

A G-quadruplex-hemin peroxidase complex as a source of oxidative stress in neurological diseases

CHARLESTOWN, MA, UNITED STATES,

December 19, 2025 /EINPresswire.com/ --

In a [paper](#) just published in the journal *Antioxidants*, the expansion of disease-causing DNA repeats is linked to the formation of a complex that generates superoxide anions toxic to neurons. The repeat expansion is found in Amyotrophic Lateral Sclerosis (Lou Gehrig's Disease)

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ALS and FTD remain challenging diseases to treat”

Alan Herbert

and in cases of Frontal Temporal Dementia. The paper, “[G-Quadruplexes Abet Neuronal Burnout in ALS and FTD](#),” by Alan Herbert of InsideOutBio, describes how these repeats fold into four-stranded structures called G-quadruplexes (GQs). The GQ formed has a propensity to bind hemin, a normal cellular constituent. The complex acts as a peroxidase, generating oxygen radicals that damage nerve

cells and contribute to disease outcomes.

Hemin is a normal cellular component. It is essential for ATP generation by mitochondria. Hemin usually complexes generate the highly reactive oxygen radicals that help mitochondria convert food into energy. The binding of hemin to GQ also enhances its production of oxygen radicals. The process occurs in the cytoplasm, where the repeat RNA can form the GQ that activates hemin. This “peroxidase” activity of the GQ-hemin complex is usually suppressed by cellular proteins that bind to it. In some cases, protein variants that are unable to suppress superoxide production increase the risk of disease. Preventing the formation of the GQ-hemin peroxidase offers a potentially new treatment option. These therapeutics are currently under investigation but are not ready for clinical use.

This paper captures the expanding knowledge on the role of [flipons](#) in health and disease.

Flipons are repeat elements present in our genome that encode RNAs able to fold into unusual structures. Besides G-quadruplexes, they can also form left-handed Z-RNA and three-stranded triplex structures. Flipons are a focus of InsideOutBio.

About InsideOutBio: InsideOutBio is a start-up focused on developing a novel class of proprietary therapeutics to 'light' up tumors for the immune system to kill by reprogramming self/nonself pathways within cancer cells. Dr. Herbert leads discovery at InsideOutBio. His work on Z-DNA was foundational to the discovery of flipons. These statements about InsideOutBio comply with Safe-Harbor laws. They are forward-looking and involve known and unknown risks and uncertainties. They are not guarantees of future performance, and undue reliance should not be

placed on them.

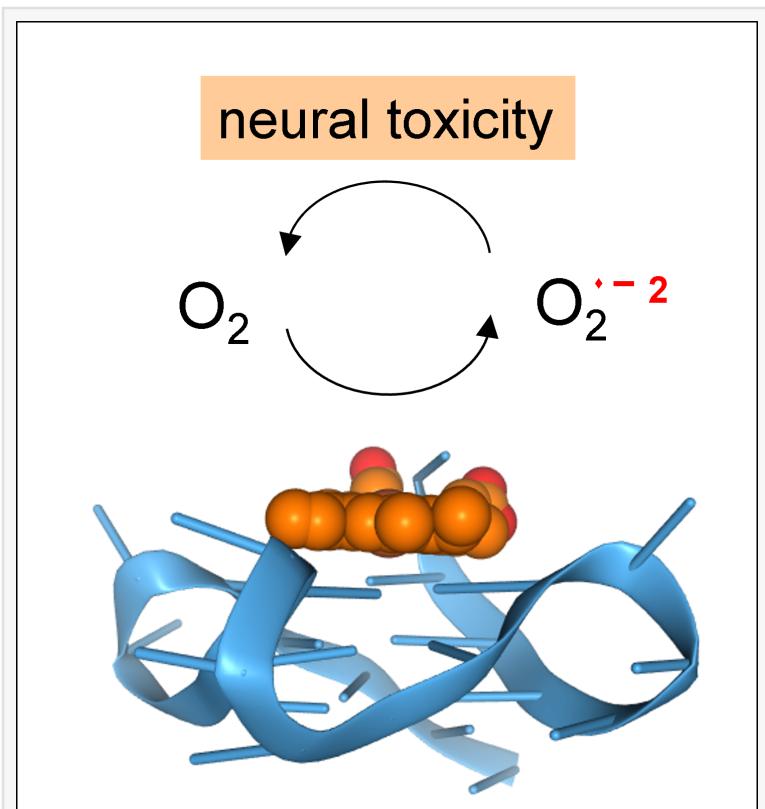
Alan Herbert
InsideOutBio, Inc

+1 617-800-7531

[email us here](#)

Visit us on social media:

[X](#)



The complex formed by an RNA G-quadruplex (blue) and Hemin (orange) catalyzes the formation of oxygen radicals (with unpaired electrons shown in red) from molecular oxygen, producing neuronal damage in LAS and FTD.

This press release can be viewed online at: <https://www.einpresswire.com/article/876952845>

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