The temporal dynamics of mild hypothermia response: from thermogenesis to protein synthesis

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Coefficien 0.00

Correlation Correlation

-0.75

32°C

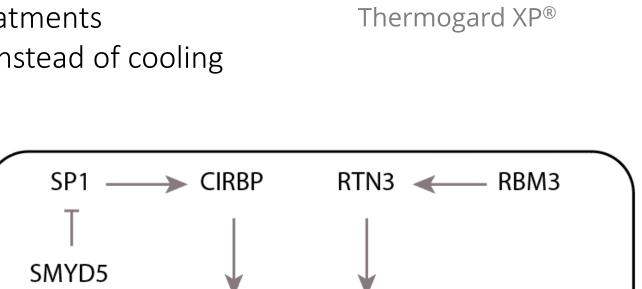
(n = 2.405 proteins

Targeted temperature management

- Benefits: → Reduces brain damage after hypoxic events as neonatal asphyxia, cardiac arrest or drowning.
- Potential risks:
 - → Systemic Inflammatory Response Syndrome (SIRS)
 - → Bradycardia, Hypotension, Coagulopathies, Pneumonia
- Understanding the pathways affected by TTM could:
- → Reveal the mechanisms behind its benefits and side effects
 - → Help identify new targets for neurodegenerative treatments
 - → Enable the use of drugs to activate these pathways instead of cooling

4. Only a few cold shock proteins are known

- a. RBM3: RNA Binding Motif Protein induced
- RTN3: Reticulon protein
- SP1: Transcription factor
- CIRBP: RNA Binding protein induced
- SMYD5: Histone methyltransferase



Neuroprotection

Ribosomal related proteins during hypothermia in HEK293 cells

n = 90 genes

n = 18 genes

n = 177 genes

n = 17 genes

RPL21/23/23A/28/36 RPS18/19/20/23/25 PB2 RPS6/7/11/12

Slope of Linear Regression



31 are ribosome related:

Cytoplasmic ribosomes

RPL proteins (60S component): RPL6, RPL19, RPL21, RPL13, RPL23, RPL23A, RPL13A, RPL36, RPL15, RPL28, RPL40/UBA52

RPS proteins (40S component): RPS6, RPS7, RPS11, RPS12, RPS18, RPS19, RPS20, RPS23, RPS25.

Mitochondrial ribosomes:

MRPS and MRPL proteins:

MRPS25, MRPL3, MRPL39, MRPL50.

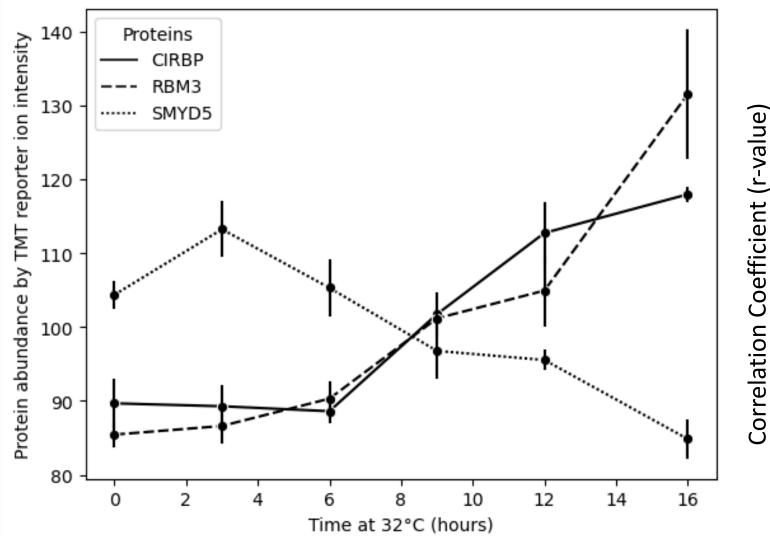
Factors:

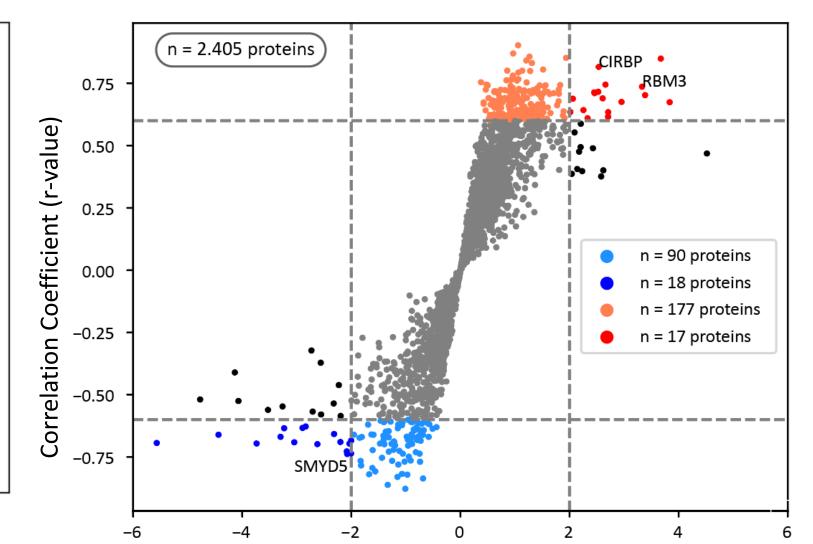
Gene expression

Ribosome biogenesis factors or splicing factors: NOC3L, NUFIP2, EFTUD2, SNRPB, SNRPB2, SNRNP40, SNRNP200

Unbiased proteomic study: target proteins detected in HEK293 cells

Proteasome



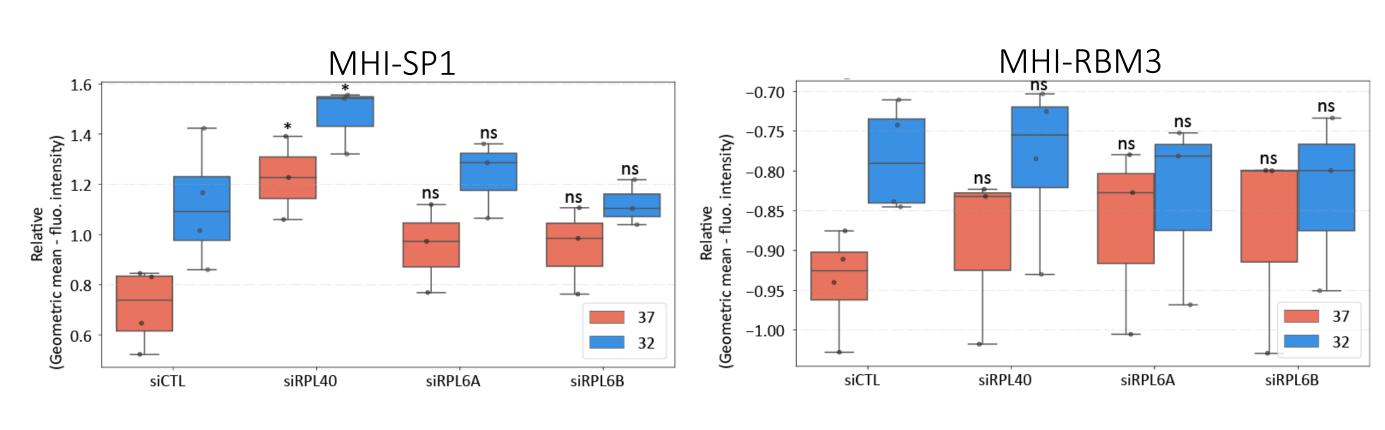


Slope of Linear Regression

Gene Rank

RPL40/UBA52 is a repressor of SP1

Flow cytometry approach using a fluorescent indicator to map promoter usage in HEK293 cells

