Geroscience
for Aging in Challenging Environments

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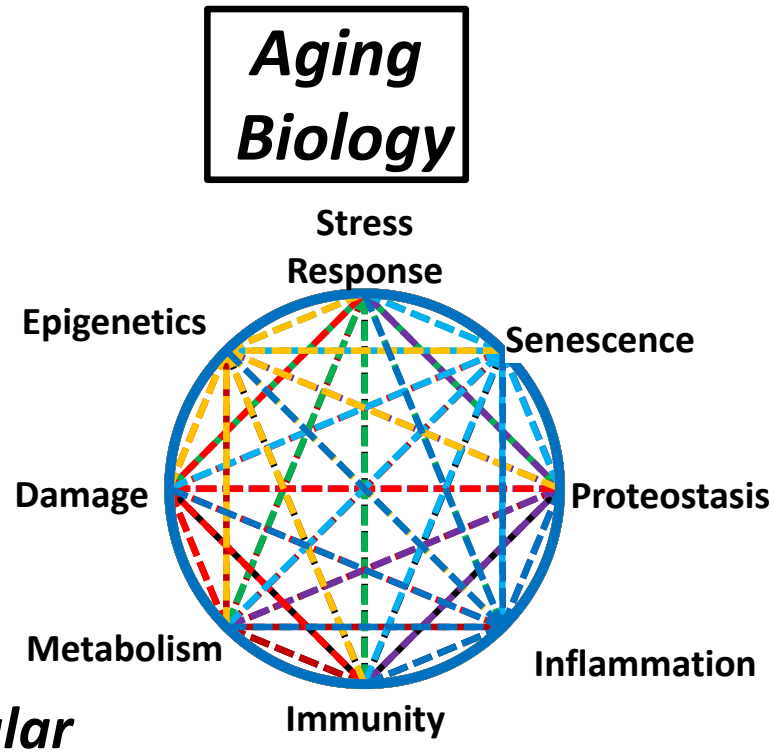
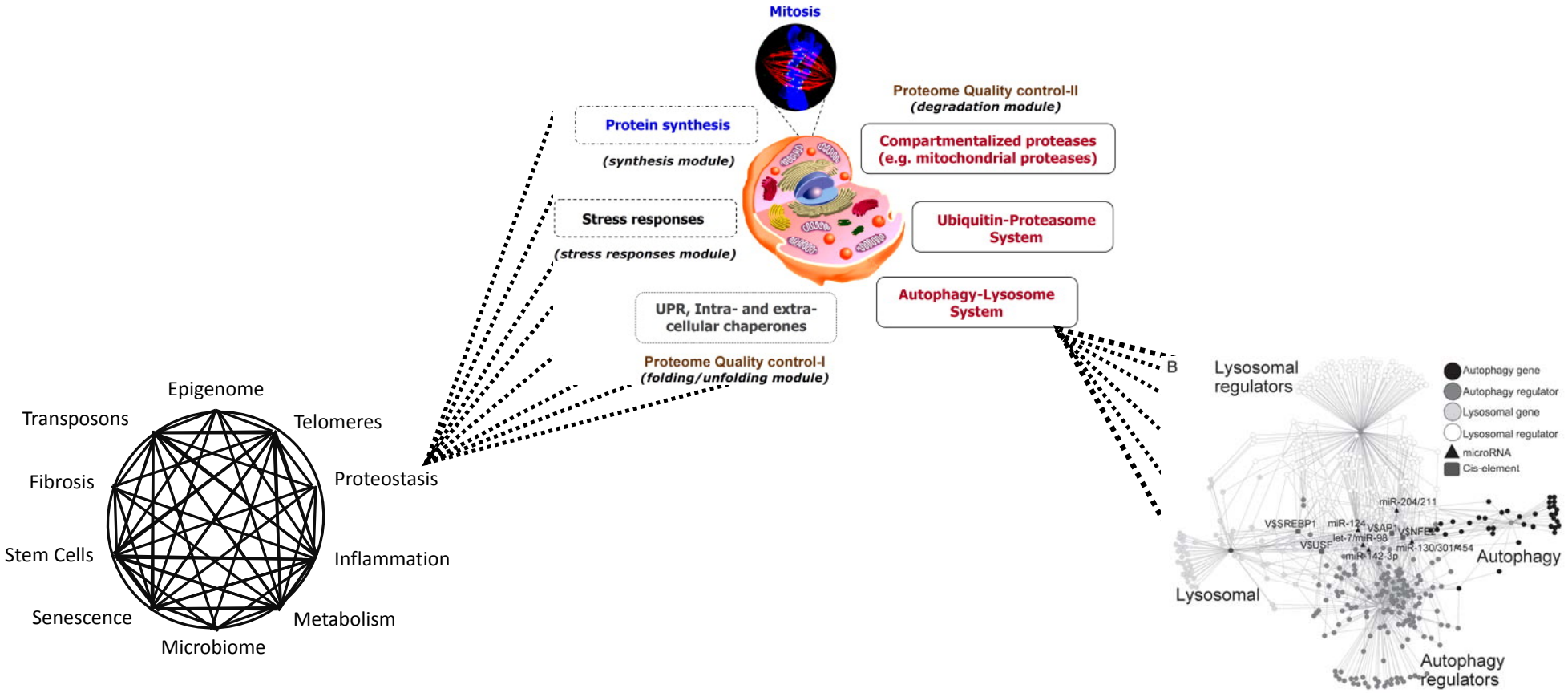
Trans-NIH Geroscience Interest Group

