TSC Research summaries

URL to summary on TS Alliance website: (TBD)

Title: The Stress-Induced Atf3-Gelsolin Cascade Underlies Dendritic Spine Deficits in Neuronal Models of Tuberous Sclerosis Complex

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What is the topic?
Tuberous sclerosis complex (TSC) is caused by deficits in genes TSC1 and /or TSC2. These genes act together and inhibit the activation of an enzyme called mTOR. A deficit in one of the genes causes loss of regulation of mTOR leading to enlarged cells seen in TSC and neurobiological abnormalities like epilepsy and autism. The focus of this study was to find out specific genes involved when there is a deficit of TSC1 and/ or TSC2 since not a lot is known about this.

What did the researchers hope to learn?
By learning what gene are regulated when there is a dysregulation of mTOR, the researchers hoped to eventually be able to find novel therapy for TSC.

Who was studied?
The scientists used experimental mice for this study. Neuronal cultures from the hippocampus from normal mice and those that were deficient in TSC2 were compared in their genetic profile.

How was the study conducted?
Instead of using conventional gene profiling, the scientists used a procedure known as Translating Ribosomal Affinity Purification (TRAP) – this method provides a clearer resolution than gene profiling.

What did the researchers find?
By using the TRAP technology in cultures of mice that were deficient in TSC2, the researchers found several important genes that were increased and others were decreased in neurons that were deficient in TSC2 gene. They also found a novel signaling pathway called Atf3-gelsolin cascade that was abnormal, and linked this to the deficits seen in TSC in dendritic spines. These spines are the area on the neuron where neurotransmission takes place.

What were the limitations of the study?
The study was done in cell cultures and is outstanding work to start teasing apart genetic profiles in TSC. However, more work in whole rodents and in human tissue would be necessary in the future.

What do the results mean for you?
This study puts forward a novel signaling pathway to the deficits in dendritic spines and gives a possible explanation for autism and epilepsy observed in TSC. With the help of more research, targeted therapies that reverse these deficits could be found.

This summary was written by Sloka Iyengar, PhD, epilepsy researcher and science writer (February 2016).