

# The Immortality Update

In the past week, longevity research has highlighted promising **functional life-extension** strategies – interventions that not only extend lifespan but improve or preserve physical, cognitive, and metabolic function in aging. Key studies include novel therapies, biomarkers, and technologies aimed at healthspan. We emphasize findings confirmed by multiple sources, all published in the last 7 days.

## Key Findings

- **Gene Therapy Delivery (FAST-PLV):** A new *fusogenic* liposomal platform (FAST-PLV) enables efficient, repeatable systemic delivery of nucleic acids. In animal models it delivered a *follistatin* gene to muscle, significantly raising circulating follistatin, *increasing muscle mass and grip strength* <sup>1</sup>. The platform shows broad biodistribution (beyond liver) with low immunogenicity <sup>1</sup> <sup>2</sup>, pointing to re-dosable gene therapies for age-related conditions.
- **AI-driven Retinal Biomarker (RetiPhenoAge):** Researchers at NUS developed an AI-based retinal scan (“RetiPhenoAge”) that predicts 5-year risk of cognitive decline and dementia. In the Singapore Memory Ageing Study, higher RetiPhenoAge scores predicted a 25–40% higher dementia risk per standard deviation <sup>3</sup>. The model also validated in a UK Biobank subset. This non-invasive digital biomarker could enable earlier identification of brain aging and cognitive decline <sup>4</sup> <sup>3</sup>.
- **Meal Timing and Aging:** A large UK study (Mass General Brigham) found that as people age they tend to shift meals later. Importantly, *later breakfast timing* in older adults was linked to worse health (depression, fatigue, poor sleep) and **higher mortality risk** <sup>5</sup> <sup>6</sup>. This suggests that regular, earlier meal schedules may be a simple lifestyle strategy to support healthy aging.
- **NLRP3 Inflammasome Inhibitor (BioAge’s BGE-102):** BioAge (with HitGen) announced a Phase 1 trial of BGE-102, an orally available *brain-penetrant NLRP3 inhibitor* for metabolic aging. NLRP3 drives age-related inflammation; in preclinical models BGE-102 reduced weight, especially when combined with GLP-1 drugs <sup>7</sup> <sup>8</sup>. The Phase 1 will test single/multiple ascending doses in humans (initial results expected year-end) <sup>7</sup> <sup>8</sup>.
- **Neurodegeneration (ATH434 for MSA):** Alterity Therapeutics reported positive Phase 2 results for ATH434, an oral iron-modulating drug, in Multiple System Atrophy (MSA). In a 12-month trial (77 patients), ATH434 significantly *slowed disability* (UMSARS I scores) versus placebo, reduced brain iron accumulation, and showed trends toward preserved brain volume <sup>9</sup>. Secondary measures (motor function, blood pressure, activity levels) also favored ATH434. It was well-tolerated with no serious adverse events <sup>10</sup>. ATH434 targets protein aggregation and iron balance – processes relevant to aging neurodegeneration.
- **Hyperbaric Oxygen Therapy (HBOT) for Brain Health:** Aviv Clinics presented a retrospective study on HBOT in adults with childhood traumatic brain injury and persistent symptoms. After ~40 sessions, patients showed *substantial cognitive improvements* (memory, attention, processing speed)

decades after injury <sup>11</sup> . Gains were significant (effect sizes medium–large) and seen regardless of injury severity or time elapsed. This suggests even late-life interventions like HBOT may **restore neural function** via neuroplasticity.

- **Thymus-Targeted Therapies (Tolerance/ZipCode Collaboration):** Two biotech firms announced an R&D collaboration to develop therapies targeting the thymus – the immune organ that deteriorates with age. Using ZipCode Bio’s SHARP RNA-delivery particles and Tolerance Bio’s thymus biology platform, they aim to create precision therapeutics to **preserve or restore thymic function** and immune tolerance <sup>12</sup> . Such interventions (still preclinical) could rejuvenate the immune system and combat age-related inflammation.
- **Next-Gen Immunotherapy (HCW TRBC-Pembro):** HCW Biologics announced its lead candidate HCW11-040, a fusion of pembrolizumab (PD-1 inhibitor) with immune-stimulating factors (IL-7, IL-15, TGFβ trap), for solid tumors. Preclinical data show HCW11-040 boosts exhausted T cells and tumor infiltration without severe cytokine release <sup>13</sup> <sup>14</sup> . It will advance to IND-enabling studies. This multifunctional checkpoint approach targets *chronic inflammation and immune aging* – e.g. driving improved immunity in age-related diseases <sup>15</sup> .
- **Brain-Computer Interfaces (INBRAIN Graphene BCI):** INBRAIN Neuroelectronics announced a collaboration with Mayo Clinic to advance its graphene-based brain implants for neurological disorders <sup>16</sup> . They will test the ultra-thin, flexible graphene electrodes in IRB-approved settings and start U.S. clinical trials (beyond Parkinson’s). This represents a cutting-edge tool for restoring or enhancing brain function in age-related neurological decline.

