# Discovering somatic mutations during aging

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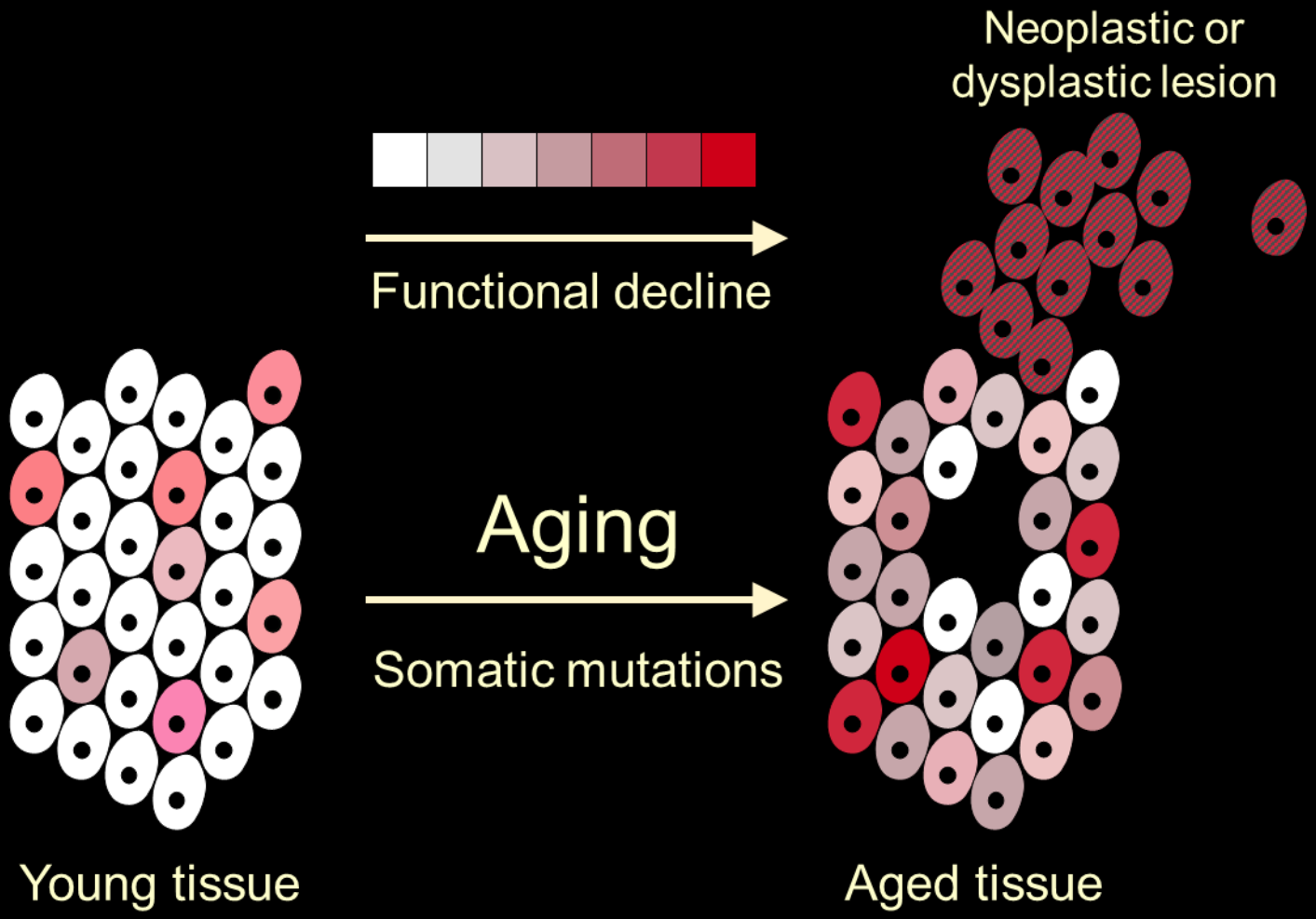
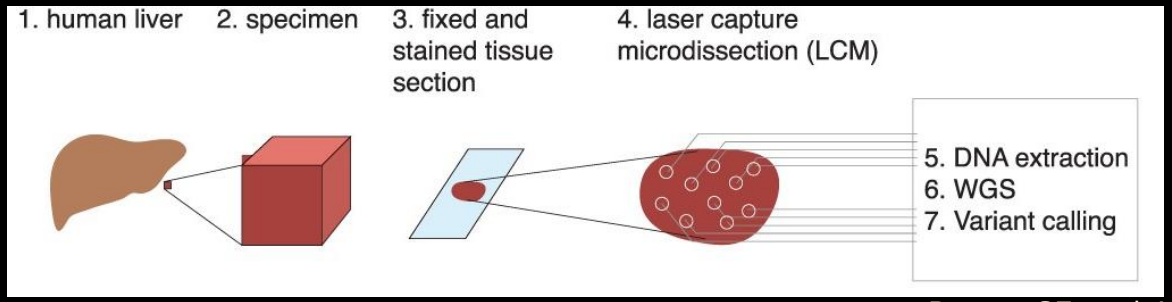
# Somatic mutation, aging and cancer




Vijg J, *Curr Opin Genet Dev, 2014.*

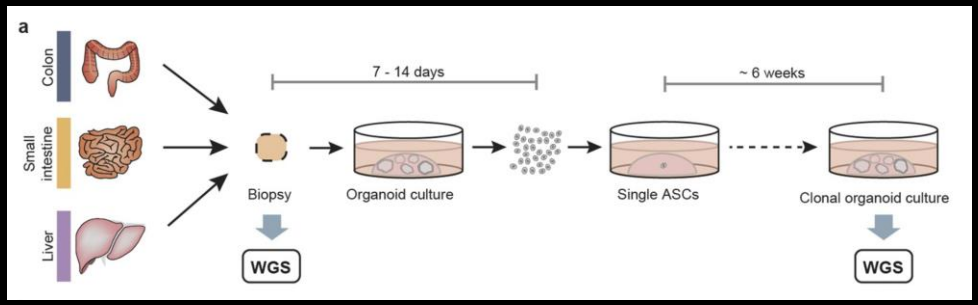
# Measure mutations as single-cell expansions

