The Geroscience Hypothesis & Hallmarks of Ageing

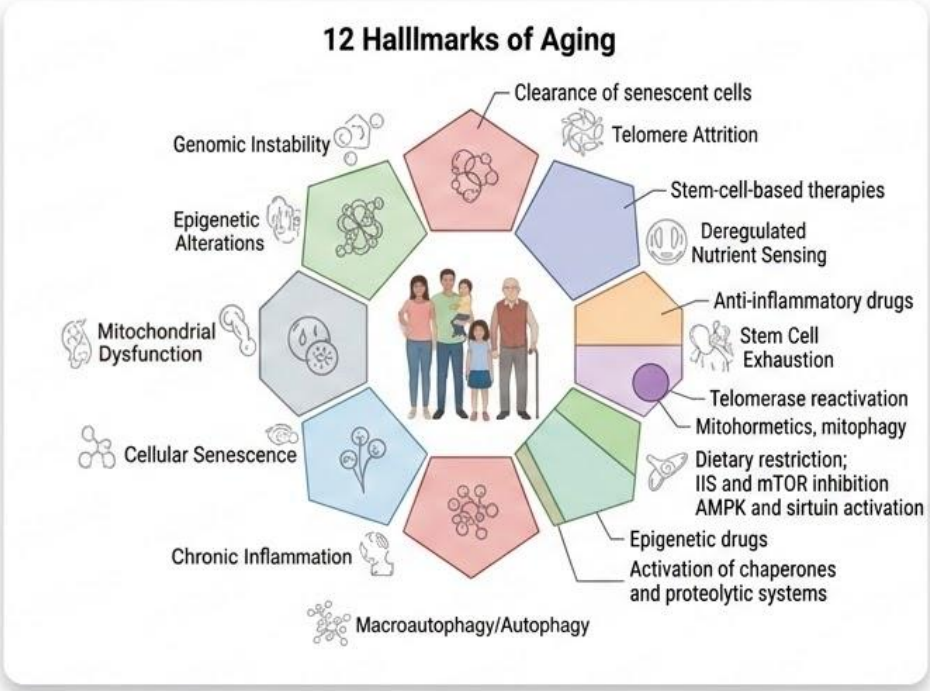
The Geroscience Hypothesis

"The core idea that cellular changes occurring during ageing can be targeted to modify age-related diseases."

Key Pillars of the Strategy:

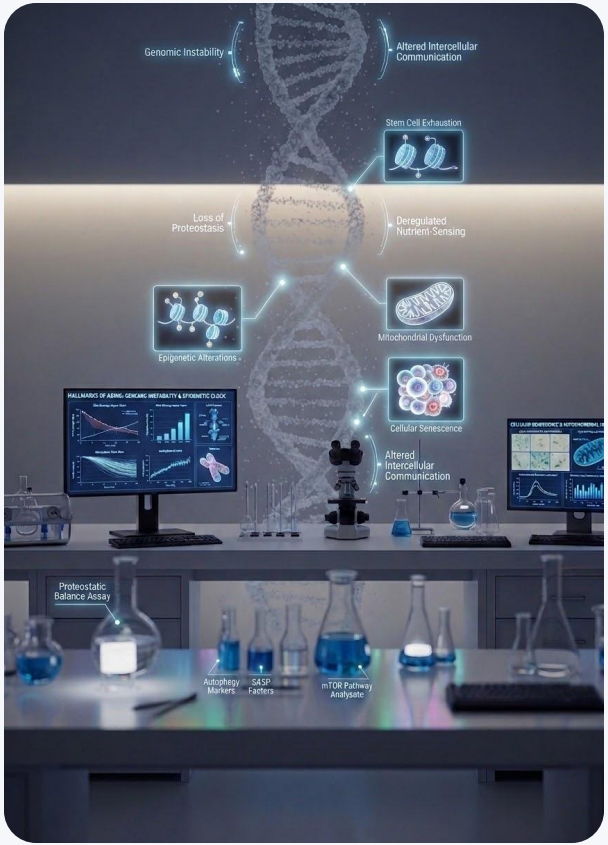
- **Healthspan:** Improving the number of healthy, functional years.
- **Lifespan:** Increasing overall longevity through biological intervention.
- **Targeted Modification:** Addressing root causes rather than symptoms of multimorbidity.