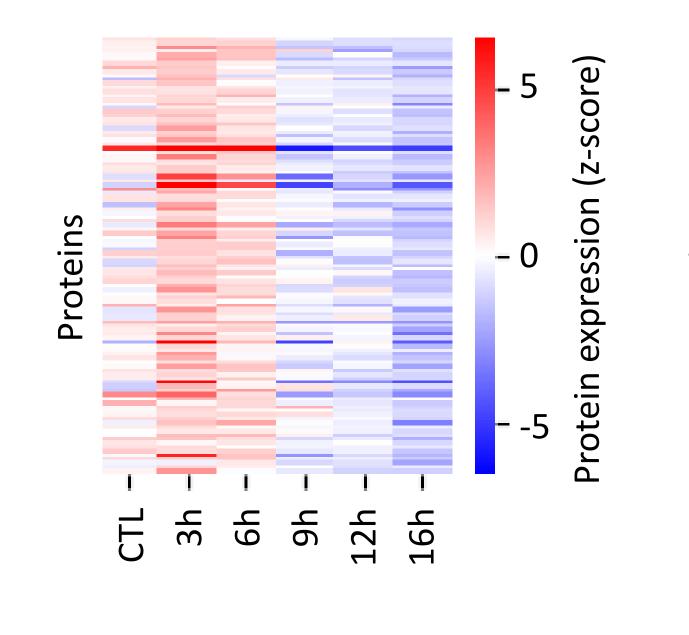


Isoform switch during mild hypothermia in HEK293 cells

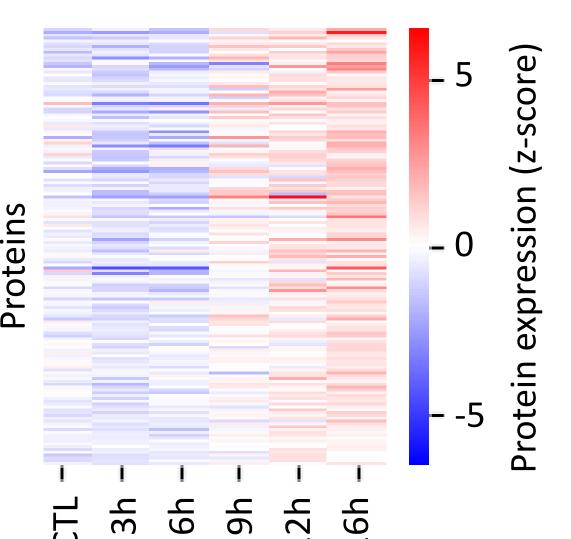
• CNOT1

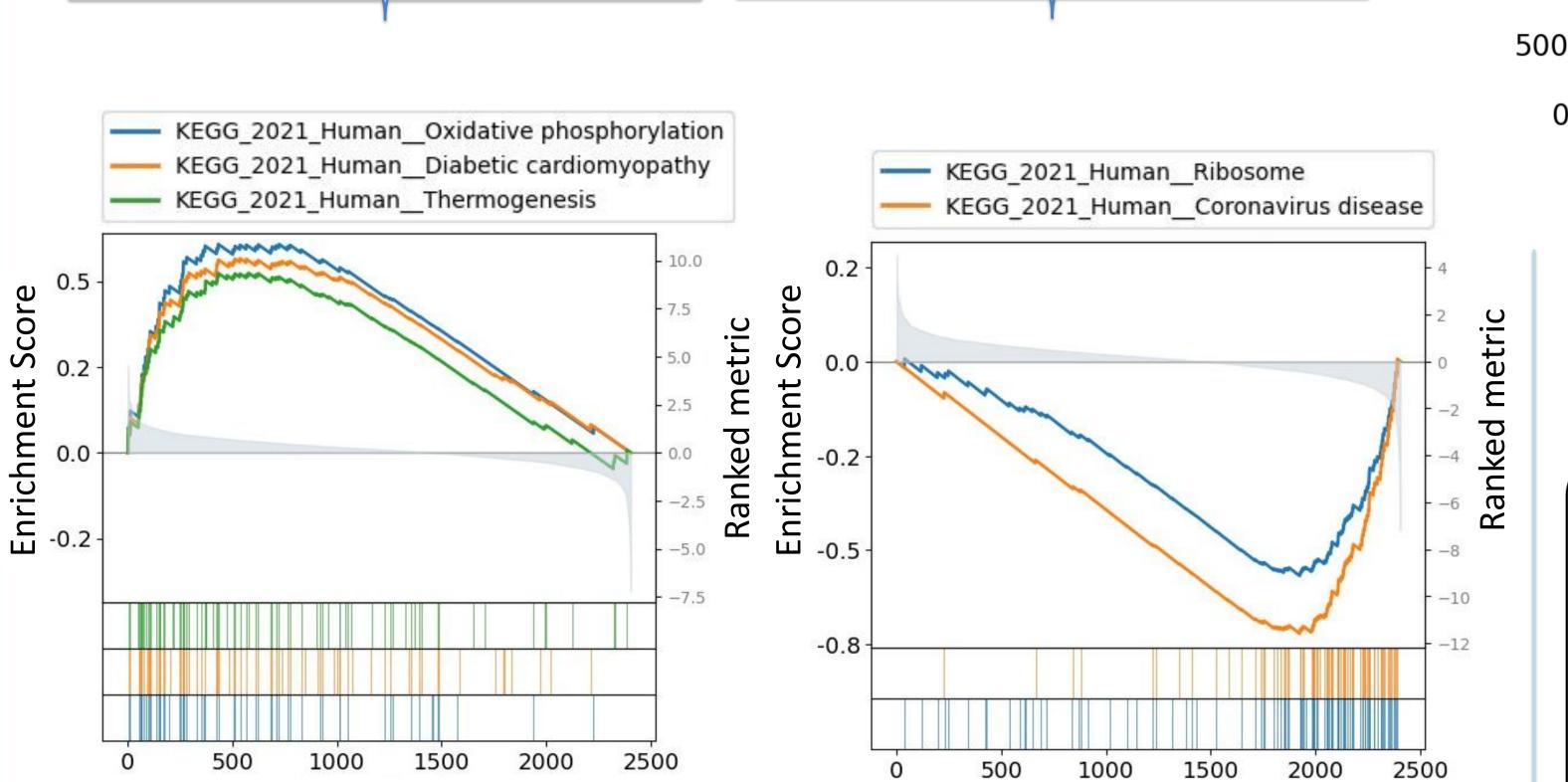
protein_coding_CDS_not_defined

Two mild hypothermia responses in HEK293 cells: thermogenesis and translation control



Gene Rank

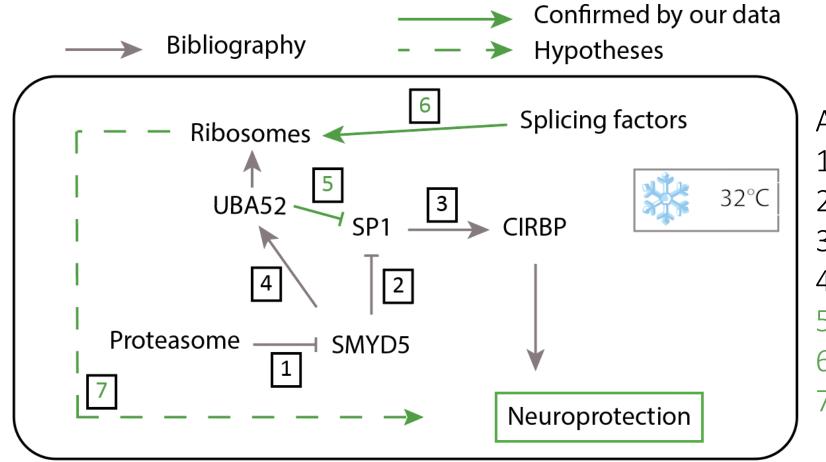




n = 15.223 genes ENST00000569263 protein_coding -log10 522 , -log10 30 Transcripts expression n = 641 from 67.460 transcripts adjp.value -01 05 Log2.FoldChange Log2 FoldChange expression log10(count) 345 Up regul. transcripts 37°C transcripts n = 67.460 transcripts 32°C transcripts 150 Down regul. transcripts 2500 2500 1500 는 1000

Schematic summary

Fanscript



10

log2(expression - count)

- At 32°C:
- 1. SMYD5 protein is degraded 2. Lack of SMYD5 leads to SP1 expression
- 3. SP1 induces CIRBP expression
- 4. SMYD5 is unable to trimethylated UBA52

3.0

log10 Total coding sequence (CDS) size (bp)

- 5. Lack of UBA52 activates SP1 expression
- 6. Isoform switch from long to short isoforms 7. Ribosomes appear key actors in MHR