

P027 Identification of genes regulated by mTOR in tuberous sclerosis

**M.E. Tyburczy¹, K. Kotulska², S. Jozwiak²,
P. Pokarowski³, J. Mieczkowski³, B. Kaminska¹**

¹ Nencki Institute of Experimental Biology, Warsaw, Poland

² The Children's Memorial Health Institute, Warsaw, Poland

³ Warsaw University, Poland

Tuberous sclerosis (TS) is a disease characterized by formation of benign tumors in the brain (subependymal giant cell astrocytoma – SEGA) and neurological disorders. TS is caused by mutations in *TSC1* (Hamartin) or *TSC2* (Tuberin) leading to enhancement of mTOR kinase activity and pathological alterations. Signaling via mTOR participates in complex genomic response but mTOR effectors in the brain are largely unknown. We sought to identify components of mTOR signaling network in the pathological brain. Gene expression profiling was done on four SEGAs and four control brain samples with Affymetrix Human Genome arrays. The differences in gene expression were validated by qRT-PCR. Identified genes encode proteins implicated in the nervous system development/ differentiation (downregulated in TS), and proteins involved in regulation of tumor cell proliferation (upregulated in TS). Several of selected genes were identified as putative mTOR effector genes in SEGA cell culture. Treatment with Rapamycin (an inhibitor of mTOR) modulated the expression of four genes in cells derived from SEGA demonstrating their association with mTOR pathway. In the present study several genes were identified, for the first time, as regulated by mTOR activity on transcriptional level in tuberous sclerosis.