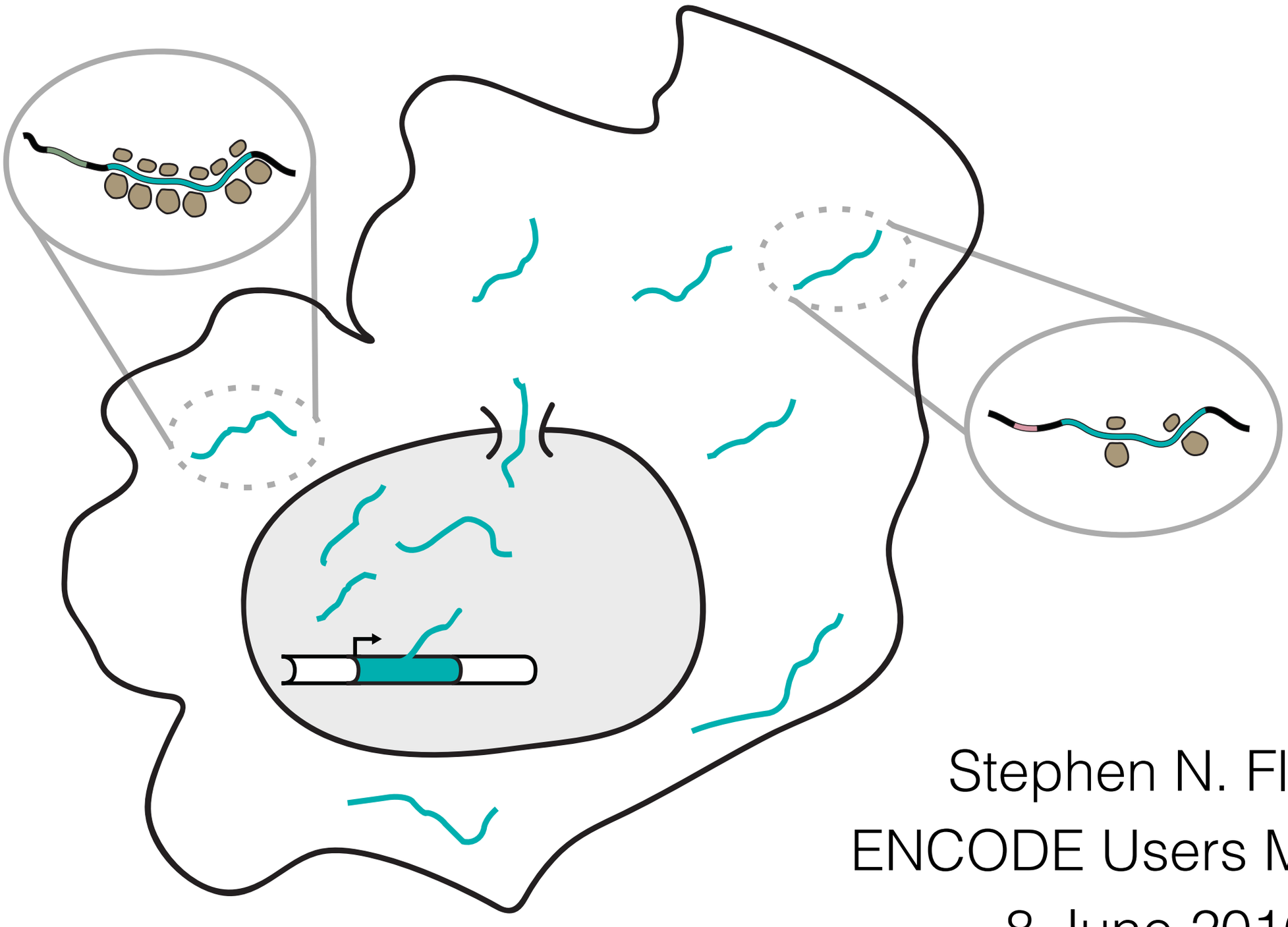
# The role of transcript-specific translation in human neuronal differentiation



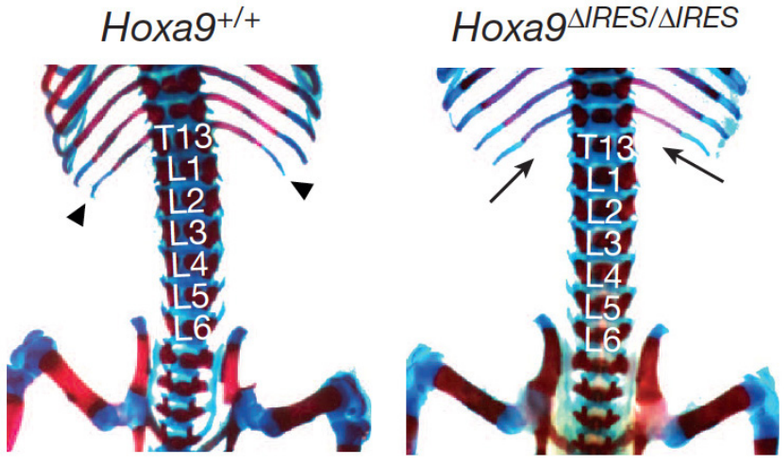
Stephen N. Floor

ENCODE Users Meeting

8 June 2016

# Control of protein translation achieves precise gene expression

Spatially or temporally localized function




Xue, S. *et al.* and Barna, M. (2015)

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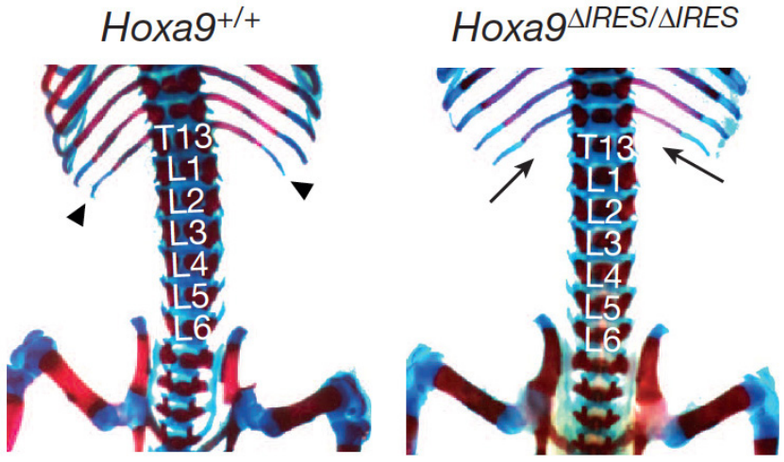
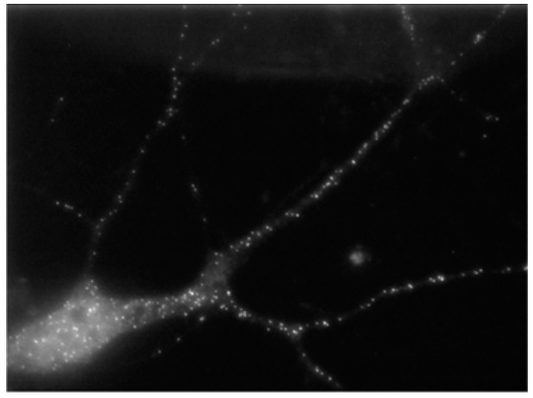



Xue, S. *et al.* and Barna, M. (2015)

*MAP2* mRNA



Batish, M. *et al.* and Tyagi, S. (2012)

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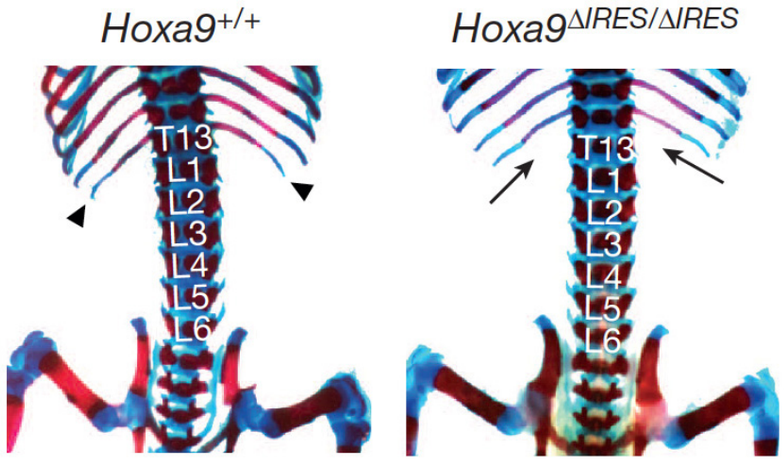


Xue, S. *et al.* and Barna, M. (2015)

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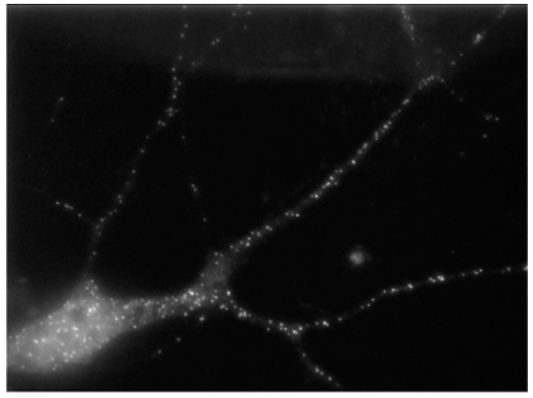
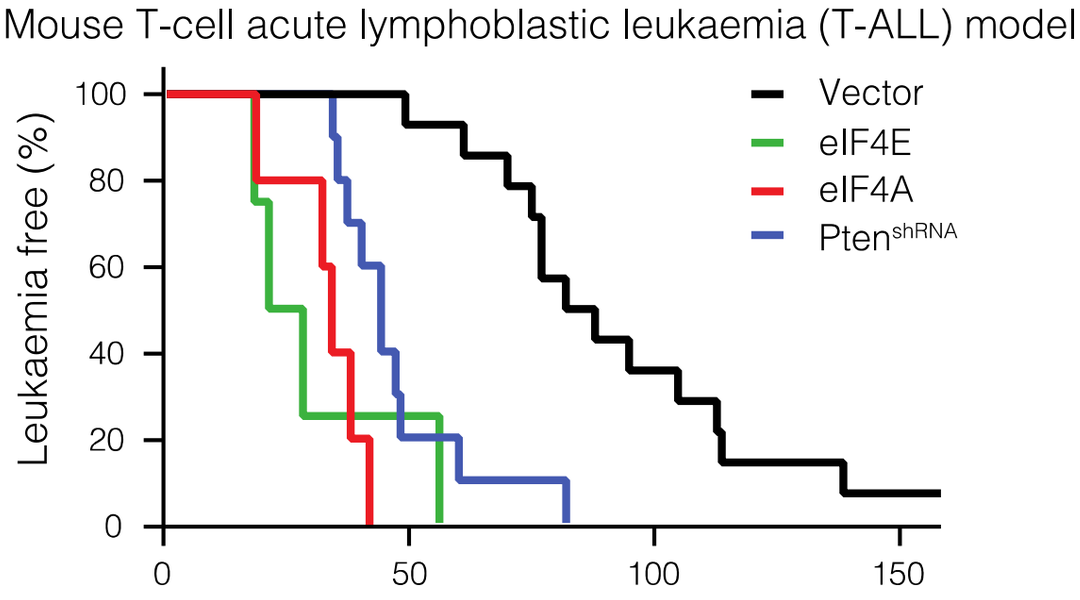


Batish, M. *et al.* and Tyagi, S. (2012)

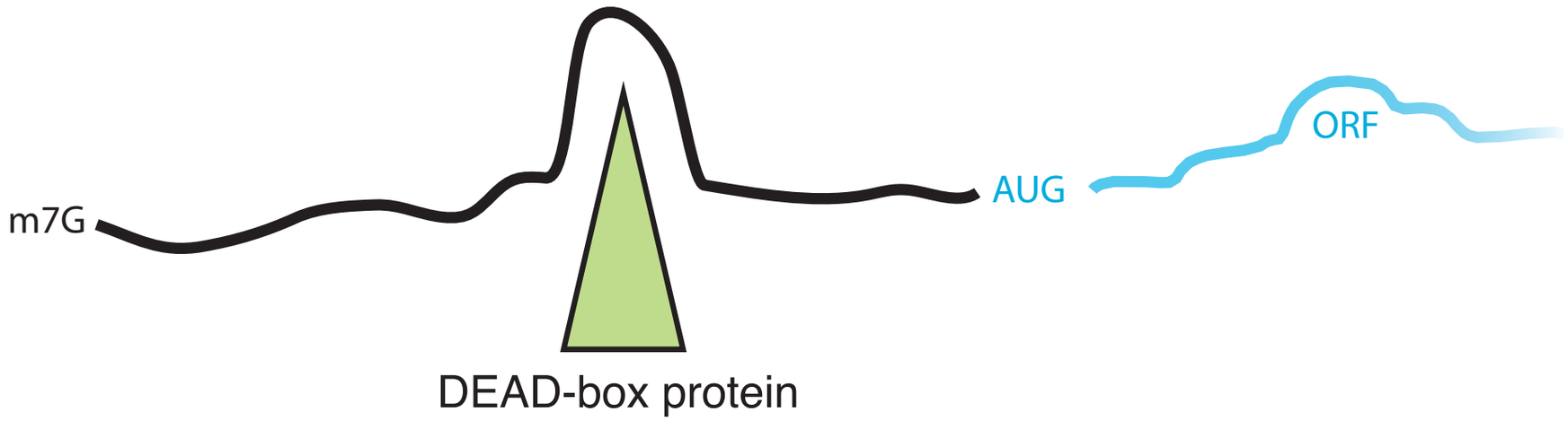
Suppression of proliferation




Wolfe A.L. and Singh, K. *et al.* and Wendel, H-G. (2014)