- **Exposures and Latent Disease Risk**
- **Identifying Hallmarks and Key Characteristics**

Building a Conceptual Framework: Hallmarks of Aging

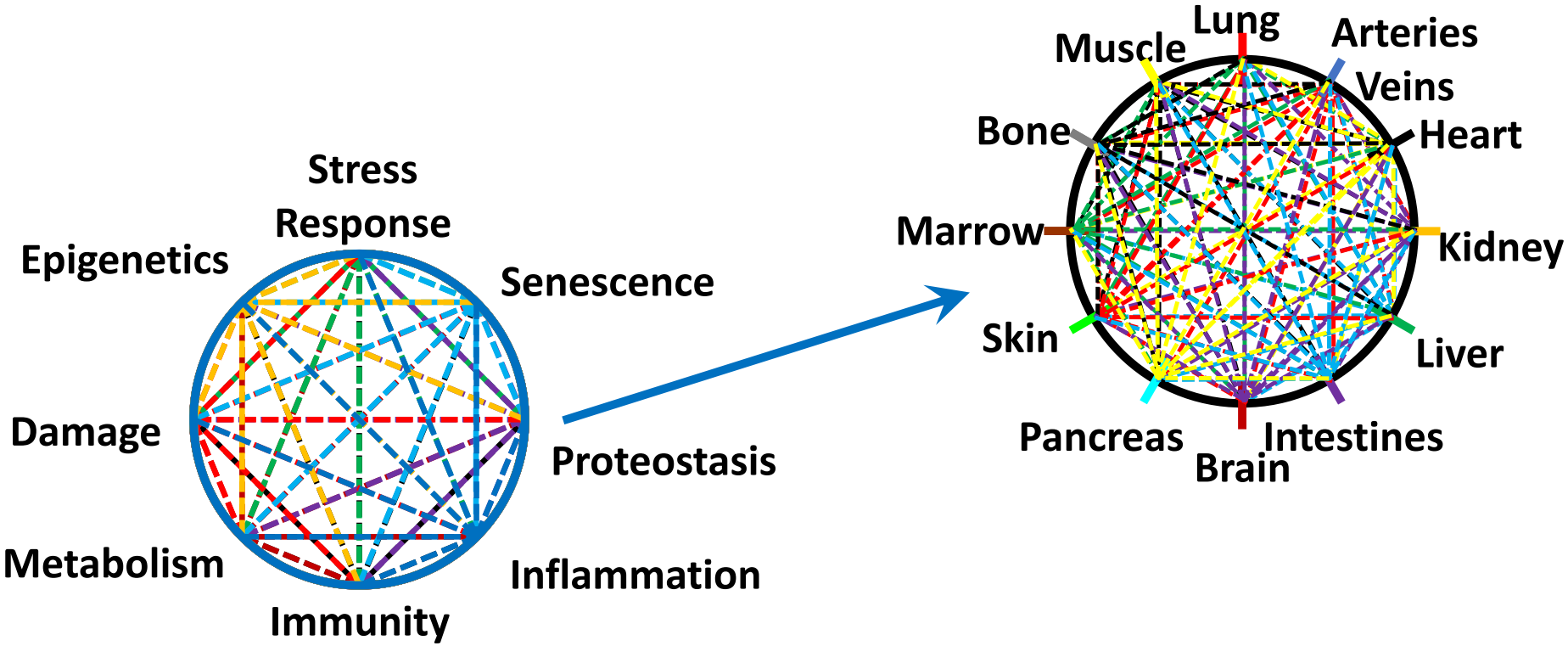


What is contained in each hallmark of aging?



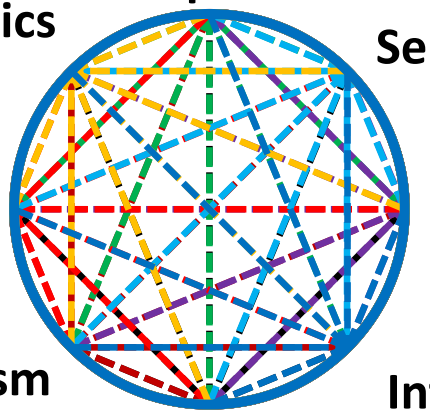
Adapted from Niforou et al. (2014).. Redox Biology. 2. 10.1016/j.redox.2014.01.017.