Deep sequencing of natural single cell expansions from micro-biopsies



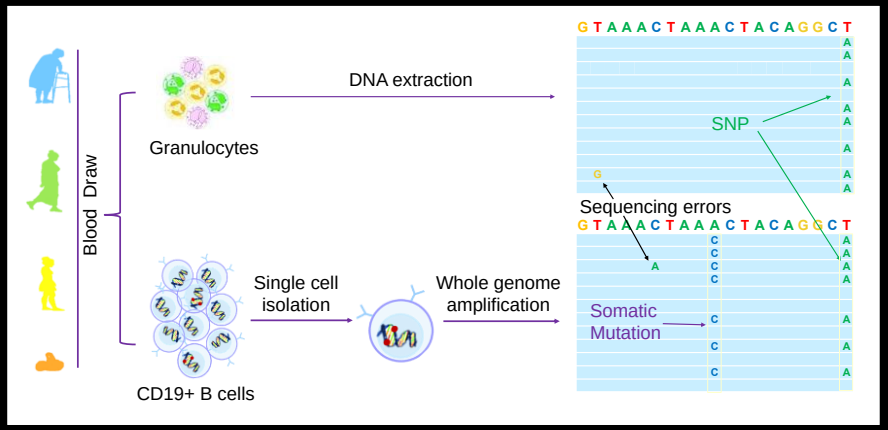

Brunner SF, et al. *Nature*, 2019.

Expand stem cells *in vitro*




Blokzijl F, et al. *Nature*, 2016.

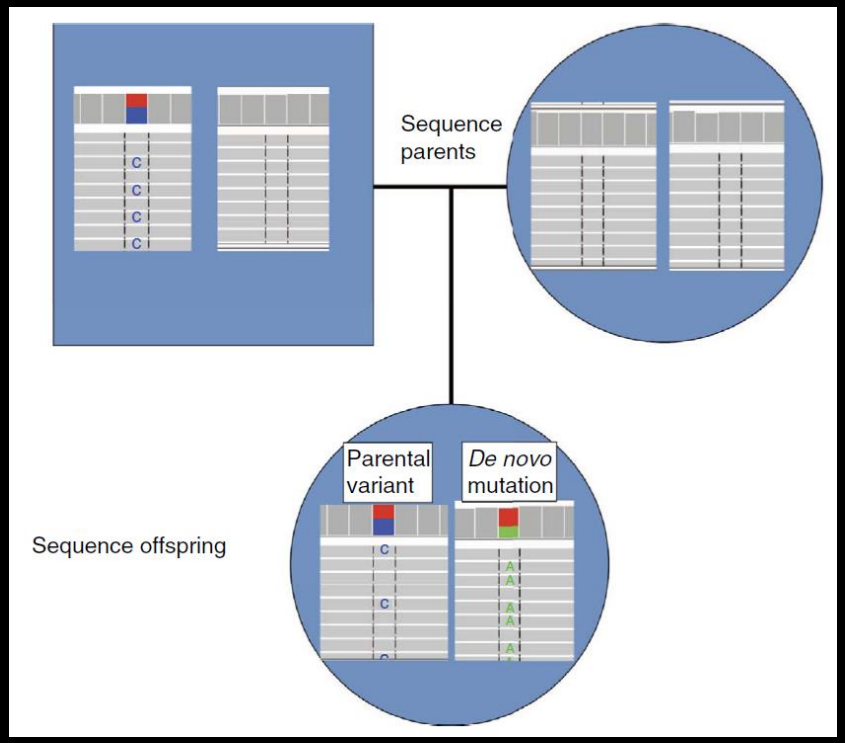
Whole genome amplification on single cells



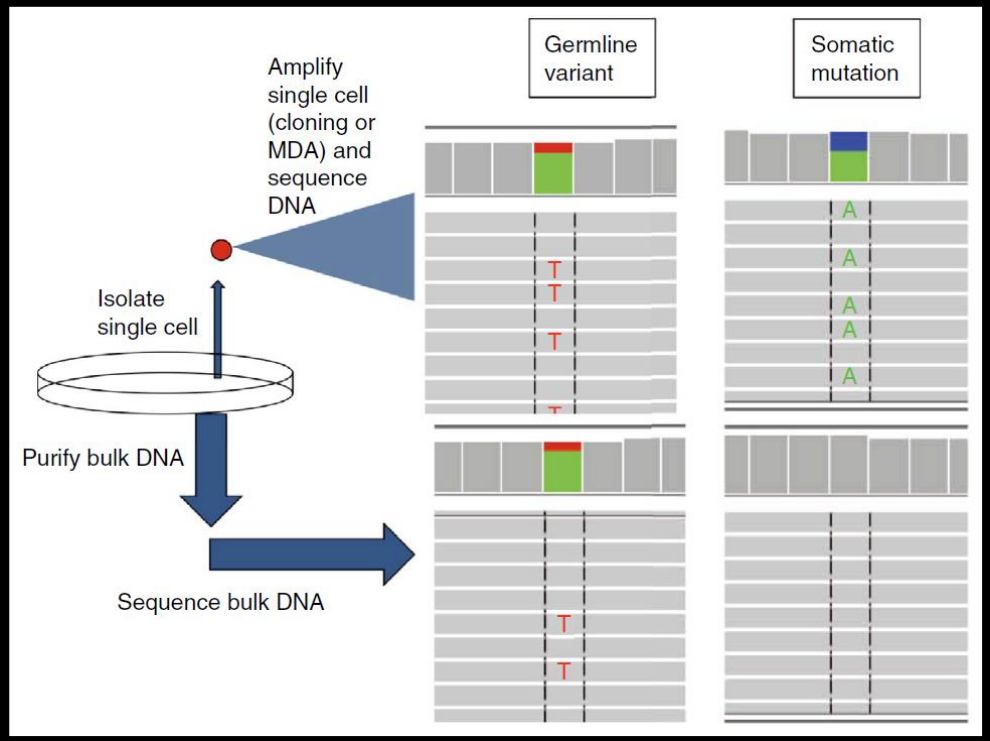

Revised from:
Dong X, et al. *Nat Methods,* 2017.
Zhang L, et al. *PNAS*, 2019.

