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New insight into the physiological activities of Amyloid Beta monomers

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Alzheimer's disease (AD) is one of the most common form of dementia in the elderly, characterized by a progressive neurodegeneration associated with synaptic dysfunction, pathological accumulation of ß-amyloid (Aß) in plaques, and neuronal loss. The self-association of Aß monomers into soluble oligomers seems to be crucial for the development of neurotoxicity (Walsh and Selkoe, 2007).
Some of the toxic effects of Aß are mediated by its adverse effect on neurotrophic factor expressions. In particular, Aβ oligomers have been found to decrease both phosphorylated CREB and BDNF mRNA in the neuroblastoma cell line, SH-SY5Y, suggesting that oligomeric Aβ could compromise neuronal functions in AD by downregulating BDNF (Garzon and Fahnestock, 2007). Accordingly, phosphorylated CREB and CREB-regulated BDNF are recently shown to be reduced in the brain of AD patients and Tg2576 mice (Pugazhenthi, 2011)
We previously reported a neuroprotective activity of monomeric Aß involving the activation of a PI3K/Akt survival pathway (Giuffrida et al., 2009). Here we demonstrate that Aß monomers are specifically able to activate CREB, a converging point for mechanisms and pathways involved in memory formation (Teich et al., 2015). Our data suggest a new model whereby Aß monomers may preserve cognitive decline.

References:

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