Scripps Research

Paving the way to new therapies for neurodegenerative disease

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ABOUT THE LECTURE

At the intersection of molecular medicine and neuroscience, Sandra Encalada showed the inner workings of the transport system inside of brain cells and how a breakdown in this system can lead to different types of neurodegeneration. She then discussed promising new molecules that have the potential to prevent neuron cell death and reverse the disease process, as well as the path to advancing these drugs toward clinical application.

TOP TAKEAWAY POINTS

1. Life expectancy across the globe has increased dramatically in the past 200 years, bringing with it a considerable rise in the incidence of dementia and other neurodegenerative diseases. **Age is the single biggest risk factor for these conditions**, while different genetic and lifestyle factors also play a role.

2. One hallmark of neurodegenerative disease is the **accumulation of abnormal, misfolded proteins in neurons**, which can then cause toxicity and cell death. Many of these toxic aggregates are observed in the axon, the long projection that acts as a connecting road to traffic important molecular components.

3. Encalada and her team are investigating **how the accumulation of these toxic proteins disrupts the machines that normally travel along the tracks of the axon**, leading to transport blockages and irregular, swollen cells.

4. In the case of fatal prion disorders, such as Creutzfeldt-Jakob disease (CJD), a mutant form of the prion protein PrP is able to convert normal PrP proteins into toxic plaques. Using high-precision imaging tools, **the Encalada lab has found that the accumulation of toxic PrP proteins occurs within special fluid-filled sacks inside the axon**. As these fluid sacks are transported along the neuron, they become swollen, eventually causing cell damage.

5. In collaboration with medicinal chemists at Scripps Research, **Encalada and her team have discovered new molecules that can break down these fluid compartments and clear the toxic aggregates**, leading to restored neuron shape and function. The lab is now optimizing these molecules to determine their effectiveness in pre-clinical animal models, as well as their potential versatility across multiple disorders, such as Alzheimer's, Parkinson's and Huntington's disease.