the site of injury in the wild type but not in the NOS null mice. Therefore, nitrative damage resulting from the formation of biologically reactive agents derived from nitric oxide can contribute to cellular injury.

Perry *et al.* suggest that nitration might be protective, possibly by preventing formation of *o-o'*-dityrosine. However, our data with different nitrating agents in vitro indicate that 3-nitrotyrosine and *o-o'*-dityrosine formation occur simultaneously at different tyrosine residues (*5*). Although it is possible that nitration could inhibit further modification of a tyrosine residue, concurrent cross-linking of nonmodified residues will surely occur.

We agree with Perry *et al.* that nitration can occur through several pathways. However, some in vitro reactions may have no physiological bearing, such as nitrylchloride, which is not an effective nitrating agent (*4, 6*), or the pathway described by Gunther *et al.* (*7*), which is limited to tyrosyl radicals. Precisely because several pathways can mediate nitration in vivo, we did not ascribe nitration of α-synuclein in human tissue to a particular nitrating agent, but the fact that several pathways can result in this modification further highlights the physiological importance of nitration. In vitro data indicate that nitrating agents are equally strong oxidizing agents (*5*); thus, nitration likely occurs concurrently with oxidation in vivo. This idea is further supported by nitrative and oxidative modifications of protein in mice challenged with MPTP (*8*).

Thus, the observation that nitration of α-synuclein, and perhaps other proteins, is present in the pathological aggregates of surviving neurons and glia in synucleinopathies (*9*) is an indicator of oxidative damage. Because of the temporal uncertainty of pathological examination, it is not possible to determine if these cells are destined for their demise. The presence of nitrative damage indicates a diminution in the normal anti-oxidative capacity and/or overproduction of reactive nitrogen species, which certainly renders them more vulnerable.

HARRY ISHIROPOULOS,[1] BENOIT GIASSON,[2] JOHN E. DUDA,[2] JOHN Q. TROJANOWSKI,[2] VIRGINIA M.-Y. LEE[2]*

[1]Stokes Research Institute and Department of Biochemistry and Biophysics, Children's Hospital of Philadelphia, Philadelphia, PA 19104, USA. [2]Center for Neurodegenerative Disease Research and Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA

*To whom correspondence should be addressed. E-mail: vmylee@mail.med.upenn.edu

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CORRECTIONS AND CLARIFICATIONS

NEWS FOCUS: "Taking the measure of the wildest dance on Earth" by D. Mackenzie (8 Dec., p. 1883). Oded Schramm's nationality and affiliation were misstated. He is a citizen of Israel and did much of the work described while at the Weizmann Institute of Science.