Building a Conceptual Framework: Hallmarks of Aging and Organ Systems



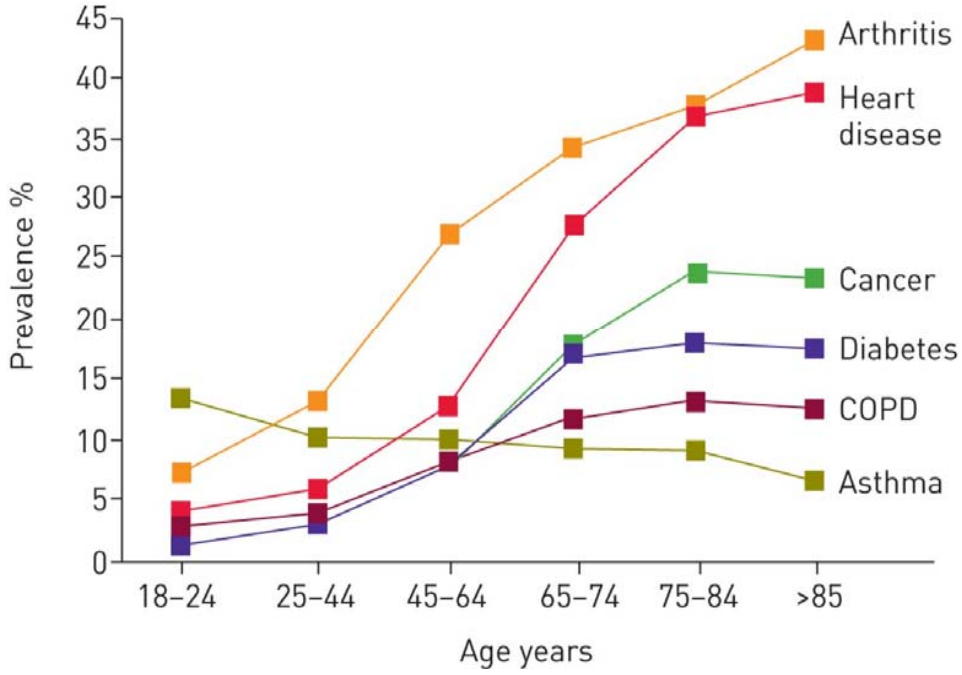
Building a Conceptual Framework: Aging as a risk factor …

Aging Biology

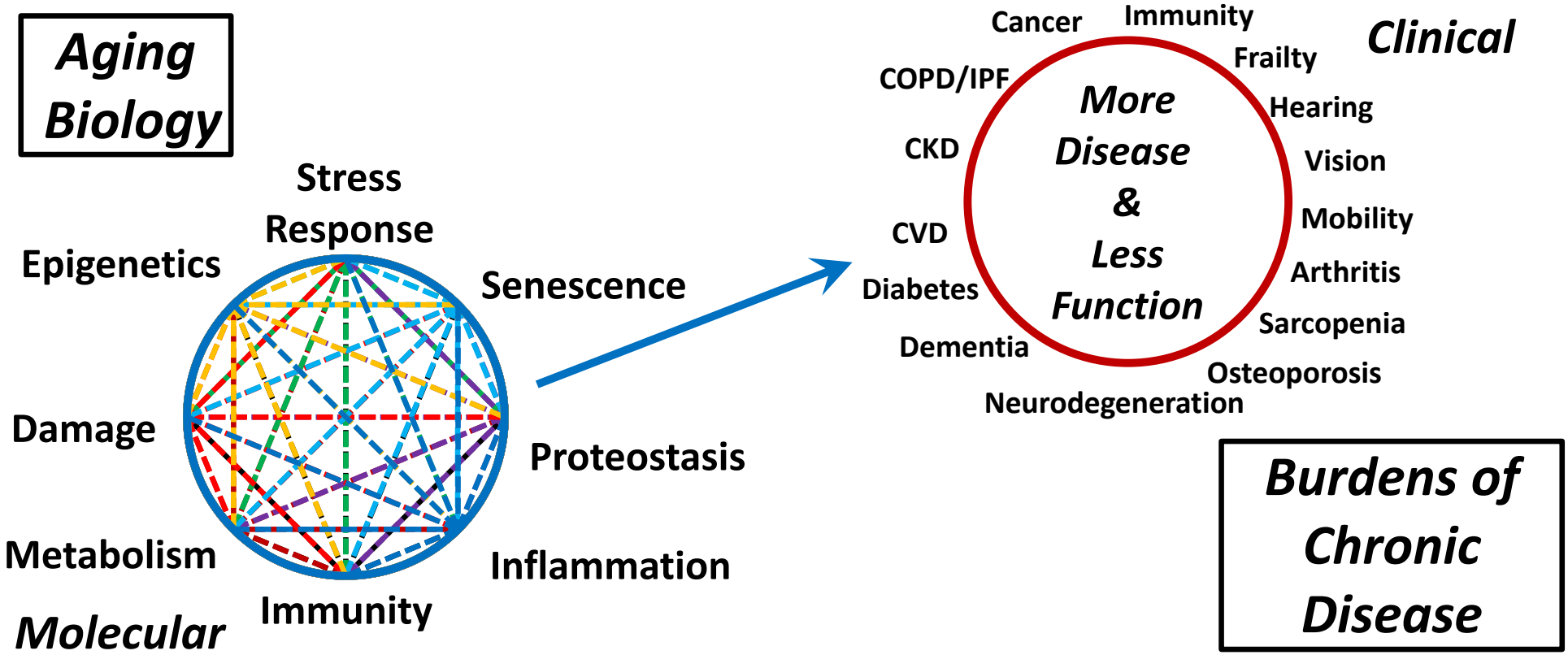


Molecular

Clinical

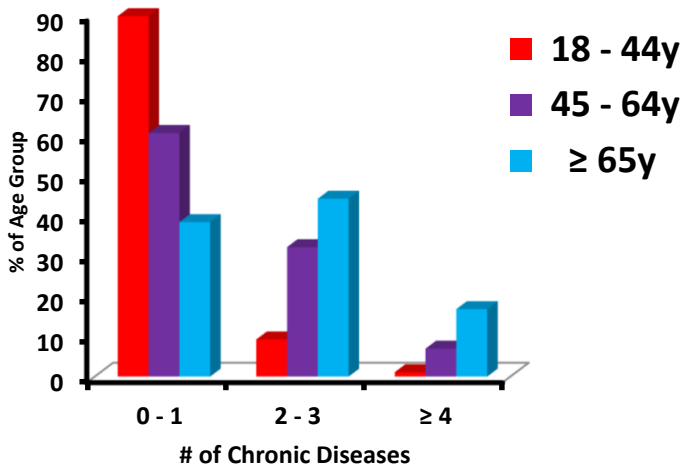


Building a Conceptual Framework: Hallmarks of Aging



Multiple Chronic Conditinos

- Age-Distribution of MCC



- Humans
  - Hypertension
  - Ischemic Heart Disease
  - Hyperlipidemia
  - Diabetes
  - Arthritis
  - Chronic Kidney Disease
  - COPD
  - Osteoporosis
  - …