# Two models of translational control

I) Alleviate inhibition through the action of proteins (or RNAs)




II) Excise inhibitory regions by altered transcription or splicing

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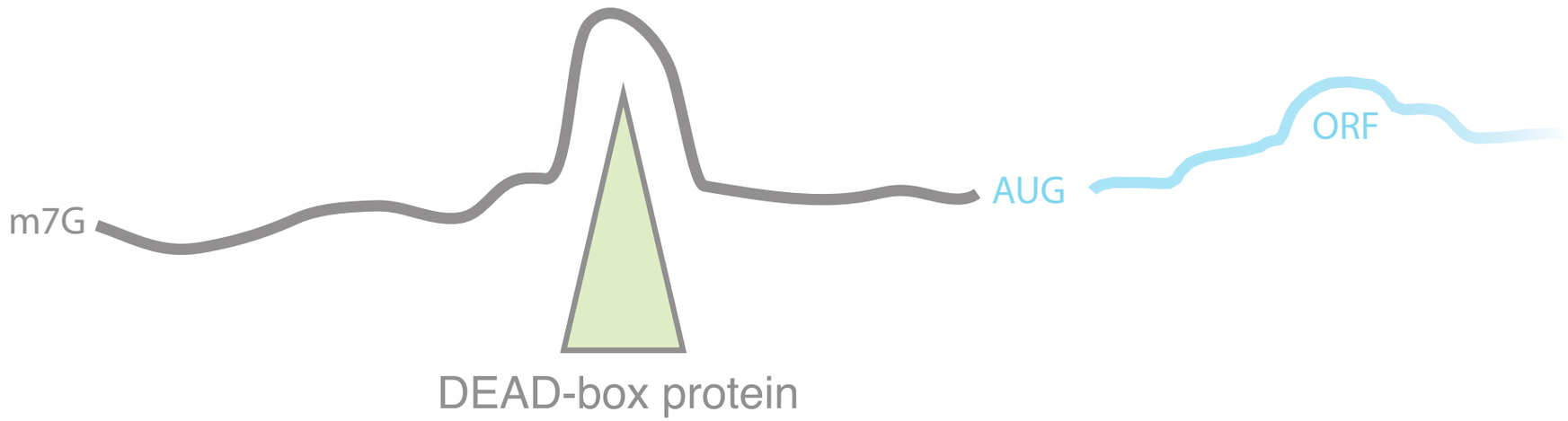
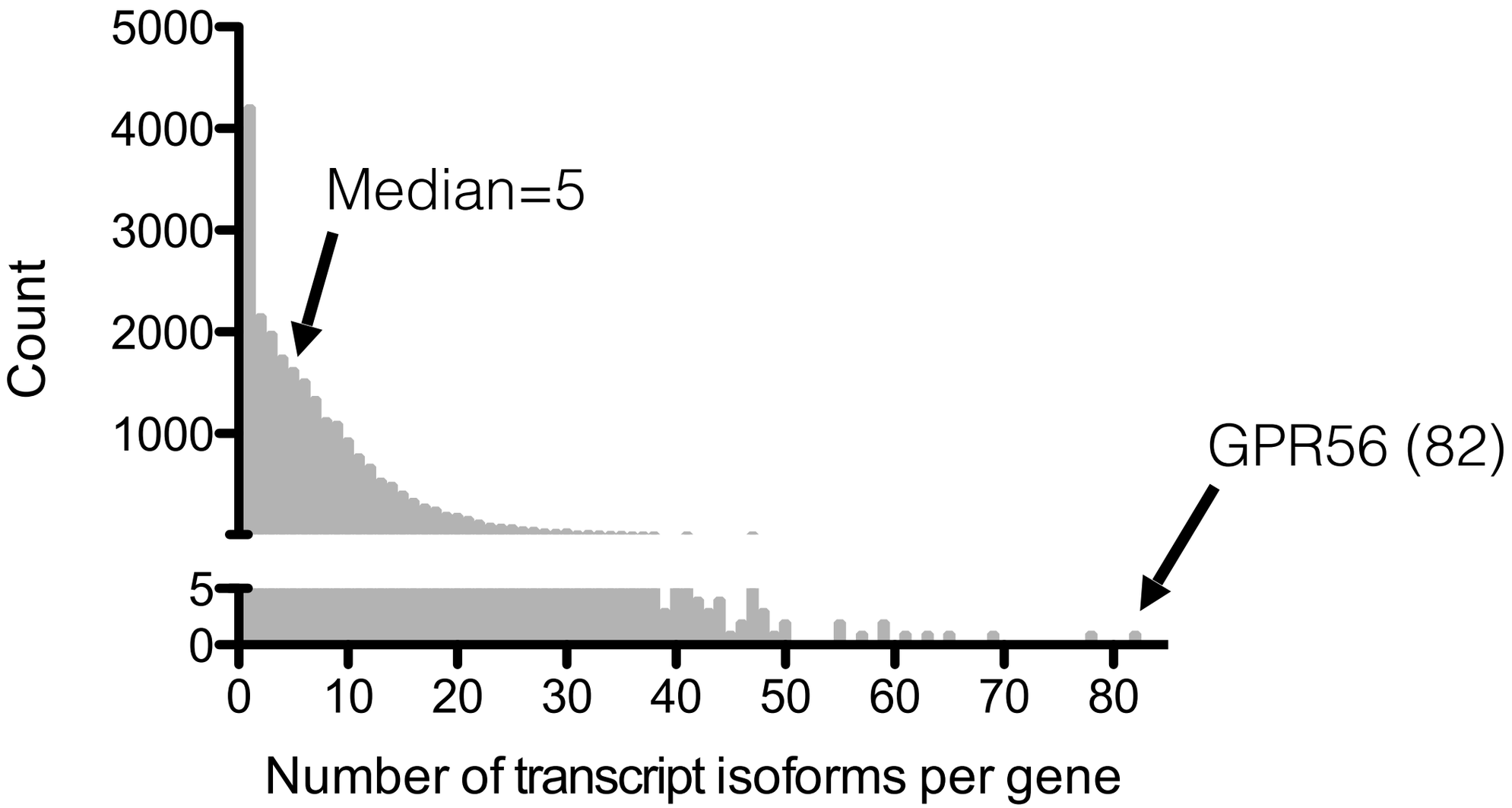



II) Excise inhibitory regions by altered transcription or splicing

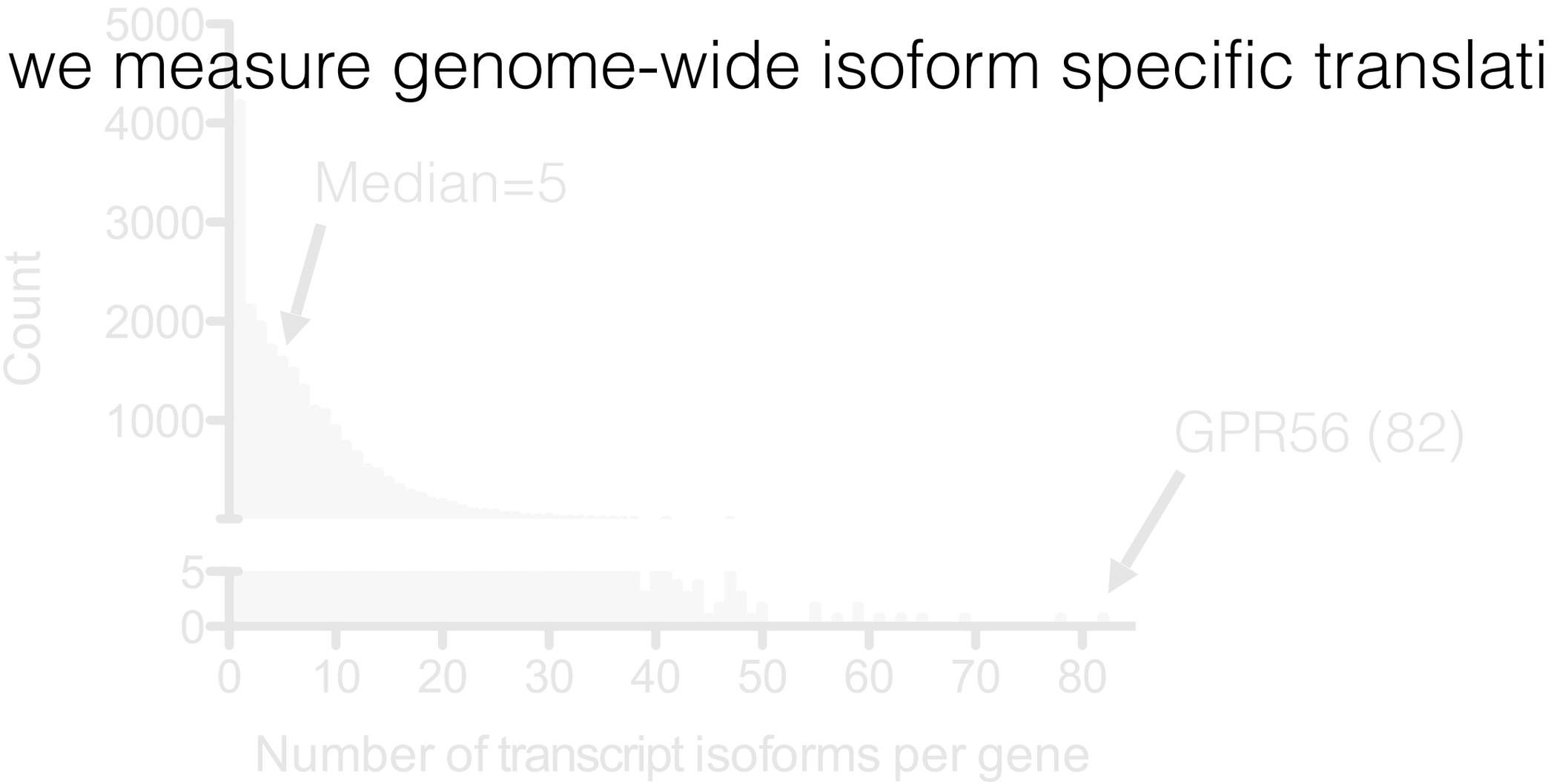
# Human genes have up to 80 annotated isoforms




