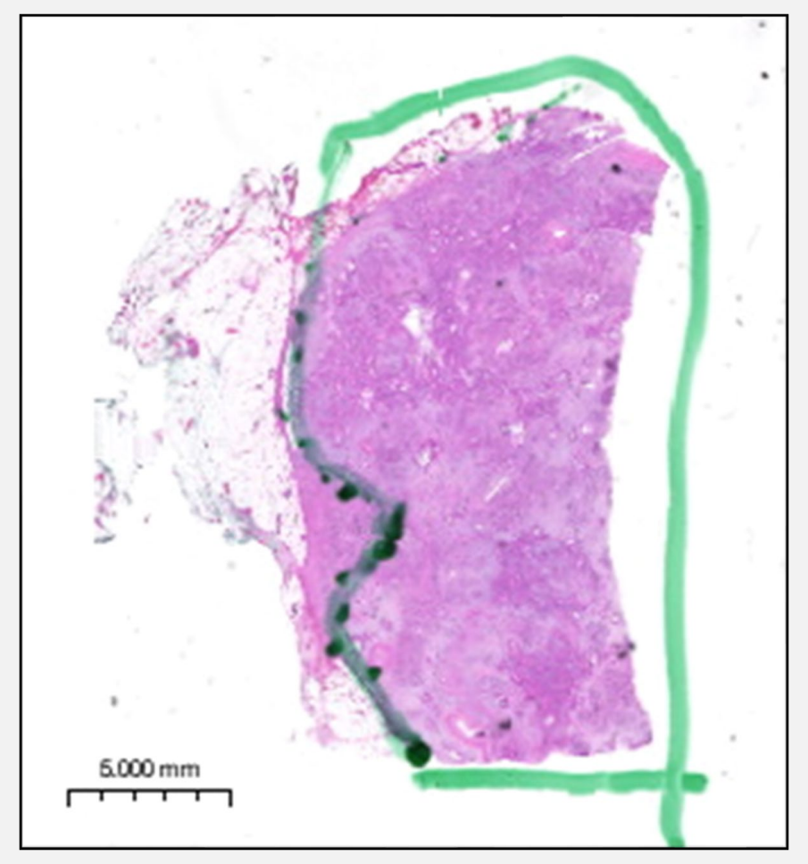
Introduction

- Health outcome differences exist among patients with pancreatic neuroendocrine tumors (pNET),
- those experiencing adverse social determinants of health (SDOH).
  - worse overall survival compared to their peers.
  - significant intratumoral transcriptomic alterations linked to neighborhood adversity.
- **Aim**: To validate the top transcriptomic changes in established pNET cell lines versus normal controls for future translational studies.

Methods

- Grade 1-2 pNETs surgically resected
- Tissue micro arrays (TMAs) created
- Transcriptomic analysis from formalin-fixed paraffin embedded (FFPE) slides
- Top 20 differentially expressed genes in adversity based on geocoded social determinants of health (SDOH)
- Qualitative IF in patient tissues from TMAs
- Evaluate expression levels in cell lines (BON-1, QGP-1) and normal pancreatic (HPNE) cells using Western Blotting, qPCR