# If mutations cause aging, is the germline protected?

Germline *de novo* mutation

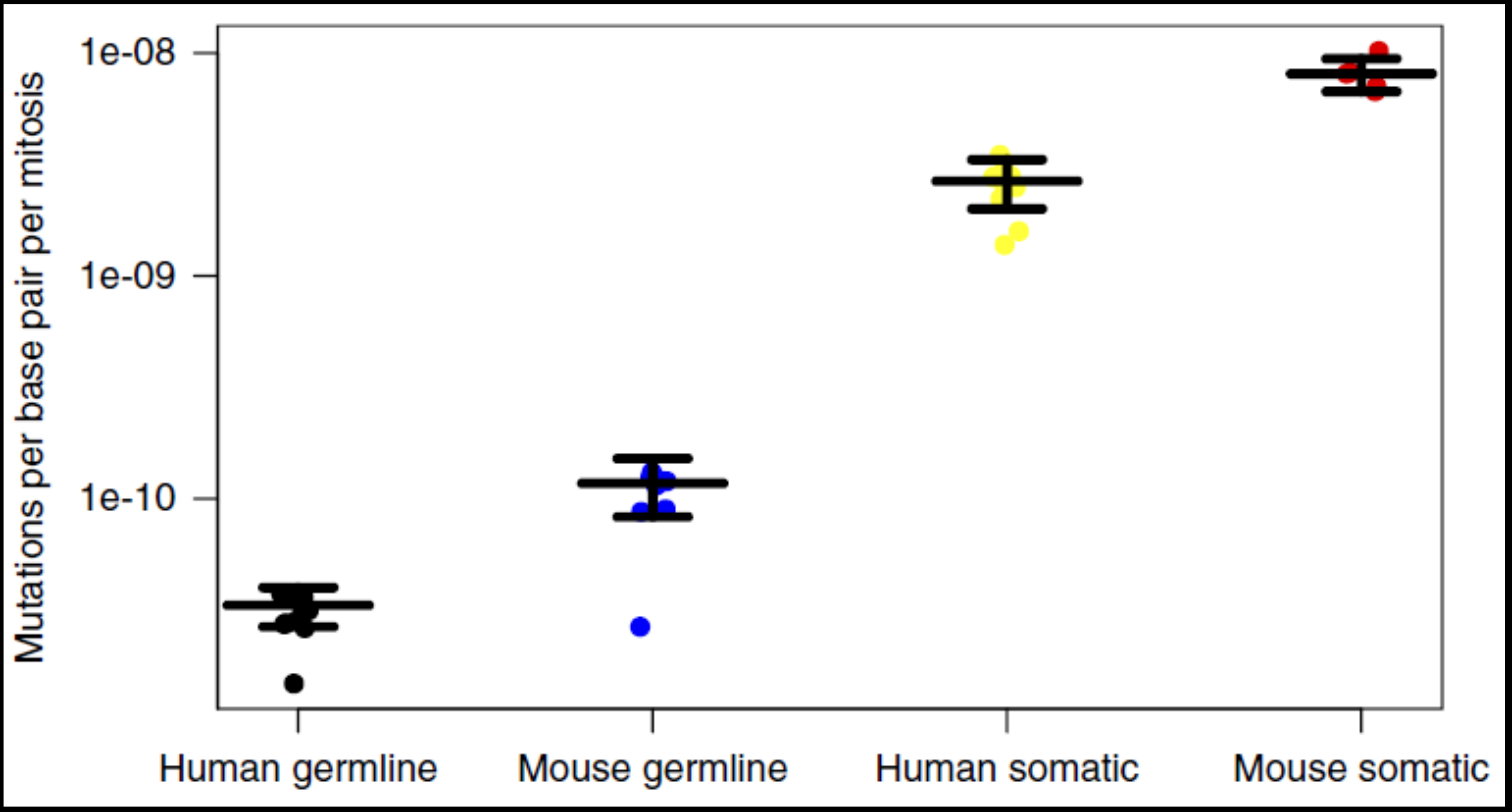



Somatic *de novo* mutation

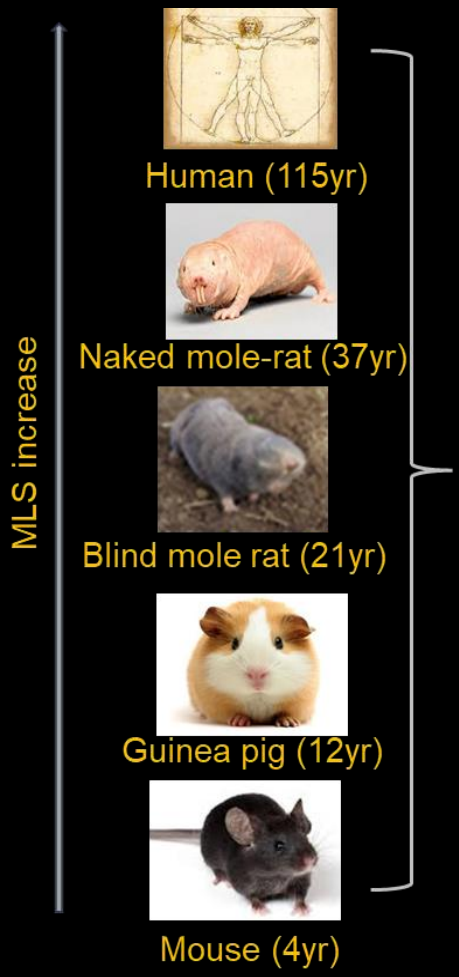


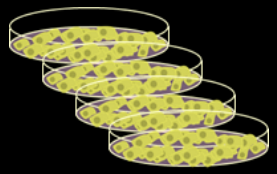

Milholland B, *et al. Nat Commun.* 2017

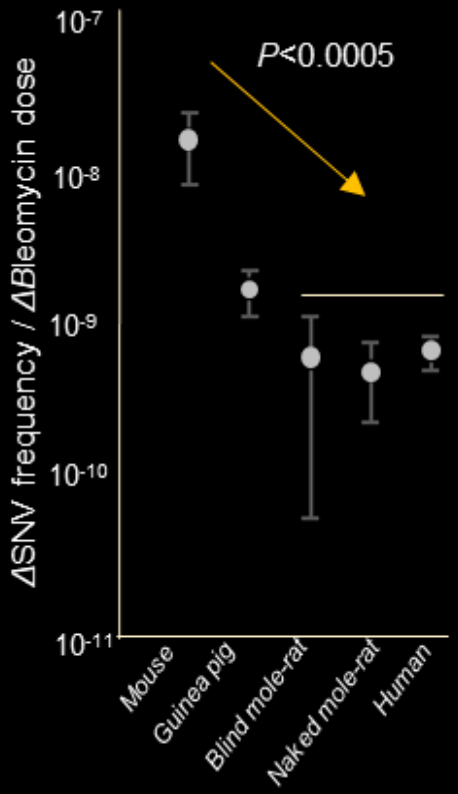
# SNV frequency is significantly higher in soma than in germline: is the soma disposable?

