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Detection of Mitogen-Activated Protein Kinase Kinase 3 (MAP2K3) Immunoreactivity in the Human Cerebral Cortex

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SuperAgers are defined as individuals aged 80 and above whose episodic memory performance is at least at the level of cognitively average individuals in their 50s and 60s. Our previous exome wide investigation revealed that the SuperAging phenotype is associated with variants in the mitogen-activated protein kinase kinase 3 (MAP2K3) gene. MAP2K3 is a dual specificity protein kinase that belongs to the mitogen-activated protein kinase signaling pathway. It is activated by different forms of stressful stimuli and inflammatory cytokines residing in a biological pathway linked to memory.

To determine if presence of MAP2K3 gene variants influence levels of its protein, it will be necessary to measure the levels of MAP2K3 protein in tissue. Detection of MAP2K3 protein levels have been reported in animal tissue and in human cells in culture. There is no information on the levels of MAP2K3 in the human brain. We sought to explore methods for detection of this protein in human cortical tissue using two commercially available antibodies in western blot and immunohistochemical experiments. We used brain tissue from the middle frontal gyrus of three cognitively normal aged individuals. To determine whether we can detect effects of neurodegeneration, we also used tissue from four patients with frontotemporal lobar degeneration (FTLD) with TDp-43 pathology. We were able to identify MAP2K3 in cortical tissue with both methods. Immunohistochemistry in aged controls showed robust staining in neurites. Western blot analyses confirmed presence of MAP2K3 in cortical tissue homogenates and revealed a 47% decrease in protein levels in FTLD.

Our findings indicate that MAP2K3 protein can be detected in human cortical tissue via both western blot and immunohistochemistry, and can be used to detect alterations in its levels.

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