

**P028** Tuberin knockdown disrupts neuronal development.

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Neuronal development is a complex, multistage process regulated by several proteins. Recently mammalian target of rapamycin (mTOR) kinase has been implicated in control of this process. Tuberous sclerosis complex (TSC), that consists of tuberin (TSC2) and hamartin (TSC1), negatively regulates mTOR due to GAP (GTPase Activating Protein) activity of tuberin towards Rheb, an immediate activator of mTOR. Hamartin, on the other hand, is known to stabilize tuberin by preventing its degradation. In our research, we focused on the role of tuberin in developing neurons, particularly in cell soma growth and dendritic branching. To approach this problem, we transfected rat hippocampal neurons cultured *in vitro* with short interfering RNA directed against tuberin. Silencing tuberin at the early stage of neuron development (3-8 days *in vitro*) resulted in an increase in the number of primary dendrites and simplification of the dendritic tree. Moreover, an increase in neuron soma size was observed. Surprisingly, while inhibiting mTOR activity in transfected neurons by rapamycin reversed the increase of cell soma size, it did not affect changes of the dendritic arbor. Thus, our data suggest that dendritic branching might be regulated by tuberin independently of mTOR Complex 1, that is rapamycin-sensitive. Such alternative pathways may involve rapamycin-insensitive mTOR Complex 2, tuberin targets distinct from Rheb or independent actions of hamartin.

This work has been financed by Polish Ministry of Science and Higher Education Research Grant PBZ-MNiI-2/1/2005