

The Guardian of the Brain

Innate Immunity, Autophagic Collapse, and the Path to Reversing Alzheimer's

Based on the Unified Hypothesis by Annelise E. Barron



The Billion-Dollar Dead End

Clinical Trials (Amyloid Targets)

Aducanumab

Lecanemab

Solanezumab

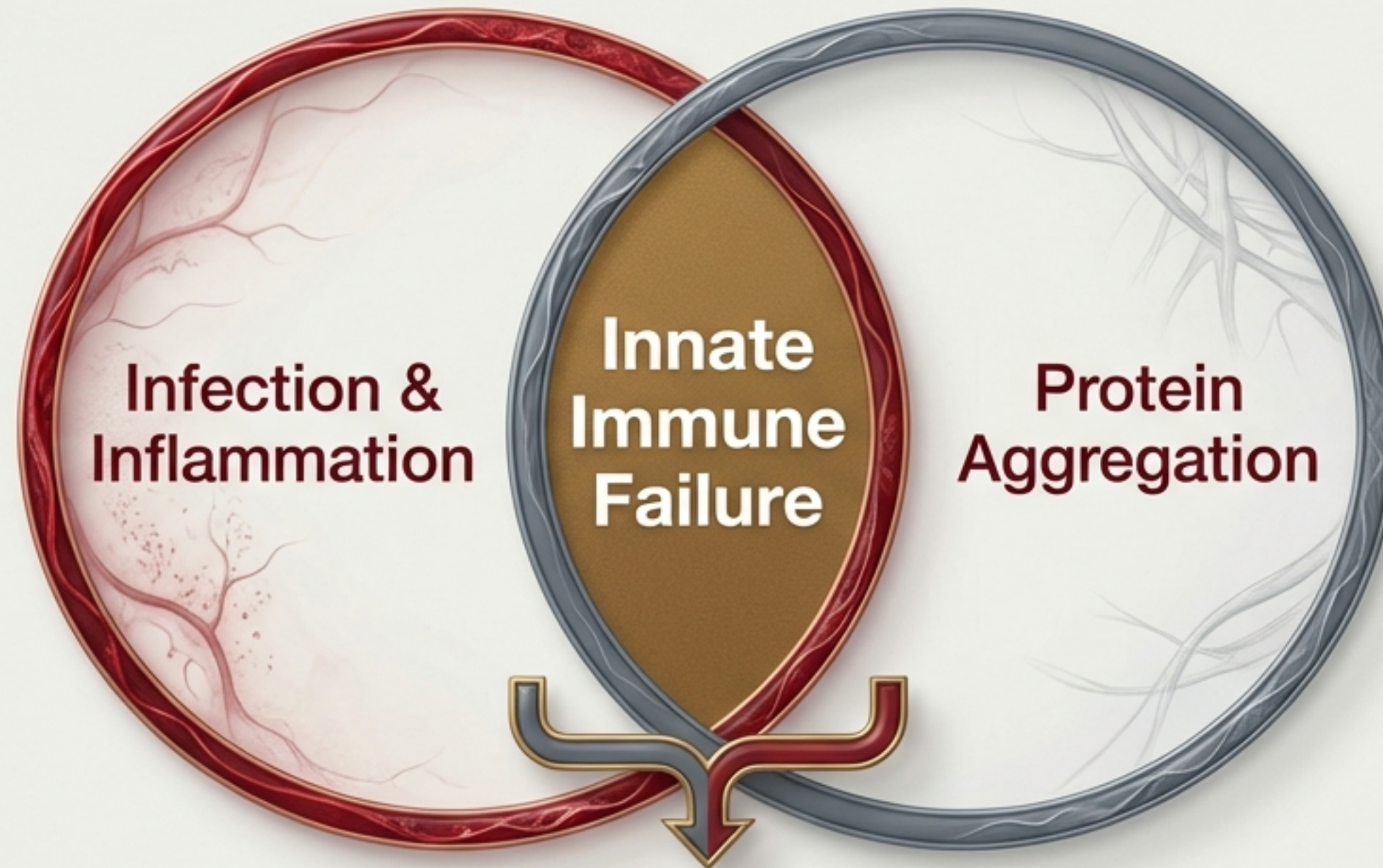
The Past

30 years of the Amyloid Cascade hypothesis.
Modest clinical benefits. Zero cures.
Are plaques the cause or the tombstone?

Global Dementia Prevalence

Unifying Infection and Degeneration

Alzheimer's is not just a protein disorder. It is an immune collapse.



The Mechanism:
Autophagic Collapse.

