NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

Jiahn Choi, PhD

Assistant Professor
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2023 Einstein NSC Pilot Awardee

Mechanisms that link Aging with Cancer Risk

How did you become interested in aging?

My interest in aging began during my doctoral studies, where my thesis focused on understanding the dynamics of intestinal stem cells. I investigated how physical perturbations of the intestinal environment affected these cells. During this research, I discovered that the stem cell niche rapidly reorganizes in response to such perturbations, effectively eliminating damaged cells. This led me to collaborate with Dr. Huffman, a renowned aging researcher at Einstein, to explore how aging alters the recovery response in this niche. We found that aging reduces the motility of niche cells, impairing their ability to repair damage efficiently, which results in incomplete recovery. In my subsequent postdoctoral work with Dr. Augenlicht at Einstein, I investigated the impact of a Western-style diet on tumor development using a mouse model and I demonstrated that time-dependent adaptive responses to diet are crucial for initiating tumorigenesis in the intestinal mucosa. This experience made me realize that aging not only causes a decline in organ functions but also exacerbates the effects of environmental stress, contributing to the development of diseases.

Briefly describe your project in non-scientific terms. What questions are you trying to answer?

My research focuses on how aging and dietary stress, particularly from a Western-style diet, interact to affect the intestinal homeostasis. Aging is a significant risk factor for diseases such as colorectal cancer, and understanding how aging intersects with environmental risk factors at the cellular level is key to promoting healthier aging and preventing disease. My goal is to uncover the mechanisms behind the aging process and how it interacts with nutritional environment. Specifically, I want to understand how these interactions lead to reprogram cellular identities in the intestinal mucosa, and how these alterations may contribute to disease development.

What previous research or experience informed the development of this proposal?

In my recent publication, I demonstrated how Western-style diet remodels the mouse intestinal mucosa that increases the probability of tumor development. Interestingly, the intestinal epithelial cells quickly adapt to this diet by triggering a switch between distinct stem cell populations. However, it can take up to two-thirds of the organism's lifespan to develop tumors. Our study highlights that prolonged exposure to this diet causes lineage reprogramming, which results in increased pro-inflammatory signaling in fully differentiated cells. This raised the important question of how the aging process interacts with environmental factors, and what triggers the development and progression of disease.

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What's exciting about your project's potential impact?

This project holds the potential to significantly improve public health by providing insights into how aging and diet influence disease development. By understanding the biological mechanisms of aging under different dietary conditions, we can develop evidence-based strategies to prevent diseases like colorectal cancer. Additionally, identifying the key factors that trigger tumorigenesis could provide new therapeutic targets and help design interventions to ameliorate or reverse disease progression.

If your project is successful, what is the next step?

If successful, the next step will be to explore whether we can intervene in the maladaptive responses that occur with aging, using nutritional or pharmacological treatments. It would be impactful to discover whether age-related pathogenesis can be reversed and identify specific targets that can be addressed through therapeutic strategies to improve health and prevent disease.

How has support from and collaboration with the Nathan Shock Centers helped further this project and/or your research overall?

The support from the Nathan Shock Center Pilot and Feasibility award has been crucial in advancing my research. This funding allowed me to investigate my initial hypothesis about the interplay between diet and aging on intestinal mucosa remodeling, using cutting-edge technologies like single-cell RNA sequencing. This powerful tool enables me to examine gene expression changes at a single-cell level under different conditions. While the analysis is ongoing, preliminary data already show significant differences in cellular gene expression in the intestines of older mice based on their diet. This award has enabled me to generate valuable data that will help identify key genes and pathways involved in disease initiation.