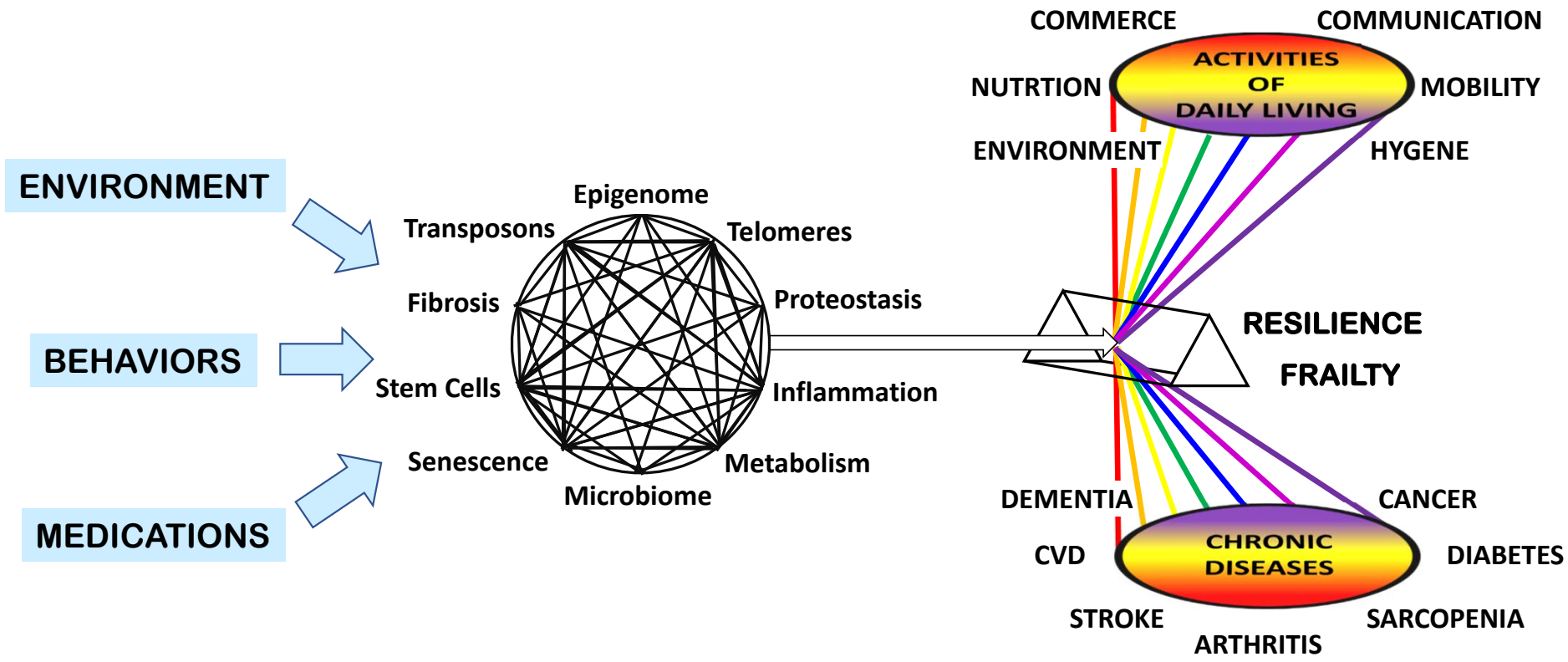
Multiple Chronic Conditions

• Human	• Lab animal
1. Cancer	A. Cancer
2. Cardiac Hypertrophy	B. Cardiac Hypertrophy
3. Kidney Failure	C. Kidney Failure
4. Hypertension	D. Splenomegaly
5. Lung Function/Disease	E. Pneumonia
6. Bones	F. Bones
7. Joints	G. Joints
8. Muscles	H. Muscles
9. Skin	I. Skin

Scoring Functions in Adults

		Newborn	ML-Adult	LL-Adult
Cognition			Response time, memory	Response time, memory
Appearance	Appearance/Complexion	blue or pale all over	BMI, skin tone, hair	Change in weight, skin tone, hair
Pulse	Pulse rate	0 to >100	+/- exertion	+/- exertion
Grimace	Reflex irritability	… when stimulated	Response to stimulation in periphery and centrally	Response…
Activity	Activity	Motion and resistance	Motion and Resistance	Motion and Resistance
Respiration	Respiratory Effort	Irregular to regular	Lung function parameters	Lung Function Parameters

Geroscience :
Aging in a Challenging Environment



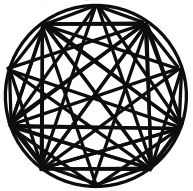
Building a Conceptual Framework: Environment as a Risk Factor



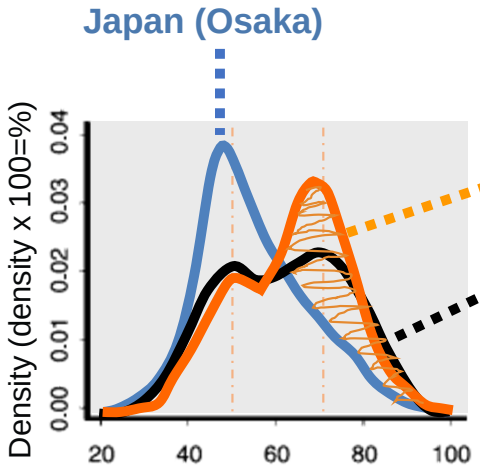



Environmental Risk superimposed on age-related risk for breast cancer?

