The question

How long is long enough?

The longevity marketplace today is saturated with influencer protocols and biological reductionism dressed up as science. Distinguishing real signal demands rigorous, evidence-based biomarkers grounded in mechanism.

Aging-genomics — extending pharmacogenomics

Pharmacogenomics asks *which drug for which person, given their genome?*

Aging-genomics asks: *which way of living and which interventions are right for which person, given their genome, epigenome, mitochondrial state, and real-time physiology?*

Mechanism — mitochondrial-inflammaging axis

Dysfunctional mitochondria release mtDNA-DAMPs + ROS → activate NLRP3 inflammasome / NF-κB → chronic inflammation → cellular senescence + tissue damage → accelerated aging.

Lifestyle modulates this axis through epigenetic regulation.
Maternal mtDNA + numts (Mills) determine the starting equilibrium.

Foundation

Three decades of mtDNA-atherogenesis collaboration between the Ballinger and Runge laboratories establish the mechanistic spine: ROS-induced mtDNA damage contributes to atherogenesis; conplastic mice show mtDNA variation alone alters metabolic phenotype.

Three aims · closed loop

Aim 1 · **LCI** — Longevity & Cardiovascular Health Index. WGS + CRF + BioButton + clinical.

Aim 2 · **EMHP** — Epigenetic & Mitochondrial Health Panel. Phase 1 small-panel + Phase 2 omics + CRISPR Perturb-seq.

Aim 3 · **Therapies** — Targets, Therapies, Precision Longevity Programs.

measure → model → intervene → **re-measure**

Cohort tiers — 5 orders of magnitude

Tier	N
WGS training (extreme phenotypes)	10K–20K
MGI (UM, recontact-friendly)	∼90K
DoDSR / USAFSAM / Cooper / VETS	750K
MPOG (Kheterpal, 85+ hospitals)	5M+
Oracle Health (Ellison)	**150M**

BioButton-paired study design (Aim 2 Phase 1)

Continuous BioIntelliSense BioButton stream (HRV · sleep · activity · stress) with strategically-timed blood draws bracketing real-world states: sleep-deprivation nights, exercise bouts, stress weeks, illness, vacation.

⇒ Quantifies *acute* epigenetic + transcriptional response.
⇒ Identifies resilience-vs-vulnerability phenotypes that static lifestyle variables cannot.

EMHP panel composition (Phase 1)

Inflammatory cytokines: IL-6, IL-1β, TNF-α
Inflammasome: NLRP3, ASC, Caspase-1
Vascular inflammation: VCAM-1, ICAM-1
Mitochondrial biogenesis: PGC-1α, TFAM
Sirtuins (longevity): SIRT1, SIRT3, SIRT6
Stress / metabolic: GDF-15, FGF-21

Each gene quantified across **methylation** × **expression** × **circulating protein**. Phase 2 adds genome-wide methylation, chromatin profiling, and CRISPR Perturb-seq for causal discovery.

Commercialization roadmap

Phase 1 · **Y1–3 — Discovery.** Biomarker discovery, panel feasibility, target identification. Initial patents.

Phase 2 · **Y4–6 — Product + regulatory.** EMHP IVD, FDA 510(k) / de novo, CE Mark, pre-clinical drug optimization.

Phase 3 · **Y7+ — Launch + therapeutics.** EMHP via Oracle Health, personalized longevity programs, therapeutic Phase 1–3 trials.

Dashboard

single-molecule-sequencing.github.io/longevity-platform-grant

28 funding-mechanism PDFs · 8 figures · 4 tables · both source drafts · status grid · "What we need from PIs"