LL-37: The Brain's Swiss Army Knife

Antimicrobial



Anti-Inflammatory



Anti-Amyloid

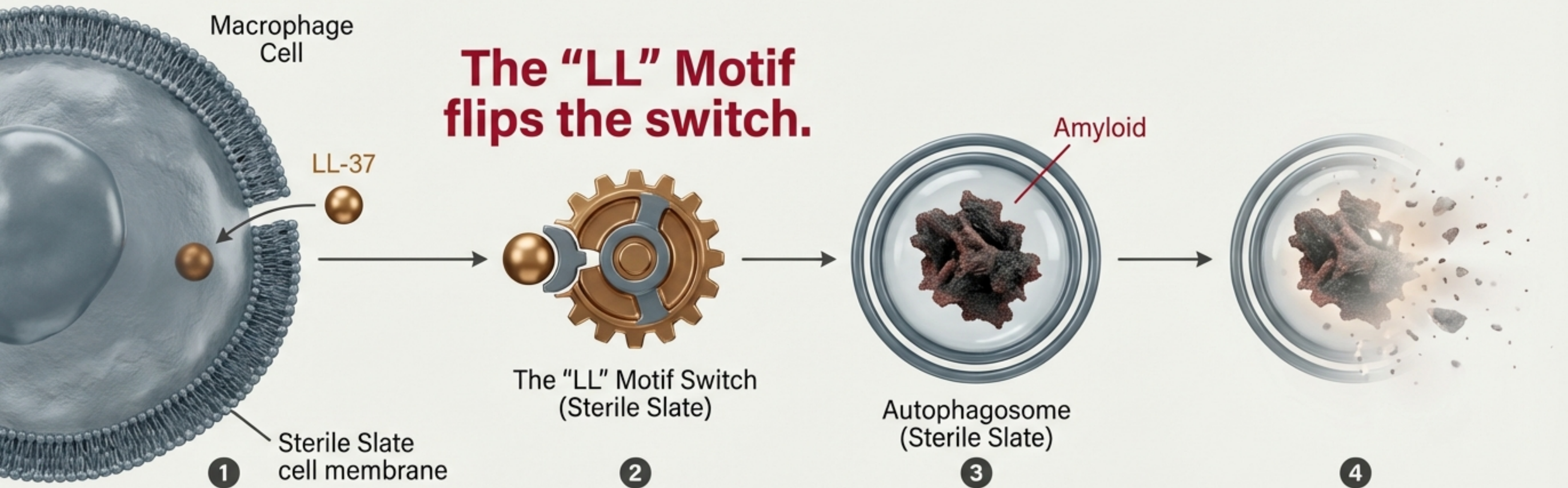


The linchpin of brain homeostasis.



Autophagy Inducer

Keeping the Engine Running



Without LL-37, the cleanup stops. Toxic proteins accumulate because the system is broken.

