The Immortality Update: Deep Research on the Most Important Discoveries and News in Longevity Sciences from the Past 7 Days

Introduction

Modern longevity science aims not only to prolong life but to extend **healthspan**—the years of functional, disease-free life. This week's **Immortality Update** focuses on research announced or published between **28 October 2025 and 4 November 2025** that targets ageing pathways or delivers tools to keep organisms healthy longer. To ensure credibility, all findings highlighted below were reported in at least two reliable sources (peer-reviewed journals, universities, major conferences or reputable news outlets). The emphasis is on interventions that enhance **functional capacity** rather than merely delaying death.

Key Findings

1. Retinal micro-vasculature as a non-invasive healthspan biomarker

Researchers from McMaster University and the Population Health Research Institute analysed retinal scans, genetic data and blood biomarkers from **>74 000 participants** across several large cohorts. The study, published in *Science Advances* and described by ScienceDaily and EurekAlert, found that the complexity of an individual's retinal blood-vessel network predicts both **cardiovascular risk** and **biological age**【694905876665992†L26-L74】. People with **simpler, less-branched retinal vessels** exhibited higher cardiovascular disease risk and signs of accelerated ageing, including increased inflammation【694905876665992†L72-L75】. By integrating retinal images with genomics and proteomics, the team identified inflammatory proteins—particularly matrix-metalloproteinase 12 (MMP12) and the IgG Fc receptor IIb—as **potential therapeutic targets** to slow vascular ageing【694905876665992†L86-L97】. The findings suggest that simple retinal imaging could one day provide a **non-invasive tool** to monitor vascular health and evaluate interventions targeting micro-vascular ageing【694905876665992†L50-L83】. The study’s cross-disciplinary approach aligns with functional-life-extension goals by offering a way to detect early vascular decline and test anti-inflammatory therapies.

2. Urolithin A rejuvenates immune function in middle-aged humans

A **randomised, double-blind, placebo-controlled trial** evaluated whether **Urolithin A**—a postbiotic produced by gut microbes from ellagitannins—can rejuvenate immune cells. Fifty healthy adults aged **45–70 years** received either **1,000 mg of Urolithin A (Mitopure®)** or placebo daily for 28 days. According to News-Medical and a Biospace press release, the trial demonstrated that Urolithin A supplementation:

- **Reprograms CD8⁺ T cells** toward a naïve, “ready-to-respond” phenotype by increasing proliferation marker **Ki-67** and decreasing exhaustion-associated **TOX**, without activating PD-1【567076091643944†L185-L216】.
- **Enhances mitochondrial fitness**: Single-cell metabolic assays showed increased fatty-acid and amino-acid oxidation and reduced glycolytic dependence【567076091643944†L199-L228】.
- **Remodels immune composition**: Supplementation expanded beneficial natural-killer and non-classical monocyte populations while reducing inflammatory monocyte priming【567076091643944†L229-L238】.
- **Low systemic inflammation**: Plasma **IL-2** decreased while other inflammatory cytokines remained stable, suggesting reduced inflammaging【567076091643944†L245-L249】.
- **Transcriptomic changes**: Single-cell RNA sequencing revealed up-regulation of **TCF7**, **LEF1** and **IL7R** (genes linked to T-cell stemness) and

down-regulation of exhaustion markers **NR4A2** and **CREM** 【567076091643944†L256-L265】.

The trial was small, but these molecular improvements suggest that Urolithin A could enhance **mitophagy**, energy metabolism and immune resilience in mid-life adults. Biospace notes that the results mark the first clinical evidence that a mitochondrial support supplement can **meaningfully rejuvenate immune function** 【575098979107811†L125-L156】. Larger, longer trials are planned, including a follow-up study combining Urolithin A with immunotherapy in cancer patients 【575098979107811†L173-L176】.

