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Time to get Personal: A Framework for Personalized Targeting of Oxidative Stress in Neurotoxicity and Neurodegenerative Disease

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## Time to get Personal: A Framework for Personalized Targeting of Oxidative Stress in Neurotoxicity and Neurodegenerative Disease

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### Highlights

- Although free radicals are necessary for certain brain functions, the brain is uniquely susceptible to oxidative stress due to factors such as aging, neurotransmitter production and high energy demands.
- Oxidative stress is a common mechanism that is involved in neurotoxicity found in various neurodegenerative diseases.
- Glial cells, such as microglia and astrocytes, are major sources of oxidative stress in the brain.
- Genetic polymorphisms in antioxidant enzymes or mitochondrial protective factors can lead to increased OS in the brain and subsequent neurodegeneration.
- Environmental contaminants, such as pesticides and metals, can lead to increased neurotoxicity through the induction of oxidative stress.
- With oxidative stress as a common mechanism mediating neurotoxicity from genetic polymorphisms and environmental exposures, a personalized medicine approach would optimize therapeutic efficiency.

### Abstract

The annual cost for neurological disorders in the United States was \$789 billion in 2014, and with an aging population these numbers are expected to significantly increase in the next 50 years [1]. Neurodegenerative diseases make up a significant portion of these costs. Neurodegenerative diseases are characterized by the loss of neuronal populations in specific regions of the brain. Although the cause is still unknown for most of these diseases, both genetic and environmental factors are thought to play important roles. There are multiple convergent mechanisms underlying the unique susceptibility of neurons to degeneration, including aging, inflammation, mitochondrial dysfunction, and oxidative stress. Oxidative stress (OS) is of particular importance because evidence indicates that the neuronal populations lost in neurodegenerative diseases are particularly susceptible to OS. OS is a complex neurotoxic mechanism that arises from excessive generation of free radicals such as reactive oxygen species (ROS), reduction in anti-oxidant factors, or a combination of the two. A complex interplay between the endogenous susceptibility of the brain, genetic factors, and environmental exposures leads to the harmful generation of OS in the brain and contributes

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