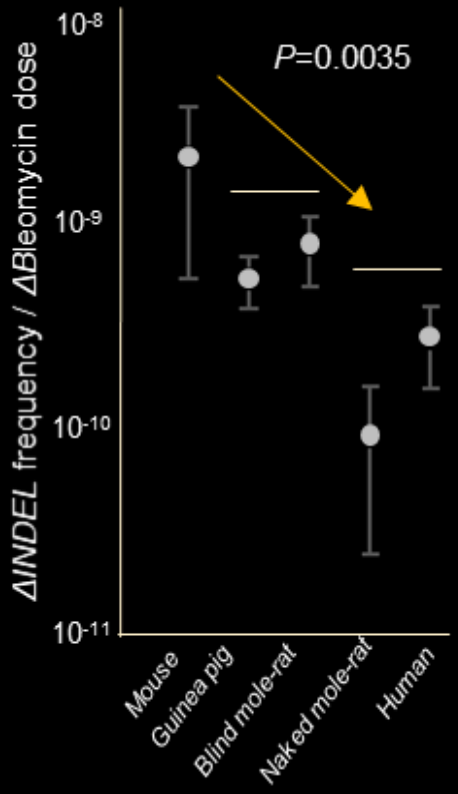


# Somatic mutation rates are inversely correlated with species-specific lifespans



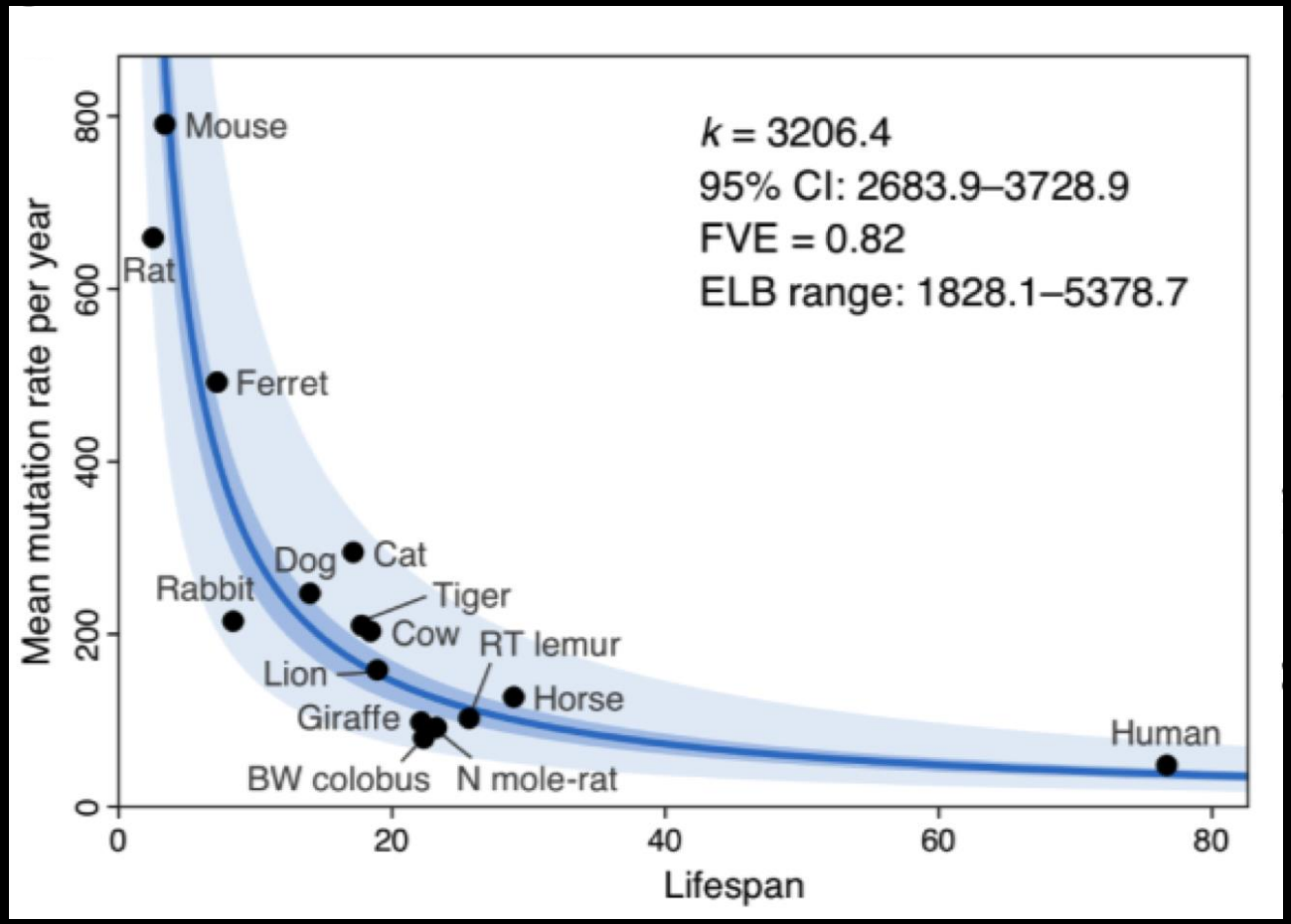



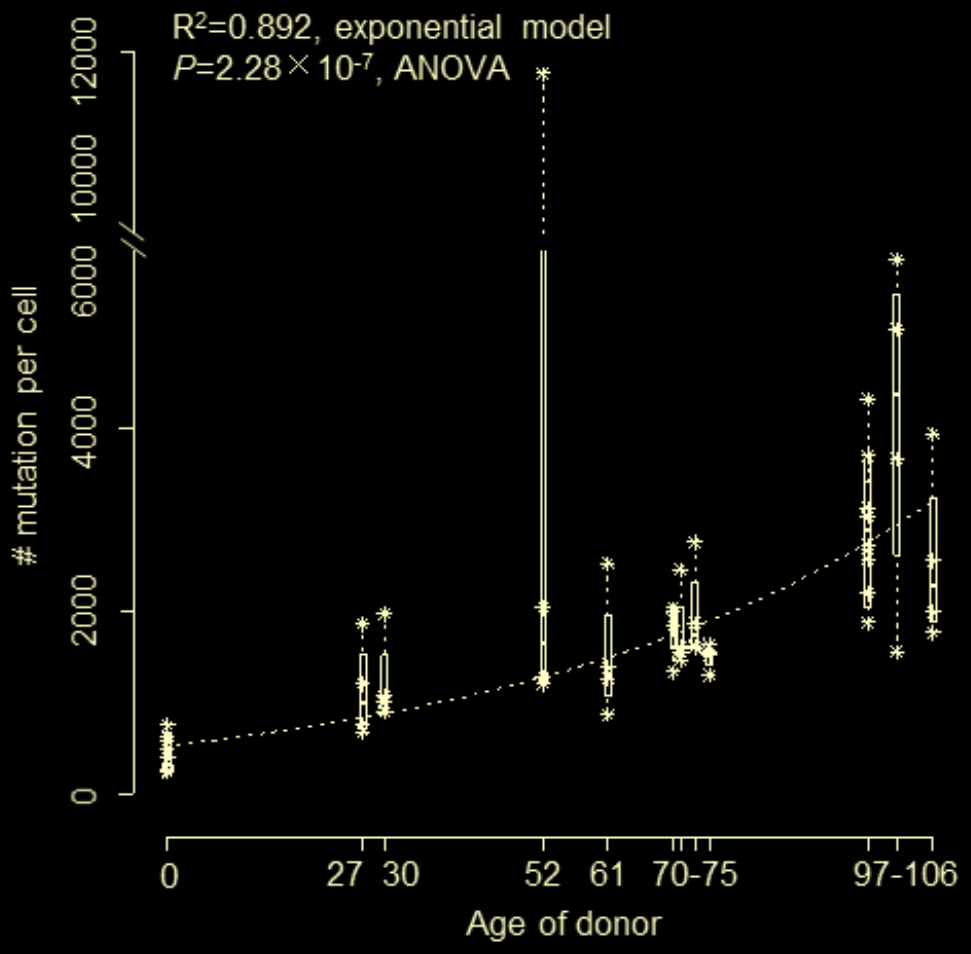