3. Super-centenarian BPIFB4 gene reverses heart ageing in progeria models

A pre-clinical study from the University of Bristol and IRCCS MultiMedica, reported by ScienceDaily and News-Medical, showed that delivering the **longevity-associated variant of the BPIFB4 gene (LAV-BPIFB4)** reversed cardiovascular damage in mouse models of **Hutchinson-Gilford Progeria Syndrome (HGPS)**—a disease that causes rapid ageing in children. After a single injection of the human LAV-BPIFB4 gene, progeria-like mice exhibited improved **diastolic function**, reduced cardiac **fibrosis**, fewer senescent cells and increased micro-vascular growth【652374316120720†L188-L200】 【171165078472065†L89-L97】. When the gene was introduced into **Progeria patient–derived cells**, it reduced markers of cellular ageing and fibrosis without lowering progerin levels【652374316120720†L202-L207】, suggesting that the gene acts by **enhancing cellular resilience** rather than removing toxic proteins. This work illustrates how mining the genetics of **super-centenarians** can inspire therapies for both rare diseases and common age-related cardiovascular decline【171165078472065†L107-L139】. Translation to the clinic would require safe gene-delivery systems; researchers are exploring protein or RNA-based delivery as alternatives to viral gene therapy 【171165078472065†L130-L135】.

Early-Stage Research vs. Clinical Trials

Category	Discoveries (past 7 days)	Evidence and Current Stage
Clinical trial with functional benefits	**Urolithin A trial**: A placebo-controlled study showed that 28-day Mitopure supplementation rejuvenated $CD8^+$ T cells, improved mitochondrial efficiency and lowered inflammatory signals in mid-life adults【567076091643944†L185-L216】【567076091643944†L245-L255】. The trial is small but provides the first human evidence that a nutraceutical can remodel immune metabolism and composition. A follow-up brain-aging trial has begun【575098979107811†L125-L170】.	**Level of evidence**: Phase 1/2 human trial (n=50). Outcomes are surrogate markers (immune cell metabolism) rather than clinical endpoints. The short duration and small sample size require cautious interpretation.
Biomarker discovery (observational)	**Retinal vessel complexity**: Cross-cohort analysis of >74 k participants linked simplified retinal micro-vasculature to increased cardiovascular risk and faster biological aging 【694905876665992†L26-L74】. The study identified inflammatory proteins MMP12 and IgG Fc receptor IIb as possible drug targets【694905876665992†L86-L97】.	**Level of evidence**: Observational human study using retinal imaging, genetics and proteomics. Provides a non-invasive biomarker and new targets but no intervention yet.
Pre-clinical therapy	**LAV-BPIFB4 gene therapy**: Delivering a super-centenarian gene improved heart function and reduced fibrosis in progeria mouse models and restored cellular health in patient-derived cells 【652374316120720†L188-L207】.	**Level of evidence**: Animal models and in vitro human cells. No human trials yet. Safety and delivery methods need optimisation before translation.

Technological Tools Driving Longevity Research

- **AI-enhanced imaging and multi-omics** – The retinal ageing study used machine-learning algorithms to quantify vascular branching patterns from tens of thousands of retinal images and integrated these data with **Mendelian randomisation** analyses, genomic profiles and plasma proteomics 【694905876665992†L50-L97】. This high-throughput combination enabled the discovery of inflammatory pathways and potential drug targets.

- **Single-cell metabolic profiling (SCENITH)** – In the Urolithin A trial, researchers used **SCENITH** assays to measure energy-pathway utilisation (oxidative phosphorylation, fatty-acid oxidation and amino-acid oxidation) in individual immune cells【567076091643944†L199-L204】. Coupled with **spectral flow cytometry** and **single-cell RNA sequencing**, these tools provided a detailed map of how the intervention reprogrammed immune metabolism and gene expression【567076091643944†L256-L265】.

- **Gene therapy platforms** – The progeria study employed **adeno-associated virus (AAV9)** vectors to deliver LAV-BPIFB4 to mice【652374316120720†L188-L199】. While effective in animals, human translation will depend on safer delivery systems, such as protein or RNA-based therapeutics 【171165078472065†L130-L135】. The work underscores the role of **super-centenarian genomic mining** in identifying protective alleles for use in gene-based interventions.