Representative demarcated pNET FFPE slide

Results

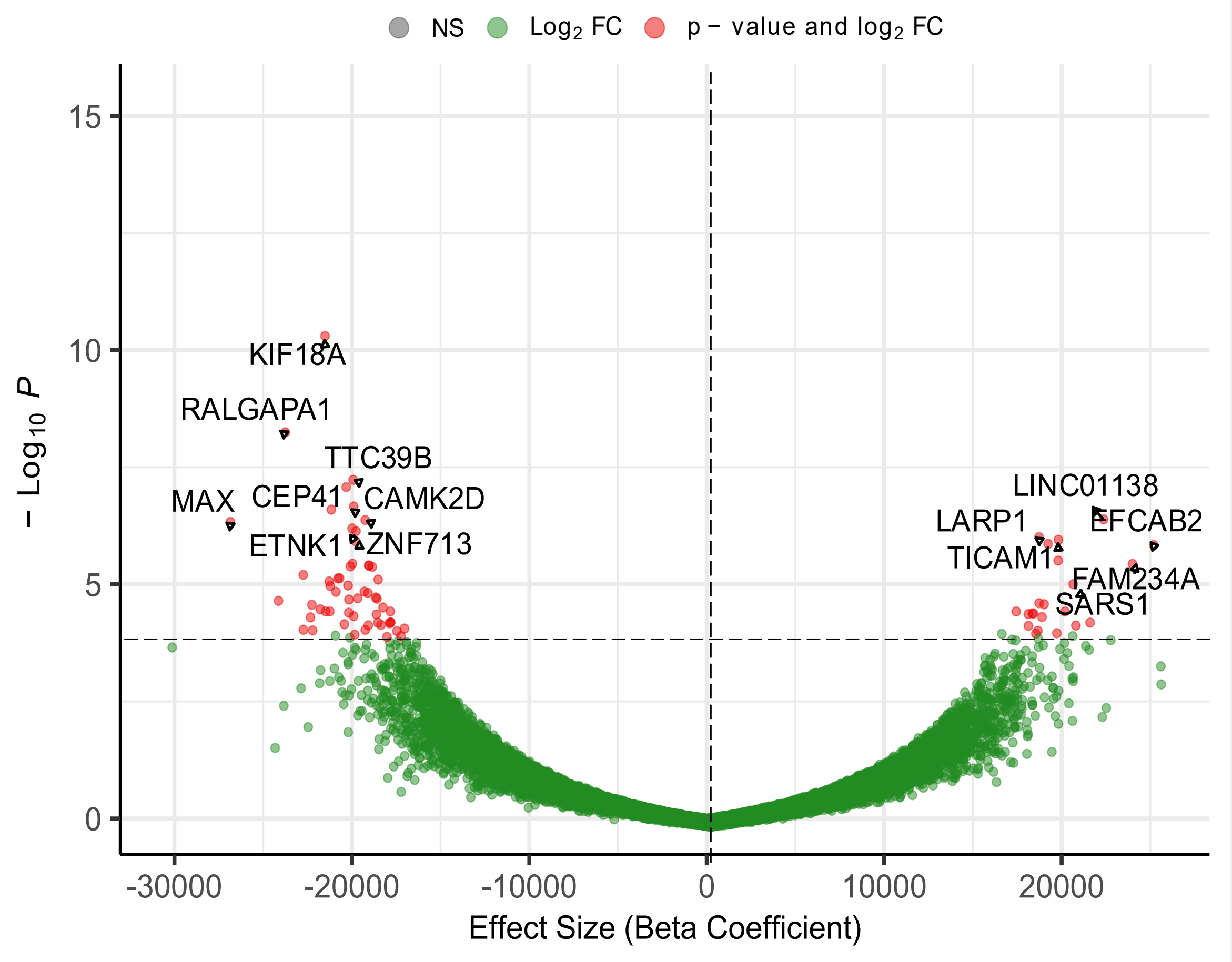
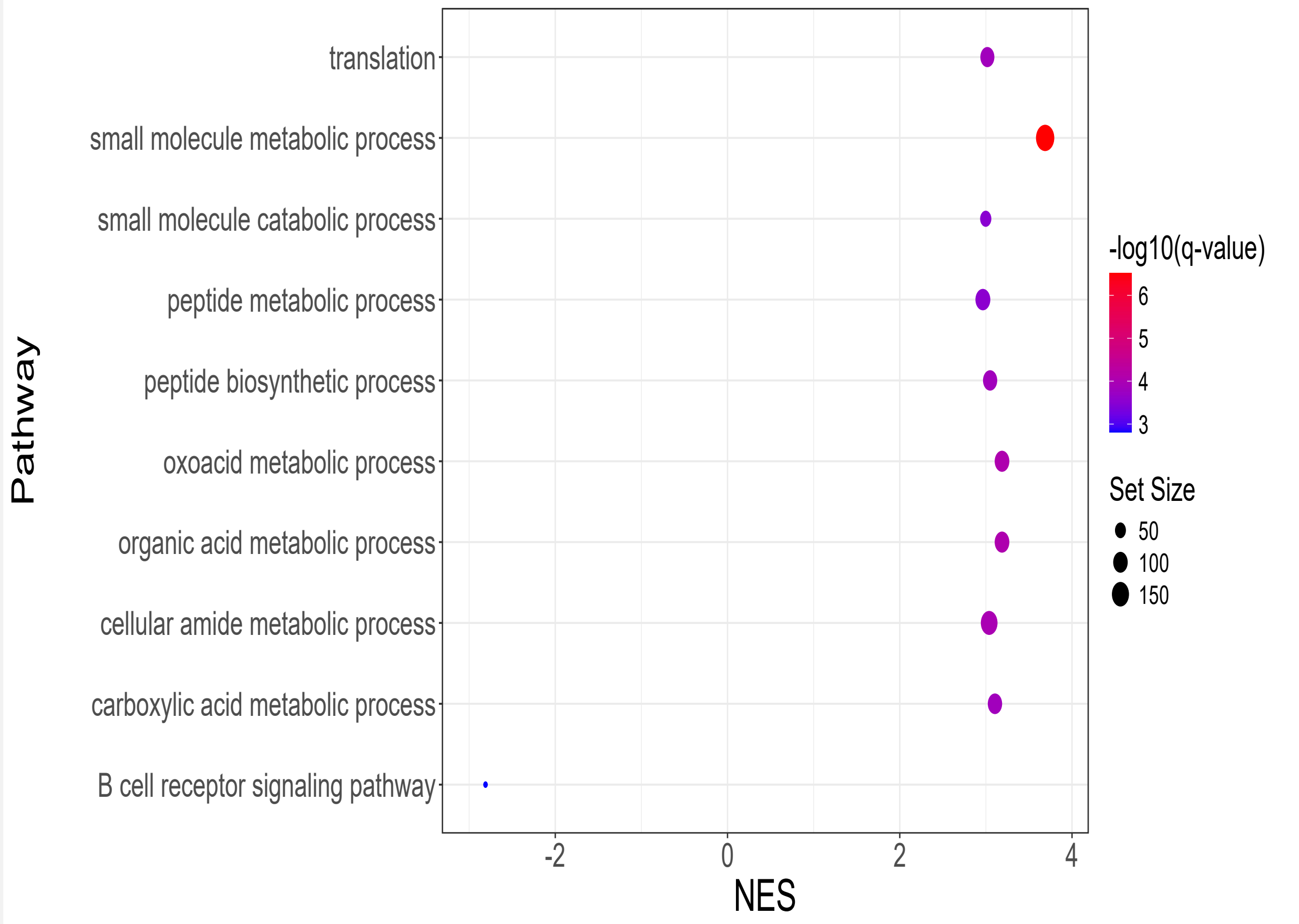


