Biological Sciences Division

PNNL team makes the first global identification of endogenous levels of nitrated proteins in the brain

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Results of the largest global proteomic study of protein nitration to date will appear in the July 2006 issue of the journal *Biochemistry*. A multidisciplinary team at Pacific Northwest National Laboratory (PNNL) surveyed 7792 proteins from normal mouse brain to identify 31 unique nitrotyrosine sites in 29 different proteins. More than half of the nitrated proteins identified are involved in neurodegenerative diseases such as Alzheimer's, Parkinson's, atherosclerosis, and Lou Gehrig's disease.

Both the sensitivity of the identified proteins to nitration and their importance for normal neuronal function suggest nitrotyrosine modification as a factor in neurodegenerative disease. Nitrotyrosine is a specific marker of inflammation and oxidative stress, which can modulate tyrosine kinase signaling pathways and, if unmitigated, lead to cellular dysfunction. Structural analysis of this proteomic dataset suggests that specific tyrosine sites within individual proteins sensitive to nitration can be predicted.

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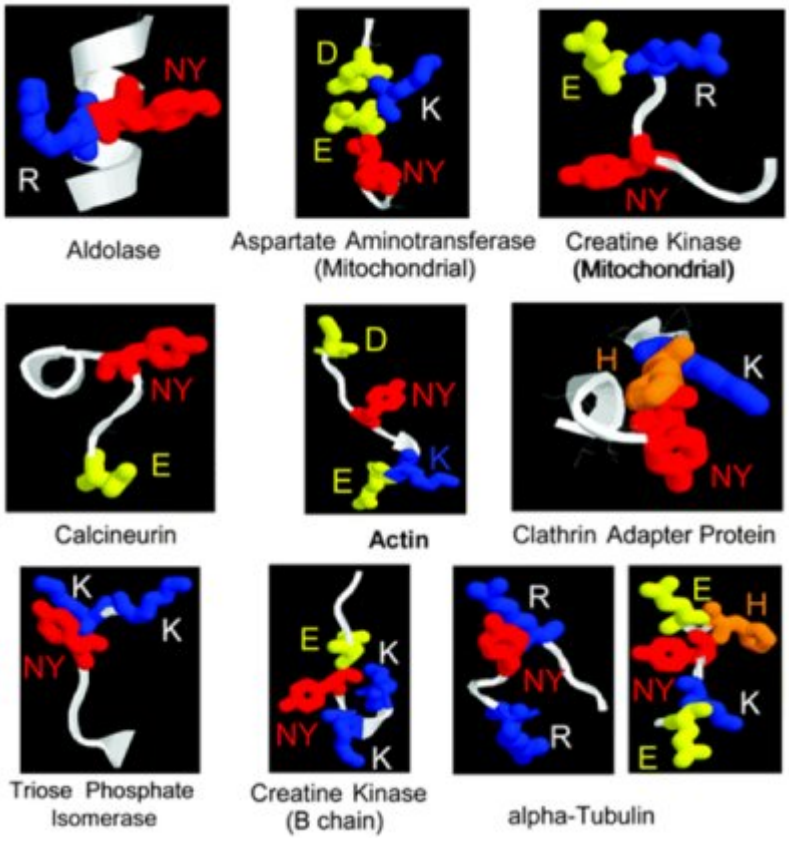
This achievement was made possible by the high-resolution separation of tryptic peptides capabilities coupled with tandem mass spectrometric analysis developed at the W.R. Wiley Environmental Molecular Sciences Laboratory at PNNL. Future studies will build upon this sensitive detection of basal levels of protein nitration to examine early events in the progression of neurodegeneration.

This work was supported by grants from the National Institutes of Health and PNNL's Biomolecular Systems Initiative. The team includes Colette Sacksteder, Weijun Qian, Tatyana Knyushko, Haixing Wang, David Camp, Dick Smith, Tom Squier, and Diana Bigelow, PNNL; and Desmond Smith, Mark Chin, Goran Lacan, William Melega, UCLA.



3-D structure of nitrotyrosine sites in selected proteins. With this information, protein sites sensitive to inflammation and oxidative stress might be predicted.
Full Image

News Release: A probable cause for Parkinson's?

Reference

Sacksteder CA, W Qian, TV Knyushko, HH Wang, MH Chin, DG Camp, II, RD Smith, D Smith, TC Squier, and DJ Bigelow. 2006. "Endogenously nitrated proteins in mouse brain: links to neurodegenerative disease." *Biochemistry* 45(26):8009-8022.