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The co-chaperone BAG2: A new piece in the complex puzzle of toxic Tau in Alzheimer's disease

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Alzheimer's disease (AD) is a neurodegenerative disorder caused by progressive loss of synapses and neurons, characterized by memory dysfunction and global cognitive impairment. The pathological hallmarks for AD are extracellular senile plaques of amyloid-β-peptide (Aβ) and intracellular neurofibrillary tangles (NFTs) of hyper-phosphorylated tau protein. Tau inclusions are not found only in Alzheimer's disease but in many others neurodegenerative diseases. Their accumulation in neurons as ubiquitinated filaments suggests a failure in the degradation limb of the Tau pathway. The components of a Tau protein triage system consisting of CHIP/Hsp70 and other chaperones have begun to emerge. However, the site of triage and the master regulatory elements are unknown. Here we report an elegant mechanism of Tau degradation involving the co-chaperone BAG2. The BAG2/Hsp70 complex is tethered to the microtubule and this complex can capture and deliver Tau to the proteasome for ubiquitin-independent degradation. This complex preferentially degrades toxic Tau. Thus we propose that ubiquitinated Tau inclusions arise due to shunting of Tau degradation toward a less efficient ubiquitin-dependent pathway.

Biography

Daniel Carneiro Carrettiero has completed his Ph.D at the age of 31 years from University of São Paulo (USP) in 2008. He was in UCSB, Santa Barbara, as visiting scientist in 2008 in Kosik's lab. He also performed his postdoctoral studies in the same university in Brasil. Now, he is a associated professor in a Federal University / Santo André / São Paulo / Brasil.

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