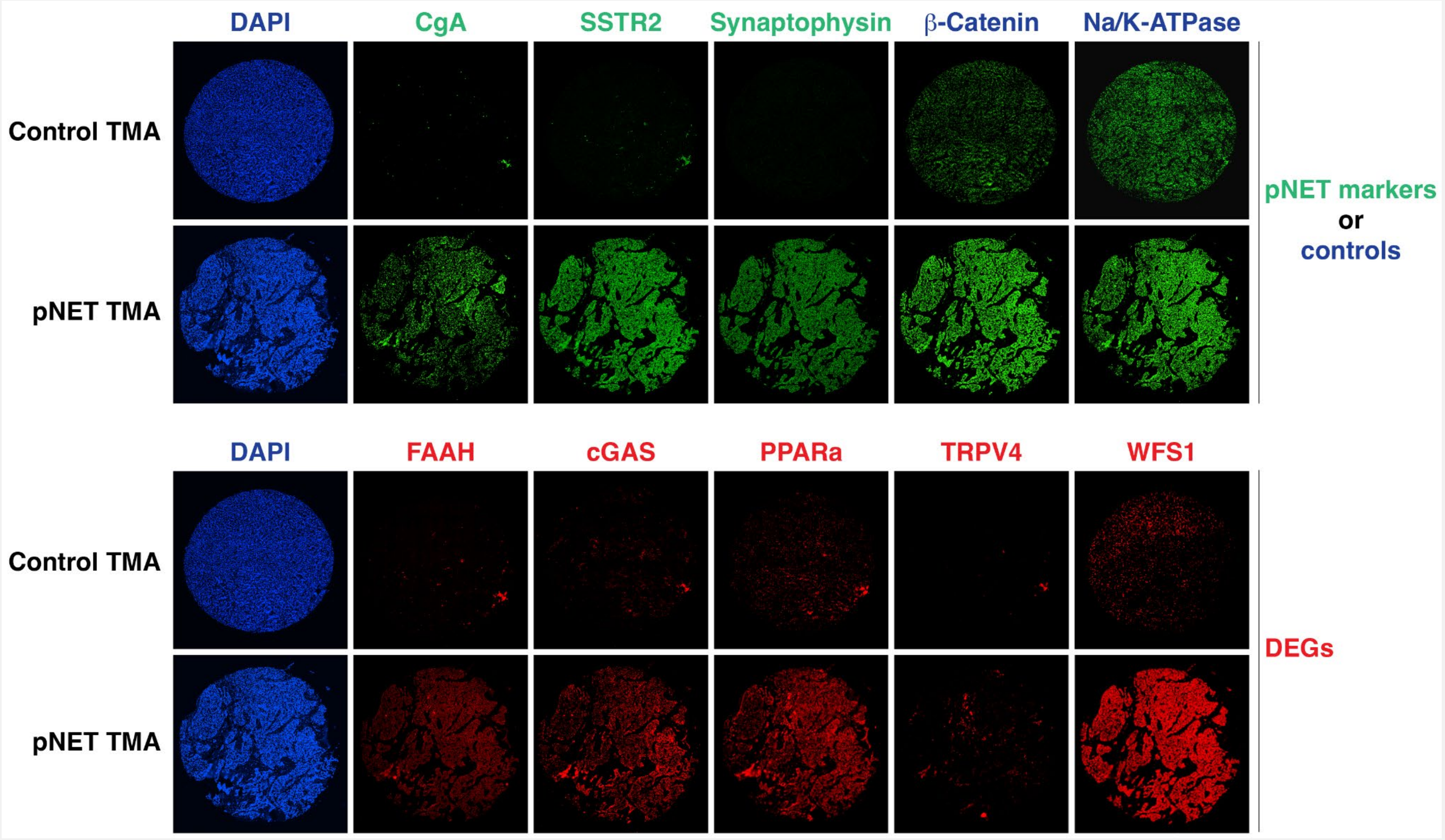
Figure 1: Differential Gene Expression Associated with **Low Income**

