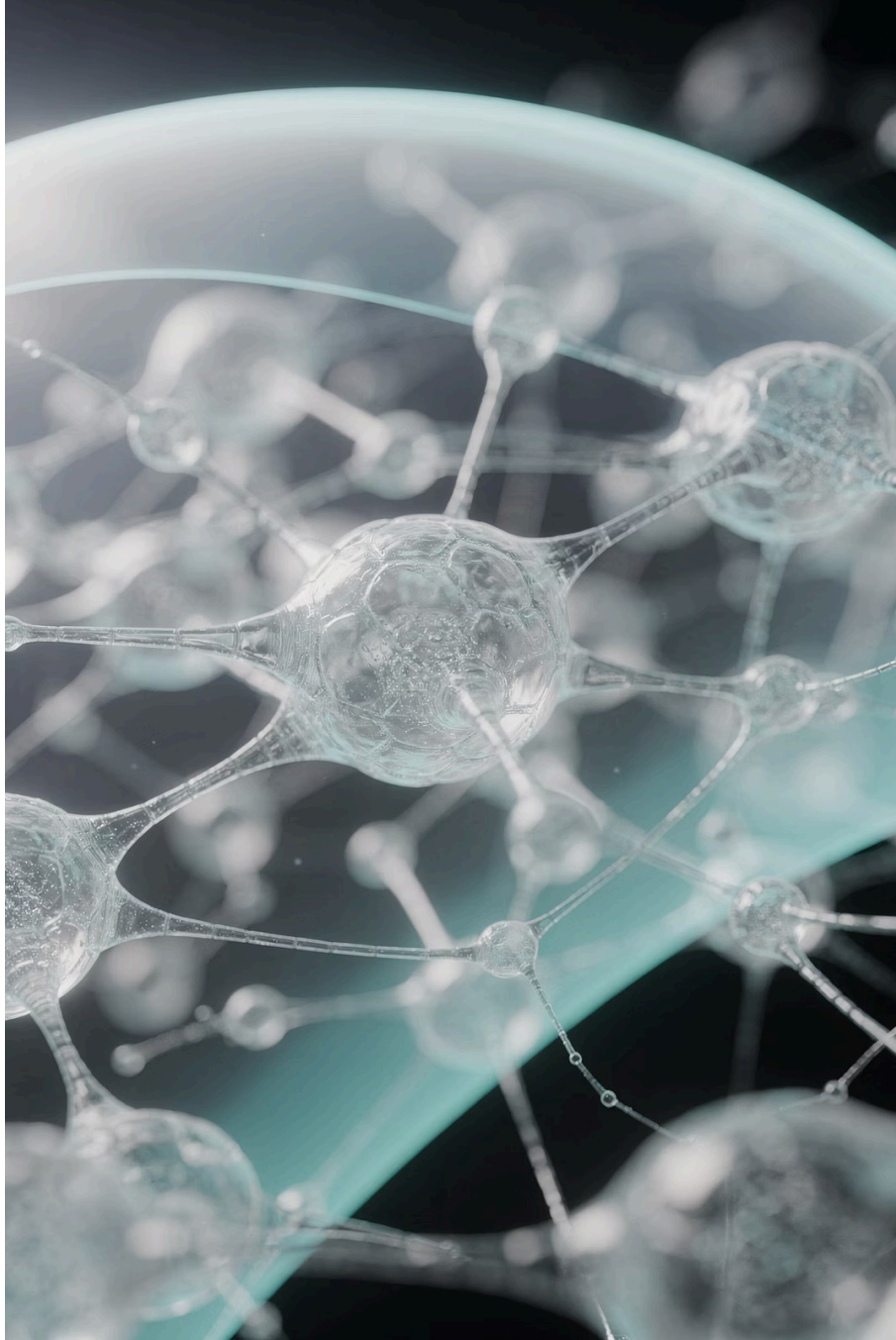
Humanin

The cell's internal survival signal

Humanin is a naturally occurring peptide that acts as an internal safety mechanism—a molecular guardian encoded in our own mitochondrial DNA. It exists to help cells survive stress, maintain function, and avoid premature failure when faced with oxidative damage, metabolic strain, or inflammatory assault.