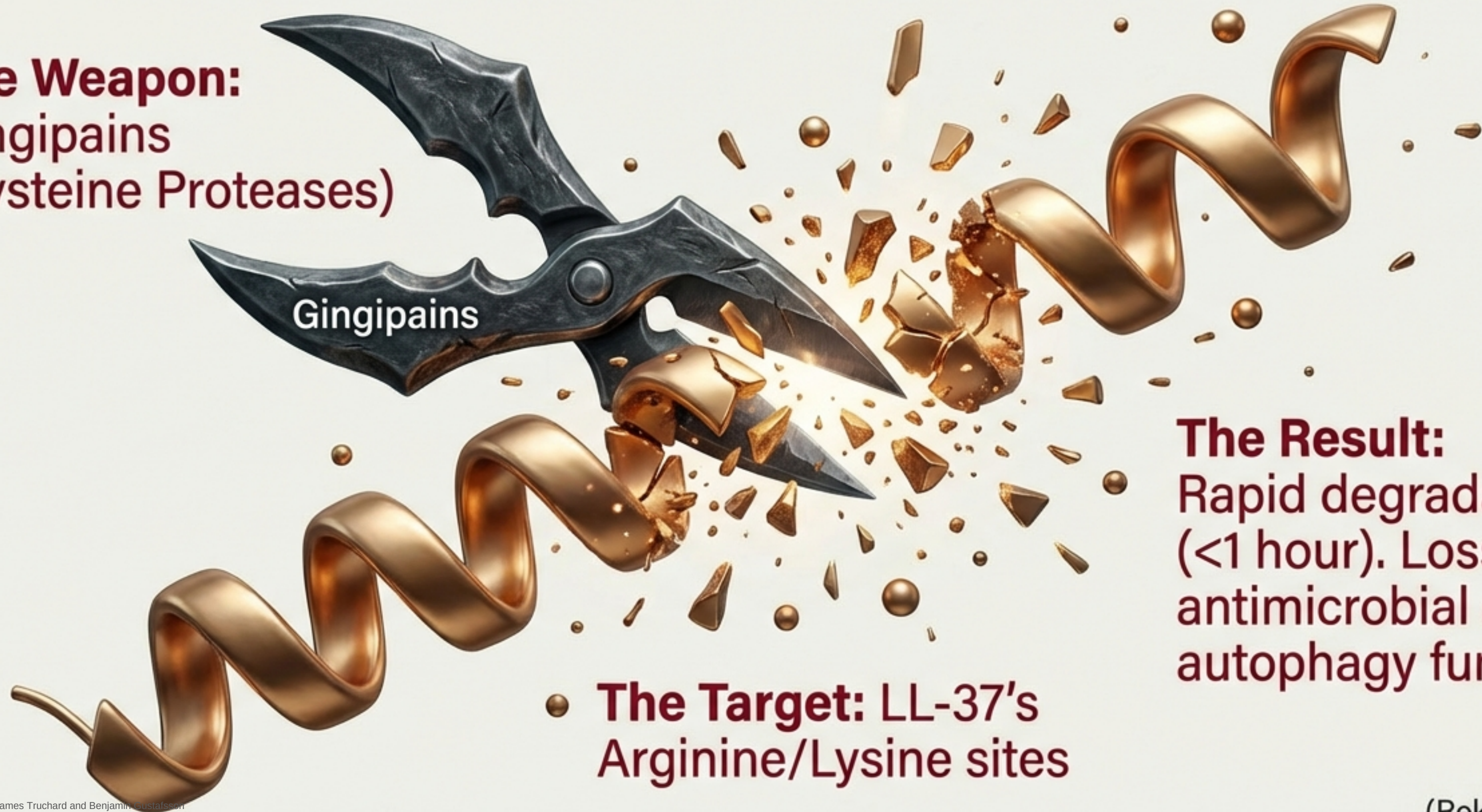
The Invader: *Porphyromonas gingivalis*



- ✓ **The Epidemiology:** Gum disease links to higher dementia risk.
- ✓ **The Invasion:** *P. gingivalis* DNA found in 7 of 10 AD brains (Control: 0/10).