Ensembl Release 75 protein coding genes

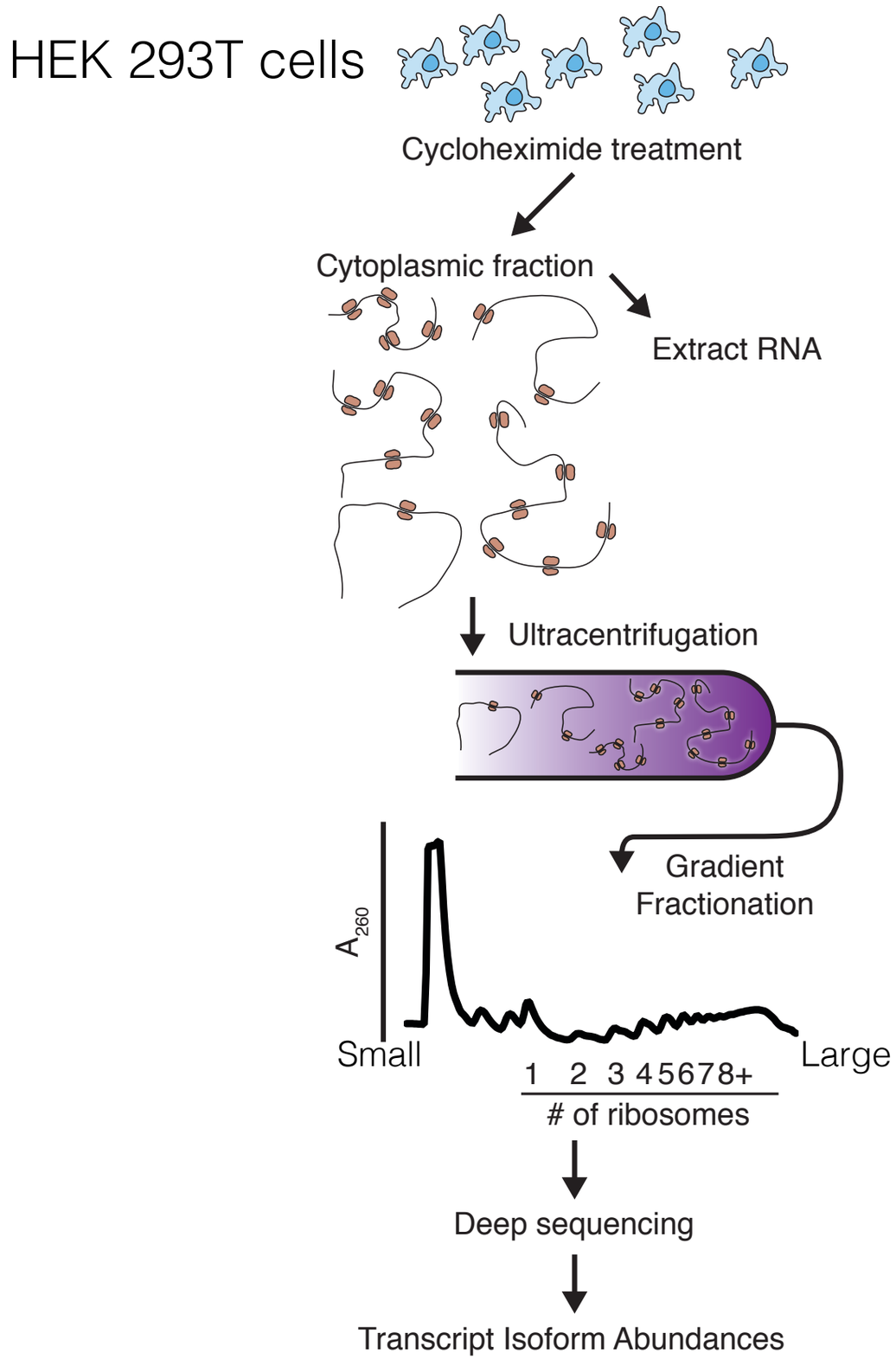
# Human genes have up to 80 annotated isoforms

Can we measure genome-wide isoform specific translation?



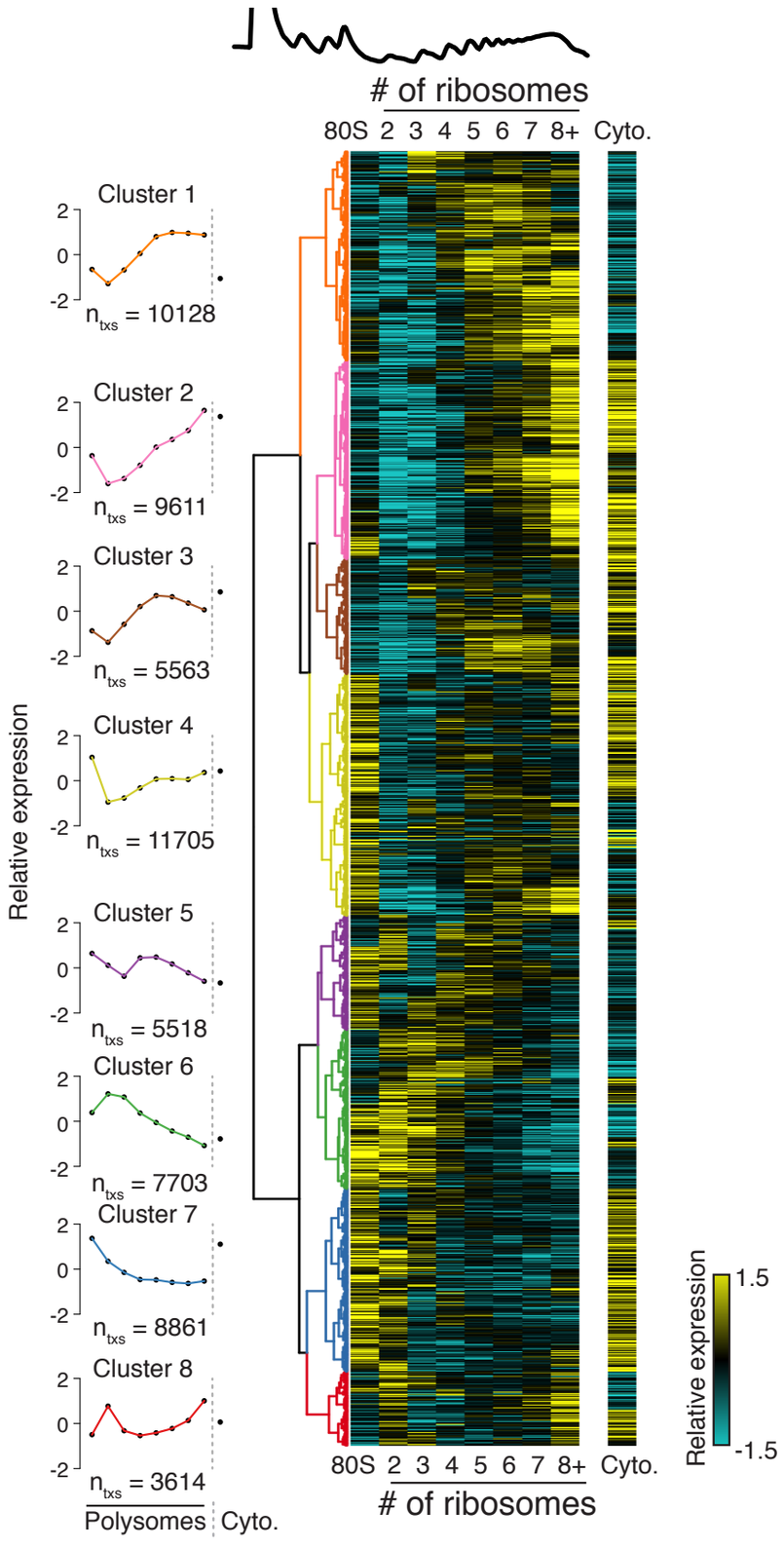

Ensembl Release 75 protein coding genes

# Transcript Isoforms in Polysomes sequencing (TrIP-seq)




**Floor, S.N.** and Doudna, J.A. (2016)

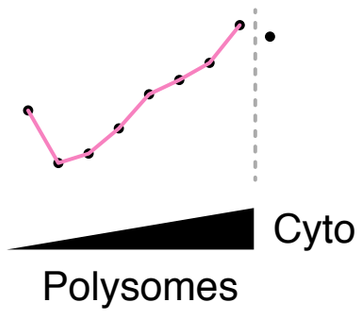
# Diverse transcript-isoform specific polysome occupancy




Hierarchical clustering of Spearman distance; partitioning by dendrogram height
62,703 transcript isoforms represented

# Dependence of transcript features on translatability

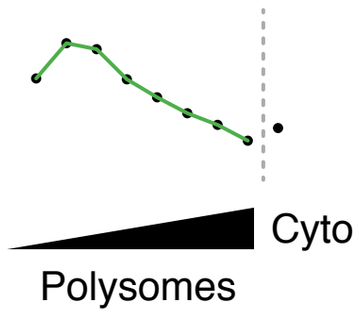
High polysomes




$n_{txs}$ = 19739

vs

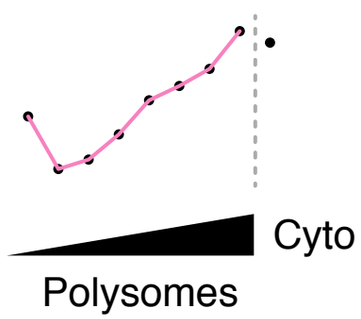
Low polysomes




$n_{txs}$ = 7703

# Dependence of transcript features on translatability

High polysomes

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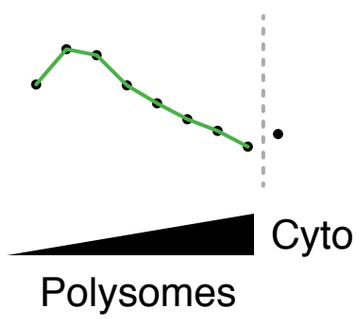


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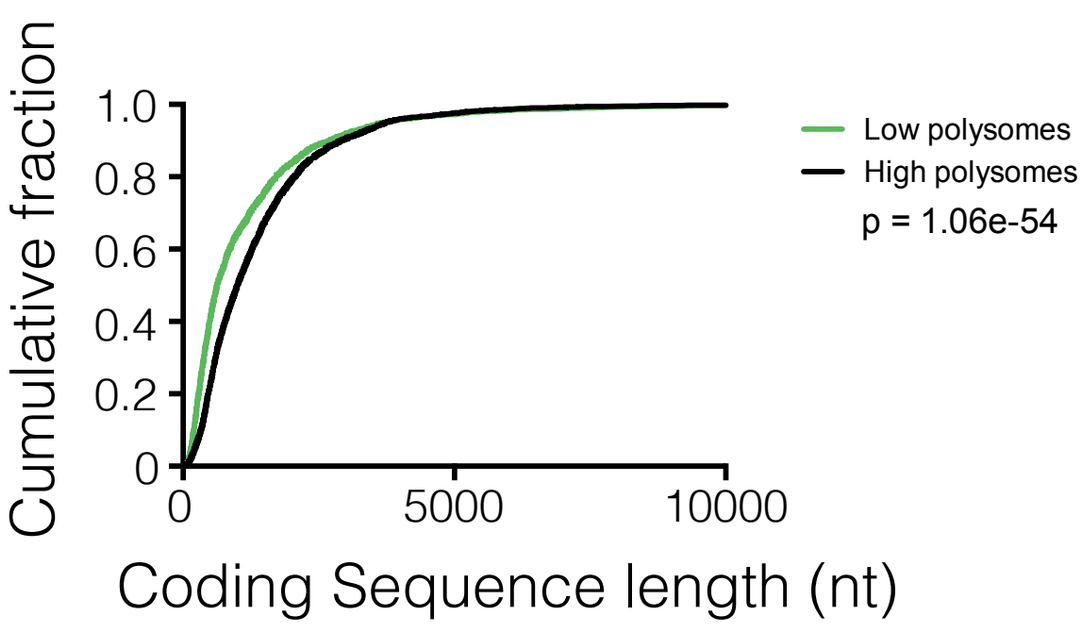

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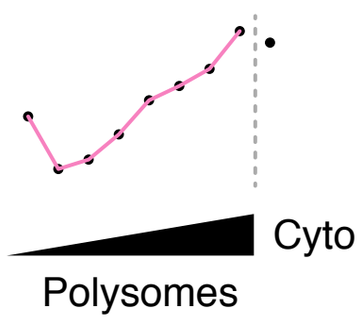
High polysomes

vs

Low polysomes

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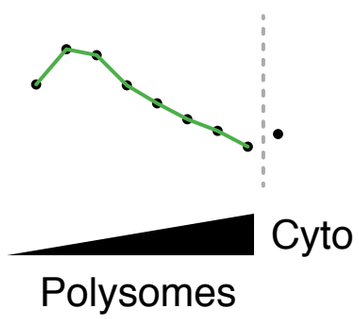