This is not a performance booster designed to push limits. It's a **resilience multiplier** that fortifies the foundation upon which all cellular performance depends. Think of it as upgrading the structural integrity of a building rather than adding more floors.



The problem no one markets well

Most decline starts long before symptoms

People think decline shows up as fatigue, brain fog, poor recovery, or visible aging. In reality, those are **late signals**—the smoke alarm going off after the fire has already started.

The real problem begins years earlier when cells lose their ability to tolerate stress without breaking down. Mitochondria become less efficient. Protein folding goes awry. Cellular cleanup systems slow. Stress tolerance erodes silently.

By the time you feel it, the infrastructure has been compromised for months or years.

The Hidden Timeline

Years 1-3: Silent cellular stress accumulation

Years 4-6: Subclinical dysfunction begins

Years 7+: Symptoms finally emerge

Why traditional approaches stall

They chase output, not stability

Most solutions push harder rather than build stronger. The playbook is predictable: more stimulation, more hormone replacement, more supplements to force outcomes. And it works—until the underlying cellular machinery can't keep up with the demands being placed on it.

More Stimulation

Caffeine, nootropics, adaptogens—pushing systems to produce

More Replacement

Hormones, precursors, cofactors—substituting what's missing

More Force

Training harder, eating less, optimizing relentlessly

That's where plateaus come from. The engine can't sustain the output you're demanding because the *engine itself* needs maintenance, not more fuel.

Humanin enters upstream

Before damage, not after

Humanin isn't trying to "fix" a broken system with downstream interventions. It exists to **prevent systems from breaking in the first place** by intervening at the earliest possible point in the stress-damage cascade.

Most therapies address consequences: inflammation, oxidative damage, protein aggregation, apoptosis. Humanin addresses the **decision point** where a cell either withstands stress or begins the path toward dysfunction.

This is a different intervention point entirely—and it's why the effects feel structural rather than symptomatic.

What Humanin actually is

A built-in cellular survival peptide

Humanin is a 24-amino acid peptide produced inside the body—specifically within mitochondria—as a protective signal in response to cellular stress. Its job is to help cells resist stress-related death and dysfunction by modulating pathways that govern apoptosis, inflammation, and metabolic stability.

It's encoded in the mitochondrial genome, making it part of an ancient evolutionary defense system. When cells detect threat signals, Humanin production increases as a molecular countermeasure.

Discovered in 2001

First identified in Alzheimer's research as a neuroprotective factor

Mitochondrial Origin

Encoded in mtDNA, transcribed during stress response

Natural Decline

Levels decrease with age, correlating with cellular vulnerability

> Think of it as the body saying: "Let's not let this cell fail today."

The key distinction

Preservation vs stimulation

Humanin doesn't:

- Increase output or force performance
- Push growth or anabolic signaling
- Force energy production beyond capacity
- Stimulate receptors to create activation
- Replace missing hormones or substrates

Instead, it:

- Protects cellular integrity during stress
- Supports mitochondrial survival and function
- Improves stress tolerance at the membrane level
- Reduces inappropriate apoptotic signaling
- Stabilizes metabolic homeostasis

That distinction matters. Stimulation creates demand. Preservation maintains capacity. One burns out systems. The other sustains them.

Why mitochondria are central

Energy systems are fragile

Mitochondria don't fail loudly with sudden collapse—they fail quietly through gradual degradation. Inflammation chips away at membrane integrity. Oxidative stress damages respiratory chain complexes. Metabolic overload impairs calcium buffering and membrane potential.

The result isn't zero energy—it's *inconsistent* energy. Some days you're fine. Other days you crash. Recovery becomes unpredictable. Performance becomes volatile. This variability is often more disruptive than a consistent lower baseline.

