**A single-cell transcriptomic view of *NEAT2* over-expressing human pancreatic islet cells**

**Background/aims:** The quality (and number) of isolated islets determines their suitability for human islet therapy. Previously (Wong et al. JCI insight, 2019), we identified two variants of a long non-coding(lnc)RNA (*MALAT1 or NEAT2*) as predictor of islet quality and survival. These observations were independently validated, confirming that *MALAT1* abundance supports cellular survival in hypoxic conditions during islet isolation (Smolander, et al. Bioinformatics, 2021). We hypothesized that *MALAT1* has a protective effect on human islets under hypoxic conditions. This study aims to investigate the regulatory networks of *MALAT1* in hypoxic human islet-derived cells at a single-cell (sc-)resolution.

**Methods:** The knockdown with Gapmers (Saini et al, STARprotocol, 2021) and overexpression with pCDH-hMALAT1 vector (Hu et al, Leukemia, 2018) of *MALAT1* in human islet-derived cells (n=3 donors) under normoxia or hypoxia (1% O2) was performed. Cells were harvested for viability assessment, qPCR and scRNA-seqeuncing. HIVE™ scRNAseq kits were used for library preparation, and sequencing was performed on Illumina™. Beenet™ was used to align/generate transcript count-matrices, and analyses was implemented using R, Seurat 5.0.

**Results:** Altered *MALAT1* expression in human islet-derived cells under hypoxia dysregulated hypoxia-related genes (such as *HIF1A*) and *MALAT1* overexpression improved cell viability.An average of ~37,800 reads/per cell from up to 12,000 cells/per a sample across six experimental conditions were obtained. Unsupervised UMAP of scRNAseq data revealed distinct single-cell clusters with cells overexpressing *MALAT1* under hypoxia and normoxia clustering together than sub-populations of *MALAT1* knockdown cells under hypoxia, which clustered more with hypoxic controls.

**Conclusion:** *MALAT1/NEAT2* expression may have a protective effect on islet-derived cells under hypoxic conditions. *MALAT1/NEAT2* is a potential target for preventing hypoxic damage to improve islet quality/yield for transplant.