By addressing these "hallmarks" early, we can potentially delay or even reverse the ageing process itself.



Visualized Hallmarks of Ageing and Biological Targets

The Geroscience Hypothesis: Hallmarks of Ageing



Cellular changes occurring during the ageing process can be targeted to modify the development of age-related diseases and multimorbidity.

Genomic Instability

Accumulation of DNA damage over time leads to cellular malfunction or cancer.

Telomere Attrition

Protective end caps shorten, triggering cell death or "zombie" senescence.

Epigenetic Alterations

Changes in gene expression "switches" adversely affecting protein manufacture.

Cellular Senescence

"Zombie cells" release SASP molecules driving chronic inflammation.

Mitochondrial Decay

Loss of cellular powerhouses leading to oxidative stress and energy decline.

Inflammaging

Chronic systemic inflammation preventing effective tissue repair.

Inflammaging: The Fire of Chronic Systemic Decay

Chronic systemic inflammation preventing effective tissue repair and driving the progression of age-related pathologies.

Persistent Immune Activation

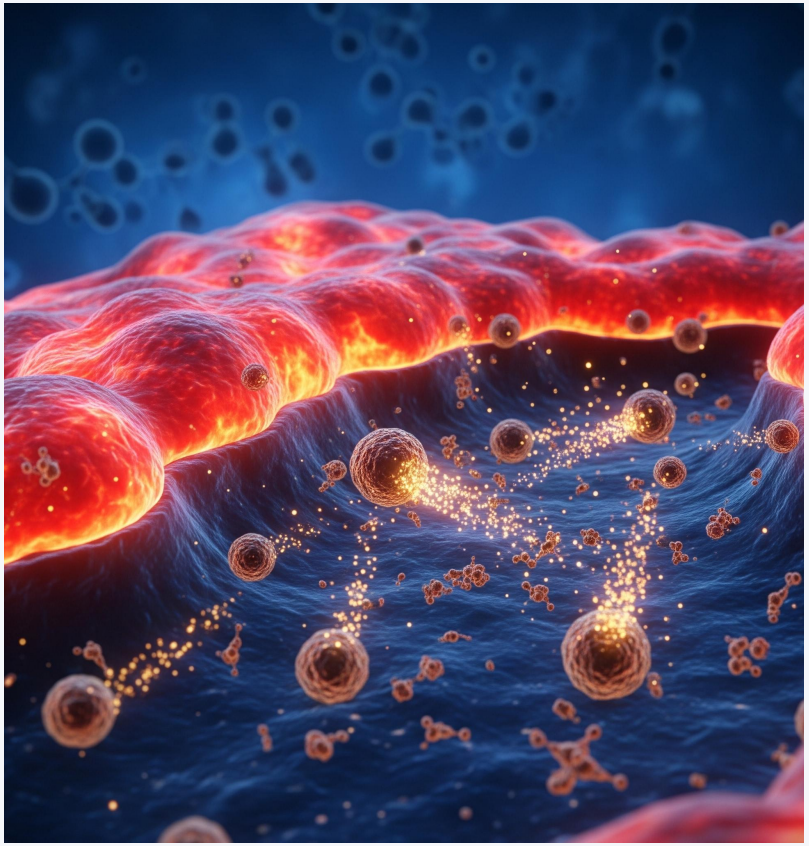
The immune system remains in a constant state of low-grade alert, exhausting cellular resources and damaging healthy structures.

Impaired Tissue Regeneration

Inflammatory signals interfere with stem cell niches, preventing the effective replacement of worn-out or damaged cells.

Cytokine Storm of Aging

Elevated levels of IL-6, TNF-alpha, and CRP circulate throughout the body, acting as systemic drivers for multi-organ decline.



Cellular Senescence: The "Zombie Cell" State

"Zombie cells" cease dividing but remain metabolically active, releasing harmful SASP molecules that drive chronic inflammation.

