

THE 12 HALLMARKS OF AGING

Quick Reference | Lesson 1.2 | Primary → Antagonistic → Integrative

PRIMARY HALLMARKS		INITIAL CAUSES OF DAMAGE
Genomic instability	Accumulating DNA damage over a lifetime	
Telomere attrition	Shortening of chromosome-protecting caps with each cell division	
Epigenetic alterations	Changes in gene expression without changes to the DNA sequence itself	
Loss of proteostasis	Declining ability to maintain properly folded, functional proteins	
Disabled macroautophagy	Reduced capacity to clear damaged cellular components (added 2023)	
ANTAGONISTIC HALLMARKS		PROTECTIVE RESPONSES THAT HARM IF CHRONIC
Deregulated nutrient-sensing	Dysfunction in pathways (e.g. insulin signalling) that respond to food intake	
Mitochondrial dysfunction	Declining efficiency of the cell's energy-producing structures	
Cellular senescence	Cells stop dividing (anti-cancer protection) but accumulate and secrete inflammatory signals	
INTEGRATIVE HALLMARKS		WHERE DAMAGE BECOMES VISIBLE DECLINE
Stem cell exhaustion	Declining capacity for tissue repair and renewal	
Altered intercellular communication	Disrupted signalling between cells, including hormonal/inflammatory	
Chronic inflammation (inflammaging)	Persistent, low-grade inflammatory activity (added 2023)	
Dysbiosis	Gut microbiome imbalance, now recognised as an active driver of systemic aging (added 2023)	

ONE ACTION, MULTIPLE HALLMARKS

A single lifestyle intervention (e.g. improving sleep) can influence multiple hallmarks across categories simultaneously — see Lesson 1.2 for a full worked mechanism.