- ✓ **The Impact:** Keystone pathogen. Creates immunosuppressed environment.

Disarming the Guardian

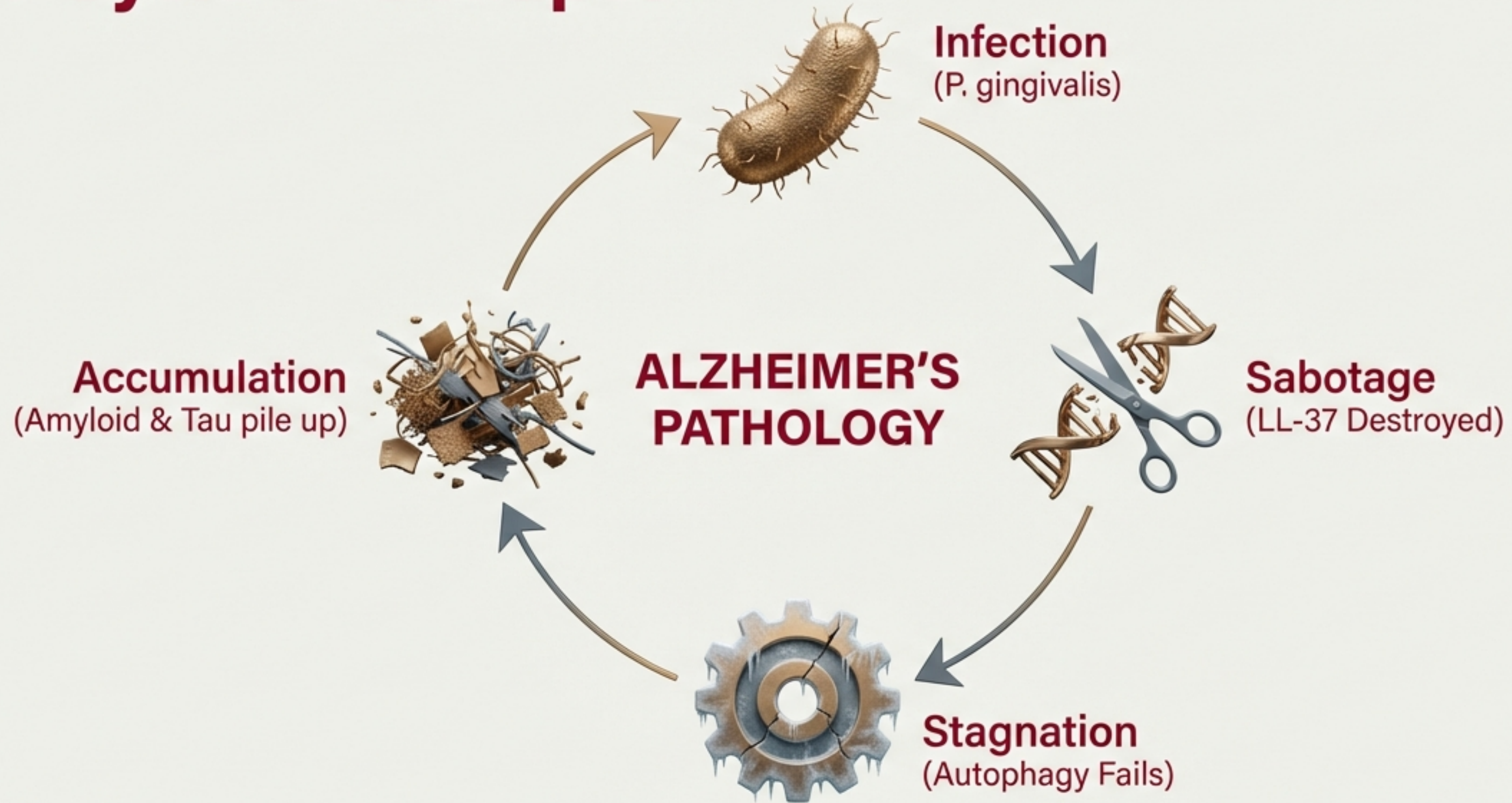
The Weapon:
Gingipains
(Cysteine Proteases)



The Result:
Rapid degradation
(<1 hour). Loss of
antimicrobial and
autophagy function.

