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Article

Single-Cell Analysis of Human Pancreas Reveals Transcriptional Signatures of Aging and Somatic Mutation Patterns

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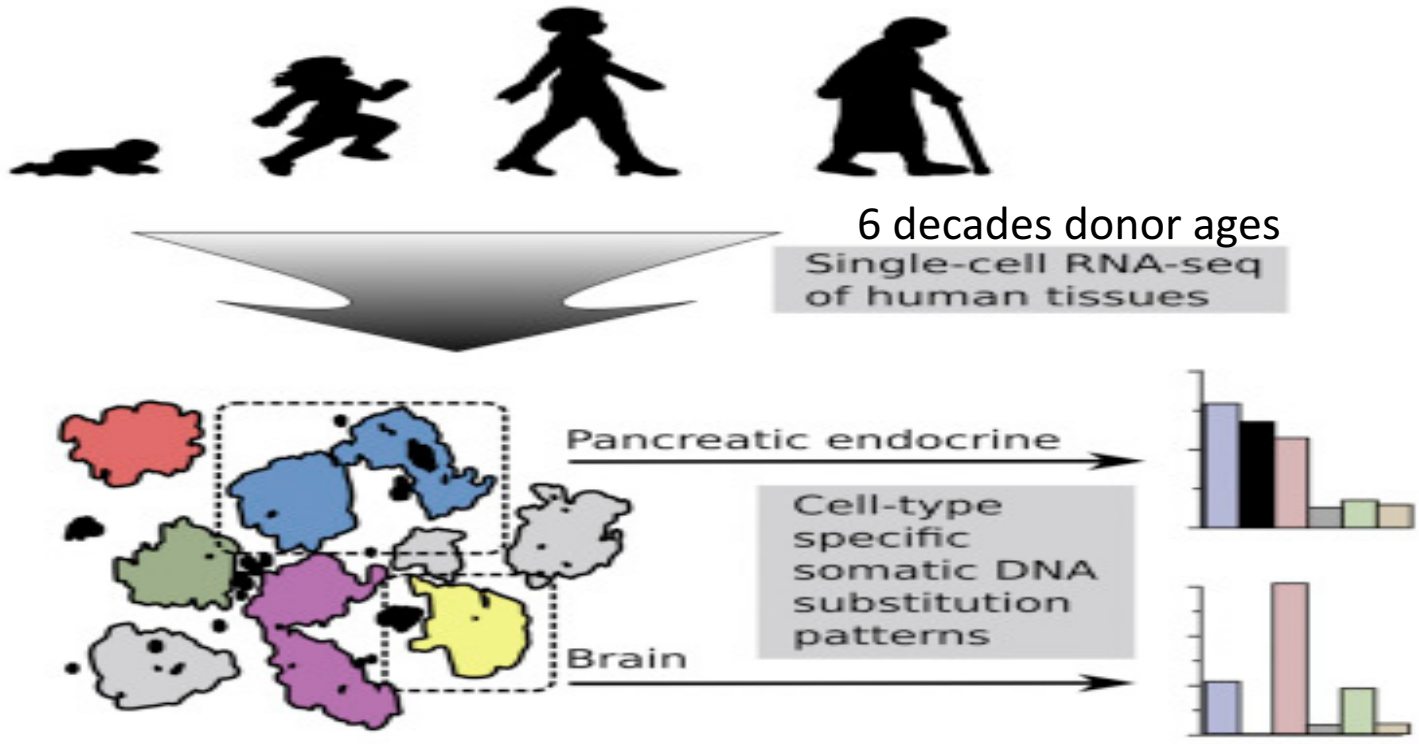


RNA-seq of single cells from donors allows detection of stochastic age-related errors:

- Cells from older donors have increased transcriptional noise and signs of fate drift
- Endocrine pancreas cells display an oxidative stress-related mutational signature
- Cellular stress and metabolic genes are high in cells with accumulation of errors

