Autophagy Mutation - FOXM1- Brain and Muscle Disorders

The following correlates ULK1 and VPS34 to the initiation of autophagy

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5869855/

Note:

Prior quantum biology modeling identified Beclin 1, Beclin 2 and phosphoinositide 3-kinase (PI3K) – a.k.a. Vps34 as forming a trefoil that functions to signal apoptosis as the intermediate step before autophagy.

Given the fact that FOXM1 is linked to mutation of autophagy and numerous studies correlate it to Vps34 is significant.

Qualified bioinformatics professionals are encouraged to contact MCFIP to discuss the role of this epigenetic signaling molecule in ALS as well as muscle disorders such as various forms of spinocerebellar ataxia.

Note: DIY using bioinformatic search to verify FOXM1 is linked to various forms of spinocerebellar ataxia.

https://www.sciencedaily.com/releases/2019/04/190410171705.htm

Biochemical switches identified that could be triggered to treat muscle, brain disorders

Date:

April 10, 2019

Source:

St. Jude Children's Research Hospital

Summary:

Scientists have found that the enzymes ULK1 and ULK2 play a key role in breaking down cell structures called stress granules, whose persistence leads to toxic buildup of proteins that kill muscle and brain cells. Such buildup is central to the pathology of three related diseases: inclusion body myopathy (IBM), amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD).

St. Jude Children's Research Hospital scientists have found that the enzymes ULK1 and ULK2 play a key role in breaking down cell structures called stress granules, whose persistence leads to toxic buildup of proteins that kill muscle and brain cells. Such buildup is central to the pathology of three related diseases: inclusion body myopathy (IBM), amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD).

IBM causes weakness in arm and leg muscles. ALS, also known as Lou Gehrig's disease, causes paralysis due to the death of nerve cells controlling voluntary muscles. FTD is a form of dementia that damages areas of the brain associated with personality, behavior and language.

Led by St. Jude researcher Mondira Kundu, M.D., Ph.D., an associate member of the St. Jude Department of Pathology, the team published their findings online in the journal *Molecular Cell*.

Stress granules are biological "storm shelters" that temporarily protect genetic molecules and proteins when the cell's health is under threat from heat, chemicals or infection. Such granules normally disassemble when the stress is removed, but mutations that cause malfunction in the disassembly machinery can cause them to persist. One such mutation is in a gene called VCP, and the St. Jude researchers found that ULK1/2 is a key activator of VCP. Thus, they believe that drugs to boost those enzymes could help treat the pathology of IBM, ALS and FTD.

The other St. Jude authors are Bo Wang, Brian Maxwell, Joung Hyuck Joo, Youngdae Gwon, James Messing, Ashutosh Mishra, Timothy Shaw, Amber Ward, Honghu Quan, Sadie Miki Sakurada, Shondra Pruett-Miller, Peter Vogel, Hong Joo Kim and Junmin Peng. Co-author Tulio Bertorini is with the University of Tennessee Heath Science Center. Co-author J. Paul Taylor is a Howard Hughes Medical Institute Investigator and chair of the St. Jude Department of Cell and Molecular Biology.

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Story Source:

Materials provided by **St. Jude Children's Research Hospital**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Bo Wang, Brian A. Maxwell, Joung Hyuck Joo, Youngdae Gwon, James Messing, Ashutosh Mishra, Timothy I. Shaw, Amber L. Ward, Honghu Quan, Sadie Miki Sakurada, Shondra M. Pruett-Miller, Tulio Bertorini, Peter Vogel, Hong Joo Kim, Junmin Peng, J. Paul Taylor, Mondira Kundu. **ULK1 and ULK2 Regulate Stress Granule Disassembly Through Phosphorylation and Activation of VCP/p97**. *Molecular Cell*, 2019; DOI: 10.1016/j.molcel.2019.03.027