Figure 2: GSEA: Results Associated with **Low Income**



- **Data set**: 179 surgical patients (n=59, QC)
- Median Age 58.8 ± 12.5y
- Tumor size: 3.4 ± 2.8 cm
- Neighborhoods below federal poverty line: 15%

Figure 3: Representative multiplexed immuno-staining pNET TMA



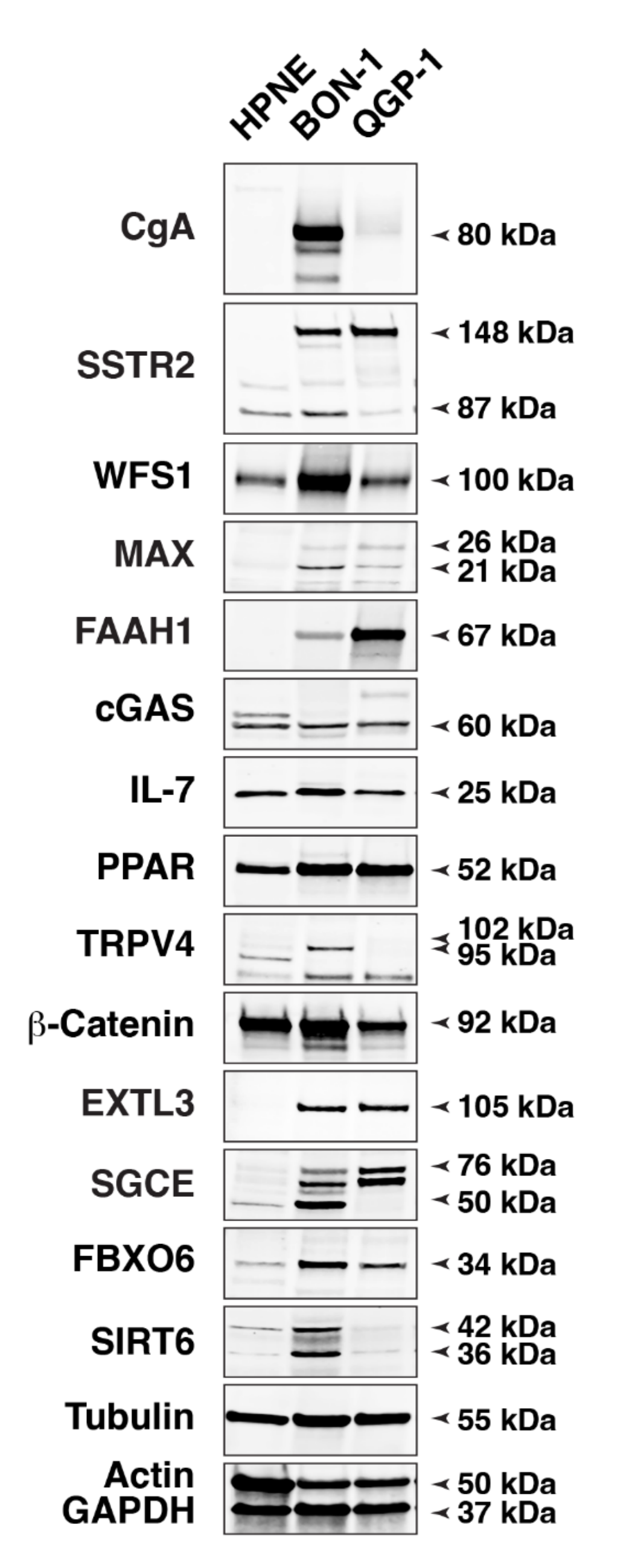


Figure 4: Western Blotting of novel DEGs using Bon-1 and QGP-1 versus hTERT

- Validated the enhanced expression of our top SDOH-associated pNET DEGs including: WFS1, MAX, cGAS, FAAH, SIRT6, SIGLEC8, and FBOX6, among others.
- Comparative immunoblotting in HPNE versus BON-1 and QGP-1 showed altered expression levels in both types of pNET cell lines.
- qPCR assessments revealed that our DEGs were overexpressed from ~5 to ~400 fold over HPNE relative expression.
- Patient TMAs confirmed co-localization of DEGs with pNET markers: Chromogranin A and Synaptophysin.