Some definitions

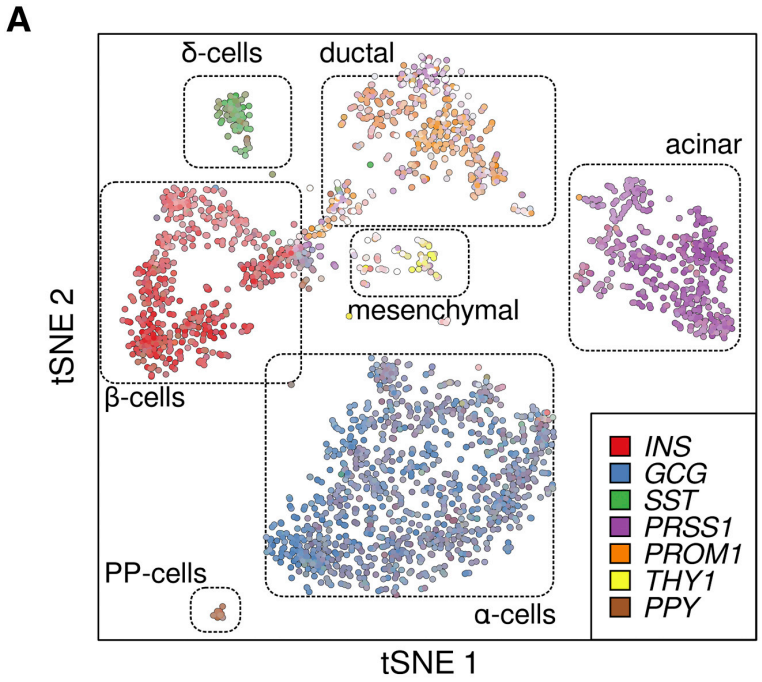
- Transcriptional Noise: ***transcriptome instability*** *or Increased disregulation of gene expression.*

- ERCC: ***RNA spike-in*** *is an* ***RNA transcript*** *of k****nown sequence*** *and* ***quantity*** *used to* ***calibrate measurements*** *in RNA hybridization assays, such as RNA-Seq.*

- Linear regression: *In statistics,* ***linear regression*** *is a linear approach for* ***modeling the relationship*** *between* ***a variable y*** *and* ***one or more explanatory variables*** *(or independent variables) denoted X.*

- CPM: *Counts per million. Unit to count gene expression level*

A Comprehensive Survey of Single Pancreatic Cells from Human Donors across Different Ages

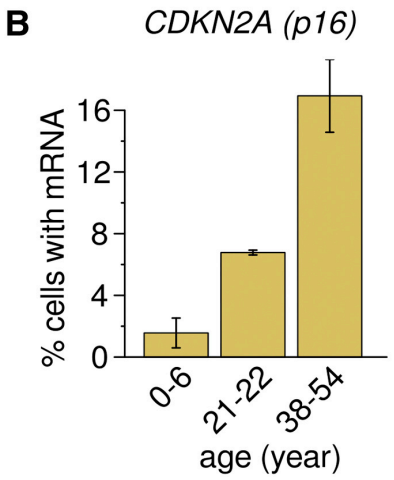


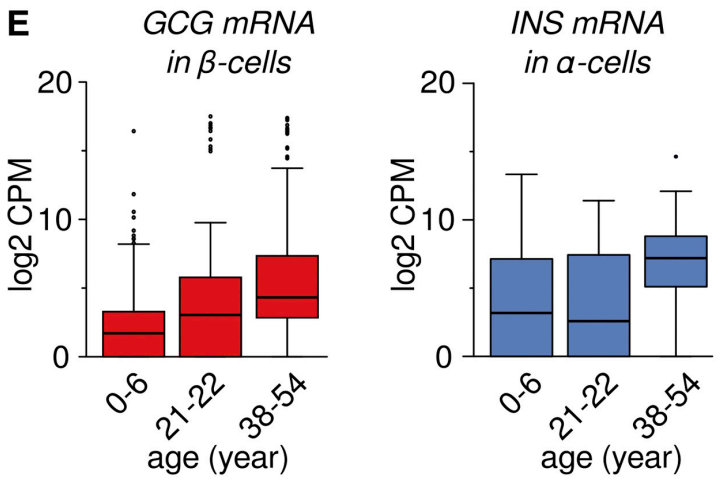
Pancreas function:

Endocrine gland: alpha- (GluCaGon), beta- (INSulin) et delta- cells and pancreatic PP .

