Novel Approaches: "Good Health and Function"

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Grand challenge II-2

- Develop strategies to identify gene variants that contribute to good health and to resistance to disease
  - Healthy cohort
    - Requires long term observation
  - Exposed yet resistant cohort
    - Genetic risk without disease
    - Environmental exposure without disease
    - Disease without illness (CHD, AD)

Life’s a drag for Winnie Langley

What does it take to live a long, healthy life?

- In utero and early life exposures
- Sex
- Lifestyle/environment/behavior
- Development of peak physiologic potential
- Late onset of age related chronic disease
- Slow rate of decline in function
- Protective capacity – stem cells, repair mechanisms, senescence and apoptosis

Evolutionary biology of aging

- Antagonistic pleiotropy – Enhancement of reproductive fitness may have negative effects in late life
  - Down regulation of reproduction and protection of soma during environmental challenge
    - E.g., thrifty phenotype and diabetes, immune responsiveness and vascular disease, sex steroids and cancer risk
- Longevity assurance - Enhancement of organism integrity throughout life
- Damage accumulation
  - Late onset mutations
  - Stochastic effects – nuclear, mitochondrial, epigenetic
  - Senescence

Models for the study of healthy aging

- Caloric restriction – reduced size and fertility, longer life span
- Progeroid syndromes – DNA repair mechanisms
- Exceptional survival/longevity – comparison group
- Delayed onset disease/slow rate of aging

Research opportunities in population studies

- Longitudinal cohort studies – identify those who survive to age 90 or 100
- Rate of change phenotypes – middle to old age
- Resistant or adapted phenotypes – protective factors
- Family studies – Centenarian offspring, twins, sib pairs, 2-3 generation families
- Life course studies – e.g. NCS

Challenges

- Heterogeneity of “normal” – Need to determine correlations between systems - or lack of correlation.
- Study age effect rather than adjust it away
- Need measures sensitive to early decline in health – potential candidates – muscle strength, vascular measures
- Measures of physiologic reserve – early disease often not detectable in absence of stress
- Life course data collection - exposures
- Biomarkers – tissue specific?