Fluorescence studies reveal a high-affinity interaction between the neurotoxic amyloid β-peptide and calmodulin

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Many works have been focused on Amyloid β-peptides (Aβ), a major hallmark of Alzheimer's disease (AD), and their interactions with different proteins. Although Aβ neurotoxicity develops with cytosolic calcium dysregulation, our knowledge about Aβ and calcium regulation and signaling is still limited. One of the proteins that plays a major multifunctional role in calcium signaling is calmodulin (CaM). In this work, using fluorescent derivatives of CaM (Badan-CaM), we show that Aβ binds with high affinity to CaM. Furthermore, we have been able to fine tune that the 25-35 domain of Aβ form a novel binding motif for CaM which is responsible for this high affinity interaction. The low values obtained for the dissociation constants of Aβ from CaM point out that CaM is one of the cellular targets with highest affinity for neurotoxic Aβ peptides. Therefore, this novel high affinity Aβ-CaM interaction opens a new gateway to further understand the mechanism involved in the neurotoxic effect of Aβ and also to consider the potential of calmodulin and calmodulin-derived peptides as therapeutic agents in AD. *This work has been supported by Grant BFU2014-53641-P of the Spanish Plan Nacional de I+D+I and by Grant GR15139 of the Junta de Extremadura to the Research Group BBB008, both with co-financing by the European Funds for Structural Development (FEDER).*