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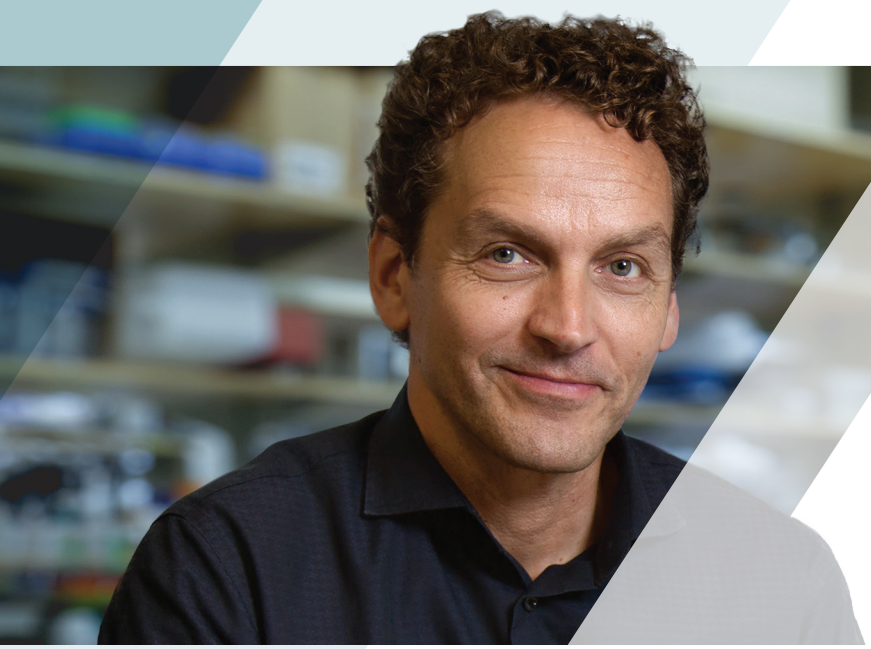

MARTIN HETZER

Professor
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Chair

THE CHALLENGE

Old age is the major risk factor for the development of neurodegenerative diseases such as Alzheimer's disease and a series of other ailments. The Hetzer lab is studying the impact of cumulative changes during adulthood on health and the development of disease, focusing on cell maintenance and repair mechanisms. They are particularly interested in understanding how non-dividing cells such as neurons function over the course of a lifetime and how cells lose control over the quality and integrity of proteins and important cell structures during aging. The ultimate goal is to utilize these mechanisms to delay age-related decline of organs with limited cell renewal such as the brain, pancreas and heart.

THE APPROACH

Martin Hetzer applies genomics, proteomics and advanced imaging techniques to pose questions about how adult tissues are maintained and repaired and why long-lived cells fail to work properly as a cell ages. He has shown that mammalian tissues are mosaics composed of cell populations with vastly different life spans ranging from days to years. The Hetzer laboratory discovered long-lived proteins (LLPs) in the nucleus, which exhibit no or very little protein turnover in the adult brain. The functional decline of LLPs could be a major contributor to age-related changes in the survival of nerve cells. A focus of his lab is to understand what allows LLPs to stay intact throughout an organism's entire life span. In people with neurodegenerative diseases, it appears that LLPs in older cells lead to the decline of the nucleus. Understanding why this happens is the first step to potentially prevent and treat disorders like Alzheimer's disease.

THE INNOVATIONS AND DISCOVERIES

- Hetzer showed that one of the ways nuclear pores (channels between the cell nucleus and the rest of the cell) manage to stay relatively stable for a cell's long life is by occasionally exchanging just one part of the channel complex at a time for a newer part. Since nuclear pore protein (nucleoporin) levels drop as a cell ages, Hetzer thinks this maintenance is limited.
- He also looked more broadly at the phenomenon of long-lived proteins (LLPs) in the rat nervous system. Most proteins in the body are replaced when they accumulate damage or begin to degrade. But LLPs—which include proteins that make up nuclear pores—last for a lifetime, Hetzer found.
- Hetzer's lab group recently developed a method to study the life spans of cells and proteins in adult tissues. They were able to show that the liver and pancreas are composed of cells with vastly different ages, many as old as the animal itself. Their findings have important biomedical implications for healthy aging of the brain, pancreas and heart and provide new insights into age-related diseases associated with these organs.

For more information, please visit:
WWW.SALK.EDU/SCIENTIST/MARTIN-HETZER

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