Zhang L, *et al. Science Advances. 2021*
In collaboration with Vera Gorbunova

# Somatic mutation rates scale with lifespan across mammals



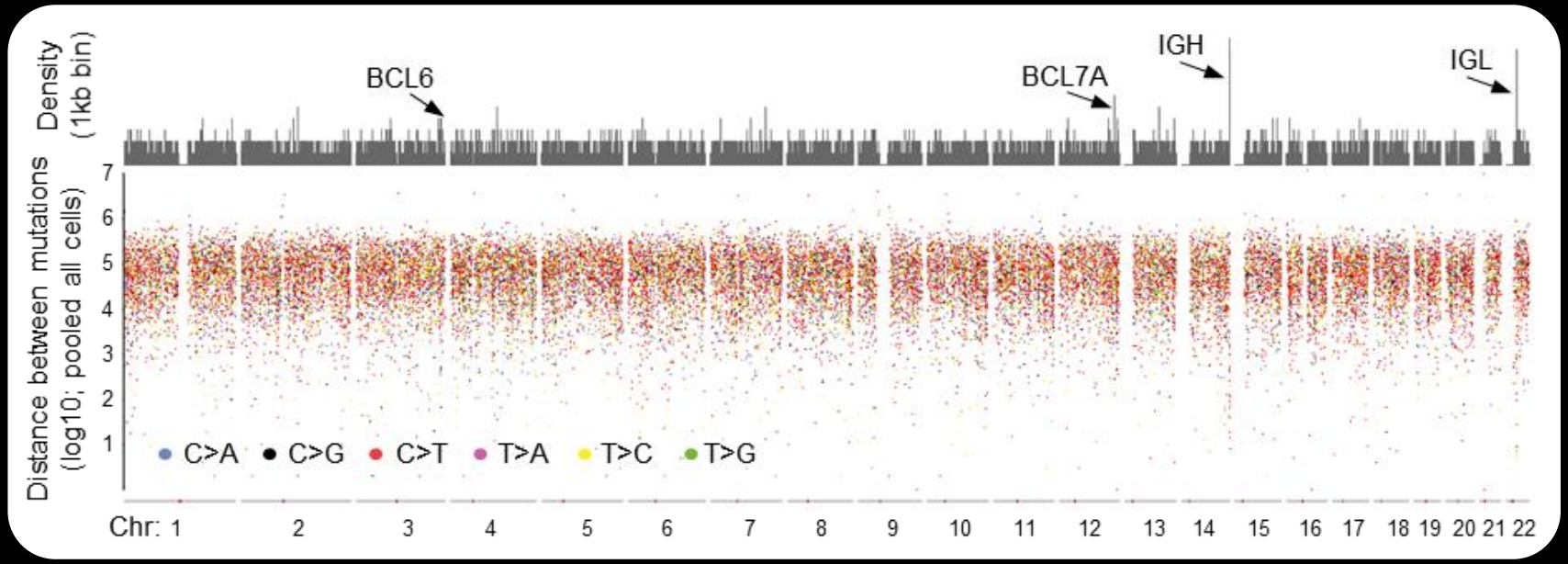

Cagan A, *et al. bioRxiv,* 2021.