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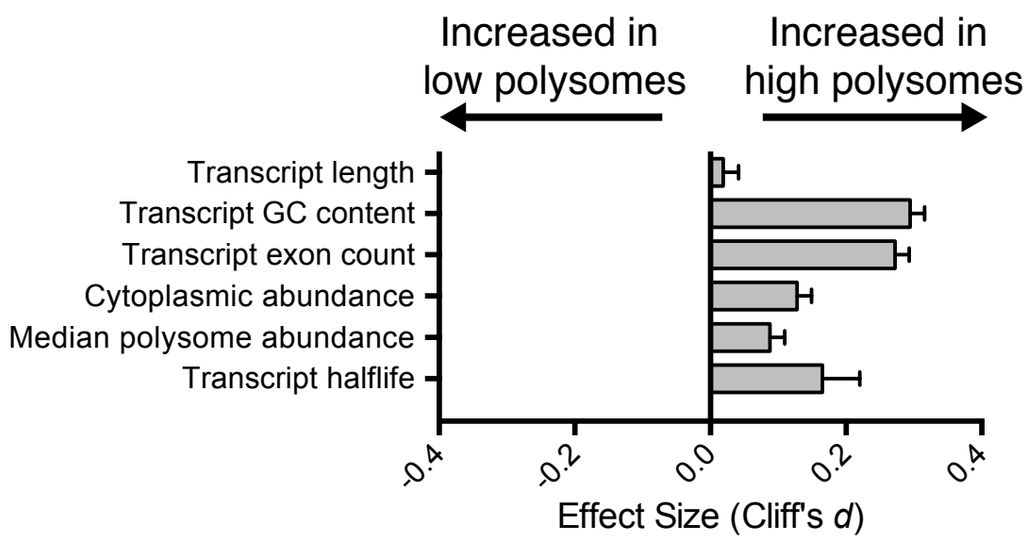
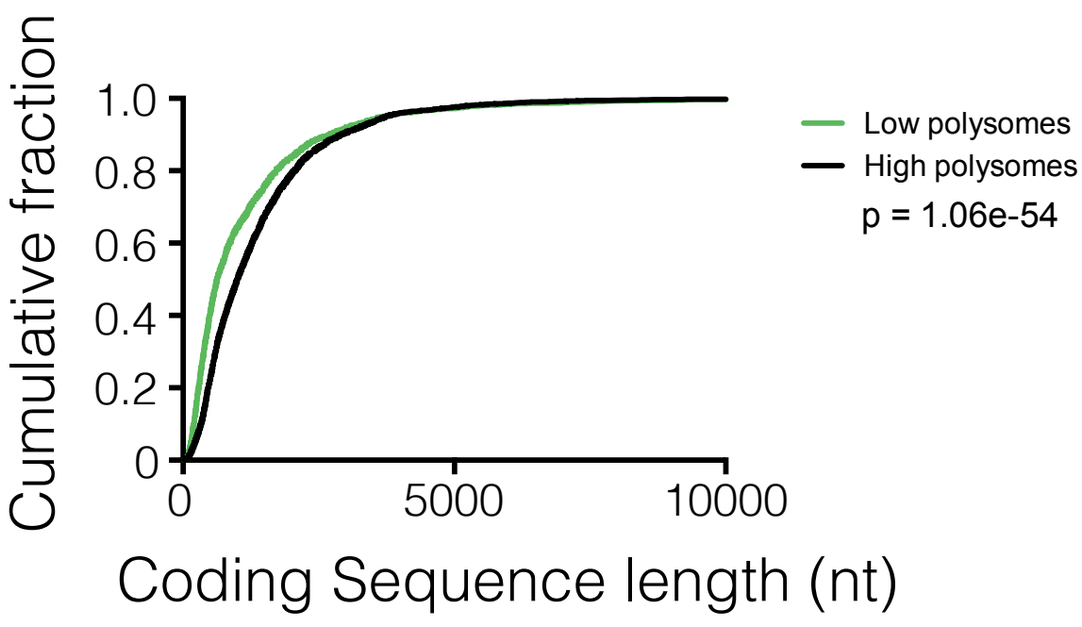
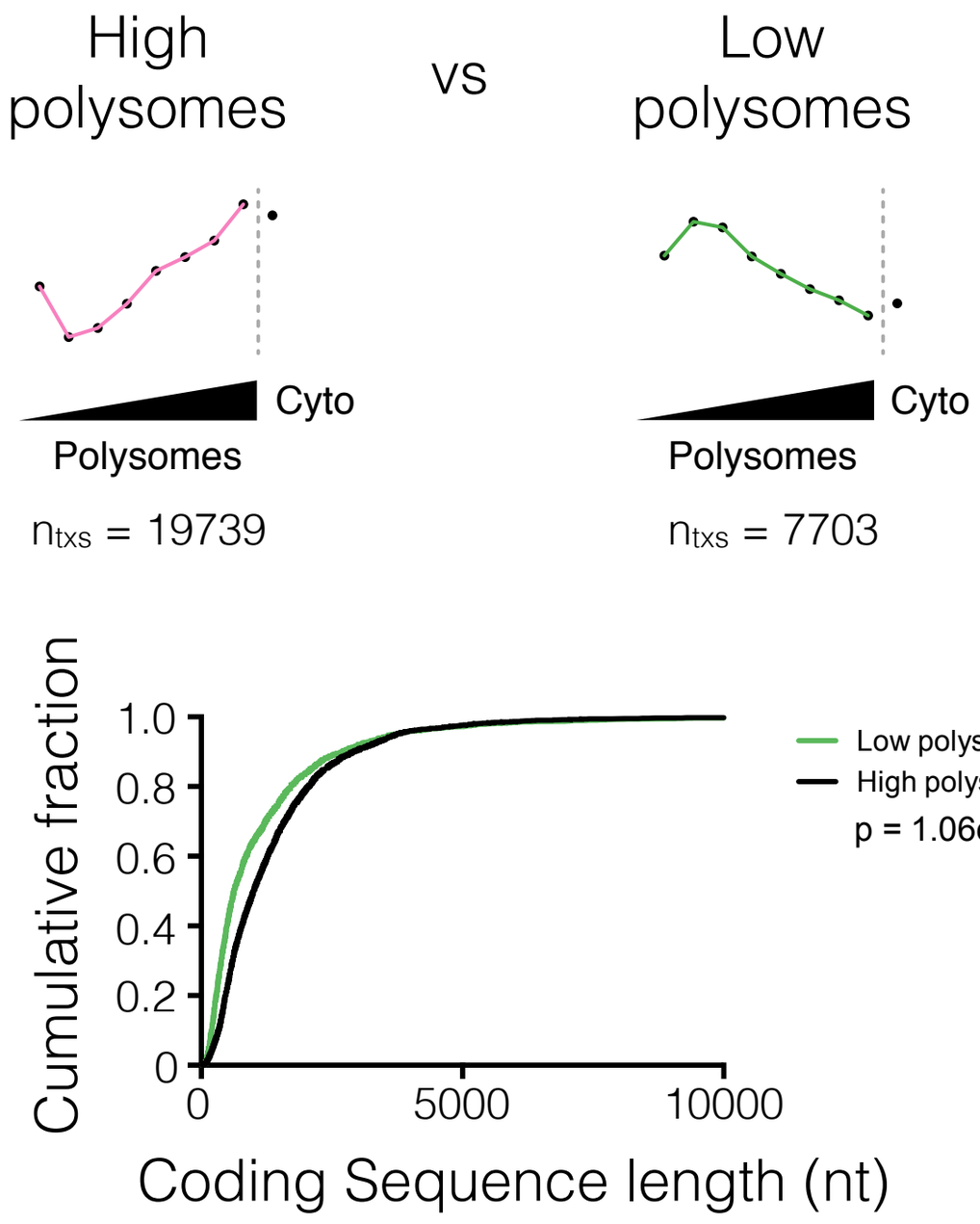
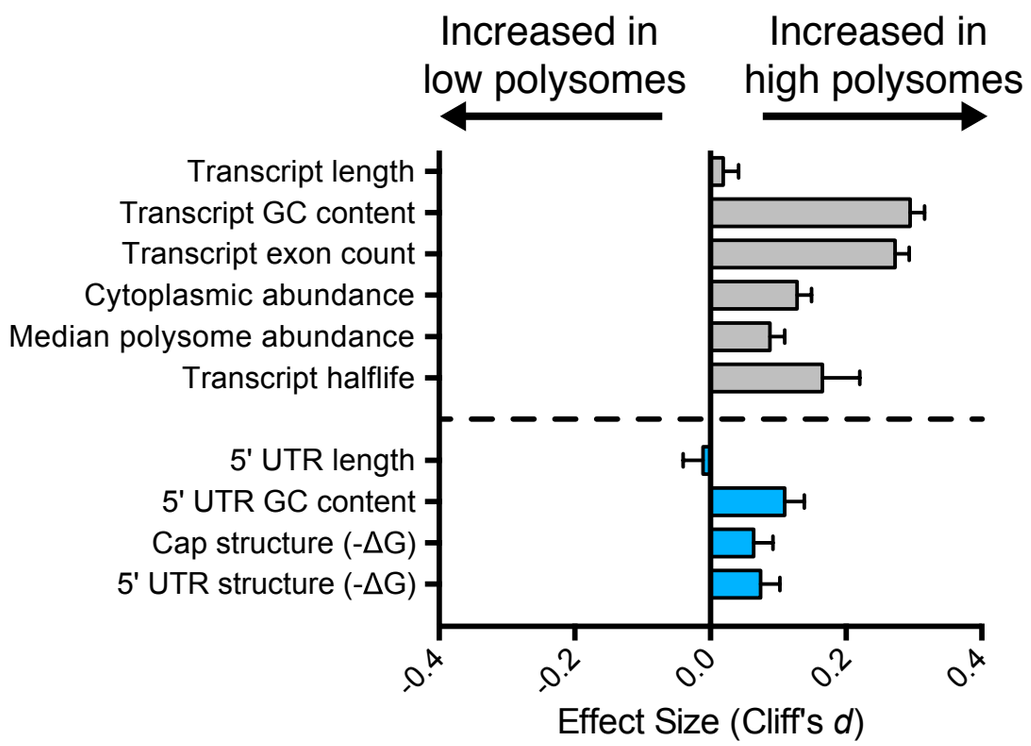


# Dependence of transcript features on translatability



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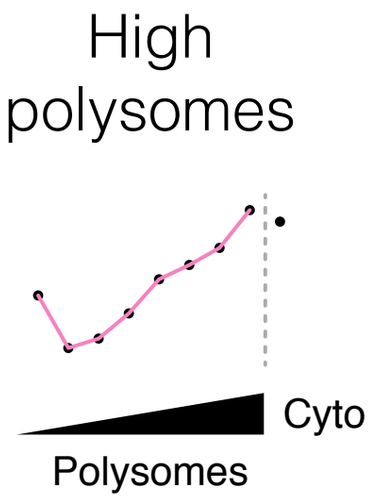
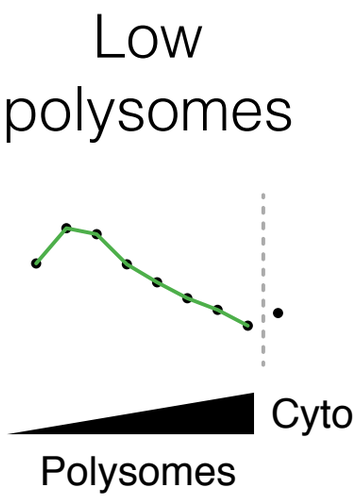



vs

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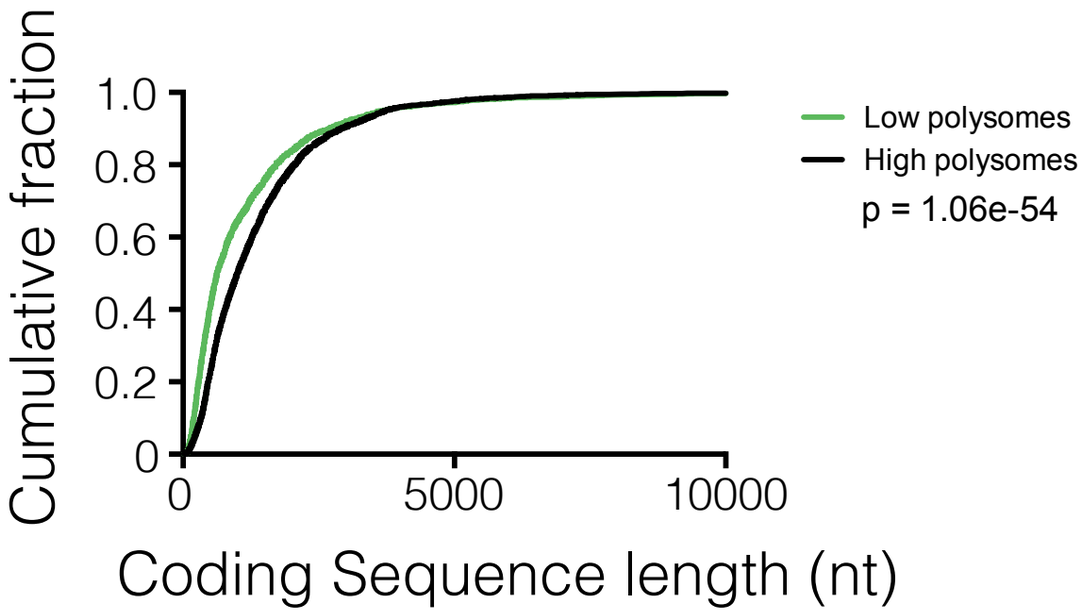