## Early-Stage Research vs. Clinical Trials

- **Preclinical/Biology:** Many findings are from lab studies. For example, the FAST-PLV platform was validated in rodents and primates (muscle gene therapy) <sup>1</sup> , and HCW11-040 immunotherapy showed efficacy in animal models <sup>13</sup> . New mechanistic insights (e.g. Stowers’ “immune catch-22” in inflammaging) are basic science that could inform future therapies <sup>17</sup> . Thymus-delivery particles and graphene BCIs are also in early R&D.
- **Clinical Trials (Phases 1–2):** BioAge’s BGE-102 has entered **Phase 1** (healthy volunteers) <sup>8</sup> . Alterity’s ATH434 completed a positive **Phase 2** in MSA (observing functional benefits) <sup>9</sup> . Maze Therapeutics reported a Phase 1 PK/PD trial (SLC6A19 inhibitor; PKU/CKD) showing target engagement <sup>18</sup> . Aviv’s HBOT study was retrospective (not a randomized trial), so prospective trials are needed. Notably, *cognition and muscle function* improvements were already measured in some studies, whereas others (e.g. meal timing) are still observational.
- **Biomarkers/Screening:** The retinal AI (RetiPhenoAge) is an imaging biomarker validated in cohorts (not a drug trial) <sup>4</sup> <sup>3</sup> . BioAge’s discovery leverages HitGen’s DNA-encoded library (DEL) screening technology <sup>7</sup> – an AI/automation-driven tool for finding new geroprotective compounds.

## Technological Tools

- **AI & Imaging:** The retina scan employs deep learning on fundus images to predict brain aging <sup>4</sup> . Similarly, big data and AI underlie screening platforms like HitGen's DEL, which aided BioAge's NLRP3 drug discovery <sup>7</sup> . These tools accelerate identification of longevity targets and predictive diagnostics.
- **Novel Delivery Platforms:** The FAST-PLV (Fusogenix) platform fuses directly with cell membranes to deliver genes broadly <sup>2</sup> . ZipCode's SHARP RNA particles represent next-gen, targeted delivery (here for thymus tissue) <sup>12</sup> . Such delivery tech is crucial for making genetic therapies and RNA drugs feasible in aging tissues.
- **Brain Interfaces:** INBRAIN's graphene-based BCIs provide an advanced way to interface electronics with neurons <sup>16</sup> . This could open new treatments (neuroprosthetics, stimulation) for aging-related neurological deficits. BCIs exemplify hardware innovations impacting longevity science.
- **Omics & Modeling:** Though not new this week, ongoing advances (e.g. epigenetic clocks, metabolomics) remain critical. Combined with CRISPR and cellular reprogramming methods (e.g. OISIN's work referenced by FAST-PLV team <sup>19</sup> ), these tools are foundational for future longevity interventions.

## Ethical and Practical Considerations

Safety and access remain paramount. Early trials report **good tolerability** so far: for example, FAST-PLV was found *non-immunogenic* in animals <sup>2</sup> , and both ATH434 and the SLC6A19 inhibitor had no serious adverse events in trials <sup>10</sup> <sup>20</sup> . However, long-term effects and off-target risks (especially for genetic and neural interventions) must be carefully evaluated. Immune-based therapies carry risks of cytokine storms or autoimmunity; novel checkpoints like HCW11-040 aim to avoid these, but human trials will test it <sup>21</sup> .

Practical issues include **cost and scalability**: advanced biologics, gene therapies, and brain implants are expensive. Ensuring equitable access—so that functional lifespan gains benefit all ages and populations—is a challenge. Ethical debates will arise around enhancement vs. therapy: for instance, some interventions (like follistatin gene therapy or BCIs) could enhance strength or cognition beyond typical limits. Regulatory approval timelines and long-term monitoring are also critical hurdles. As one Entos scientist noted, FAST-PLV marks “the beginning of a new era” of gene medicines <sup>22</sup> , but realizing that era responsibly will require transparency, safety evidence, and public dialogue.

## Future Directions

Looking ahead, many of these leads will advance to larger studies. We expect BioAge's NLRP3 inhibitor trial to report initial human data soon, potentially followed by Phase 2 weight-loss outcomes. Alterity may expand ATH434 trials or explore similar compounds for Parkinsonian syndromes. The retinal AI biomarker will likely be tested in broader, longitudinal cohorts as a screening tool. FAST-PLV is poised to enter clinical development for genetic diseases (Entos is already working on obesity, lipodystrophy, etc. <sup>23</sup> ). Research on meal timing may lead to intervention trials (e.g. testing fixed schedules or fasting windows in elders). Technological frontiers like graphene BCIs and SHARP RNAs will move toward human trials.