# Somatic SNVs accumulate with age in human B lymphocytes



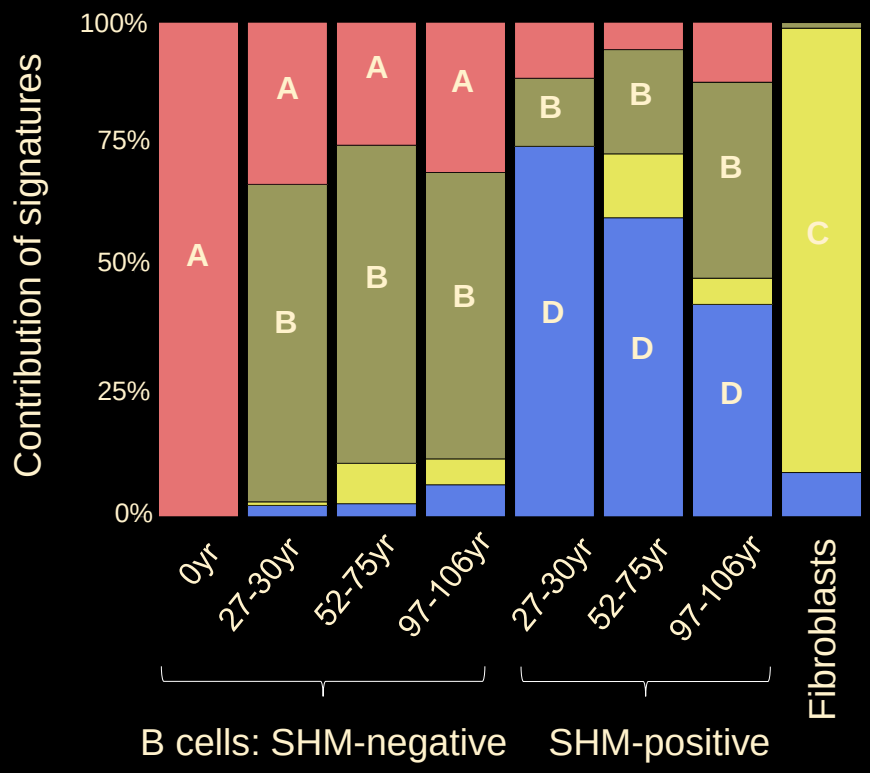

Zhang L, *et al. PNAS*. 2019

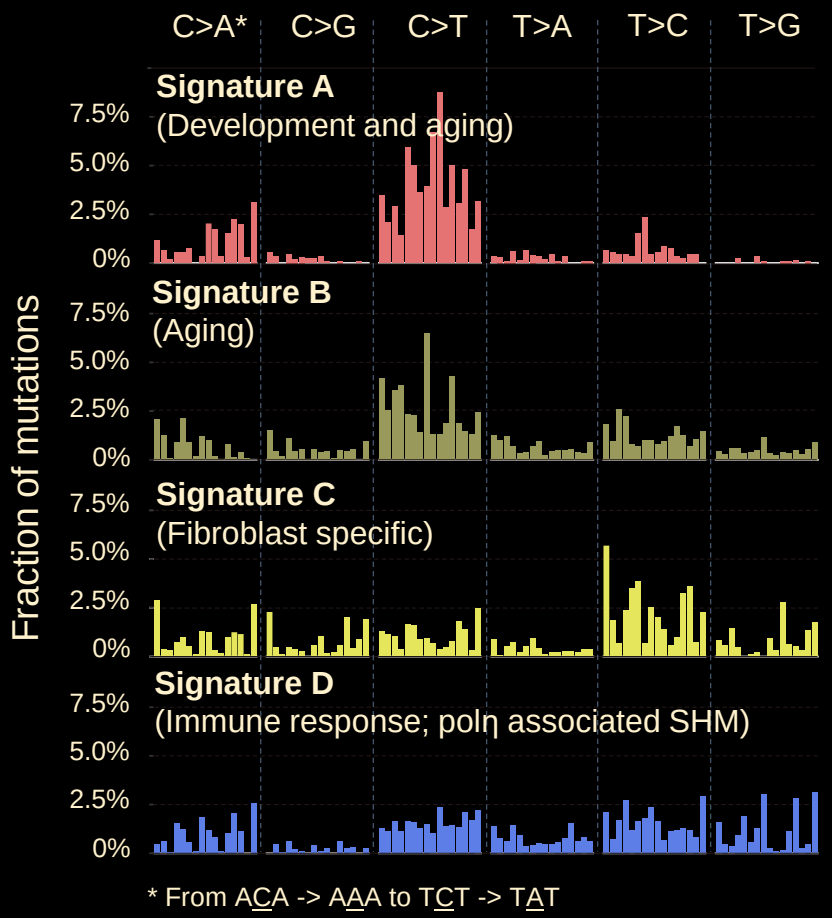
# Distribution of mutations and mutational hotspots in pooled 56 B cells




24 hotspots observed
Hotspots: >4 SNVs in a ~5kb region
Genome average: 0.05 SNV in a 5kb region