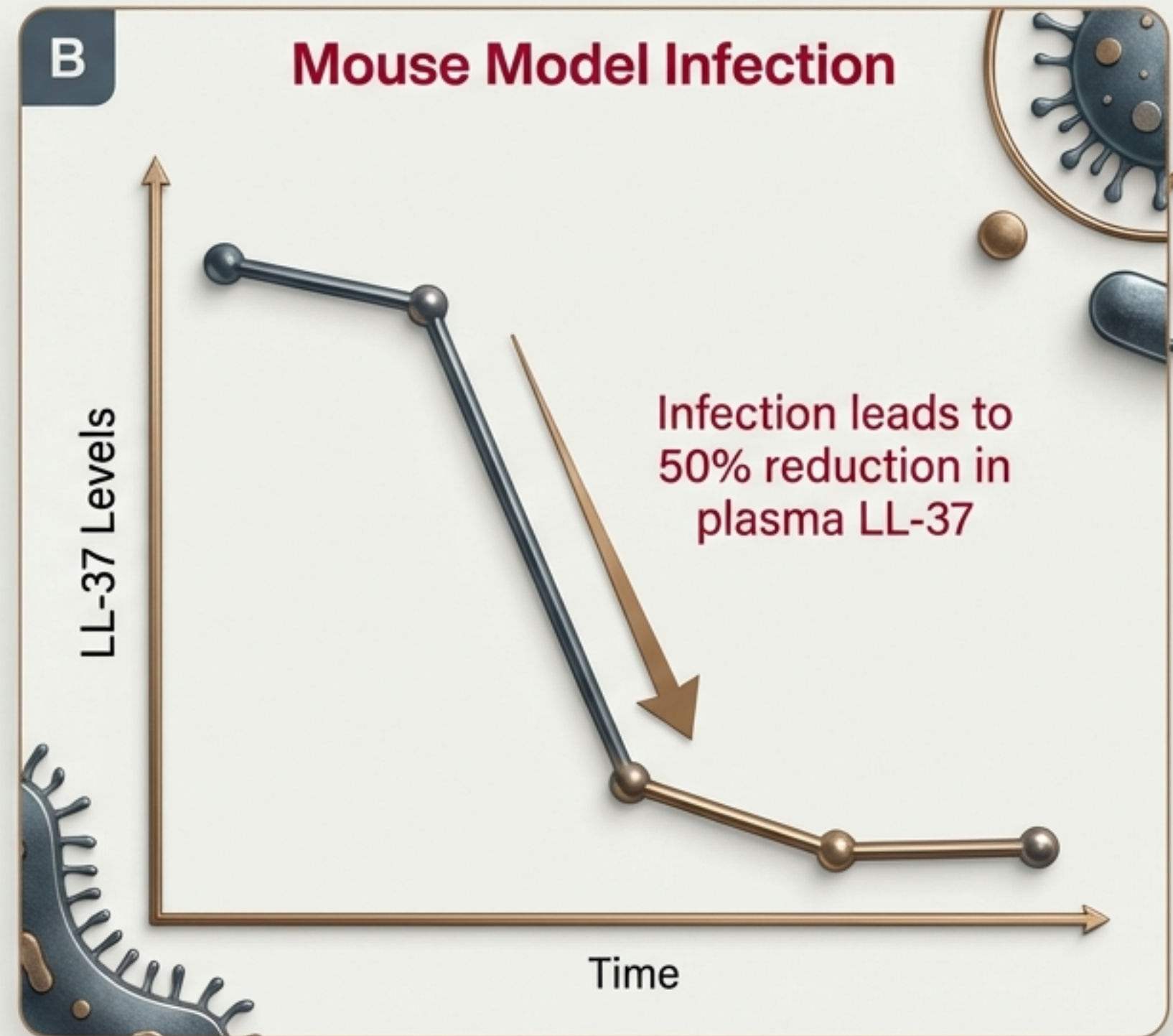
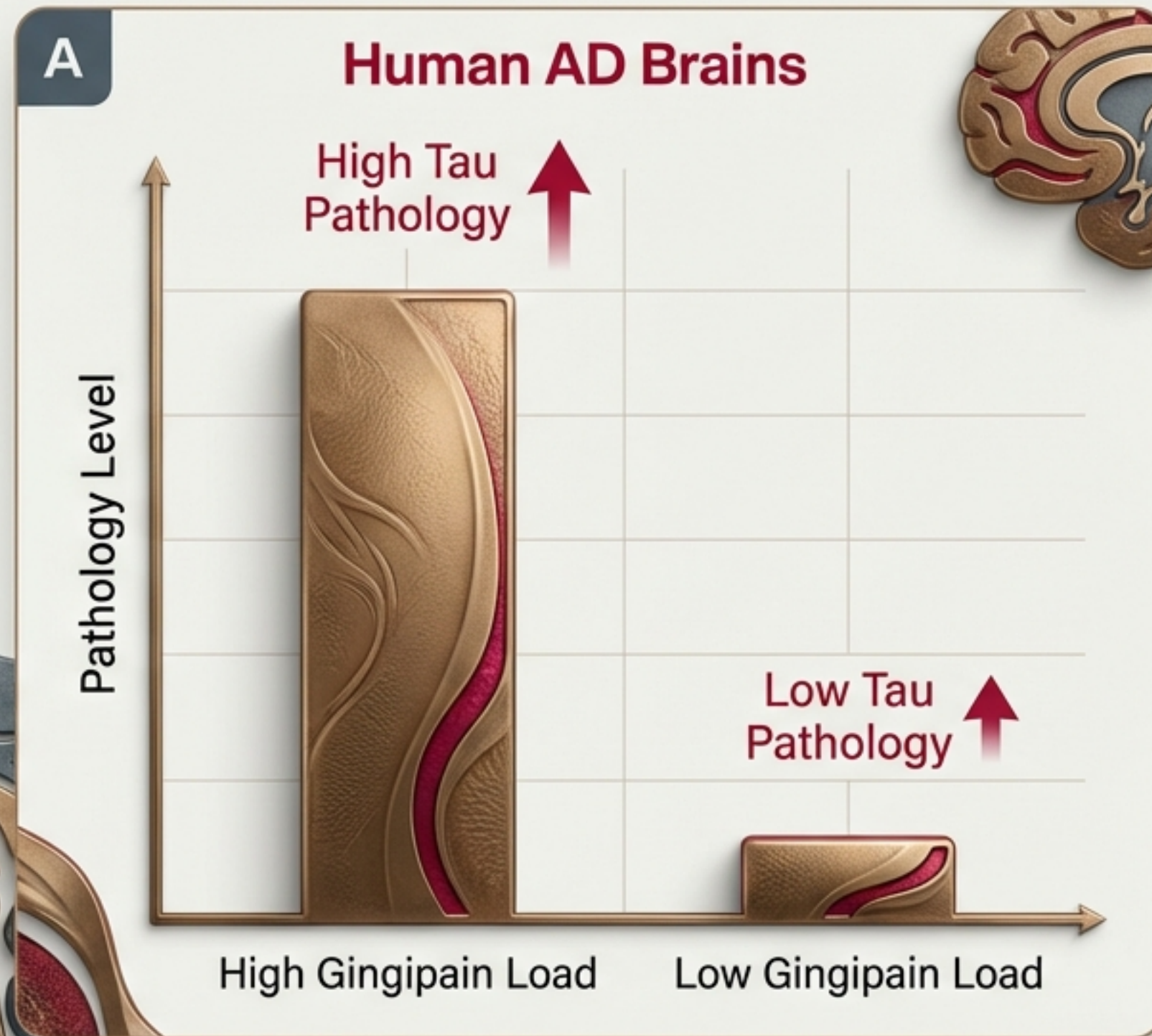
- **The Target:** LL-37's
Arginine/Lysine sites