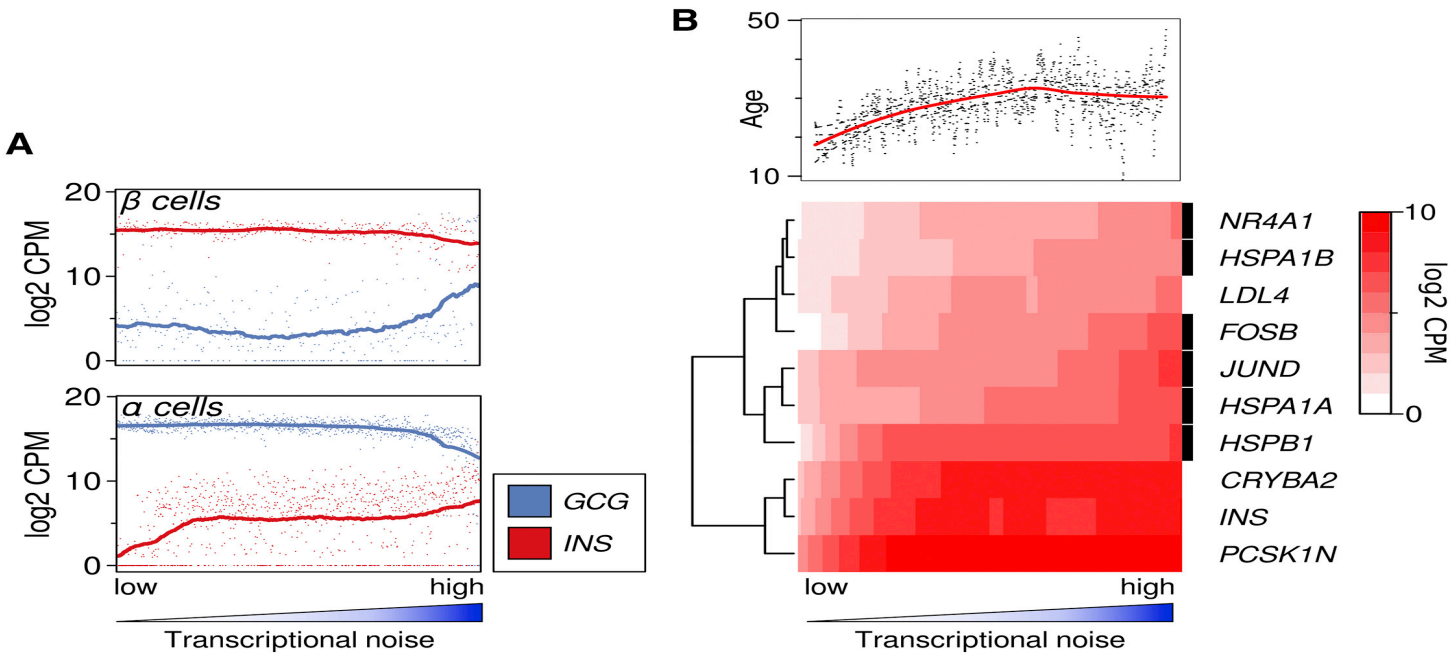
- Glucagon: UP glucose levels in blood.
- Insulin: DOWN glucose levels in blood.

Type2 Diabetes (age-related disease)