Humanin helps stabilize this environment so energy production remains consistent instead of erratic. It doesn't boost mitochondrial output—it protects mitochondria so they can **sustain their output** under real-world stress.

The mental model

Seatbelts, not horsepower

The Seatbelt

You don't feel seatbelts when things are smooth. You're grateful for them when things go wrong.

The Engine

Horsepower is what you feel immediately—acceleration, speed, raw output.

Humanin functions like the seatbelt: **Invisible when things are good. Critical when stress hits.** It's not designed to make you feel supercharged. It's designed to keep your cells alive and functional when metabolic, oxidative, or inflammatory stress would otherwise push them toward failure.

The value becomes apparent not in perfect conditions, but during the inevitable periods of challenge—illness, overtraining, sleep deprivation, psychological stress, aging.

What people usually notice

Less volatility

This isn't a "feel it Day 1" compound with acute stimulation or immediate mood lift. What tends to show up instead is a **narrowing of the volatility range**—fewer extreme highs and lows, more predictable baseline function.

More stable energy

Energy levels become more consistent throughout the day, with fewer unexplained crashes or dips in the afternoon

Better stress tolerance

Physiological and psychological stressors feel less overwhelming; recovery from acute stress improves

Fewer crashes

The post-workout, post-work, or post-travel collapse becomes less severe and shorter in duration

Improved recovery consistency

Day-to-day variability in how you feel upon waking decreases; baseline becomes more reliable

It's structural, not flashy. The benefit accumulates in the *absence of problems* rather than the presence of enhancement.

Why Humanin plays well with others

It doesn't compete — it reinforces

Humanin doesn't overlap with performance compounds in mechanism or outcome. It doesn't compete for the same receptors, pathways, or resources. Instead, it strengthens the cellular environment those compounds rely on to work effectively.

Performance peptides and hormones create demand on cellular systems—they ask cells to produce more, adapt faster, recover quicker. That's valuable, but it only works if the underlying cellular machinery is resilient enough to meet those demands without breaking.

Stack Amplifier

Humanin improves the **substrate** that other interventions act upon, making them more effective and sustainable.

That makes it a **stack amplifier**, not a stack hog. It doesn't steal the spotlight—it makes sure the stage doesn't collapse.

Best stacked with

Humanin works best in a systems stack

SS-31 (Elamipretide)

Mitochondrial membrane protection + efficiency

Humanin preserves the cell and prevents apoptosis → SS-31 optimizes energy flow inside mitochondria by stabilizing cardiolipin and improving electron transport efficiency

MOTS-c

Metabolic signaling + stress adaptation

MOTS-c drives metabolic adaptation and improves insulin sensitivity → Humanin improves cellular survival during the stress of adaptation, allowing changes to take hold

Epitalon

Longevity signaling + circadian repair

Epitalon handles telomere protection and circadian rhythm optimization → Humanin handles cellular durability so those long-term benefits can accumulate without attrition

