

## Editor's Corner

# High anxiety

## Recognizing stress as the stressor

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Anxiety disorders can lead to uneasiness, apprehension and ultimately become manifest with compulsions and panic attacks. These disturbances may even be a component of other behavior or psychiatric disorders such as depression, mania or psychosis. The biological basis of emotional disorders are broad and can be the result of multiple components that involve cellular pathways as well as environmental influences. Surprisingly, oxidative stress is one significant component for behavior and emotional disease that has a large impact during psychological illnesses. For example, some clinical studies have suggested that recollection of life events that lead to anger or depression could increase oxidative activity and potentially weaken immune system function within thirty minutes of recalling such events. These oxidative pathways, which may either mediate emotional disturbances or, on the contrary, may be the product of emotional behavior, also can affect other biological pathways that control metabolism and aging to affect disorders such as diabetes and Alzheimer disease. Interestingly, in circumstances that psychological disorders lead to increased oxidative stress, these pathways also may serve as biomarkers for disease progression.

In this issue of *Oxidative Medicine and Cellular Longevity*, our studies highlight the intimate role played by oxidative stress in several clinical disorders that also may be accompanied by emotional stress in patients. Bouayed et al. delve into the novel role oxidative stress plays with anxiety related disorders and discuss how specific genes can be correlated with anxiety-related phenotypes. They further discuss the interesting and intricate relationship among metabolic pathways, oxidative stress and anxiety. Yet, it is clear that oxidative pathways that emerge as a result of emotional stress may have more protean effects. For example, Gupta et al. evaluated patients with head and neck squamous cell carcinoma for several parameters of oxidative stress and illustrate that the presence of cancer itself, in addition to other confounding

variables such as tobacco consumption, can lead to systemic oxidative stress in individuals. Furthermore, immune system dysfunction during oxidative stress that has been reported in patients with cancer also may lead to other abnormalities such as male infertility during acute infections. In the study by Abd-Allah et al., experimental models of sepsis with oxidative stress lead to marked reductions in sperm count and motility, obstruction in seminiferous tubules and congested blood vessels in testicular sections, suggesting that therapeutics directed against oxidative stress may impart protection against or lead to the resolution of conditions that result in the loss of fertility. Interestingly, immune system modulation that can be altered by oxidative pathways also may play a role during autologous and allogenic hematopoietic stem cell transplantation. Although the primary factors influencing stem cell transplantation reported in this issue by Goncalves et al. are the graft source and the disease type, an additional significant variable was the conditioning regimen that allowed for quicker immune system responsiveness with neutrophil and platelet engraftment.

As a means to counteract these detrimental effects of oxidative pathways, three of our studies in this issue of *Oxidative Medicine and Cellular Longevity* discuss highly unique pathways to regulate oxidative cellular damage. For example, the brain may contain specific intrinsic pathways to ameliorate oxidative stress. Bharti and Srivastava show that administration of pineal protein can reduce makers of oxidative stress and enhance cellular anti-oxidant pathways with increased activities of superoxide dismutase catalase. In addition, new strategies with urate oxidase gene silencing also may offer unique therapies for disorders such as cardiovascular and metabolic disorders. Prior work with serum urate levels has noted an association with cardiac injury, hypertension, obesity, renal dysfunction and diabetes. As a result, reduction or elimination of pathways responsible for uric acid generation per the work of Cleveland et al. in this issue may be beneficial for a number of disorders. Furthermore, naturally occurring plant products such as Aloe vera, which is popular for dermatological care, also may have more far reaching implications than initially considered. In this issue, Ozsoy et al. demonstrate the antioxidant potential of *Aloe vera* extract and its influence upon cellular pathways by the ability to inhibit the peroxidation of liposomes and reduce malondialdehyde levels, indicating that the active components in

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*Aloe vera* extract may provide treatment support for a number of degenerative disorders.

We complete this issue of *Oxidative Medicine and Cellular Longevity* with two Extra Views articles that provide new insight into on-going studies. Eugene Weinberg presents evidence for the newly recognized role of iron load and toxicity in aging muscle atrophy, viral replication, rosacea and pulmonary alveolar proteinosis. In our second Extra View article, Léveillé et al. extend their current work that has shown that neuronal antioxidant defenses are influenced by synaptic activity through N-methyl-D-aspartate receptors. This process occurs through the enhancement of thioredoxin activity to result in the reduction of hyperoxidized peroxiredoxins. However, more importantly, the authors new work in *Oxidative Medicine and Cellular Longevity* now illustrates that a fine line exists in this biological system in that both insufficient as well as excessive synaptic activity can lead to peroxiredoxin hyperoxidation and oxidative-induced neuronal injury, providing important insight that close modulation of these systems will be required during the treatment neurodegenerative disorders. Our papers for this issue of *Oxidative Medicine and Cellular Longevity* provide our readers with a host of significant insights for the role of oxidative stress in the body, but also drive home the point that “stress” at any level also may become the generator of toxic oxidative products, or the “stressor”.