Epigenome

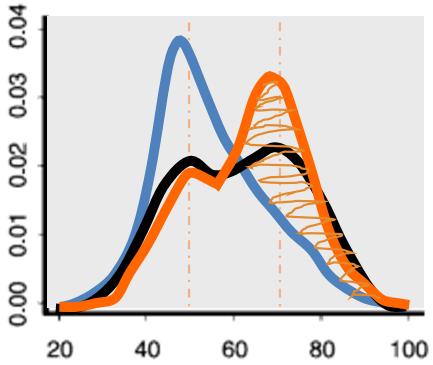


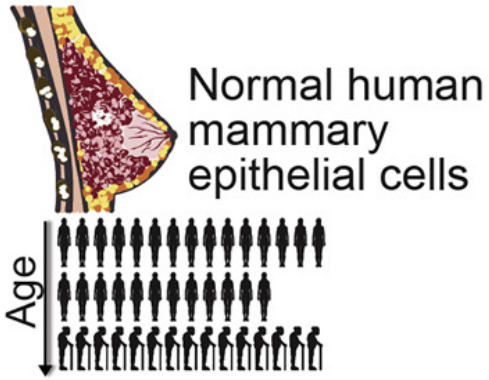
Stem Cells



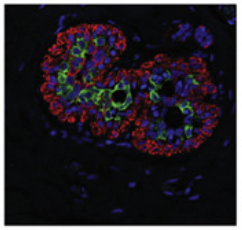
1993-1997

The aging biology of age-related risk for breast cancer

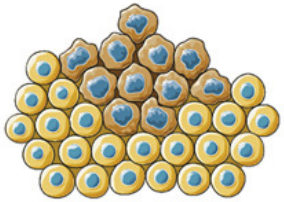




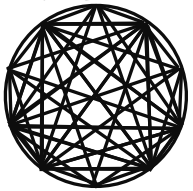
Age-emergent luminal cell subpopulations predict the chronological age