The Cycle of Collapse



Amyloid isn't just waste; it is a failed immune response.

Evidence from the Crime Scene



Infection creates a 'two-hit' impairment: consuming LL-37 locally and degrading it systemically.

The Engineering Challenge

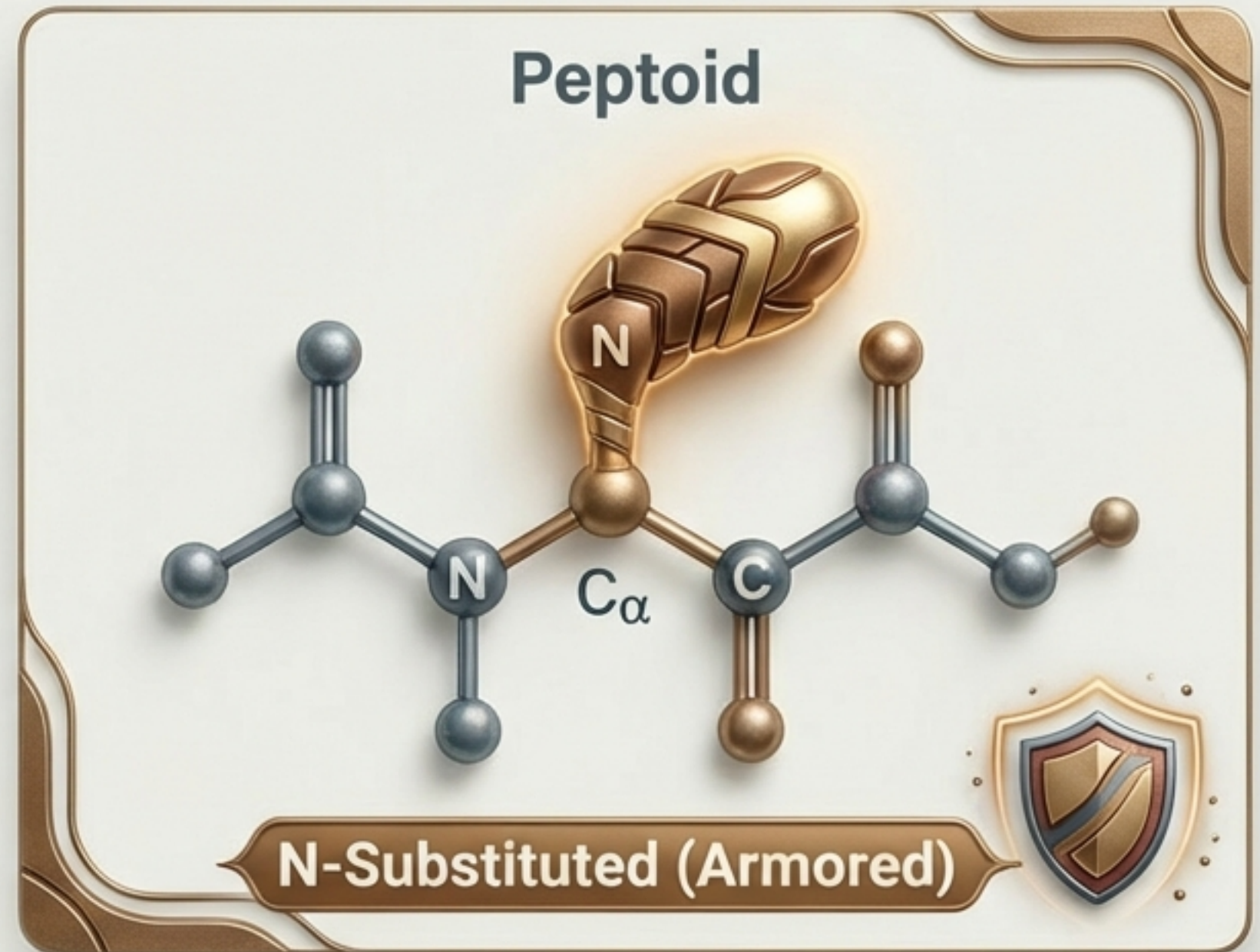
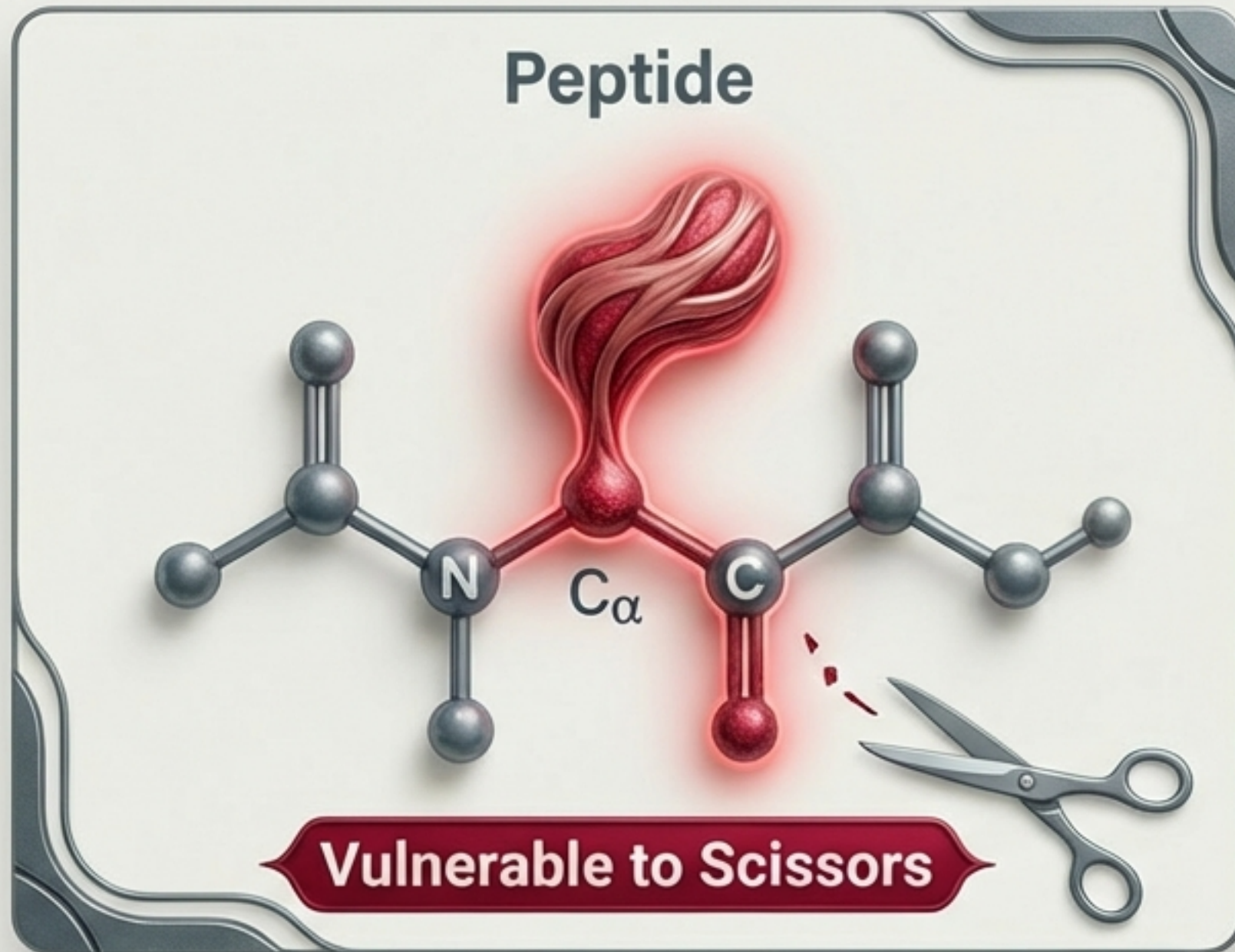