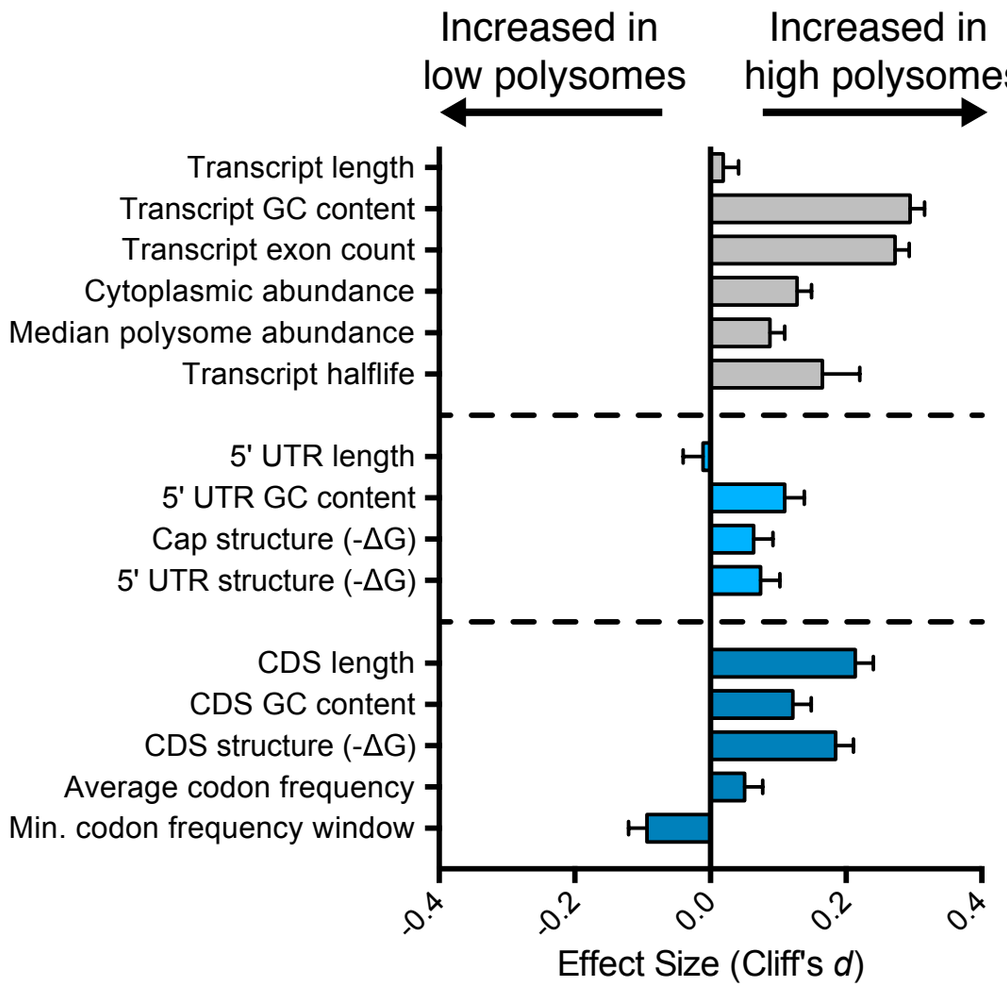

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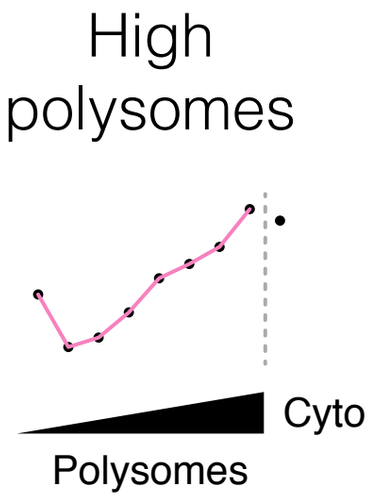
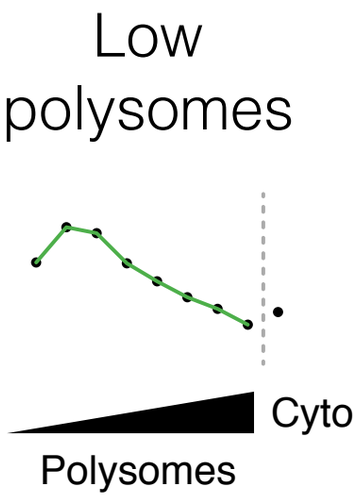



vs

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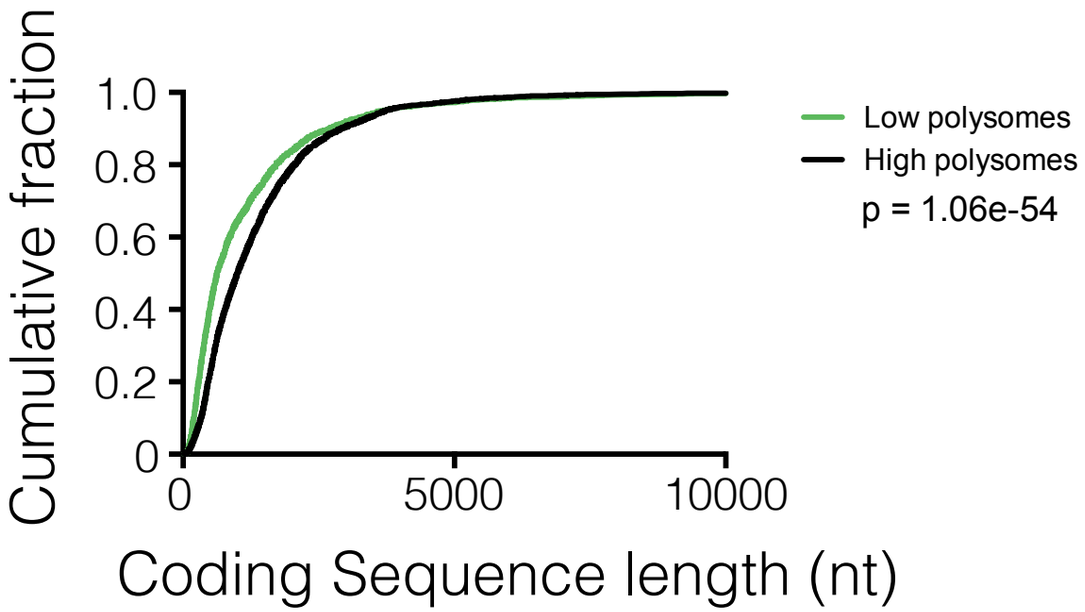
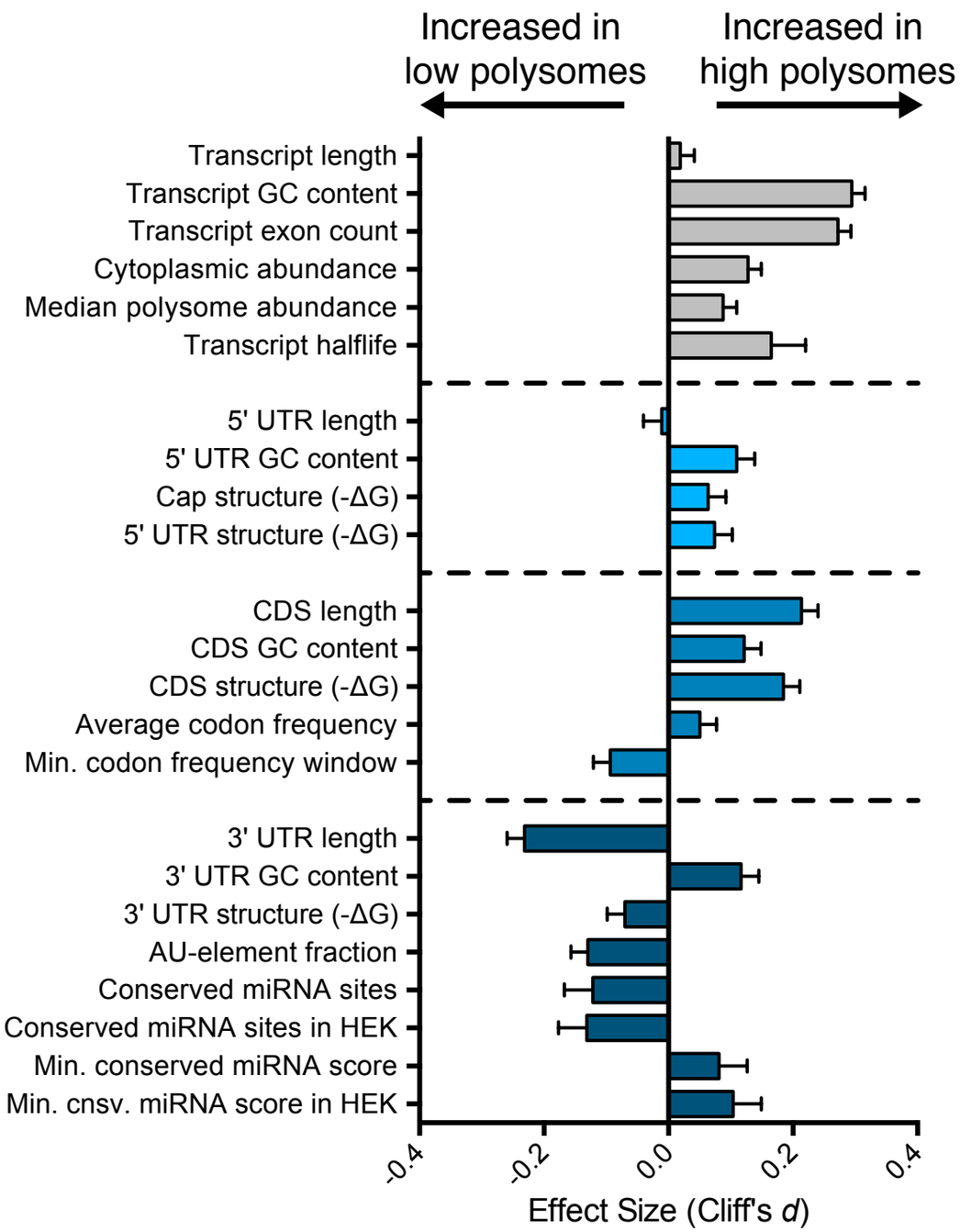
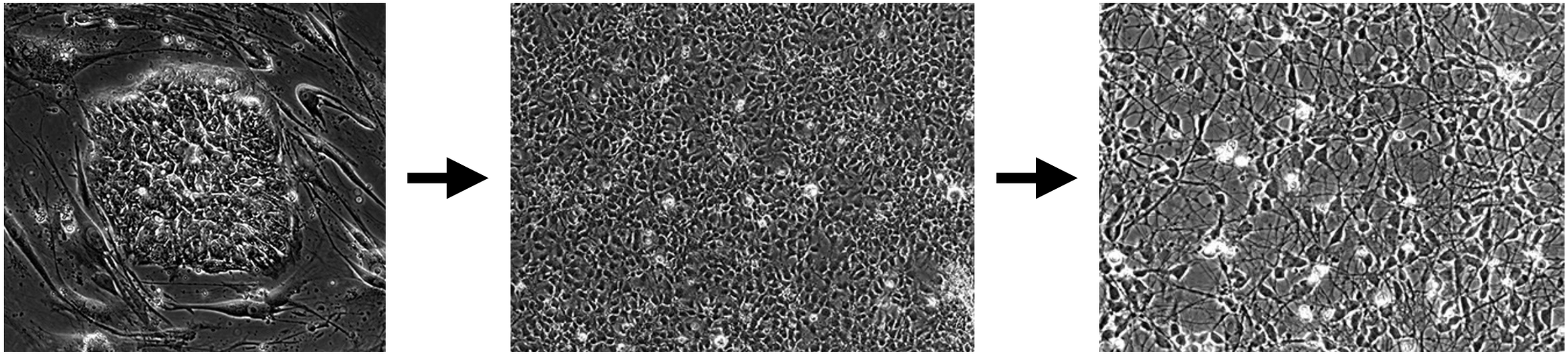


