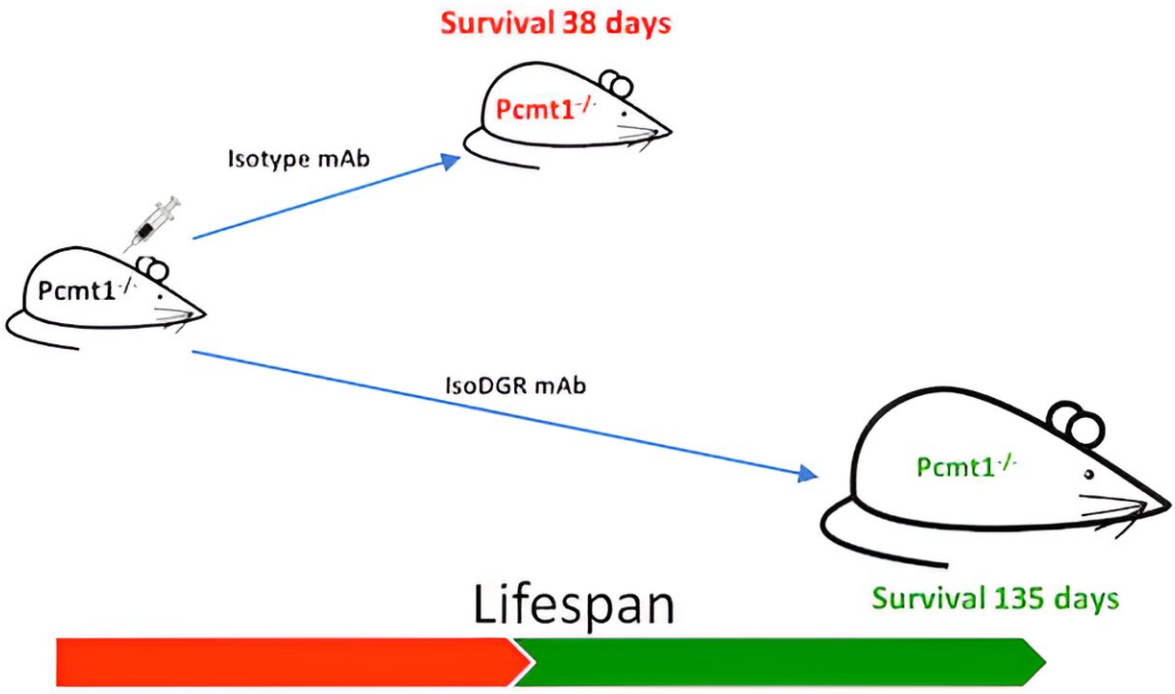
Immunotherapy research shows potential to extend healthy lifespan of humans

November 21 2023, by Doug Hunt



Anti-isoDGR immunotherapy enhances the healthspan of naturally aged mice and extends the lifespan of Pcmt1 KO mice by reducing chronic inflammation. The health benefit is mediated by immune clearance of damaged proteins by antibody-dependent cellular phagocytosis (ADCP). Credit: *EMBO Molecular Medicine* (2023). DOI: 10.15252/emmm.202318526

A Brock-led international research team has discovered an

immunotherapy method that could potentially add years to healthy aging. The research, published in the journal *EMBO Molecular Medicine*, introduces an innovative method to address health issues arising from poor lifestyle choices, which can cause damage to biomolecules and contribute to the development of diseases later in life.

Professor of Health Sciences Newman Sze and his team developed an approach that involves directing the immune system to clear out accumulated proteins damaged by inactive lifestyles, unhealthy diets, various stresses and genetic factors, root causes of aging and age-related diseases.

"Age-related chronic diseases are a major health care burden," says Sze, the Canada Research Chair in Mechanisms of Health and Disease. "We therefore developed a first-of-its-kind monoclonal antibody drug that harnesses the immune system to target and remove these abnormal proteins, providing an effective treatment for age-related health problems."

As time passes, environmental stresses and physiological conditions cause biomolecular damage in tissues. One of these changes, called isoDGR, triggers chronic inflammation in the body and leads to tissue degeneration.

Uncontrolled chronic inflammation, in turn, can lead to conditions such as cardiovascular disease, cancer, type 2 diabetes, arthritis and Alzheimer's disease.

While the accumulation of isoDGR has been identified as a "molecular clock" of aging, the new research paper says the potential benefits of targeting these structures with specific immunotherapies remain largely unknown.

Sze and his team created monoclonal antibodies called isoDGR-mAb. These lab-engineered proteins are designed to boost the immune system's ability to attack unhealthy cells or abnormal molecules. Such immunotherapies are already being used to treat various cancers, autoimmune disorders and infectious diseases.

Using animal models, the team found that these lab-engineered molecules stimulated the immune system to clear out the proteins in tissues that had been damaged by isoDGR. Treatment with isoDGR-mAb not only doubled lifespan but also preserved behavior and coordination functions and reduced pro-inflammatory cytokine levels in the circulation and body tissues.

Sze says the team's findings could lead to the development of immunotherapy-based interventions to extend the healthy lifespan of humans.

"The existing treatments for age-related diseases primarily address symptoms," says Sze. "Our pioneering mAb, uniquely focused on targeting the root causes of chronic diseases, is anticipated to substantially extend human health span."

As Canada Research Chair, Sze studies diseases that occur as people age, specifically diseases related to the brain and the blood vessels becoming damaged. His lab has developed new research methods that investigate how body tissues deteriorate over time and created new drugs to guide the immune system to eliminate abnormal biomolecules.

This latest paper, "Immunotherapy targeting isoDGR-protein damage extends lifespan in a mouse model of protein deamidation," involved researchers from Brock as well as universities in Singapore, China, New Zealand and the United Kingdom.

More information: Pazhanichamy Kalailingam et al, Immunotherapy targeting isoDGR-protein damage extends lifespan in a mouse model of protein deamidation, *EMBO Molecular Medicine* (2023). DOI: 10.15252/emmm.202318526