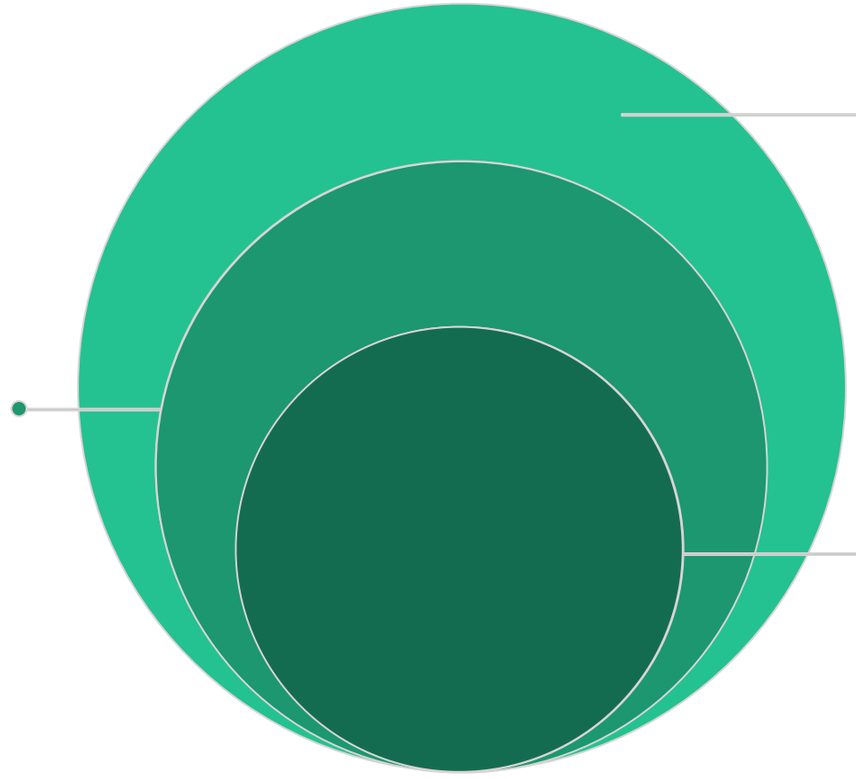
Tesamorelin / GH-axis support

Structural repair and recovery

Growth hormone signaling drives tissue repair, lipolysis, and anabolic processes → Humanin improves cellular resilience so those processes don't create unsustainable metabolic strain

How to think about stacking logic

Order matters



Top: Performance & Recovery

Growth factors enhance recovery and function

Middle: Metabolic Optimizers

MOTS-c and SS-31 improve metabolism

Foundation: Humanin

Cellular resilience and baseline protection

Humanin belongs at the **foundation** of a longevity or performance stack—not as an afterthought or finishing touch. It creates the conditions that allow other interventions to work more effectively and sustainably.

01

Early in a stack

Establish cellular resilience before adding performance or adaptation stressors

02

As foundational infrastructure

Think of it as upgrading the operating system before installing demanding applications

03

Supporting long-term resilience

The value compounds over months and years, not days

Not as a finisher. Not as a stimulant. Not as a rescue tool. As a *foundation*.

Old model vs modern model

Old Model

Push systems until they fail

- Maximize output at all costs
- Replace what breaks
- Ignore upstream fragility
- Accept crashes as inevitable
- Measure success by peak performance

Modern Model

Protect systems so performance lasts longer

- Optimize for sustainable capacity
- Prevent breakdown before it starts
- Address cellular resilience first
- Reduce volatility and crashes
- Measure success by consistency over time

Humanin is firmly modern. It represents a shift from heroic intervention to intelligent preservation—from asking "how much can I push?" to "how long can I sustain?"

Why this matters long-term

Resilience compounds quietly

Cells that survive stress age better than cells that barely cope. Each time a cell successfully weathers oxidative damage, inflammatory signaling, or metabolic strain *without* accumulating dysfunction, it remains in the viable pool longer.

Humanin shifts the system toward **survival instead of attrition**. Over years, this creates a meaningful difference in the proportion of cells that remain functional versus those that have senesced, become dysfunctional, or undergone apoptosis.

1

Months 1-3

Subtle improvements in energy stability and stress tolerance

2

Months 6-12

Reduced frequency of crashes; more predictable baseline function

3

Years 2-5

Cumulative preservation of cellular populations; sustained performance capacity

4

Years 5+

Measurable difference in healthspan markers and functional resilience

That pays dividends over time—not in flashy ways you'll notice day-to-day, but in the *absence of decline* you would have otherwise experienced.

In short...

Humanin doesn't make you stronger.

It helps your cells last longer under pressure.

Not a stimulant

Doesn't force output or create acute effects

Not a replacement

Doesn't substitute for missing hormones or substrates

A resilience tool

Protects cellular integrity during inevitable stress

The value isn't in what you feel immediately. It's in what you *don't* lose over time. That's the essence of intelligent longevity intervention—not chasing peaks, but preserving capacity.