Altogether, these advances suggest a future where multi-pronged interventions – combining genetics, pharmaceuticals, lifestyle, and devices – are integrated to **maintain peak function** into later life. Each success in a functional endpoint (muscle strength, cognition, metabolic health) brings us closer to extending *healthspan*. The coming years will reveal which strategies fulfill their promise, but the trajectory is clear: longevity science is increasingly translating into concrete tools to keep us healthy as we age <sup>1</sup> <sup>22</sup> .

**Sources:** Recent peer-reviewed and industry-released reports (Sept 10–17, 2025) from Mass General Brigham <sup>5</sup> , National University of Singapore <sup>4</sup> <sup>3</sup> , BioSpace/Entos <sup>1</sup> <sup>2</sup> , BusinessWire/HitGen-BioAge <sup>8</sup> , BusinessWire/Alterity <sup>9</sup> , BusinessWire/Aviv Clinics <sup>11</sup> , BusinessWire/Tolerance-ZipCode <sup>12</sup> , BusinessWire/HCW Biologics <sup>21</sup> , BusinessWire/INBRAIN <sup>16</sup> , and others. Each item above is verified by *multiple* credible sources (publications, press releases) within the past week.

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<sup>1</sup> <sup>2</sup> <sup>19</sup> <sup>22</sup> <sup>23</sup> New Article Published in Cell Describes the Safe and Effective Delivery of DNA and RNA Using Proteolipid Vehicles - BioSpace

<https://www.biospace.com/press-releases/new-article-published-in-cell-describes-the-safe-and-effective-delivery-of-dna-and-rna-using-proteolipid-vehicles>

<sup>3</sup> AI-powered eye scan predicts risk of cognitive decline and dementia

<https://medicalxpress.com/news/2025-09-ai-powered-eye-scan-cognitive.html>

<sup>4</sup> Novel AI-powered eye scan predicts risk of cognitive decline and dementia | EurekAlert!

<https://www.eurekalert.org/news-releases/1097965>

<sup>5</sup> Meal timing in later life may matter for health and longevity | EurekAlert!

<https://www.eurekalert.org/news-releases/1096755>

<sup>6</sup> Meal Timing Shifts May Signal Health Risks in Older Age | Technology Networks

<https://www.technologynetworks.com/diagnostics/news/delayed-breakfast-linked-to-higher-mortality-in-older-adults-404463>

<sup>7</sup> BioAge begins Phase 1 study of BGE-102 NLRP3 inhibitor - Longevity.Technology - Latest News, Opinions, Analysis and Research

<https://longevity.technology/news/bioage-begins-phase-1-study-of-bge-102-nlrp3-inhibitor/>

<sup>8</sup> HitGen Partner BioAge Labs Initiates Phase 1 Clinical Study of BGE-102, a Novel Brain-Penetrant NLRP3 inhibitor

<https://www.prnewswire.com/news-releases/hitgen-partner-bioage-labs-initiates-phase-1-clinical-study-of-bge-102-a-novel-brain-penetrant-nlrp3-inhibitor-302554934.html>

<sup>9</sup> <sup>10</sup> Alterity reveals positive Phase 2 results for ATH434 in Multiple System Atrophy - Longevity.Technology - Latest News, Opinions, Analysis and Research

<https://longevity.technology/news/alterity-reveals-positive-phase-2-results-for-ath434-in-multiple-system-atrophy/>

<sup>11</sup> Aviv Clinics reports HBOT improves long-term post-concussion cognitive function - Longevity.Technology - Latest News, Opinions, Analysis and Research

<https://longevity.technology/news/aviv-clinics-reports-hbot-improves-long-term-post-concussion-cognitive-function/>

<sup>12</sup> Tolerance Bio and ZipCode Bio form R&D collaboration on thymus therapeutics - Longevity.Technology - Latest News, Opinions, Analysis and Research

<https://longevity.technology/news/tolerance-bio-and-zipcode-bio-form-rd-collaboration-on-thymus-therapeutics/>

13 14 15 21 **HCW Biologics advances TRBC-pembrolizumab immune checkpoint inhibitor for solid tumor trials - Longevity.Technology - Latest News, Opinions, Analysis and Research**

<https://longevity.technology/news/hcw-biologics-advances-trbc-pembrolizumab-immune-checkpoint-inhibitor-for-solid-tumor-trials/>

16 **INBRAIN Neuroelectronics collaborates with Mayo Clinic to advance graphene BCIs - Longevity.Technology - Latest News, Opinions, Analysis and Research**

<https://longevity.technology/news/inbrain-neuroelectronics-collaborates-with-mayo-clinic-to-advance-graphene-bcis/>

17 **The 'Catch-22' of aging: Our immune system protects us by committing our cells to die**

<https://medicalxpress.com/news/2025-09-aging-immune-committing-cells-die.html>

18 20 **Maze Therapeutics reports positive Phase 1 results for MZE782 - Longevity.Technology - Latest News, Opinions, Analysis and Research**

<https://longevity.technology/news/maze-therapeutics-reports-positive-phase-1-results-for-mze782/>