Altered progenitor cell populations accumulate during aging

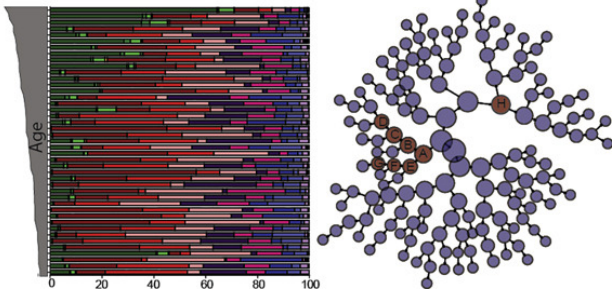


Epigenome

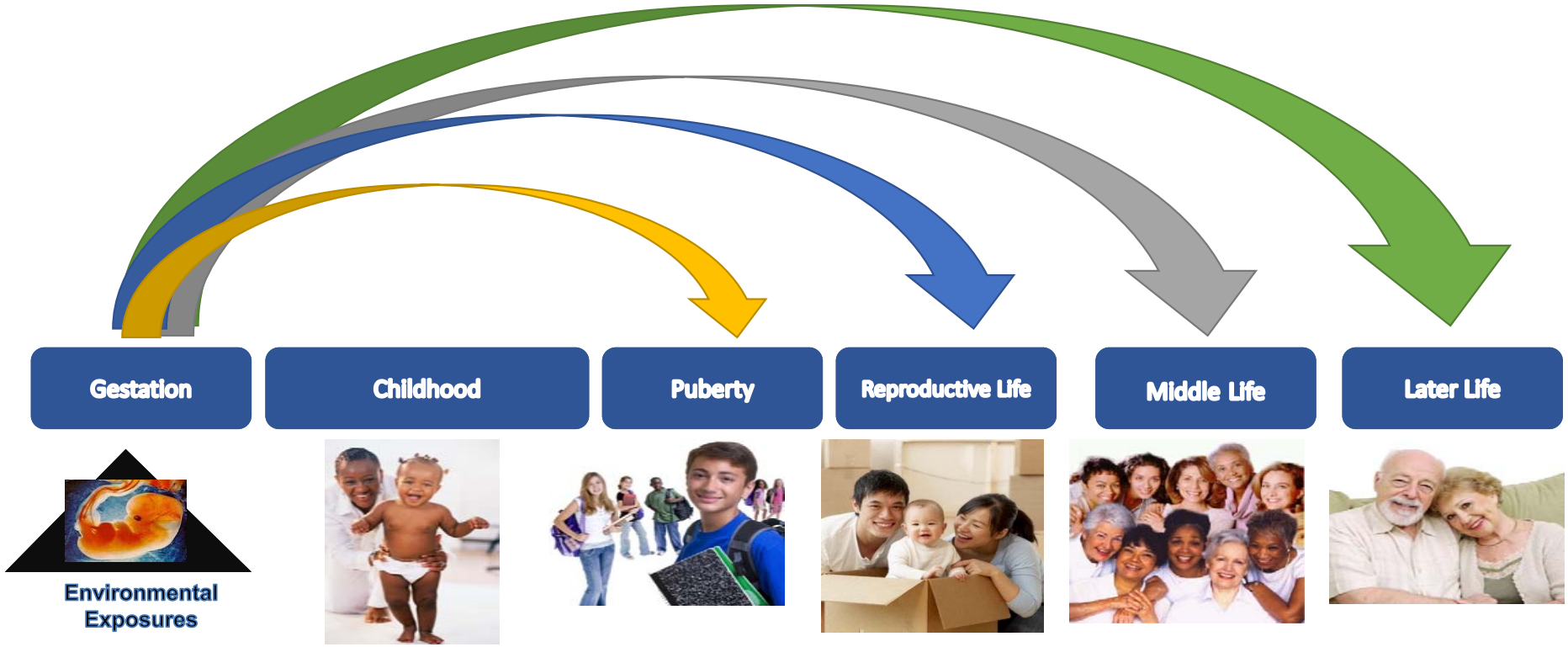


Stem Cells

Computational analyses

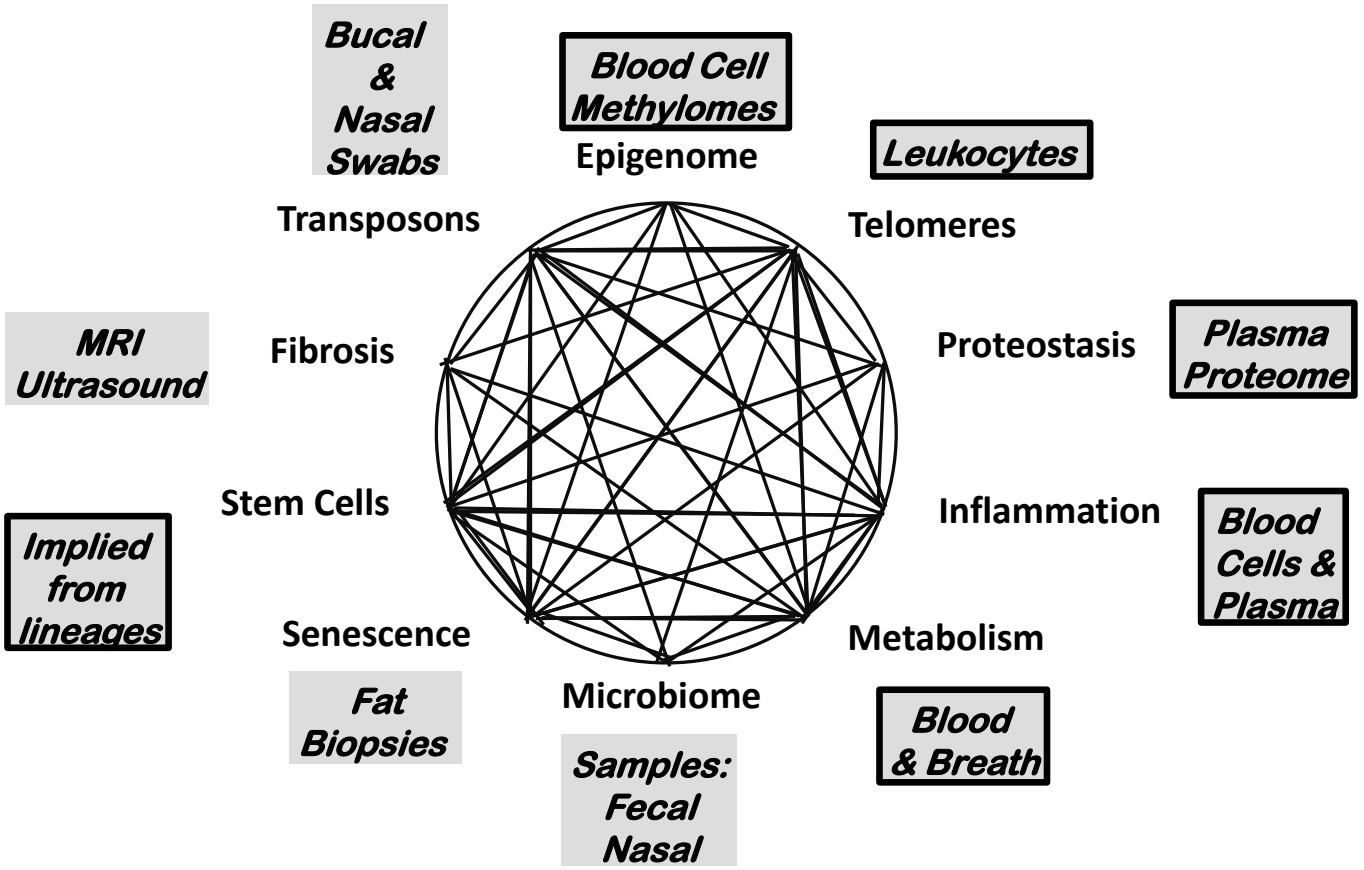


Individual susceptibility across the life span

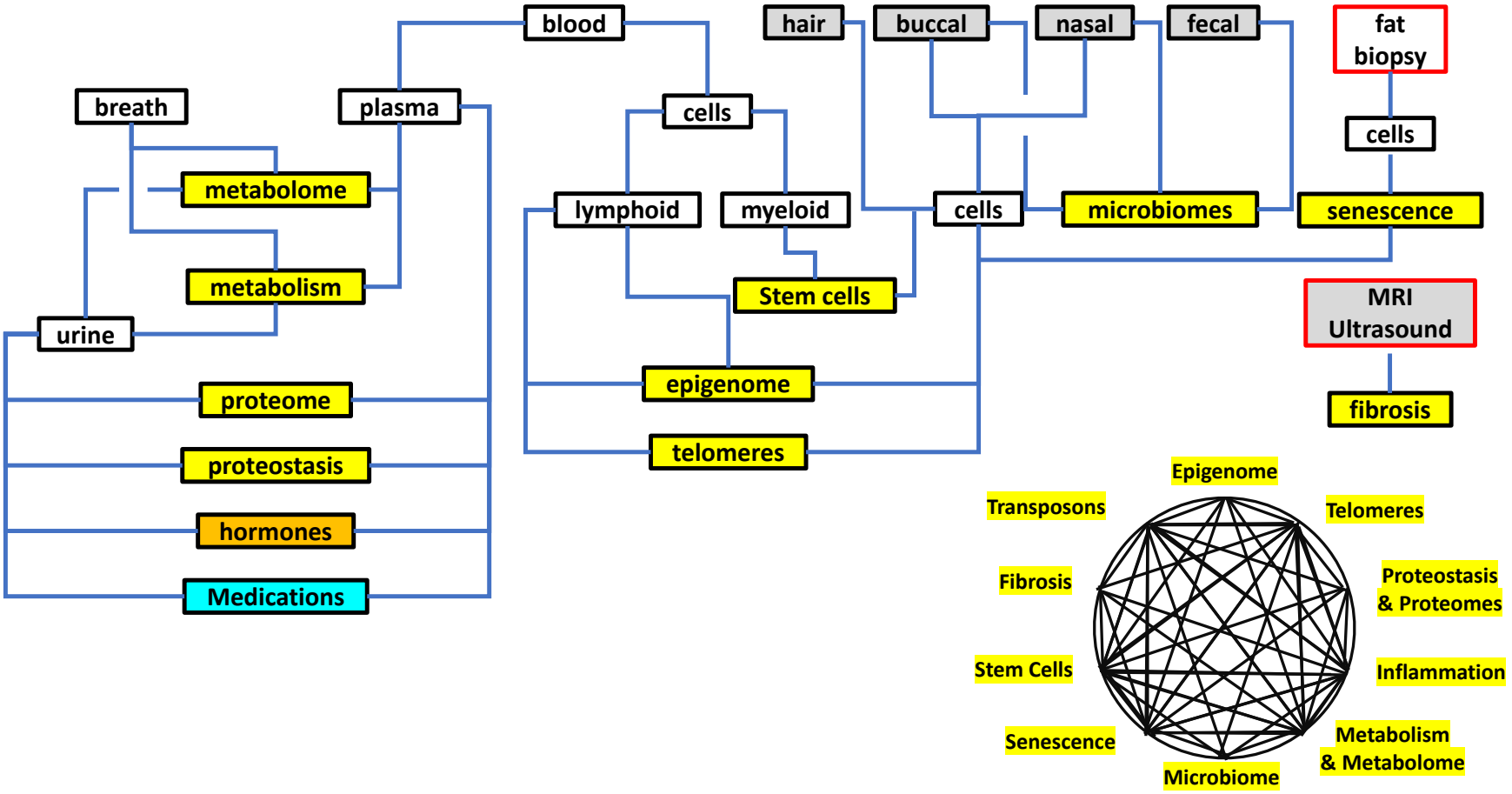


Individual susceptibility across the life span: Outcomes for aging

For environmental exposures: sample collection mapped to the hallmarks of aging



Samples in a doctor's visit



Combining Functional and Molecular Metrics in Adults

	Newborn		Adult	LL-Adult
Cognition			Response time, memory	Response time, memory
