

# A balancing act in Parkinson's disease: Phosphorylation of alpha-synuclein

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Both genetic and pathologic data indicate a role for the neuronal protein alpha-synuclein in Parkinson disease. Previous studies have indicated that phosphorylation of alpha-synuclein at amino acid 129 (Ser129) is a key event in alpha-synuclein-mediated nerve cell toxicity. However, Mel Feany and colleagues, at Brigham and Women's Hospital, Boston, have now identified a counterbalancing role in nerve cell protection for phosphorylation of alpha-synuclein amino acid 125 (Tyr125).

In the study, [phosphorylation](#) of human alpha-synuclein Tyr125 was detected in [Drosophila](#) transgenic for human alpha-synuclein and shown to protect from alpha-synuclein-mediated nerve cell toxicity in a *Drosophila* model of Parkinson disease. That the two phosphorylated amino acids have opposing roles was indicated by the observation that Tyr125 phosphorylation decreased levels of toxic soluble alpha-synuclein oligomers in the *Drosophila* [brain](#), whereas Ser129 phosphorylation increased them.

More importantly, Tyr125 phosphorylation was found to decrease as both humans and *Drosophila* aged and was reduced in cortical tissue from patients with synucleinopathy [dementia](#) with Lewy bodies, a disease related to Parkinson disease. The authors therefore suggest that changes in the balance between Ser129 and Tyr125 phosphorylation — which promote nerve cell toxicity and protection, respectively — might cause alpha-synuclein-mediated nerve cell toxicity in Parkinson disease and related disorders.

More information: View this article at: [www.jci.org/articles/view/3908...59af0a7e79b38662c2ee](http://www.jci.org/articles/view/3908...59af0a7e79b38662c2ee)

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