Scripps Research

Getting to the heart of the matter

Precision therapies for age-related neurodegenerative diseases

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ABOUT THE LECTURE

Professor Jeff Kelly illustrated the importance of molecular shapes in the process of aging. He outlined why structural abnormalities can cause cellular degeneration, leading to disorders of our central and peripheral nervous system, as well as heart disease. Kelly showed how his lab is addressing neurodegenerative conditions and heart failure with novel molecular "stabilizers" that can halt disease progression and restore a patient's quality of life.

TOP TAKEAWAY POINTS

1. Neurodegenerative diseases are disorders of protein shape. Proteins are the molecular machines that carry out critical processes inside our cells. A correctly folded protein normally has a spherical shape, while abnormal proteins are larger and rectangular.

2. The shape of a protein dictates how well it will function. An abnormal shape confers abnormal functions, leading to problems with the way a cell transports its cargo, produces energy or fights inflammation.

3. Our bodies can normally degrade these misassembled structures, but this process becomes less efficient as we age. In the brain, the accumulation of misfolded proteins can cause neuron cell death, compromising the brain's communications signals and leading to neurodegeneration.

4. The Kelly lab developed the FDA-approved drug Tafamidis, which can stabilize a protein's structure and prevent it from misfolding and accumulating into toxic clumps. The breakthrough therapy has significantly improved the prognosis of those with neurological disorders, or even heart failure, caused by protein plaques.

5. Early diagnosis and treatment are crucial. Emerging evidence suggests that as a neurodegenerative disease progresses, the brain's immune cells can become hyperactivated and worsen the destruction of neurons. Scientists are increasingly studying these autoimmune pathways.

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