Appearance		blue or pale all over	BMI, skin tone, hair	Change in weight, skin tone, hair
Pulse		0 to >100	+/- exertion	+/- exertion
Grimace		… when stimulated	Response to stimulation in periphery and centrally	Response…
Activity		Motion and resistance	Motion and Resistance	Motion and Resistance
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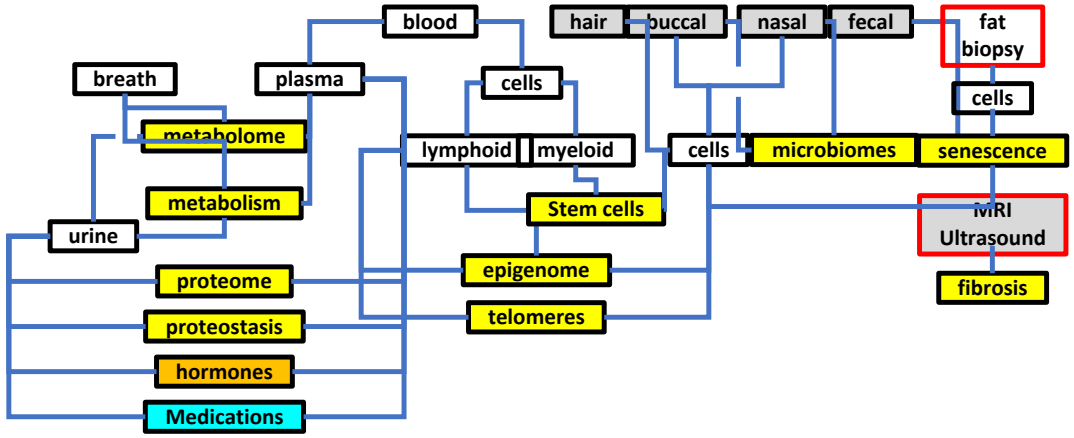
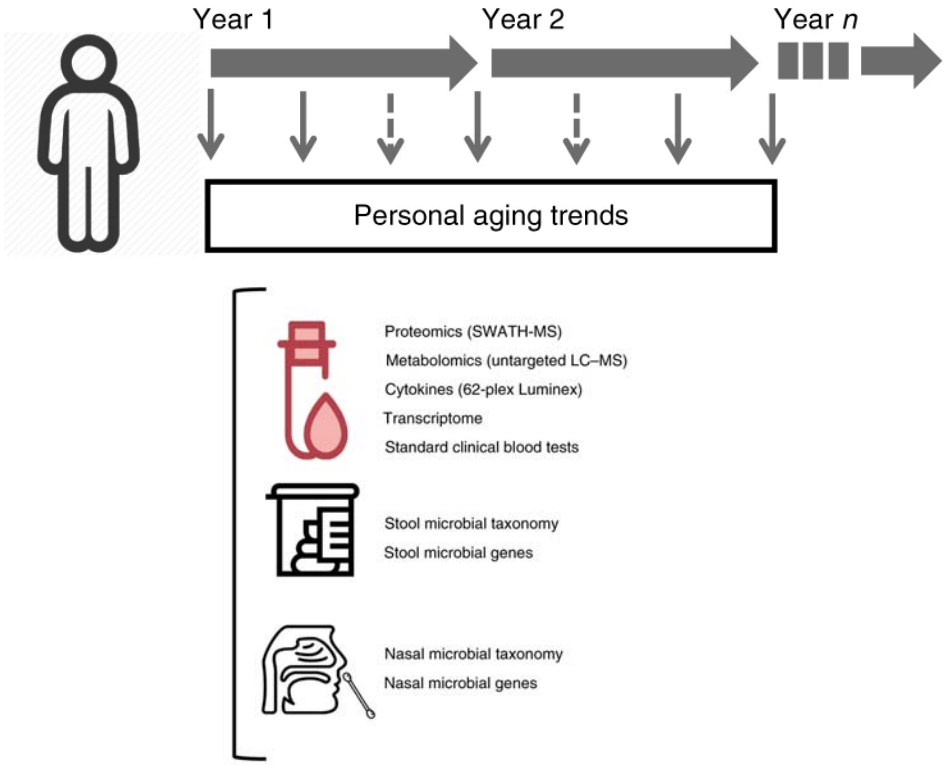
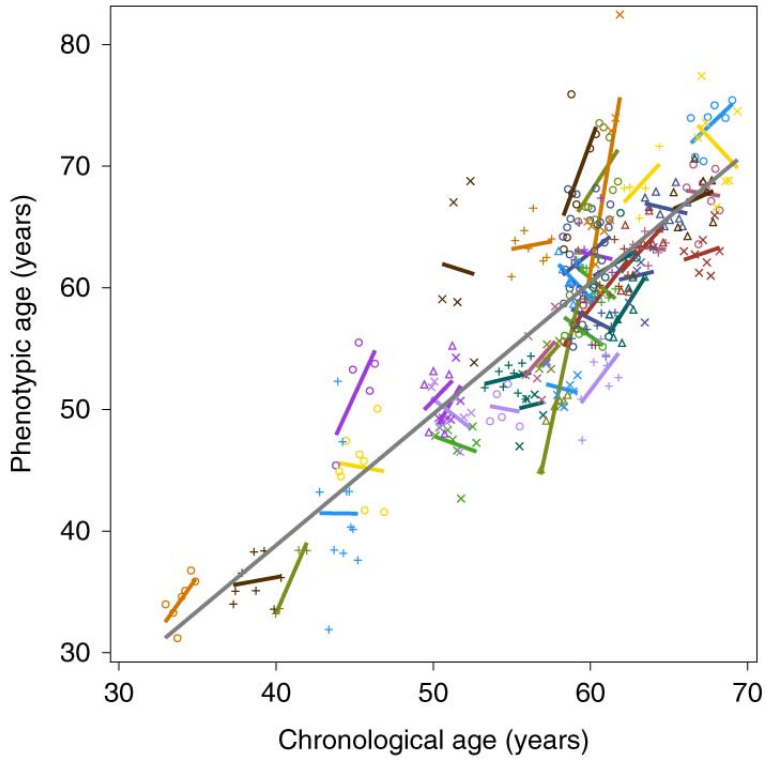


Rates of Aging in Humans





Ahadi et al. Nat Med . 2020 Jan;26(1):83-90

Conclusions for Aging

- Molecular hallmarks can be used to understand interactions between the environment and aging
  - Example from breast cancer
- Clinically useful information about the trajectories of human aging can be obtained in 2-3years of doctor's visits
  - Trajectories are individual
- Studies in laboratory animals establish principles and validate useful tools
  - Biology of aging and geroscience can be done in humans

Conclusions for
Aging in Challenging Environments

- Explore how a variety of environmental factors influence the aging process and disease outcomes in aging populations
- Environmental effects that are chronic, acute, and combined

- PAR-19-249 Aging Processes
  - (NIEHS, NIA, OBSSR)
- PAR-19-250 Aging Populations
  - (NIEHS, NIA, NINR, NIMHD, OBSSR)