The Mitochondrial Peptide Trio

Three peptides, three mechanisms, one integrated system

Humanin: Cell Survival & Resilience

Role: Protective signal

Function: Helps cells tolerate stress without breaking down

Mental model: Insurance

Character: Quiet, foundational, upstream

MOTS-c: Metabolic Signaling & Adaptation

Role: Metabolic messenger

Function: Encourages cells to adapt to energy stress

Mental model: Training signal

Character: Active, adaptive, performance-adjacent

SS-31: Mitochondrial Efficiency & Repair

Role: Membrane optimizer

Function: Improves energy production efficiency

Mental model: Engine tuning

Character: Mechanical, targeted, performance-supportive

How they work together:

Humanin keeps the cell alive under pressure → MOTS-c tells the cell how to adapt → SS-31 makes the mitochondria run cleaner.

No redundancy. No competition. Each handles a different layer of the system.

Stack Logic

Humanin (Durability)

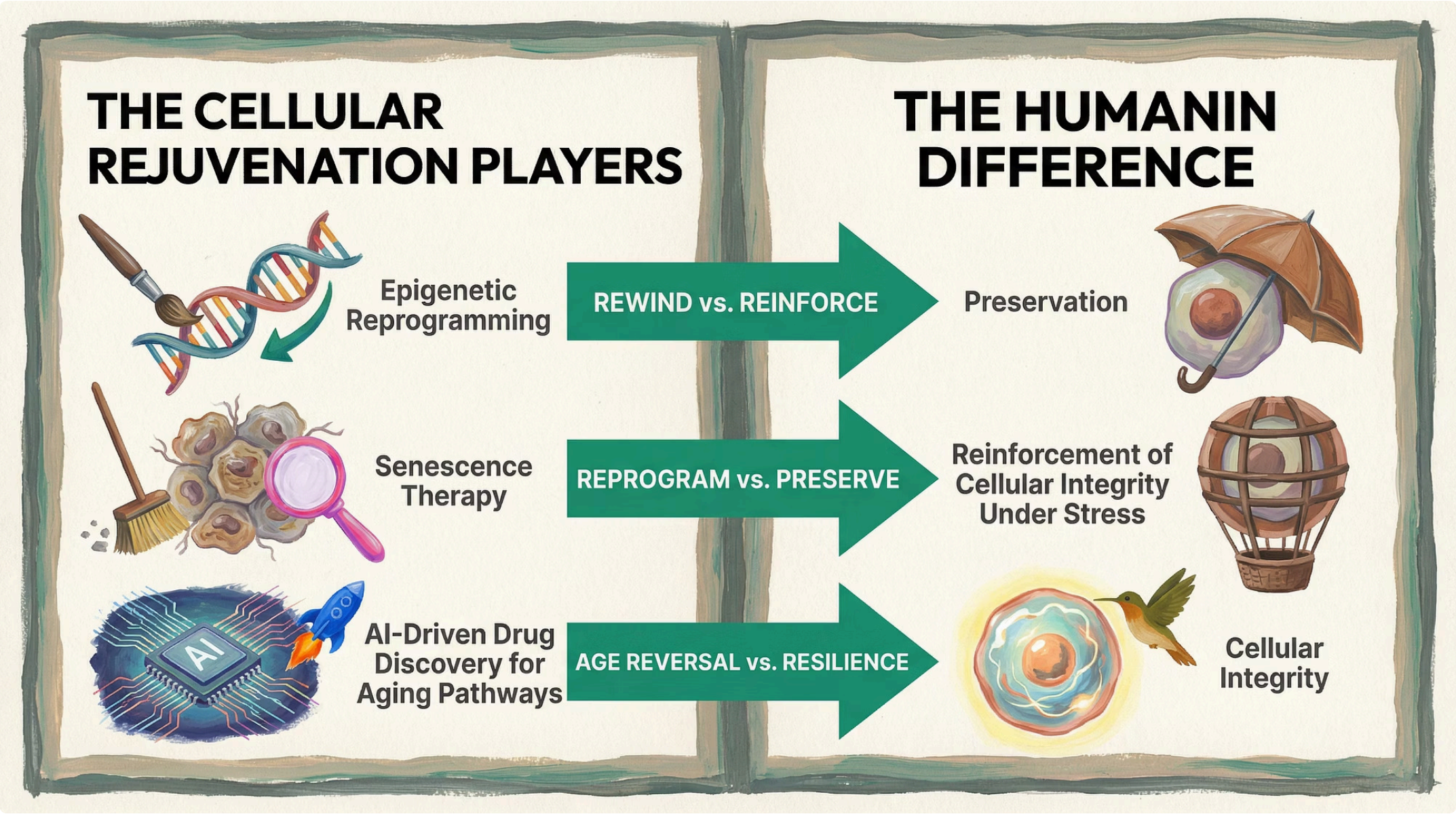
MOTS-c (Adaptation)

