New study reveals how to rejuvenate the immune system of elderly people and reduce their risk of infectious disease

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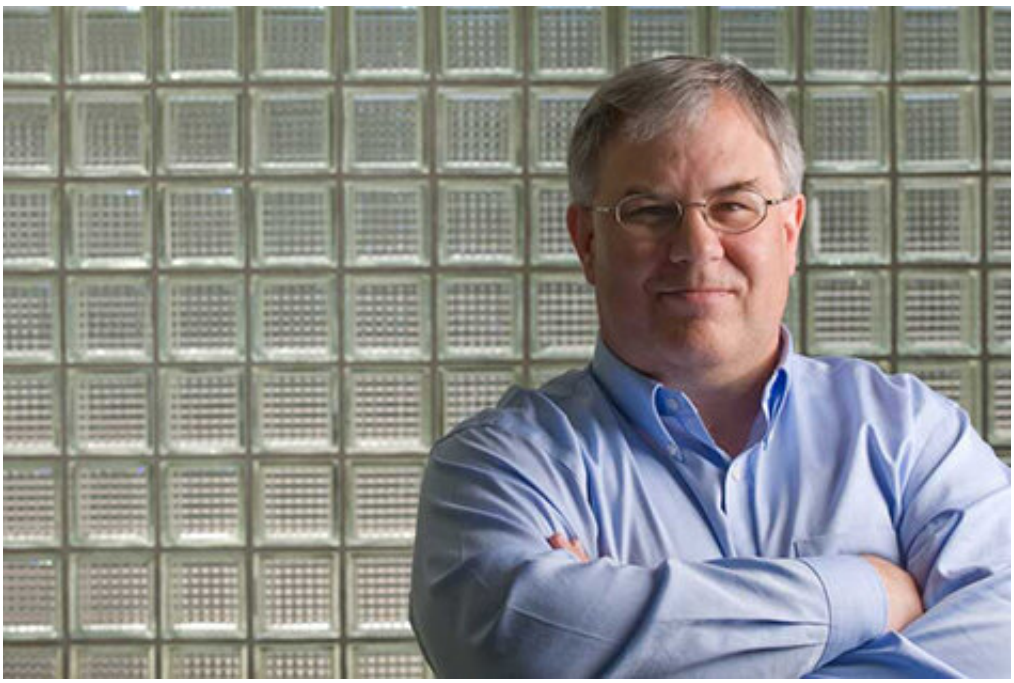

Results from new study, led by Michael Demetriou, MD, PhD, may pave the way for new potential therapeutic targets to rejuvenate the immune system in older adults and thereby reduce their risk of infectious disease. Credit: UCI/Steve Zylius

A new study, led by researchers from the University of California, Irvine, identifies a reason for why older adults are significantly more susceptible to infectious diseases than younger people, a critical societal

issue most recently exemplified by the COVID-19 pandemic.

Study results also pave the way for new potential therapeutic targets to rejuvenate the immune system in older adults and thereby reduce their risk of infectious disease.

"Through this study, we have gained a new understanding of why older adults are more susceptible to infectious diseases, which will enable us to identify potential new treatments," said senior author Michael Demetriou, MD, Ph.D., a professor of neurology at the UCI School of Medicine and chief of the Division of Multiple Sclerosis and Neuroimmunology at UCI. First author and assistant professor in the UCI Department of Pathology, Haik Mkhikian, MD, Ph.D., added, "We've identified a potential fountain of youth for the immune system."

The study, titled, "Age-associated impairment of T cell immunity is linked to sex-dimorphic elevation of N-glycan branching," was published in *Nature Aging*.

T cell immunity declines with aging, thereby increasing severity and mortality from infectious disease. T cells are the quarterback of the immune system and coordinate immune responses to fight off infections. The addition of complex and branched carbohydrate chains ('glycans') to proteins suppresses T cells function.

In this study, researchers show that the branched glycans increase with age in T cells from females more than in males due to age-associated increases in an important sugar metabolite (N-acetylglucosamine) and signaling by the T cell cytokine interleukin-7.

"Our research reveals that reversing the elevation in branched glycans rejuvenates human and mouse T cell function and reduces severity of *Salmonella* infection in old female mice," said Demetriou.

Mkhikian added, "This suggests several potential novel therapeutic targets to revitalize old T cells, such as altering branched glycans or the age-triggered elevation in serum N-acetylglucosamine and IL-7 signaling."

Aging-associated immune dysfunction, referred to as immunosenescence, contributes to increased morbidity and mortality from both infectious and neoplastic diseases in adults aged 65 years and older. In the U.S, for example, around 89 percent of annual deaths from influenza are in people at least 65 years old, despite this age group representing only around 15 percent of the nation's population. More recently, the vulnerability of older adults to viral infections has been tragically highlighted by the recent emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Increased morbidity and mortality in older adults also occurs with common bacterial infections such as those caused by the enteric pathogen *Salmonella*. Furthermore, efficacy of immunizations declines with age, further increasing risk of infection in older adults. The rapidly aging population in the developed world exacerbates this issue and heightens the need for interventions that effectively target immunosenescence.

Previous studies examined transcriptome changes in highly purified aged T cell subsets. In this study, researchers analyzed T cell populations by age and sex, with results suggesting sex-specific differences that imply that effective interventions to reverse immune dysfunction in older adults may require sex-specific strategies.

More information: Haik Mkhikian et al, Age-associated impairment of T cell immunity is linked to sex-dimorphic elevation of N-glycan branching, *Nature Aging* (2022). DOI: 10.1038/s43587-022-00187-y

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