# Currently analyzing translation in differentiating neurons



Human ES cells

Neural progenitor cells

Neurons

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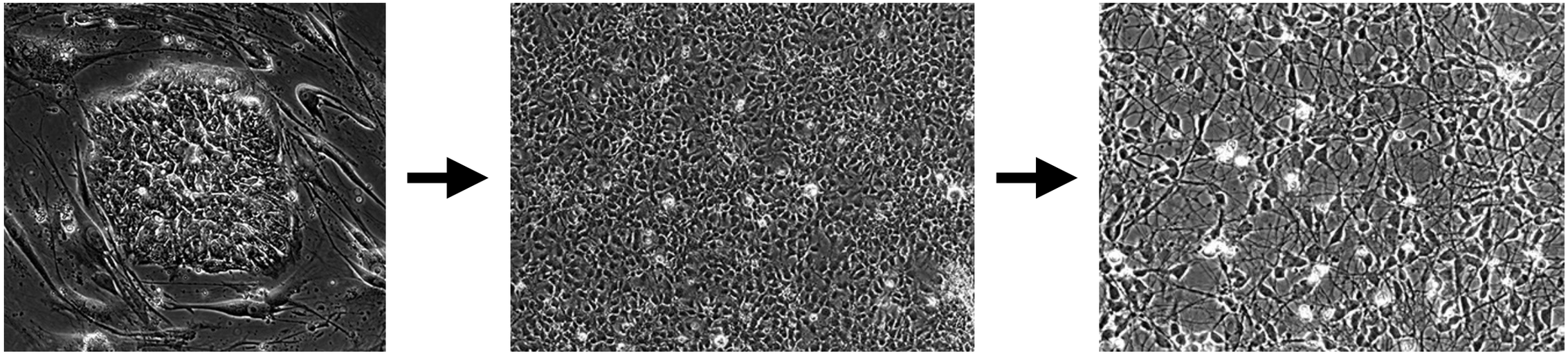

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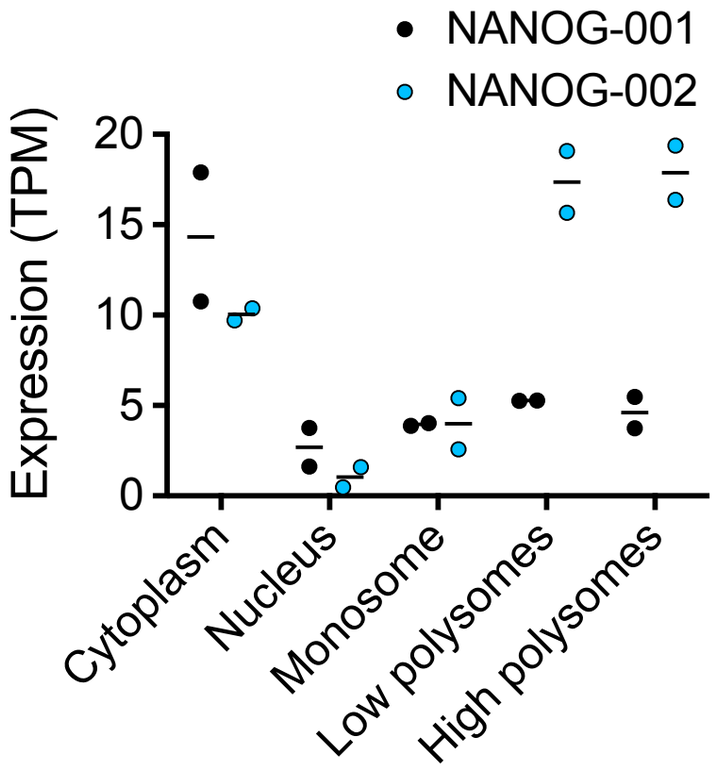
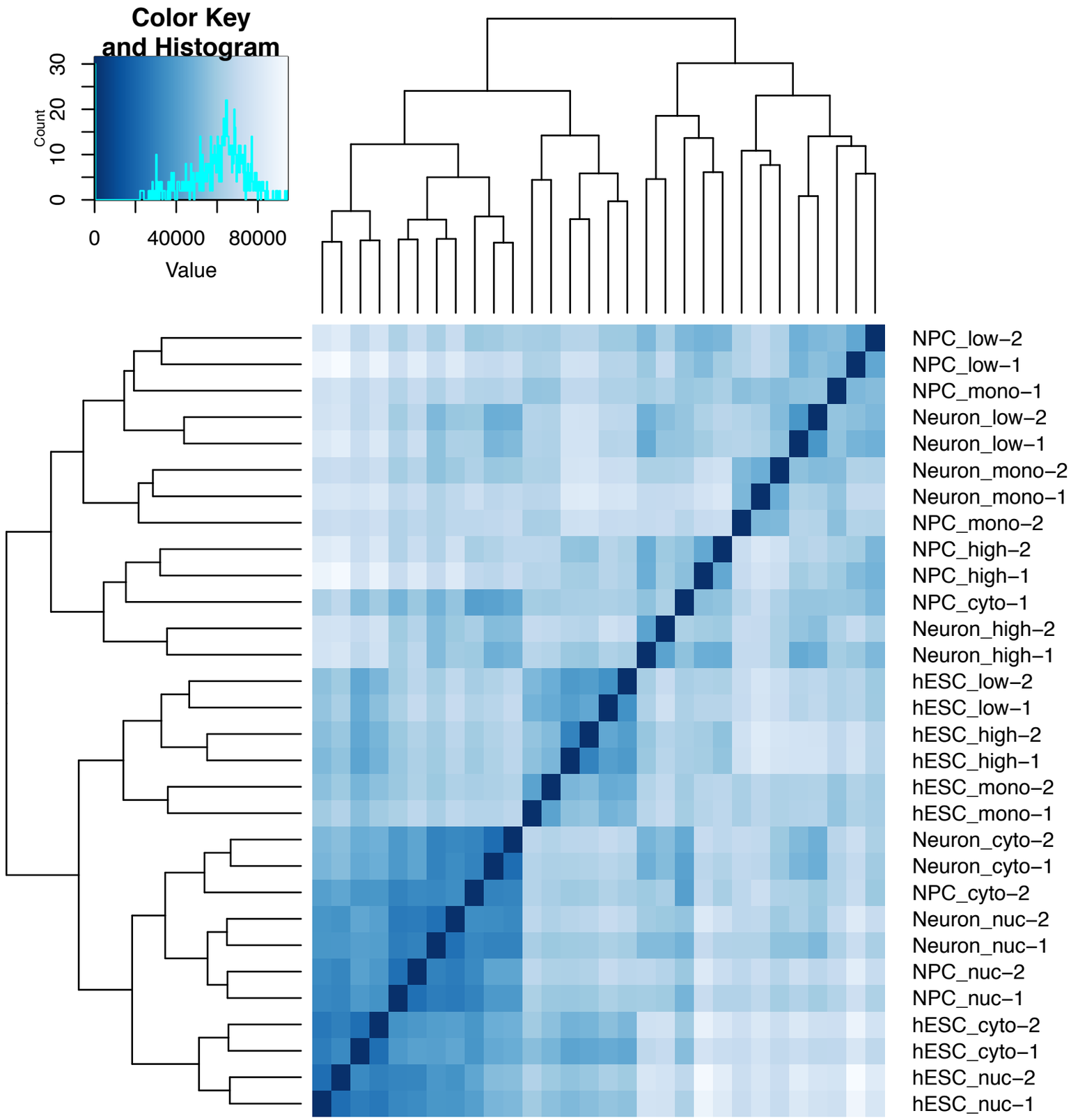


# Translated RNA clusters by cell type



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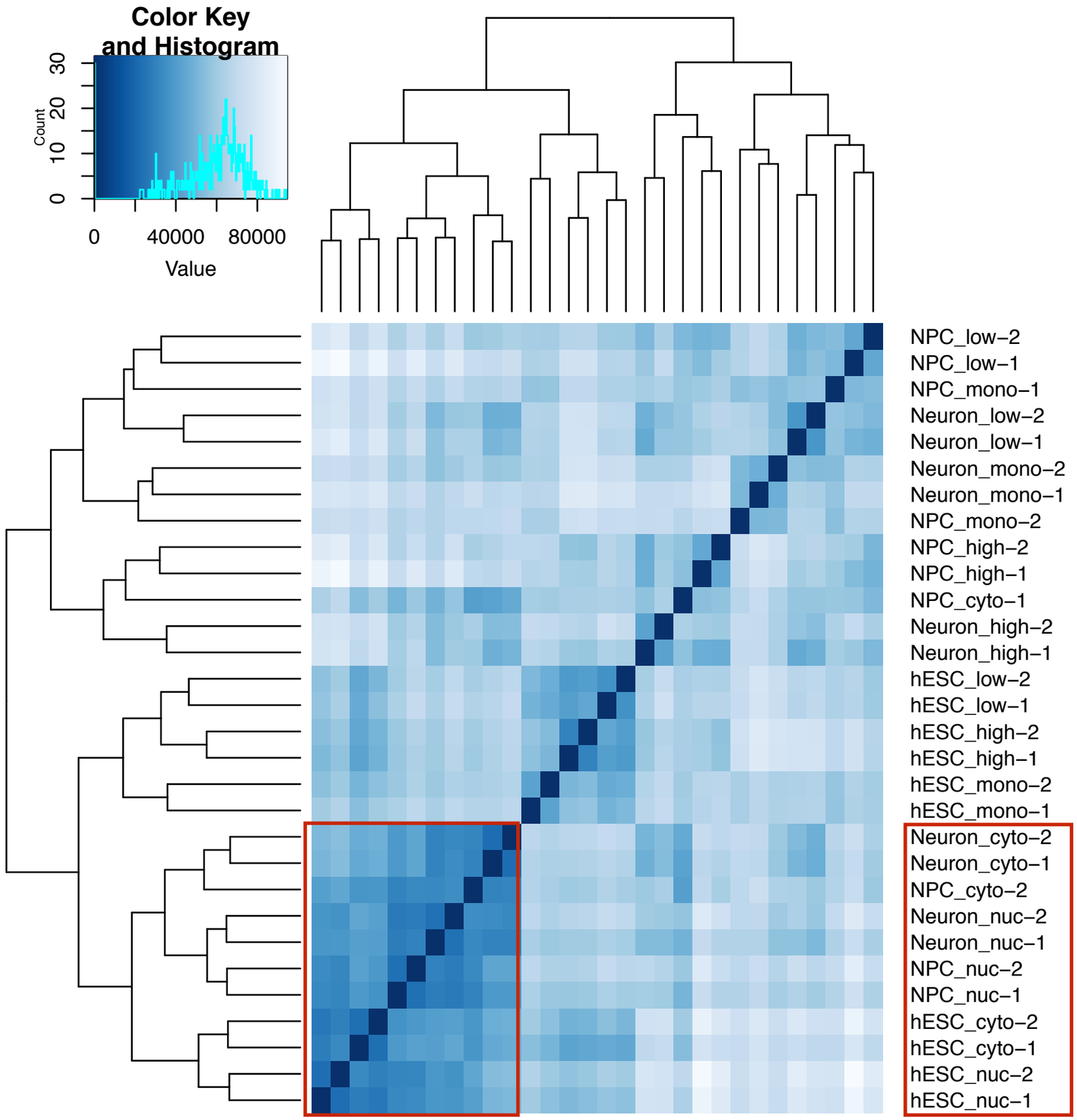
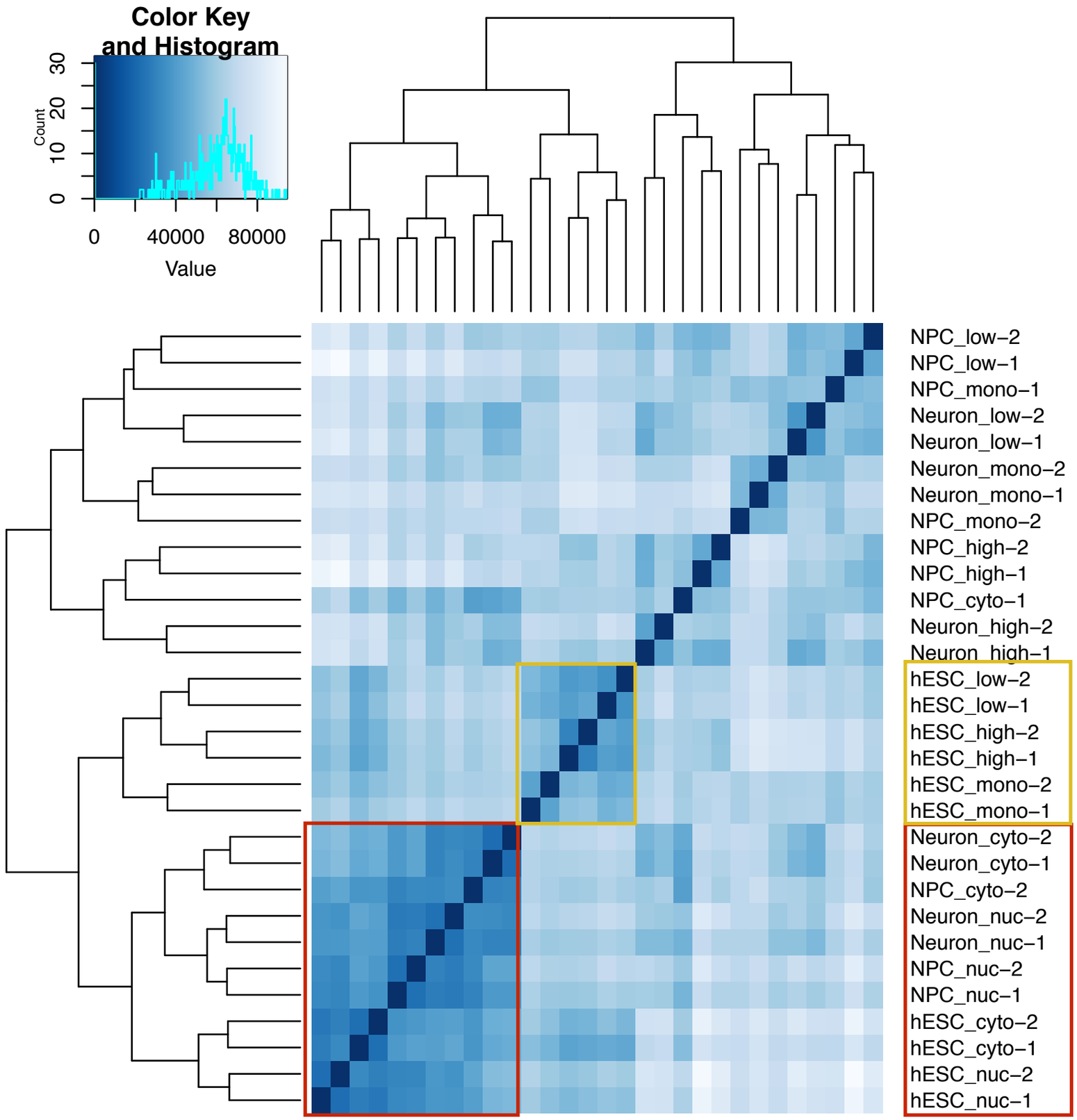



