

## John Q. Trojanowski

Internationally renowned neuropathologist and scientist John Q. Trojanowski died at the age of 75 years on 8 February 2022, following complications from a fall. John had an immeasurable impact on the field of neurodegenerative diseases and was responsible for many ground-breaking discoveries that continue to drive our understanding of Alzheimer disease, Parkinson disease, frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS).

Born in 1946 to a military family, John's childhood was spent across many air force bases in the USA and abroad. As a man with a towering physique, John played collegiate American football, but his sporting career was cut short owing to an injury. He spent his remaining college years in the Netherlands and Austria, before graduating from King's College (Wilkes-Barre, Pennsylvania, USA). Fulfilling his dream to be a doctor, John obtained his medical and doctoral degrees from Tufts University (Medford, Massachusetts, USA), followed by clinical training in medicine, pathology and neuropathology at Harvard University (Boston, Massachusetts, USA) and the University of Pennsylvania (Philadelphia, Pennsylvania, USA). While in Boston, John met a postdoctoral fellow, Virginia M.-Y. Lee, who had trained as a classical pianist before turning to science, and was already known for her amazing sharp intellect and penchant for high fashion. This athlete-musician pair moved to Philadelphia and forged a partnership in science and life, combining his expertise in neuropathology and her talent in biochemistry with remarkable success.

In 1981, John joined the faculty ranks at the University of Pennsylvania as an assistant professor in the Department of Pathology and Laboratory Medicine, where he stayed for the rest of his career, rising to full professor in 1990 and receiving the William Measey-Truman G. Schnabel, Jr., M.D. Professorship of Geriatric Medicine and Gerontology in 2002. He served as the director of the Institute on Aging (2002–2021), director of the Penn Alzheimer's Disease Core Center (1991–2020), co-director of the Center for Neurodegenerative Disease

Research (1991–2022), director of the Penn Udall Center of Excellence for Parkinson's Disease Research and the Penn U19 Center on Alpha-Synuclein Strains in Alzheimer Disease and Related Dementias (2007–2022), and Biomarker Core Leader for the Alzheimer's Disease Neuroimaging Initiative (2004–2022). These leadership roles speak to John's remarkably giving and collaborative nature, which has spawned a generation of scientists and clinicians dedicated to neurodegenerative disease research. He was the recipient of numerous awards and accolades, including the Potamkin Prize, the American Association of Neuropathologists Meritorious Contribution to Neuropathology Award, the Alzheimer's Association Lifetime Achievement Award and induction into the Institute of Medicine (National Academy of Medicine).

John's foundational discoveries are too numerous to be fully catalogued here, but some of his major accomplishments include demonstrating unequivocally that phosphorylated tau is the protein that forms the paired helical filaments in Alzheimer disease neurofibrillary tangles<sup>1</sup>; that  $\alpha$ -synuclein is the protein that forms Lewy bodies in Parkinson disease and dementia with Lewy bodies<sup>2</sup>; and that TAR DNA-binding protein 43 (TDP43) is the protein that forms inclusions in FTLD and ALS<sup>3</sup>. Together, these three proteins have been implicated in a wide range of ageing-related neurodegenerative proteinopathies. Also evident from these discoveries is John's unique ability to integrate knowledge across different diseases, which informed his prescient warning that ageing-related neurodegenerative diseases are characterized by mixed proteinopathies and are likely to require multiple complementary therapeutic approaches.


John was also responsible for mapping the spread of neurodegenerative proteinopathies in the human brain for several diseases, including ALS, FTLD with TDP43 inclusions, progressive supranuclear palsy, Pick disease and limbic-predominant age-related TDP43 encephalopathy. These pathological studies inspired basic research into the mechanisms that affect the cell-to-cell spread of proteinopathy through the neuronal connectome, and the biochemical elucidation



Credit: Image courtesy of Brandon Lausch, Penn Medicine, Philadelphia, PA, USA.

of proteopathic strains linked to disease phenotypes.

Aside from John's remarkable scientific discoveries, he is remembered for his boundless energy and ever-present personality. His probing questions at conferences were legendary. John's passion and dedication remains a driving force for all who had the privilege to know him, and our memories remind us that his was an extraordinary life.

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#### Competing interests

The author declares no competing interests.