Problem:
Natural LL-37 is fragile.

- Instantly degraded by bacterial proteases.
- High doses are toxic.
- Potential immunogenicity.

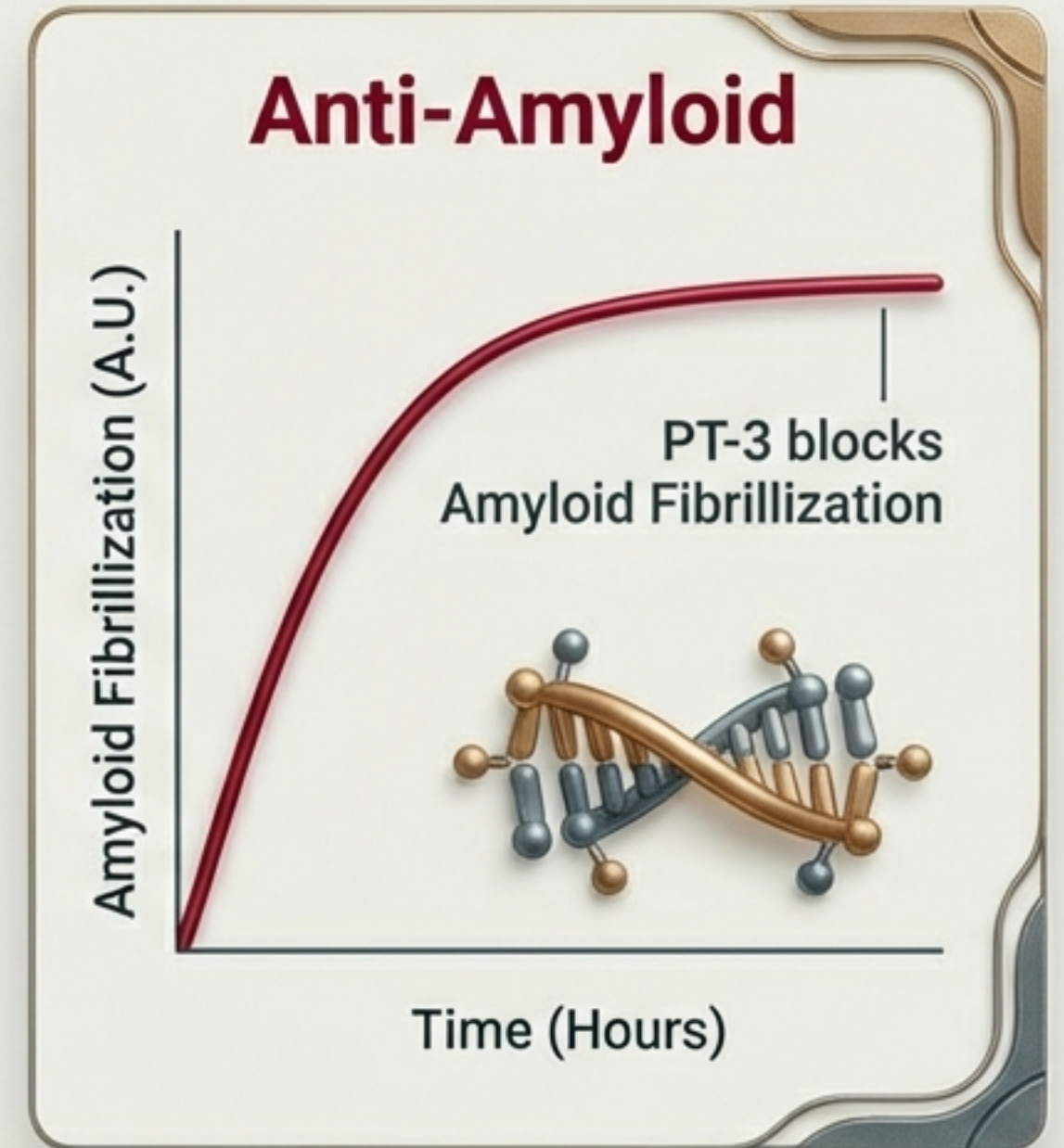
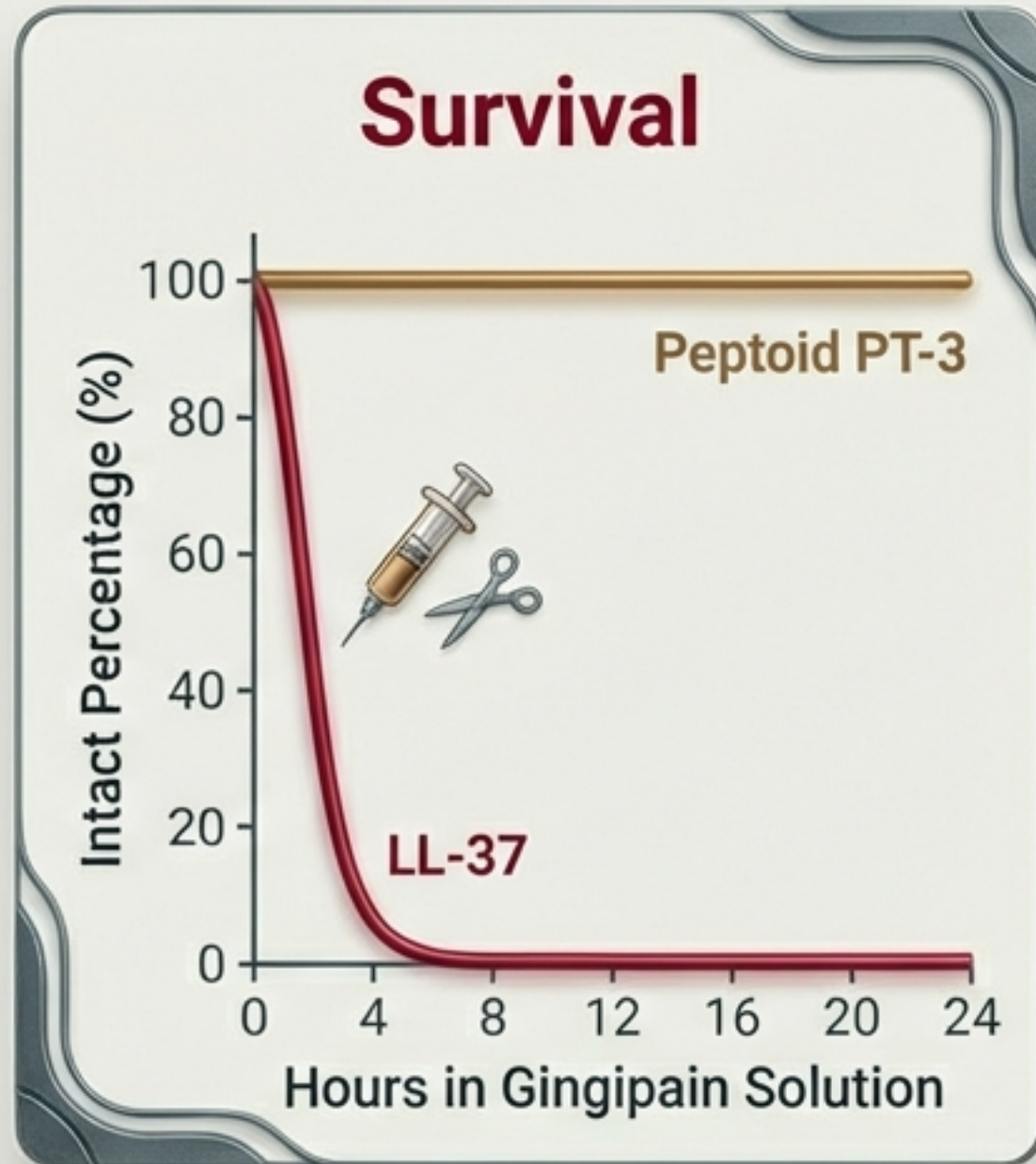
**We need a molecule that acts like LL-37
but is invisible to the scissors.**

Enter the Bionic Shield: The Peptoid



- **Protease Resistant:** Invisible to Gingipains.
- **Biomimetic:** Identical function, superior stability.

Engineering Superiority (In Vitro)



**The mimic survives the villain
and retains the hero's powers.**

Reversing Pathology (In Vivo)

Untreated Mouse (5xFAD)



Heavy Plaque Burden

Peptoid PT-3 Treated



Reduced Plaque Burden

- 🛡️ Significant reduction in plaque burden.
- 🛡️ Reduced microglial inflammation.
- 🛡️ Cognitive improvement in maze tests.

A New Era: Innate Immunotherapy



Protect the Guardian, Save the Mind



Alzheimer's is not inevitable. By fortifying the body's own defenses, we can turn the tide.

Advance Peptoid Mimics to Clinical Trials.