INTRODUCTION TO INTEGRATIVE MODELS OF AGING CORE

• THE CHALLENGE OF STUDYING AGING
• TECHNOLOGIES
• SERVICES OFFERED
• WHO WE ARE
• PROJECT EXAMPLE
• HIERARCHICAL DATA VISUALIZATION METHODS
• CONTACT INFORMATION AND Q&A
Aging is a challenging problem

- Dysregulation across virtually all cellular processes
  - 9 hallmarks of aging (López-Otín et al, 2013)
- Heterogeneous
  - Not all cells age at the same rate (Arrojo e Drigo et al., 2019)
- Organ-specific
  - Each organ has its own aging phenotype (Schaum et al, 2020)
  - Interactions between organs (e.g. liver->blood->brain; Currais et al, 2019; Schaum et al, 2020)
- Varies between individuals in a population.

Technologies for addressing these challenges

- High-throughput sequencing
  - RNA-Seq, Cut&Tag/ChIP-Seq, ATAC-Seq, ...
- Single-cell sequencing
  - scRNA-seq, scATAC-seq, Spatial transcriptomics
- Mass spectrometry
  - Proteomics
  - Metabolomics
- Microscopy
  - Measure age-associated features in high-resolution images
Services offered

- Brainstorming / Project Design
  - Assay selection, replicates, controls, timelines
- Data storage and curation
  - Redundant storage, data sharing, submission to online repositories
- Quality control
- Standard and customized analyses
  - Ask us about our pipelines and tools, or we can help implement new ones
- Data integration
  - Mathematical modeling, machine learning, hyperbolic embedding
- Access to analyses through online tools
  - Interactive data visualization and tool development
- Training
  - Workshops, 1-on-1, online materials
A dedicated team

Prof. Tatyana Sharpee (Core Lead)
Dr. Max Shokhirev (Director)
Dr. Ling Huang
Dr. April Williams
Dr. Jingting Yu

Co-authored over 60 publications in the last 4 years on a wide array of topics (including 14 aging papers)

An example of a recent aging collaboration

Biological Questions:
- How does old age affect gene expression and metabolism?
- How do the drug treatments affect expression and metabolism?

Assays:
- RNA-Seq
- Metabolomics

Conditions:
- Middle-Aged vs Old Age
- Old Age vs Drug treatments
A novel multi-omics integration tool

SUMMER, a shiny utility for metabolomics and multiomics exploratory research

Ling Front. - Antonio Canab / Shayan N. Shafazand

Input

Gene Expression (FPKM/Microarray)

Protein Abundance (raw intensity)

Metabolite Abundance (raw intensity)

SUMMER is freely available at https://www.surfer.com/features/surfing-blacks-beach-1998-2016/
• Describing hierarchical data
  – Identifying driver nodes & causal interactions in networks
  – Visualization methods for hierarchical data
  – Custom methods for “batch correction”

Hierarchical data -> Hyperbolic geometry
3D Hyperbolic space

Representing 3D Hyperbolic Space with Poincare Sphere
Hyperbolic geometry in gene expression data

Zhou & Sharpee, *iScience* 2021
Comparison with Klimonvksaia et al. Nature Communications 2020

Summary of current methods for analyzing hierarchical data

• Visualization methods (t-SNE, UMAP, PCA, hyperbolic SNE, hyperbolic MDS).
• Methods for geometry detection, dimensionality reductions
• Methods for identifying driver nodes
Contact information


Prof. Tatyana Sharpee sharpee@salk.edu
Dr. Max Shokhirev mshokhirev@salk.edu