Growth Arrest

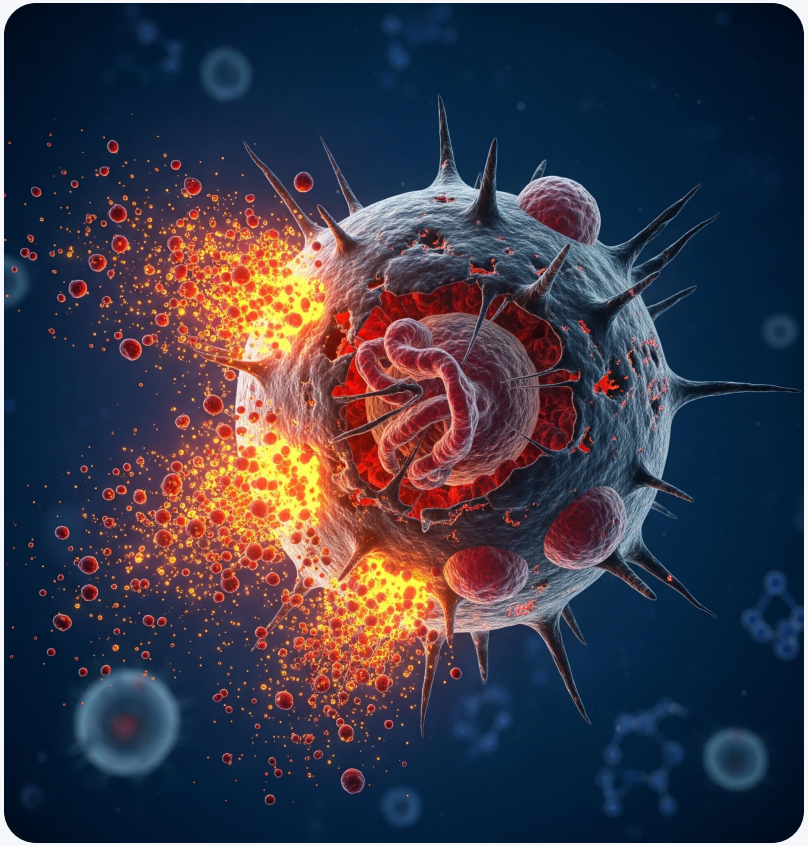
Cells permanently stop dividing in response to damage, acting as a double-edged sword for tumor suppression and aging.

The SASP Profile

The Senescence-Associated Secretory Phenotype (SASP) releases pro-inflammatory cytokines that damage neighboring healthy cells.

Tissue Dysfunction

Accumulation of senescent cells leads to impaired regeneration, chronic disease, and the progressive decline of organ function.



Telomere Attrition: The Cellular Aging Clock

Protective end caps shorten, triggering cell death or "zombie" senescence as biological limits are reached.

End-Cap Erosion

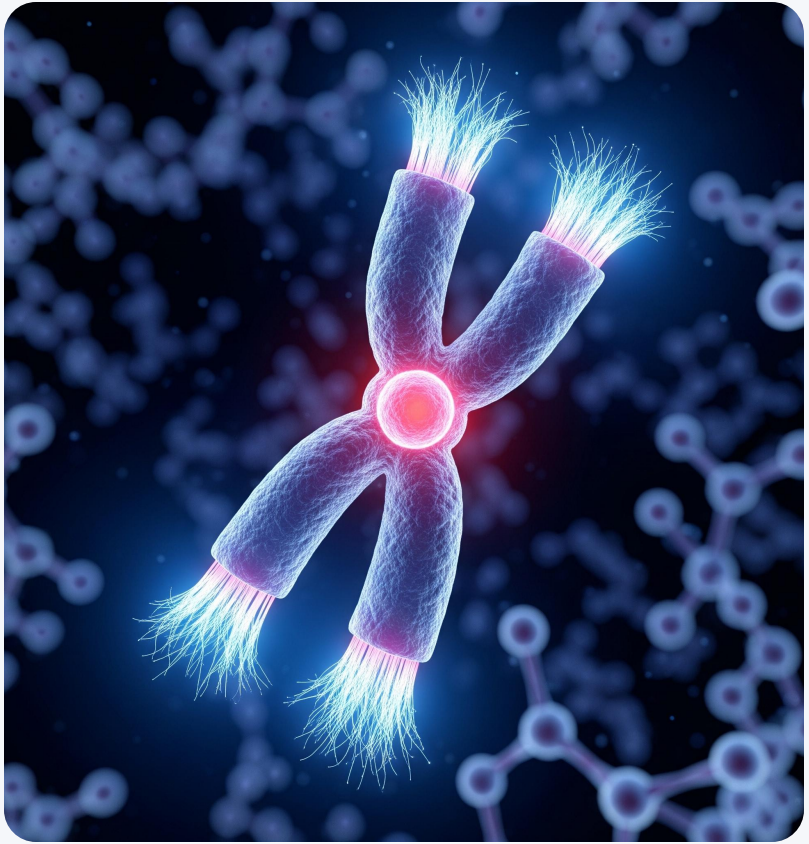
Repeated cell division whittles away the repetitive DNA sequences that protect the chromosome tips.