SS-31 (Efficiency)

You don't pick one—you **sequence them** based on what your system needs most.

Competitor Landscape

How others approach cellular longevity



The Cellular Rejuvenation Players

- **Altos Labs** (Backed by Jeff Bezos): Epigenetic reprogramming to "rewind the cellular clock" - focuses on reversing age-related cell decline
- **Juvenescence**: Developing therapies targeting senescence and stem cell regeneration
- **Insilico Medicine**: AI-driven drug discovery for cellular senescence and aging pathways

The Humanin Difference

Preservation vs. Reprogramming

While competitors focus on reversing or reprogramming cellular age, Humanin takes a fundamentally different approach: protecting existing cellular integrity under stress.

- They rewind → We reinforce
- They reprogram → We preserve
- They target age reversal → We target resilience

Most longevity biotech chases the 'fountain of youth.' Humanin protects the foundation you already have.

Clinical Evidence

What the research shows

USC Centenarian Study (2020)

Published in *Aging*

Key finding: Children of centenarians—who are statistically more likely to become centenarians themselves—had **significantly higher circulating humanin levels** than age-matched controls.

Additional findings:

- Humanin levels decline with age in most species
- Levels remain stable in naked mole-rats (a model of negligible senescence)
- First study to demonstrate humanin's link to both lifespan and healthspan

HNG Analog Trials

Published in *Heliyon* (2023) and *Aging* (2020)

S14G-humanin (HNG), a potent humanin analog, showed:

- Cardioprotective effects in heart failure models
- Improved metabolic healthspan in middle-aged mice treated twice weekly
- Reduced inflammatory markers
- Enhanced protection against toxic insults

Disease Correlation Research

Alzheimer's Drug Discovery Foundation (2020)

Humanin levels were significantly **decreased** in:

- Alzheimer's disease patients
- MELAS syndrome (mitochondrial disease)

