NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

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Aging enhances plasma cell competition

How did you become interested in aging?
Our laboratory is focused on how long-lived plasma cells survive in the body. These are the cells in the body that produce antibody and as long as they are alive, they can provide protection against pathogens like measles, SARS-Cov-2, or influenzae, just to name a few. We and others have been trying to understand how these cells can survive in the body for more than 50 years, in spite of a constant influx of new plasma cells generated every day.

Briefly describe your project in non-scientific terms. What questions are you trying to answer?
Plasma cells are the specialized cells in the body that make antibody. We are trying to see what changes occur in long-lived plasma cells as they age, that give them a selective survival advantage against new plasma cells. We also want to know if having all of these old plasma cells make it harder for humans to generate new long-lived plasma cells in old age, such after a vaccination.

What previous research or experience informed the development of this proposal?
In our recent Cell Reports study (Benet, Jing, Fooksman 2020), we reported that as plasma cells age in mice, they increase CXCR4 expression, and we also found that with age, plasma cells form more and larger clusters in the bone marrow and are also more motile, in a CXCR4-dependent manner. We think CXCR4 may give some plasma cells a selective advantage to survive in the bone marrow and allows them to better compete for survival factors. We have not extended this work into aging mice yet.

What's exciting about your project's potential impact?
This idea that plasma cells are getting stronger with age is counter-intuitive to what we would expect with aging, that everything breaks down, particularly in immune cells. If competition between old and new plasma cells is what is limiting duration of new antibody responses, then we may understand what it takes to get more durable immune responses in older adults.

If your project is successful, what is the next step?
The next step would be to understand what factors control plasma cell maturation and longevity and determine ways to improve vaccinations to activate these pathways.

How has support from and collaboration with the NSCs helped further this project and/or your research overall?
For certain, we would not be working on aging of plasma cells without this pilot grant, as well as additional support from the Einstein NSC Aging center through their core facilities, faculty, and access to unique tools and specimens. This is an exciting new avenue in our laboratory research program, which I hope will continue to expand in the future.