

GEOFFREY BEENE

2013 Global NeuroDiscovery Challenge

21 CBT INNOVATION AWARD (\$50,000)

ONLINE VOTING

NOVEMBER 1-5

Three Finalists Submissions

HYPOTHESIS #2: 075 USP9Y

MALE/FEMALE DIFFERENCES IN AGING BRAINS IN A GENE FOR UBIQUITIN-SPECIFIC PEPTIDASE 9 (USP9) AS A POSSIBLE CAUSE FOR INCREASED INCIDENCE OF ALZHEIMER'S DISEASE IN OLDER WOMEN

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The Science: Aging is considered one of the primary risk factors for Alzheimer's Disease. Studies of the aging human brain show that changes in gene expression may be different between men and women. This investigator analyzed two datasets and looked for genes that are deregulated only in aging men and only in aging women in Alzheimer's compared to unaffected controls.

Hypothesis: One of the genes with the largest difference between aging adult men and women across multiple brain regions was the male Y-chromosomal gene for ubiquitin-specific peptidase 9 (*USP9Y*); the differences were not shown with the similar female gene, *USP9X*. Therefore the hypothesis is that *USP9Y* is important to men and may be protective against Alzheimer's.

Innovation: These observations suggest that higher *USP9Y* levels in unaffected males as compared to *USP9X* levels in females may provide a protective effect in men against Alzheimer's. In brain samples from male Alzheimer's patients, there was a down regulation of *USP9Y* compared to unaffected male controls. Supportive findings come from other studies that show that *USP9* is known for involvement in multiple pathways related to Alzheimer's – microtubule-associated protein tau (*MAPT*), a biomarker of Alzheimer's; *SIRT1*, a gene linked with longevity and Alzheimer's; and another signaling pathway which is neuroprotective.

Proposed Research: Dr Glaab and his team would like to verify these findings by datamining other datasets in males only and also extend this work to cell cultures and animal mouse models. They have been studying other neurodegenerative disorders as Parkinson's.

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