**Definition of Normal Biological Aging**

- Aging is defined as the decline and deterioration of functional properties at the cellular, tissue and organ level.

  - Loss of functional capacity
  - Loss of homeostasis
  - Decreased adaptability
  - Increased vulnerability to disease and mortality

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**Dysregulated Cytokines: Sickness Behavior**

- IL-1ra
- IL-1β
- IL-6
- TNFα
- IL-10

- Fever → Anorexia/Weight Loss
- IL-6 → Muscle Loss

- IL-1ra stimulate
- IL-1β inhibit

- TNFα, IL-6, IL-1ra, sTNFRs

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**Dysregulated Cytokines: Nutrition**

- ↑ Leptin
- ↑ IL-1β
- ↓ food intake
- ↑ energy consumption
- IL-1ra
- Weight Loss

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Mouse Studies

Cytokine dysregulation can have multiple causes
- disrupted tumor suppressors
- structural proteins
- feedback signaling

P53-/-, BubR1-/-, p63-/-, B6C3FeCcl2-/-, IL-10tm/tm

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Mouse Studies

Models exhibit facets of aging/frailty:
- Weight loss
- Sarcopenia
- Osteopenia
- Reduced stress tolerance
- Elevated pro-inflammatory cytokines

Overlap: apoptosis, senescence, inflammation