Total RNA

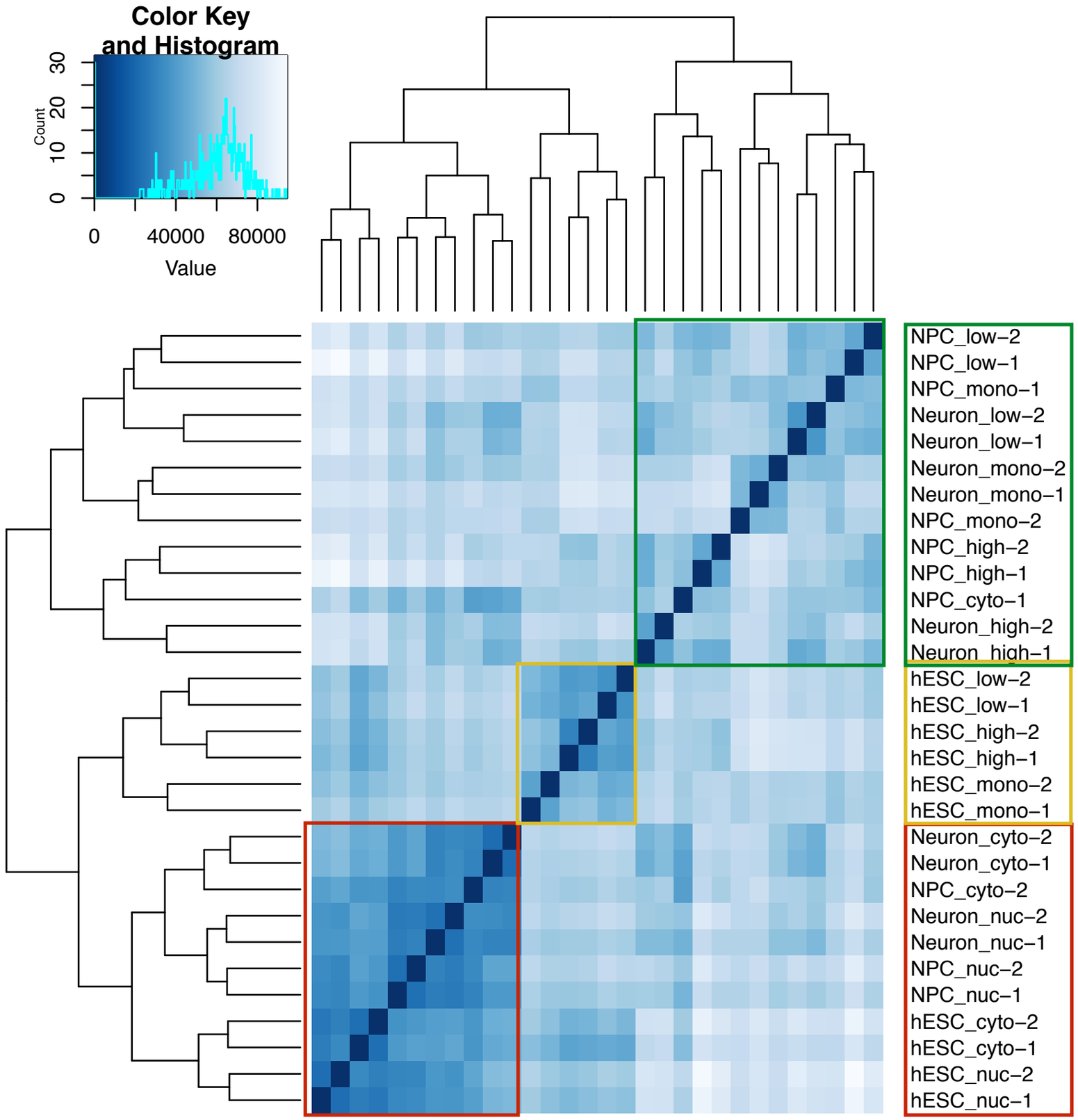
# Translated RNA clusters by cell type




hESC
polysomal RNA

Total RNA

# Translated RNA clusters by cell type

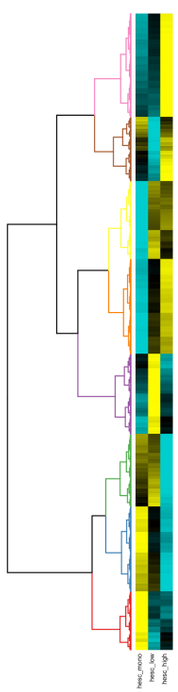



Neuron/NPC polysomal RNA

hESC polysomal RNA

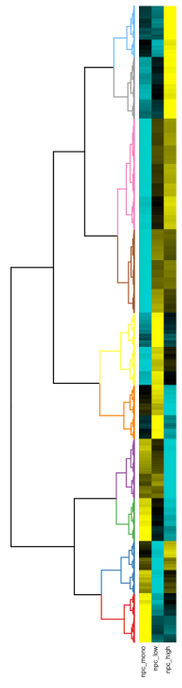
Total RNA

# 3′ UTRs have cell type dependent effects on translation



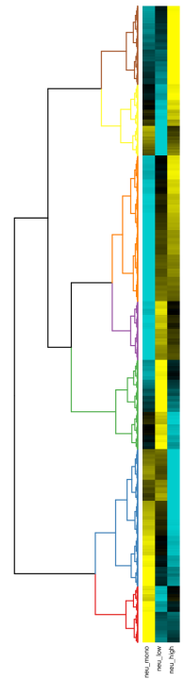
hESCs

47096 transcripts



NPCs

49002 transcripts

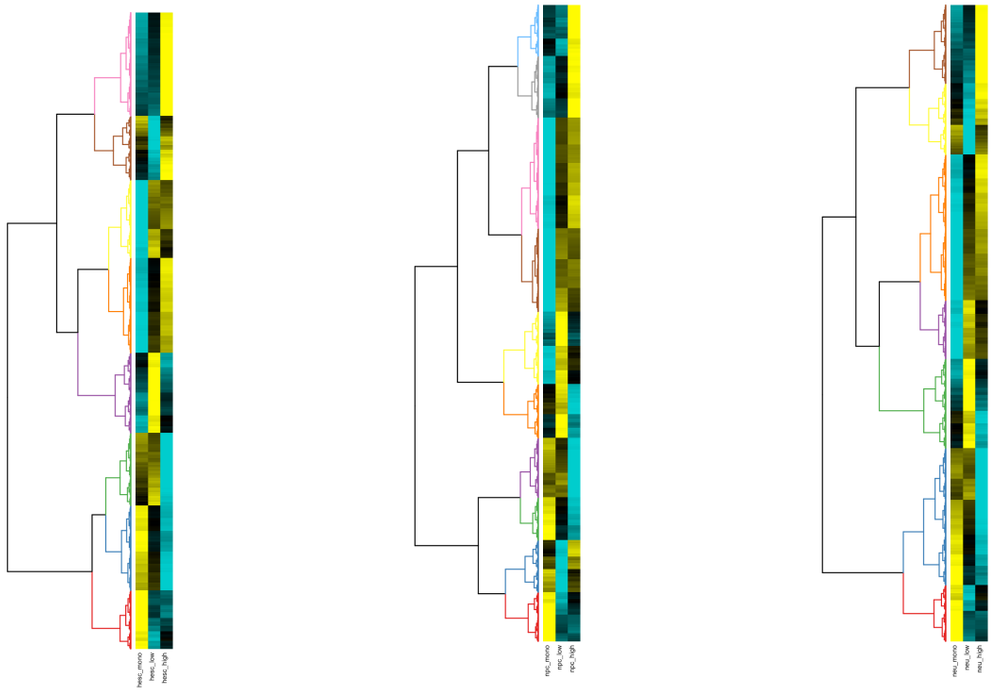


Neurons

47766 transcripts

Hierarchical clustering of regularized log transformed data by Euclidean distance
cluster partitioning by dendrogram height

