Periphilin is a novel interactor of synphilin-1, a protein implicated in Parkinson's disease.

Parkinson's disease (PD) is a common neurodegenerative disorder characterized by the loss of dopaminergic neurons and the presence of Lewy bodies. Alpha-synuclein and its interactor synphilin-1 are major components of these inclusions. Rare mutations in the alpha-synuclein and synphilin-1 genes have been implicated in the pathogenesis of PD; however, the normal function of these proteins is far from being completely elucidated. We, thus, searched for novel synphilin-1-interacting proteins and deciphered periphilin as a new interactor. Periphilin isoforms are involved in multiple cellular functions in vivo, and the protein is broadly expressed during embryogenesis and in the adult brain. We show that periphilin displays an overlapping expression pattern with synphilin-1 in cellular and animal models and in Lewy bodies of PD patients. Functional studies demonstrate that periphilin, as previously shown for synphilin-1, displays an antiapoptotic function by reducing caspase-3 activity. Searching for mutations in the periphilin gene, we detected a K69E substitution in two patients of a PD family. Taken together, these findings support for the first time an involvement of periphilin in PD.