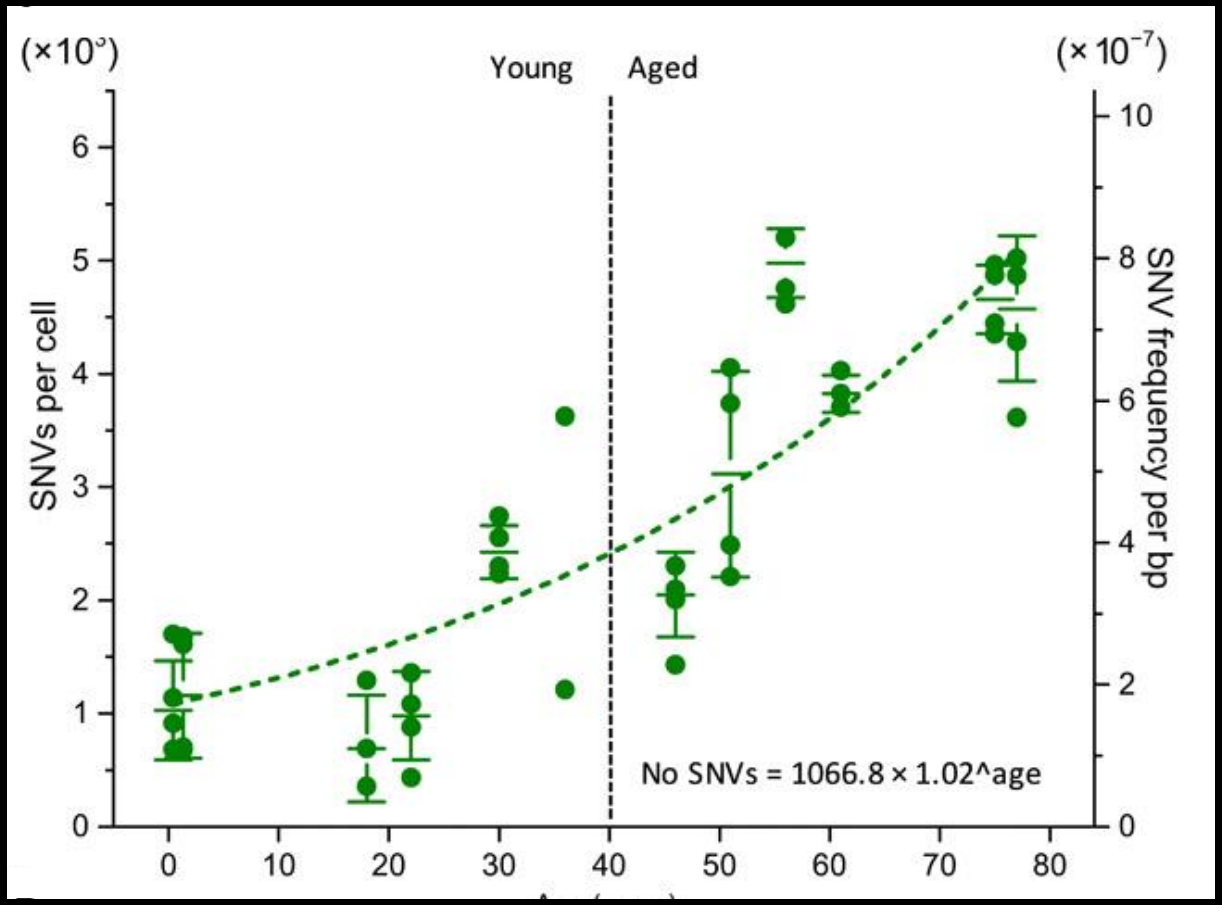
# Mutational signatures in normal B lymphocytes during aging



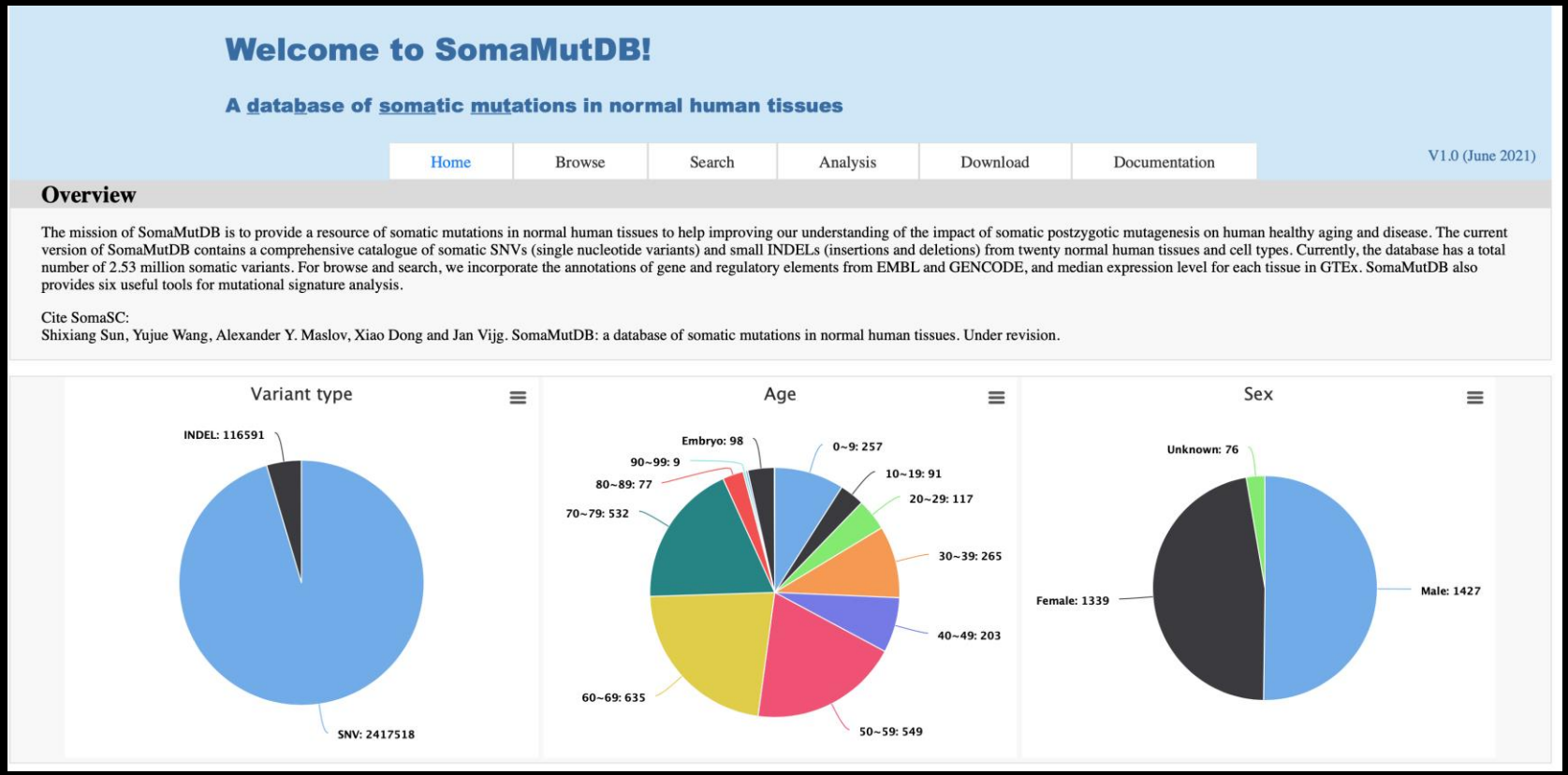

* From ACA -> AAA to TCT -> TAT

# Somatic SNVs accumulate with age in human hepatocytes and other cell types




Brazhnik K, *et al. Science Advances*. 2020

# SomaMutDB: a database of 2.5 million discovered mutations in normal somatic human tissues




Sun S, *et al. Nucleic Acids Research* 2022

# Conclusions and prospects

- Using the single-cell approaches we can now characterize the landscapes of somatic mutations in humans in relation to aging

- Is the accumulation of somatic mutations a direct cause to functional decline during aging?

