

**P042** JNK regulates dendritic architecture: role of MAP2 as an effector

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Normal functioning of the nervous system requires precise regulation of dendritic shape and synaptic connectivity. Here we report a severe selective impairment of dendritic structures in the cerebellum and motor cortex of JNK1 deficient mice. Using an un-biased screen for candidate mediators we identified dendrite-specific high molecular weight microtubule-associated protein 2 (MAP2) as a JNK substrate in brain. We subsequently show for the first time that MAP2 was phosphorylated by JNK in intact cells and that MAP2 phosphorylation was decreased in JNK1<sup>-/-</sup> brain. We developed compartment-targeted JNK inhibitors to define whether a functional relationship existed between the physiologically active, cytosolic pool of JNK and dendritic architecture. Using these, we demonstrated that cytosolic but not nuclear JNK determined dendritic length and arbor complexity in cultured neurons. Moreover, we confirmed that MAP2-dependent process elongation was enhanced upon activation of JNK. Together these results suggest that JNK phosphorylation of MAP2 plays an important role in defining dendritic architecture in the brain.