# 3′ UTRs have cell type dependent effects on translation



hESCs

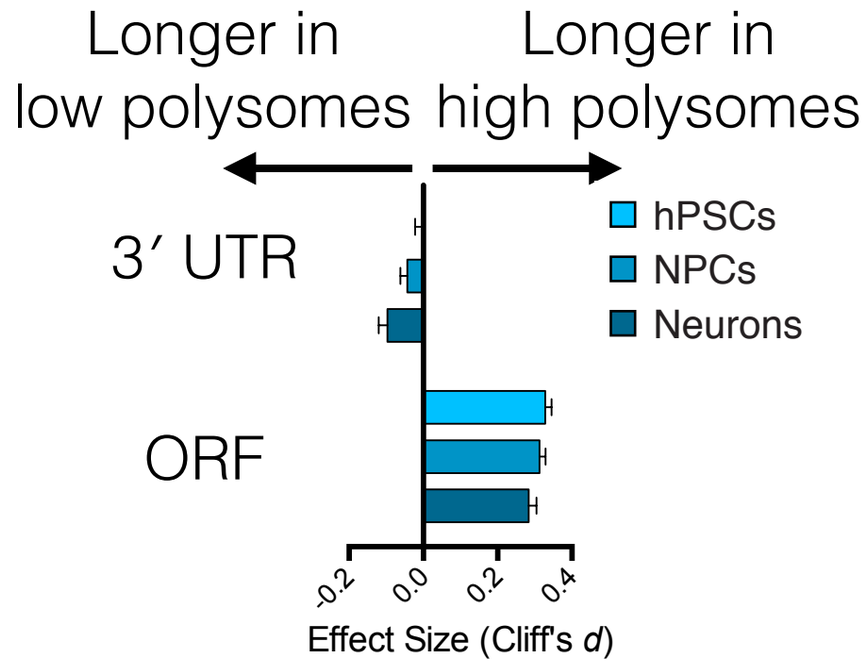
47096 transcripts

NPCs

49002 transcripts

Neurons

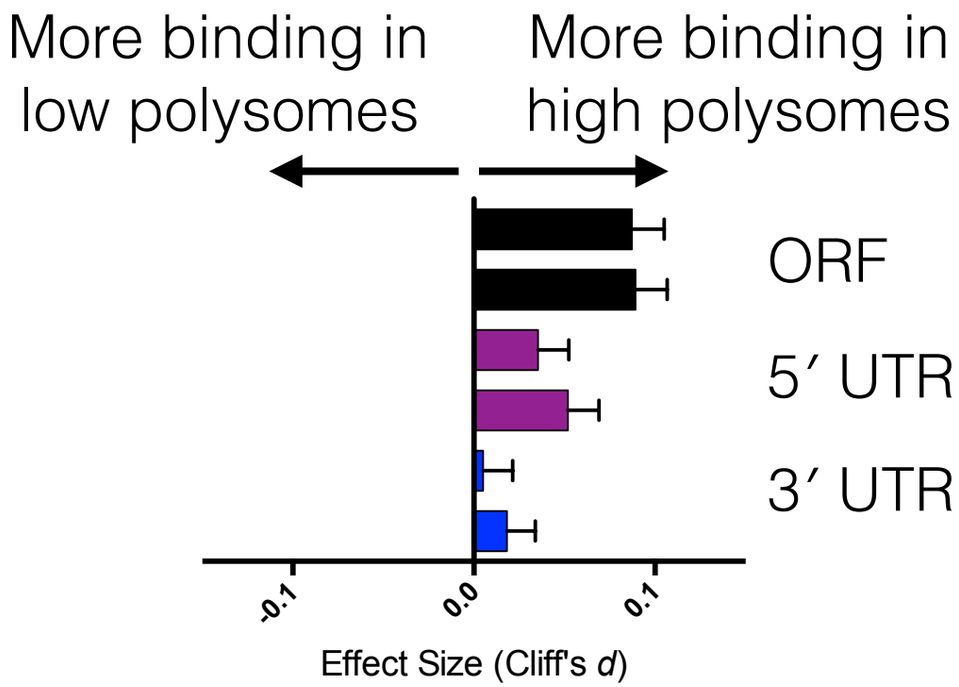
47766 transcripts




Features contrasted between transcripts of the same gene

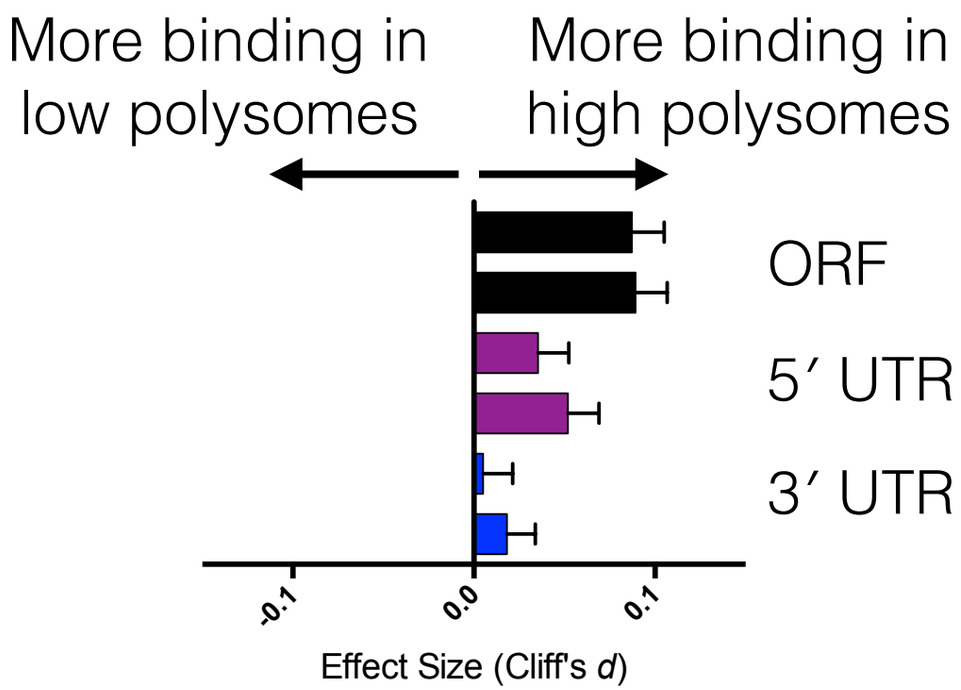
Hierarchical clustering of regularized log transformed data by Euclidean distance
cluster partitioning by dendrogram height

# Insights from ENCODE RNA binding protein data

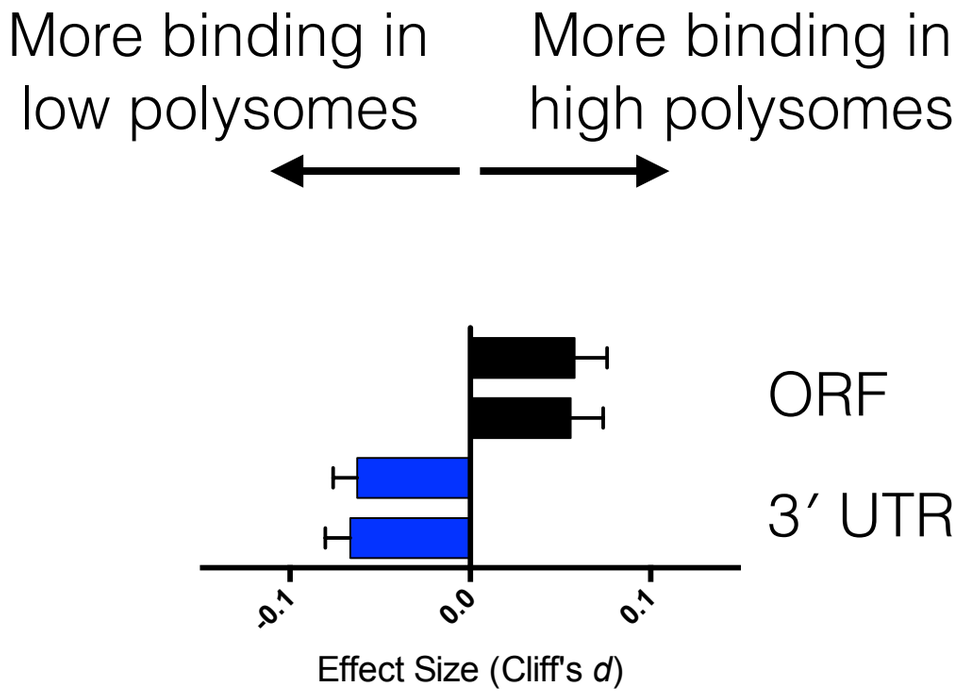



FMR1

# Insights from ENCODE RNA binding protein data

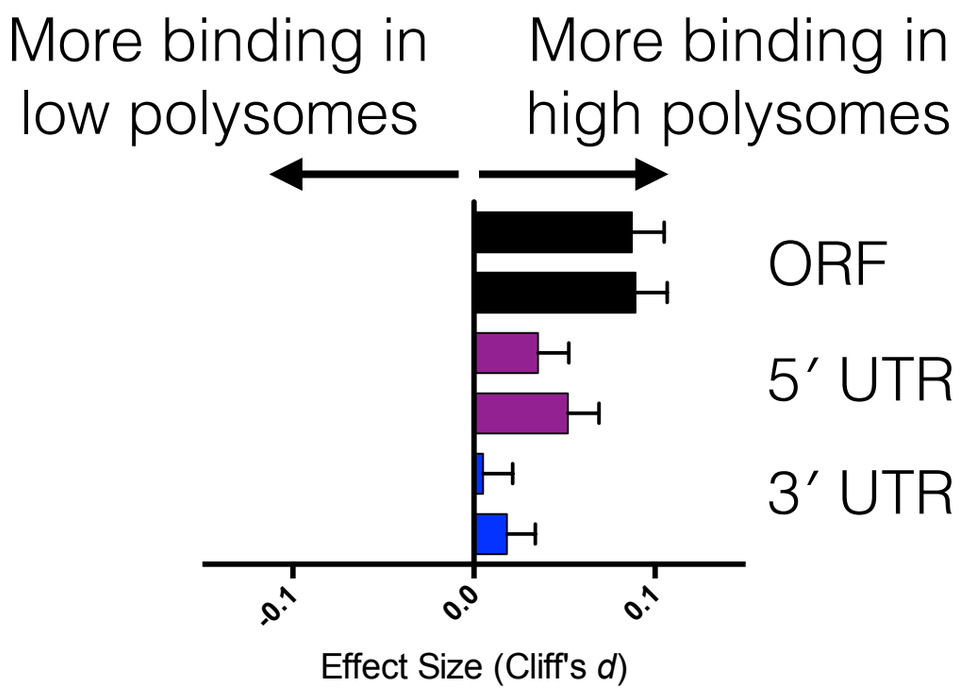


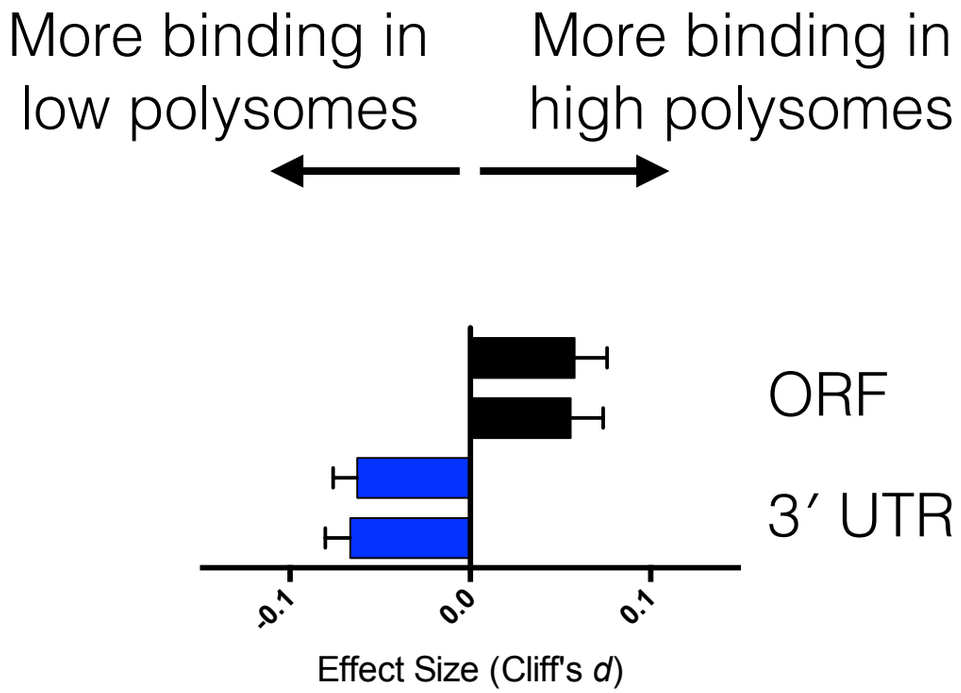

FMR1




SF3B4

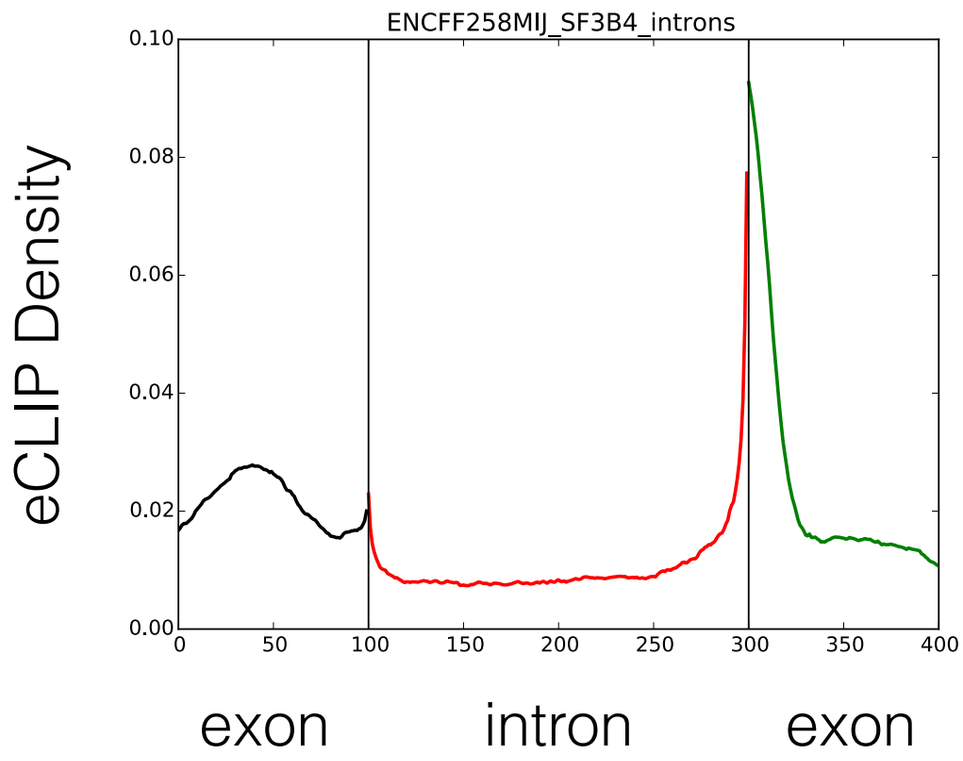
# Insights from ENCODE RNA binding protein data




FMR1

SF3B4



# Acknowledgements


Collaborators:

DDX3:
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Eckhard Jankowsky

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Yun Bai
Akshay Tambe
Amy Lee

Doudna Lab

Computing:

Doudna lab
Pachter lab
LBL
UC Berkeley BRC

hhmi

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