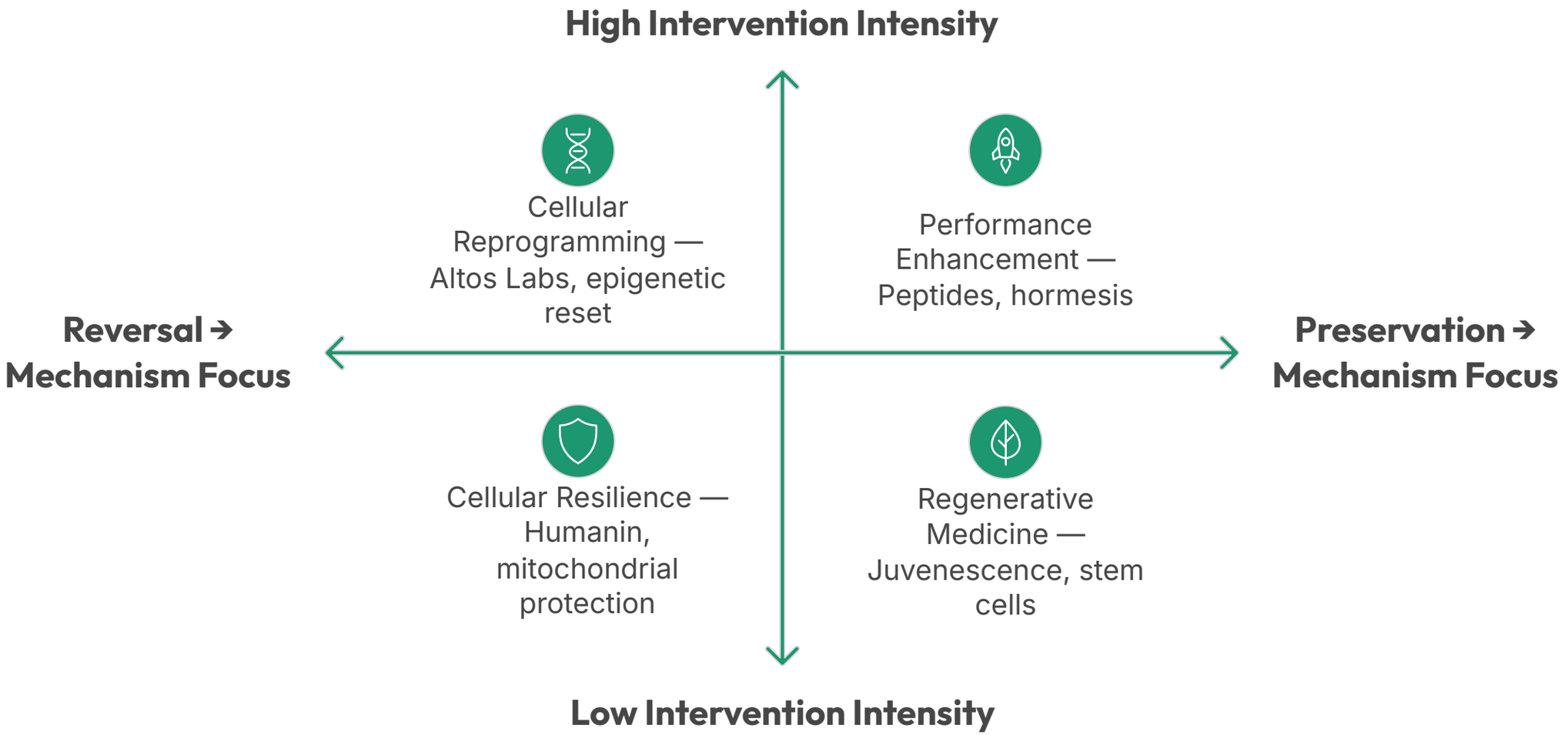
Higher humanin levels correlated with:

- Lower Alzheimer's risk
- Better metabolic health
- Improved insulin sensitivity

Sources: USC Leonard Davis School of Gerontology (2020); Heliyon, 2023; ADDF Cognitive Vitality Report, 2020

Market Positioning

Where Humanin fits in the longevity landscape



The strategic advantage: While billion-dollar biotechs chase dramatic cellular reversal, Humanin occupies the underserved 'cellular resilience' space—lower risk, complementary to existing protocols, and focused on what cells already do naturally.

Humanin: Mitochondrial Survival & Apoptosis Regulation

How Humanin protects cells from programmed death

The Mechanism

Humanin is a mitochondrial-derived peptide that directly regulates apoptosis—the process of programmed cell death. When cells face oxidative stress, inflammatory signals, or metabolic strain, Humanin:

- Binds to BAX (a pro-apoptotic protein) and prevents it from triggering mitochondrial membrane permeabilization
- Stabilizes mitochondrial membrane integrity under stress
- Preserves cellular energy production when it matters most
- Allows cells to survive transient stress rather than self-destruct prematurely

Why This Matters

Most performance protocols create cellular stress as a byproduct. Without adequate protection:

- Neurons become vulnerable to excitotoxicity
- Muscle cells face increased breakdown during recovery
- Metabolic tissues lose resilience over time

Humanin acts as **cellular insurance**—it doesn't enhance output, but it prevents unnecessary loss.

Think of it as: Protection before performance. Preserve the cell, extend the runway.