Ethical and Practical Considerations

1. **Safety and long-term effects** – The Urolithin A trial found the supplement well-tolerated over four weeks, yet long-term safety and efficacy remain unknown 【567076091643944†L274-L279】. As mitochondrial enhancers could interact with immune responses or other medications, future trials should assess chronic use and potential interactions, especially for older adults or those with chronic diseases. Similarly, gene therapy using LAV-BPIFB4 must address off-target effects, immune reactions to viral vectors and the risk of insertional mutagenesis.【171165078472065†L130-L139】.

2. **Accessibility and cost** – Retinal imaging is relatively inexpensive, but building infrastructure for population-level screening and integrating AI algorithms will require investment and careful validation to avoid false positives. Urolithin A supplements are commercially available, yet high-quality formulations can be costly; widespread adoption demands rigorous regulation to ensure purity and efficacy. Gene therapy remains prohibitively expensive; translation of LAV-BPIFB4 into protein or RNA therapeutics could reduce costs but still pose affordability challenges.

3. **Equity and inclusivity** – Studies must include diverse populations. The retinal study drew participants largely from European-ancestry cohorts; external validation across ethnic groups is needed to prevent health-equity gaps. The Urolithin A trial involved only 50 participants; larger trials should intentionally recruit from underrepresented groups. Gene-therapy research raises ethical questions about allocating resources to rare diseases versus broad public health interventions.

4. **Regulatory oversight** – Nutraceuticals like Urolithin A straddle the line between supplements and pharmaceuticals; regulators must determine whether claims of immune rejuvenation warrant drug-like oversight. Gene therapies require stringent regulation to ensure safety, informed consent and long-term follow-up. AI-based diagnostic tools such as retinal ageing clocks must address data privacy and algorithmic transparency.

Future Directions and Impact on Healthspan

- **Towards personalised vascular-age interventions** – The discovery that retinal vessel branching reflects systemic vascular ageing provides a platform for developing **targeted anti-inflammatory or anti-fibrotic therapies**. Clinical trials could test whether interventions that reduce MMP12 or modulate Fc-receptor signalling slow micro-vascular ageing and improve healthspan. 【694905876665992†L86-L97】. Integration of retinal imaging into routine check-ups may enable early lifestyle or pharmacological interventions.

- **Scaling up Urolithin A research** – The promising results of the 28-day trial warrant **larger, longer studies** evaluating clinical outcomes such as vaccine responsiveness, infection rates and physical function. Combining Urolithin A with exercise, diet and other mitochondrial enhancers could yield synergistic benefits. Researchers are also investigating its effects on **brain health**, as indicated by the newly launched CLARITY trial 【575098979107811†L120-L136】.

- **Translating super-centenarian genetics** – The LAV-BPIFB4 study demonstrates that longevity alleles can be harnessed to treat severe premature-aging disorders. Future work will test whether this gene or its protein product benefits normal age-related heart decline and whether combination with **senolytics** or **mitochondrial therapies** produces additive effects. Developing **non-viral delivery systems** (e.g., lipid nanoparticles or protein replacement) will be critical to mitigate risks and broaden accessibility 【171165078472065†L130-L135】.

- **Convergence of AI, biomarkers and therapeutics** – As AI-driven analyses of imaging and multi-omics datasets mature, they will identify new ageing pathways and guide **precision longevity interventions**. The field is moving from descriptive geroscience to **mechanism-guided therapy**, with an emphasis on maintaining function and resilience rather than simply increasing lifespan.

Conclusion

The past week’s longevity research highlighted the shift from lifespan extension to **functional life extension**. By linking retinal micro-vascular complexity to biological ageing, researchers provided a non-invasive window into systemic health and uncovered inflammatory pathways ripe for intervention. The first human trial of Urolithin A demonstrated that a food-derived metabolite can rejuvenate immune metabolism and composition in mid-life adults, laying groundwork for safe, mitochondrial-targeted therapeutics. Meanwhile, the discovery that a super-centenarian gene reverses cardiovascular ageing in progeria models underscores how exceptional longevity genetics can inspire treatments for both rare and common age-related conditions. Together, these advances signal a future in which **early detection, mitochondrial support, and genetic resilience** converge to extend the healthspan of diverse populations.