

SUMO defeats protein aggregates that typify Parkinson's disease

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A small protein called SUMO might prevent the protein aggregations that typify Parkinson's disease (PD), according to a new study in the July 11, 2011, issue of *The Journal of Cell Biology*.

Insoluble protein clusters are the hallmarks of several neurodegenerative diseases. In PD, neurons harbor insoluble clumps of the protein alpha-synuclein. What triggers these protein pileups remains obscure. A possible clue for PD came when researchers overexpressed alpha-synuclein in human kidney cells and found that the protein was modified by the addition of the small, ubiquitin-like molecule SUMO. Since sumoylation generally boosts the solubility of proteins, the result raised the possibility that SUMO proteins affect the aggregation of alpha-synuclein.

Researchers tested whether sumoylating purified alpha-synuclein hindered its clustering into fibrils, filaments similar to those detected in neurons of PD patients. If all of the alpha-synuclein molecules in a solution were sumoylated, no fibrils appeared. And even if only 10 percent of the molecules were sumoylated, fibril formation slowed dramatically.

SUMO molecules typically attach to two sites on alpha-synuclein, the researchers found. Compared with controls, cells that produced alpha-synuclein variants lacking these two sites contained more protein clusters and were more likely to die by apoptosis. The scientists then genetically altered rats to manufacture the alpha-synuclein variants specifically in neurons. Cell death surged in the substantia nigra, the brain region where large numbers of neurons perish in PD patients. But whether sumoylation goes awry in these patients remains unknown.

More information: Krumova, P., et al. 2011. *J. Cell Biol.* doi:10.1083/jcb.201010117

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