The Hayflick Limit

Cells reach a critical threshold where telomeres are too short to support further healthy replication.For humans 50 cell divisions are the maximum.

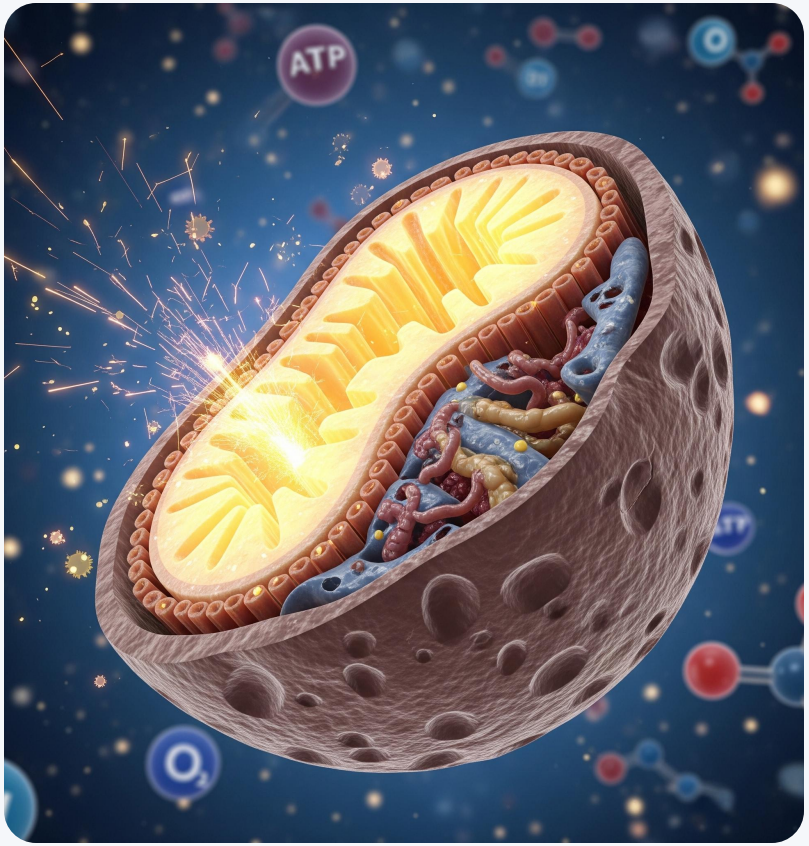
Apoptosis vs. Senescence

Critically short telomeres trigger a DNA damage response, leading to programmed cell death or "zombie" states.



Mitochondrial Decay: The Cellular Powerhouse Crisis

Loss of cellular powerhouses leading to oxidative stress, energy decline, and a "perfect storm" of decay.



Decreased ATP Production

Declining mitochondrial efficiency results in lower energy levels for vital organs like the brain and heart.

Oxidative Stress & ROS Leakage

Dysfunctional mitochondria leak electrons, dramatically increasing Reactive Oxygen Species (ROS) that damage DNA.

NAD+ & Glutathione Depletion

Age-related decline in vital coenzymes compromises repair mechanisms and the body's master antioxidant protection.

Genomic Instability: The Root of Aging

Accumulation of DNA damage over time leads to cellular malfunction or cancer.

DNA Damage Accumulation

Environmental factors and metabolic byproducts cause persistent lesions in the genetic code.

Cellular Malfunction

Errors in protein synthesis and signaling pathways disrupt normal tissue homeostasis.

Oncogenic Transformation

Unrepaired mutations can trigger uncontrolled cell division and cancer development.



Epigenetic Alterations: The Genetic "Switches"

Changes in gene expression "switches" adversely affecting protein manufacture.

DNA Methylation

Chemical tags added to DNA that can turn genes on or off, affecting cell identity.

Histone Modification

Changes to the proteins DNA wraps around, altering how easily genes are read.

Chromatin Remodeling

The structural reorganization of chromatin that controls the access of repair proteins.

