2026 IMPACT CIRCLE

Project Title: The Mitochondrial Switch: A Path to Restoring Aged Human Immune Cells

Investigator(s) and collaborations: Olga Bielska, PhD, Eric Verdin, MD

Unmet Need/Primary Question:
Think back to the last time you had a severe flu. You weren't just coughing; you were exhausted. That's because your immune system is the most "expensive" system in your body to run. When it fights an infection, it redirects every spare calorie to the front lines; it is an energetically massive undertaking. As we age, our immune system enters a state called "Inflammaging." It's like a smoke alarm that won't stop going off, even though there's no fire—and on top of that, it comes with a huge bill. This chronic, low-grade inflammation is incredibly "leaky," wasting your body's precious energy resources every single day. The culprit? Aging mitochondria (our cellular power plants) become damaged. They stop producing the energy we need and start broadcasting constant "distress signals" that drain our vitality. Currently, there are no therapeutic interventions to repair aged mitochondria.

Novel Hypothesis:
Our research at the Buck Institute focuses on the fundamental differences between young and aging mitochondria. We have identified a proprietary 'master-switch' protein, which we refer to as EV001, that is essential for both building new mitochondria and recycling damaged ones. In aging organs, this protein virtually disappears, leaving mitochondria unable to repair or replenish themselves.

By leveraging mRNA-LNP technology—the same breakthrough delivery system used in COVID-19 vaccines and next-generation cancer therapies—we can deliver a 'recharge' instruction directly to these exhausted immune cells. By rejuvenating their mitochondria, we do more than just silence the false alarms of inflammation; we stop the "energy leak." We are essentially giving the body back the vital energy it has been wasting on a dysfunctional defense system. Utilizing the Verdin Lab's extensive biobank of human immune cells, we will test whether this treatment can functionally reprogram aged mitochondria, narrowing the performance gap between aged and young donors to restore a more youthful immune response.

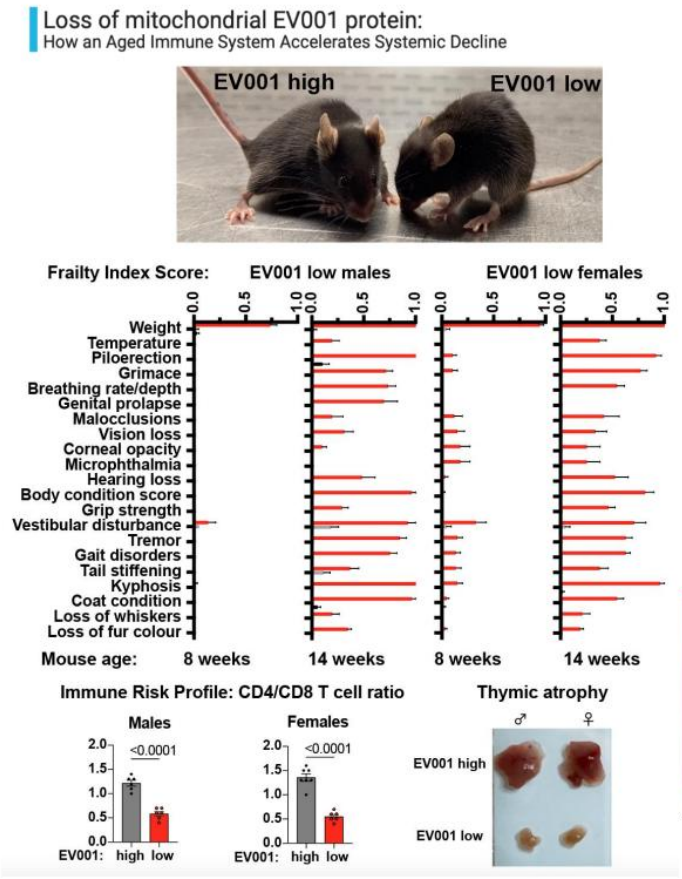
Project Proposal:
We will utilize the Verdin Lab's extensive human biobank to treat immune cells from aged donors with either control or EV001 mRNA-LNPs. Our study will include a comparative screening of multiple EV001 RNA isoforms to identify the most potent candidate for cellular rejuvenation. Before and after the treatment period, we will monitor:

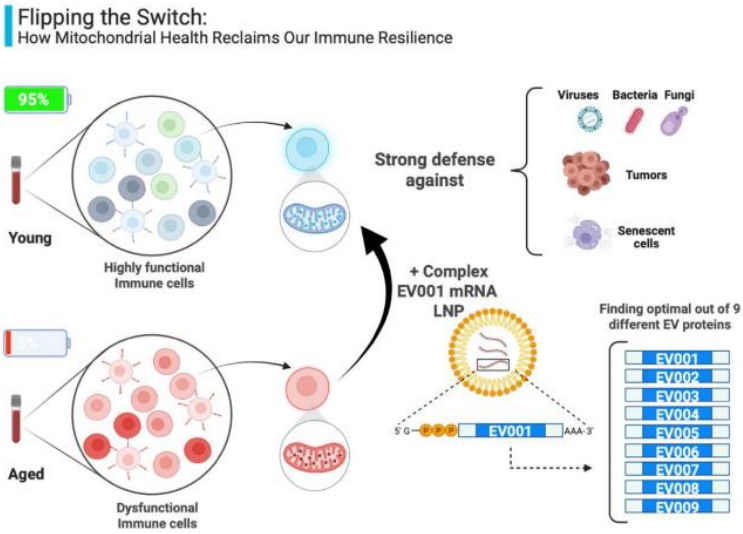
- Cellular Vitality: Assessing viability, growth rates, and metabolic "fitness."

- Immune Competence: Testing the cells' ability to respond to challenges, mimicking an exposure to senescent cells or active infection or a vaccine response.
- Safety & Toxicity: We will monitor for any signs of over-activation or cellular stress to ensure our 'rejuvenation pulse' remains within a safe, physiological range.

To capture the full scope of this "rewiring," we will leverage the Buck Institute's state-of-the-art Core facilities. By integrating high-dimensional flow cytometry, transcriptomics, and proteomics, we will create a high-resolution map of how our therapy shifts the aged immune landscape toward a more youthful state.

Description of Potential Impact:
This project represents a critical bridge between mouse-based discovery and human clinical application. By identifying the optimal isoform and delivery parameters in human cells, we provide the essential "Proof of Concept" needed to move mRNA-based rejuvenation therapies toward the clinic.





Applicants Background:

Eric Verdin, MD, is the President and CEO of the Buck Institute for Research on Aging. A global leader in the field of immunometabolism, Dr. Verdin has spent decades uncovering how metabolic shifts drive the aging process.

Olga Bielska, PhD, is a postdoctoral fellow in Dr. Verdin's lab. Originally from Ukraine, I am on a mission to re-energize aging mitochondria and bring more healthy years to our lives. Mom. Scientist. Entrepreneur.