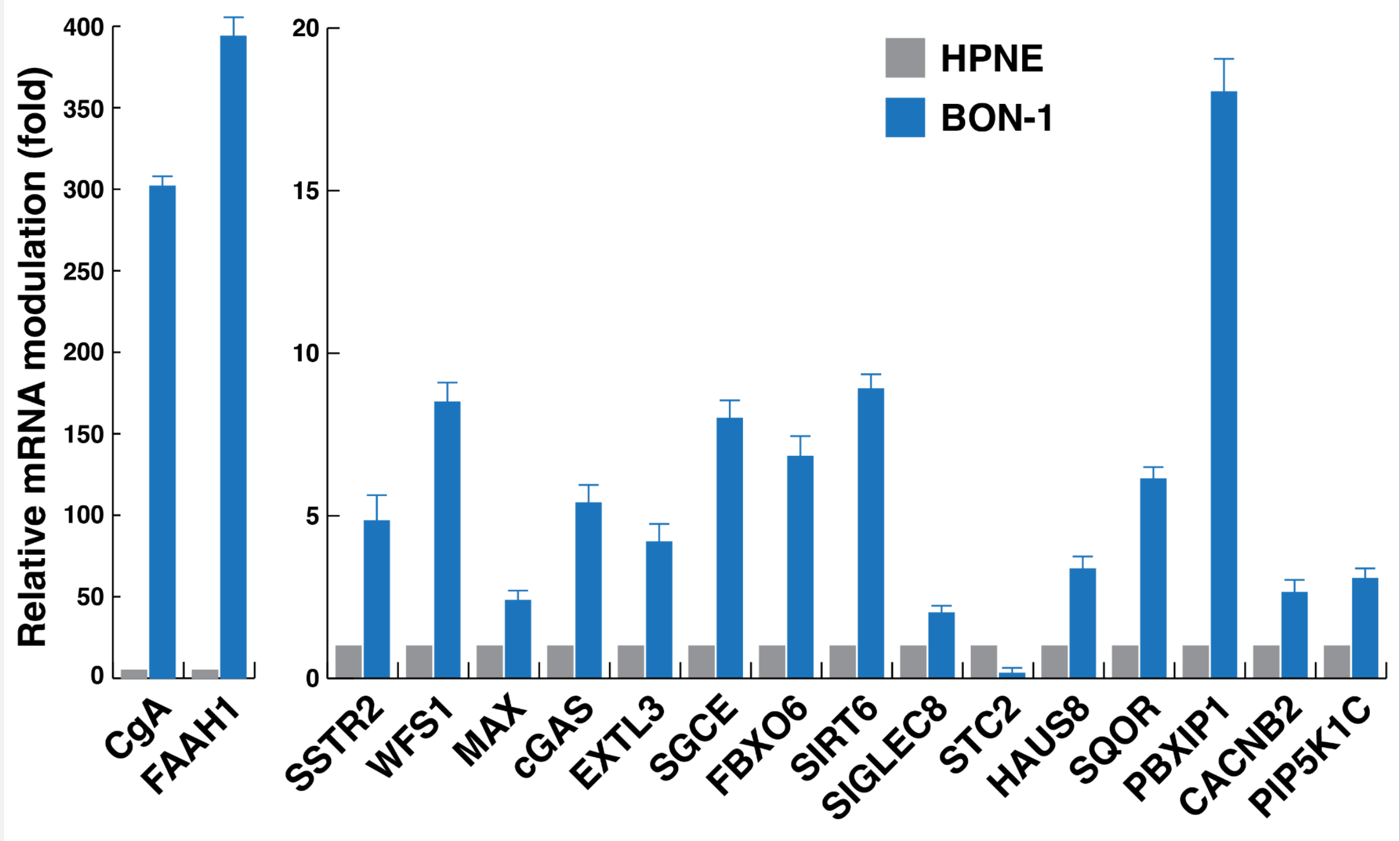


Figure 5: DEG qPCR expression comparing BON1 versus hTERT cell lines

Conclusion

- Our novel adversity associated genes have been validated experimentally with protein and mRNA expression levels in established pNET cell lines. Future directions will focus on exploring the role of these genes in driving more aggressive disease.