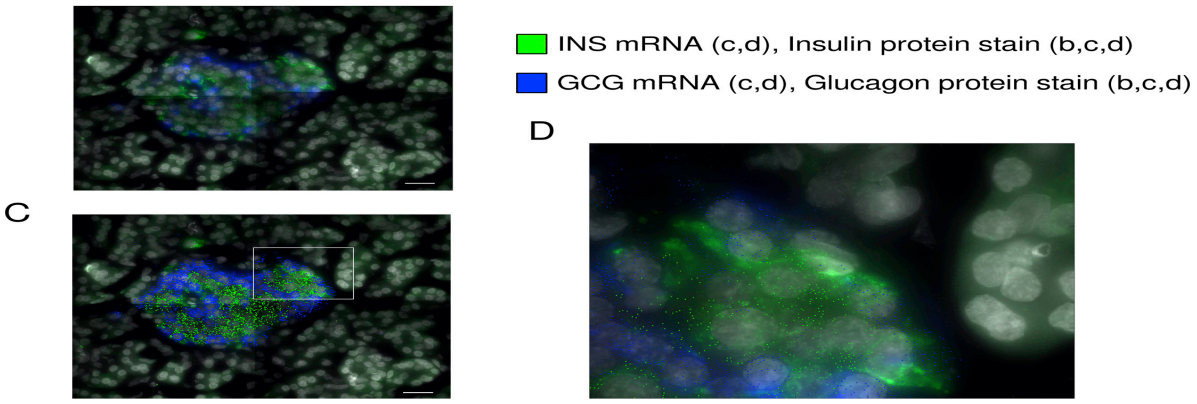




Transcriptional Instability and Fate Drift in Cells from Older Donors

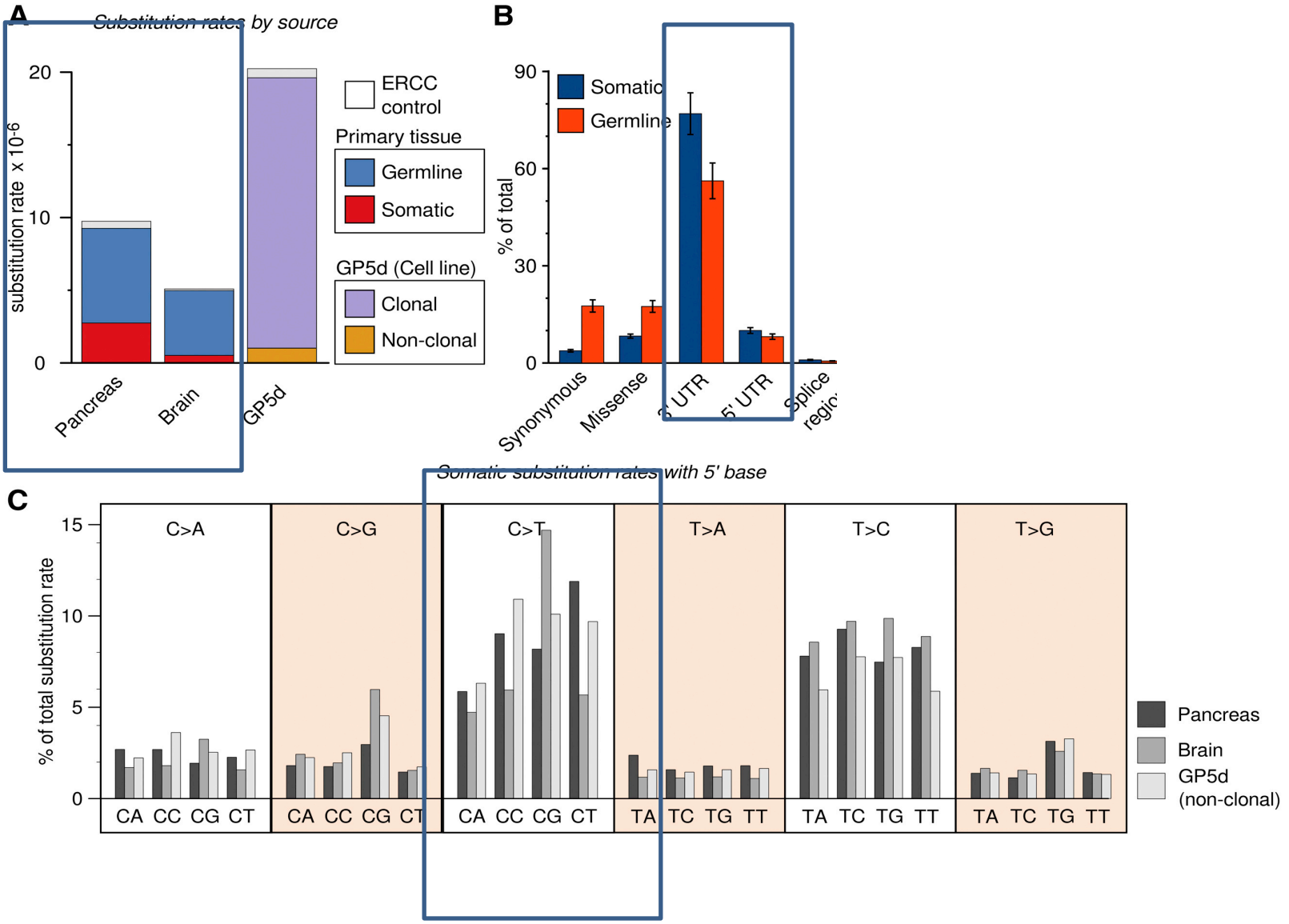


pancreatic islet containing cells with atypical hormone expression

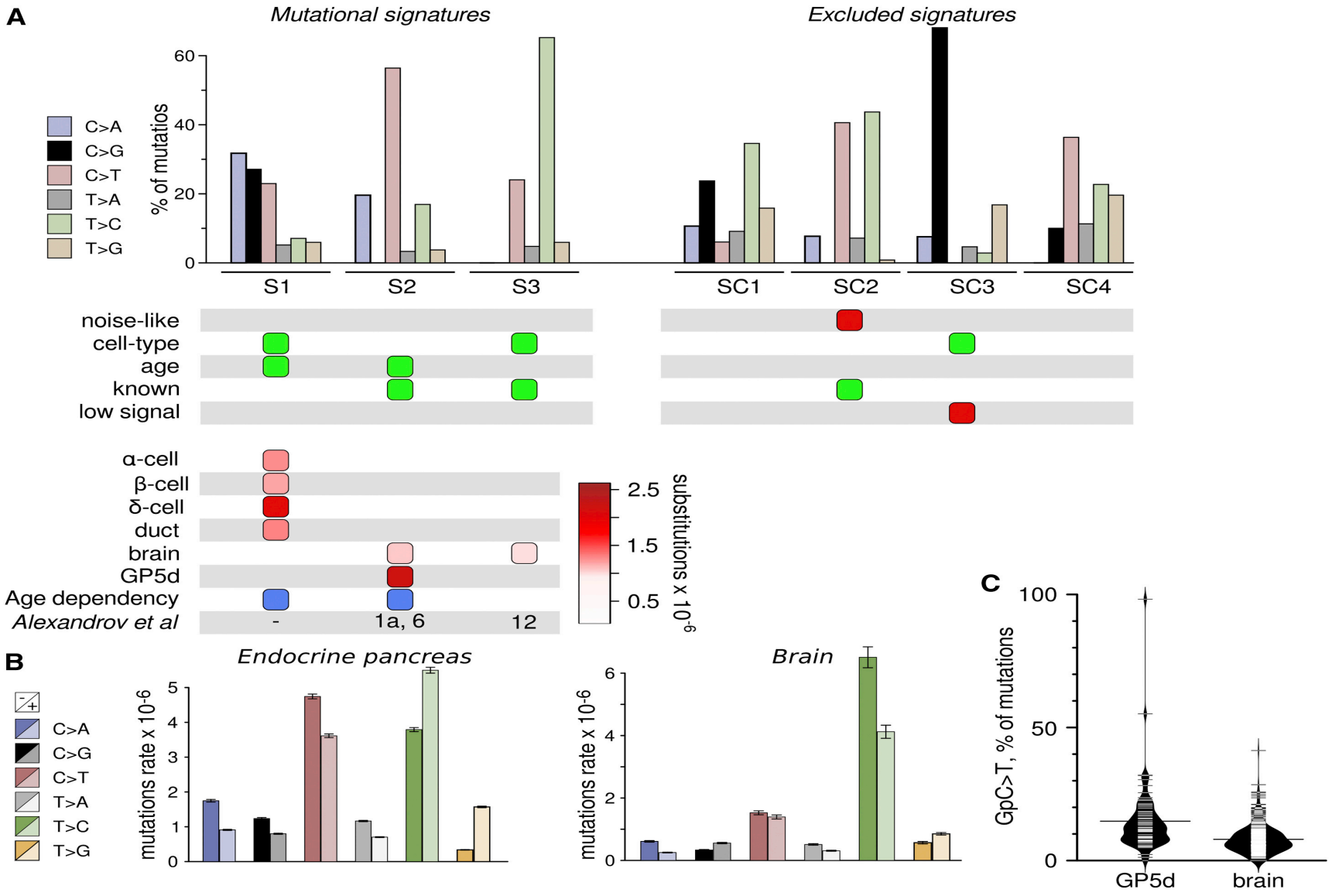


Aging is accompanied by the accumulation of somatic mutations

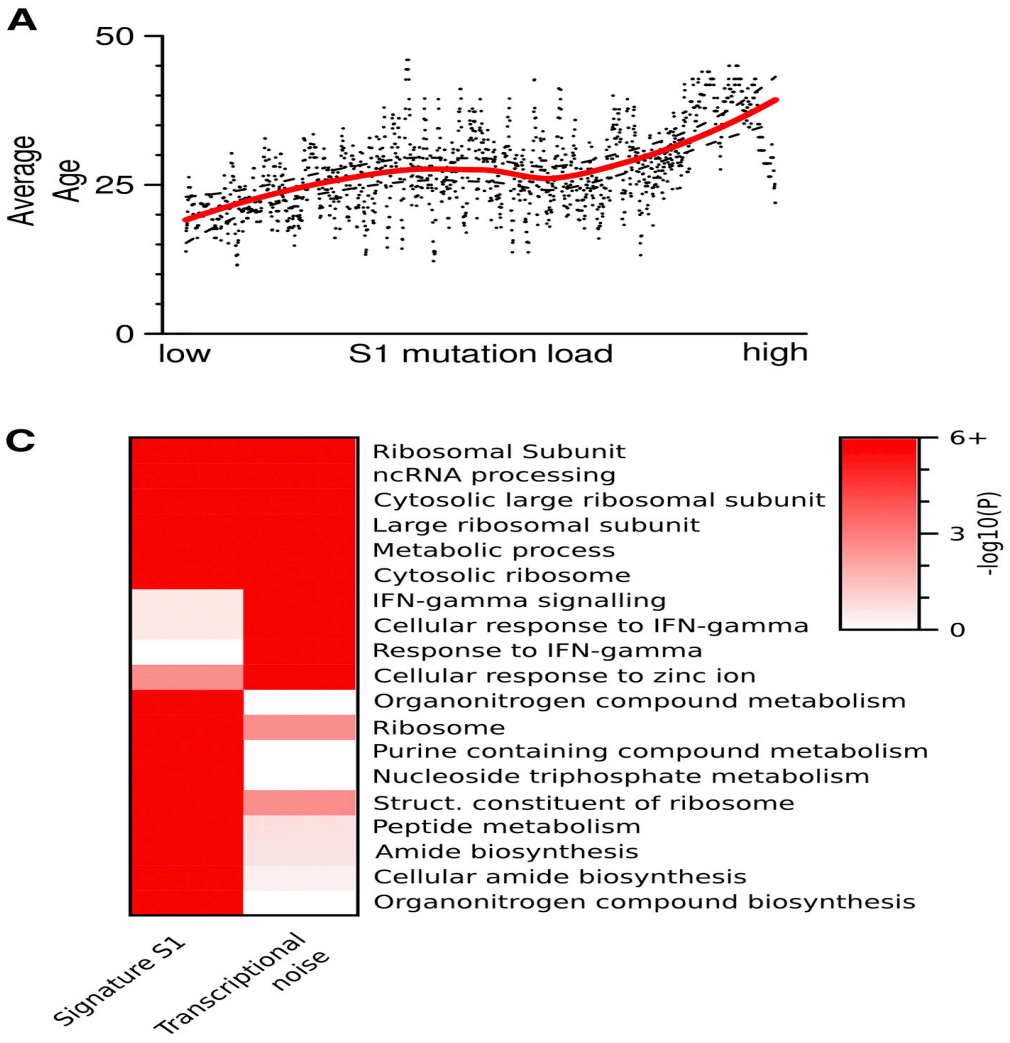
Somatic Mutation Profiles Derived from Single Primary Human Cells



Endocrine Cells Display a Specific Mutational Signature Related to Oxidative Stress



Mutational Load of Signature S1 Is Higher in Endocrine Cells from Older Donors and Correlate with Induction of Protein Synthesis-Related Genes



Conclusion

- Aging is accompanied of increase in transcriptome noise and accumulation of genetic errors.
- Absence of causal link between transcriptional instability and mutational load.
- The cellular heterogeneity suggests that aging-dependent changes are due to events in a subset of cells.
- Age specific mutational signature observed in endocrine is due to ROS-dependent lesions of DNA.
- They defined a method to determine transcriptome instability and mutations signatures from scRNAseq on arbitrary cells on primary tissue.