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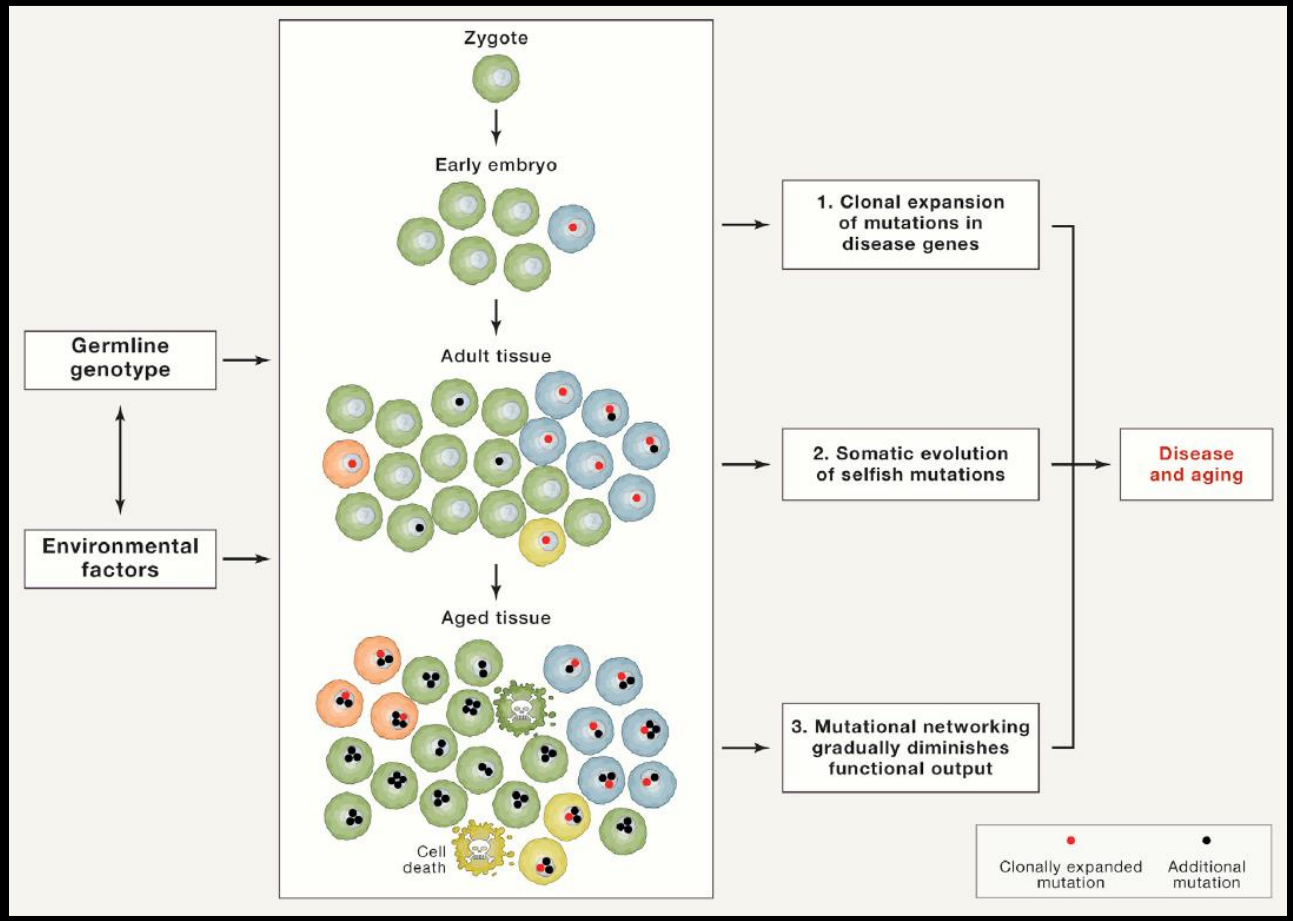


Vijg J & Dong X, *Cell* 2020

# Acknowledgement

Jan Vijg

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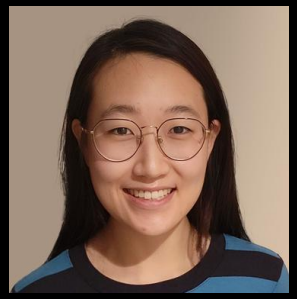
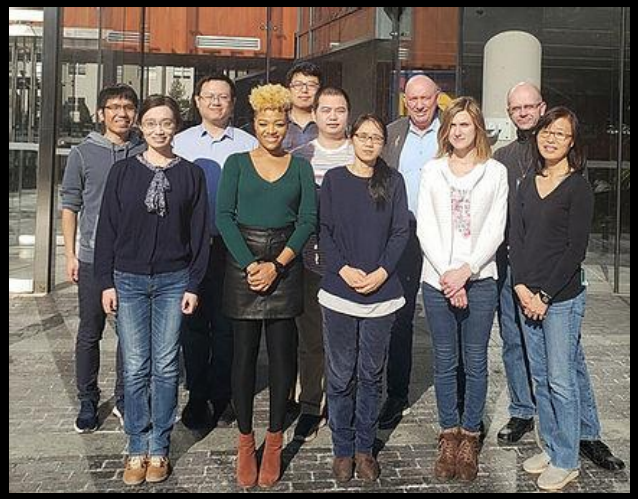


Hannim Jung

Josh Bartz



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