

Naturally occurring peptide could serve as a novel protective agent for 'inflammaging'

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A naturally occurring peptide called PEPITEM could potentially rejuvenate the immune response in older individuals and protect against "inflammaging," which is widely believed to be the root cause of many

age-related diseases.

The study, [published](#) today in the journal *npj Aging*, raises the exciting possibility of a protective agent that could dampen age-related inflammation and restore normal immune function in older adults.

PEPITEM (Peptide Inhibitor of Trans-Endothelial Migration) was initially identified at the University of Birmingham in 2015. While the role of the PEPITEM pathway has already been demonstrated in immune-mediated diseases, this is the first data showing that PEPITEM has the potential to increase healthspan in an aging population.

Researchers, led by Drs. Myriam Chimen, Asif Iqbal, and Helen McGettrick, investigated how aging adversely influences the [inflammatory response](#) and how it can be rescued by PEPITEM.

In a healthy immune system, PEPITEM regulates the trafficking of immune cells between blood and body tissues, ensuring that the [immune response](#) is not exaggerated. In immune-mediated diseases such as [rheumatoid arthritis](#), type 1 diabetes, and lupus, the PEPITEM pathway is dysregulated, leading to increased trafficking of immune cells into tissues and resulting in chronic inflammation.

The researchers used an [animal model](#) to study the effect of an immune challenge in young and older mice and the extent to which PEPITEM influences leukocyte (white blood cell) trafficking in both groups.

Their findings revealed that older mice exhibited an exaggerated response in terms of the number, subtype, and migration of immune cells (including T-cells), which could be reduced by administering PEPITEM. This indicates a decline in the activity of the PEPITEM pathway with age.

The second aspect of the study examined the potential cause for this decline in PEPITEM activity with age by using B-cells harvested from younger (under 45 years) and older (over 60 years) human donors.

PEPITEM originates from a larger protein secreted by B-cells ([white blood cells](#)), and its production is triggered by a circulating hormone called adiponectin. In the bloodstream, PEPITEM acts on receptors on cells that line blood vessel walls.

The researchers found that B-cells from [older adults](#) had a deficit in the [signaling pathway](#) that triggers the production of the parent protein for PEPITEM (14-3-3ζ).

Dr. Chimen said, "We have shown an age-related decline in the PEPITEM-adiponectin pathway and demonstrated the influence this has on T-cell trafficking, as seen in inflammaging. These truly exciting results raise the possibility of developing a geroprotective agent that not only reduces excessive inflammation in old age but also supports good immune function in older people."

University of Birmingham Enterprise has filed several patent families related to PEPITEM and the components of the PEPITEM molecule responsible for maintaining a normal immune response.

More information: Rejuvenation of leukocyte trafficking in aged mice through PEPITEM intervention, *npj Aging* (2024). [DOI: 10.1038/s41514-024-00160-6](https://doi.org/10.1038/s41514-024-00160-6)

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