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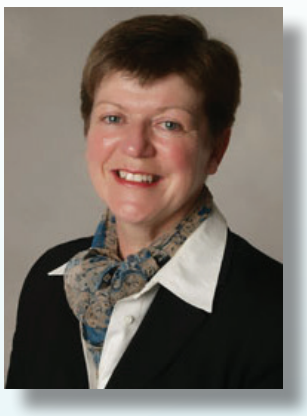
# PAPER OF THE MONTH • MARCH 2014

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Cell Death & Differentiation


## Caspase-6 activity in the CA1 region of the hippocampus induces age-dependent memory impairment


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Active Caspase-6 is abundant in the neuropil threads, neuritic plaques and neurofibrillary tangles of Alzheimer disease brains. However, its contribution to the pathophysiology of Alzheimer disease is unclear. Here, we show that higher levels of Caspase-6 activity in the CA1 region of aged human hippocampi correlate with lower cognitive performance. To determine whether Caspase-6 activity, in the absence of plaques and tangles, is sufficient to cause memory deficits, we generated a transgenic knock-in mouse that expresses a self-activated form of human Caspase-6 in the CA1. This Caspase-6 mouse develops age-dependent spatial and episodic memory impairment. Caspase-6 induces neuronal degeneration and inflammation. We conclude that Caspase-6 activation in mouse CA1 neurons is sufficient to induce neuronal degeneration and age-dependent memory impairment. These results indicate that Caspase-6 activity in CA1 could be responsible for the lower cognitive performance of aged humans. Consequently, preventing or inhibiting Caspase-6 activity in the aged may provide an efficient novel therapeutic approach against Alzheimer disease.



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