

## Editor's Corner

# Marking the onset of oxidative stress

## Biomarkers and novel strategies

Kenneth Maiese, Editor-in-Chief

Wayne State University; School of Medicine; Detroit, Michigan USA

The term “biomarker” can refer to any entity that occurs in the body and can be measured to predict the diagnosis, onset or progression of a disease process. The definition of a biomarker is intentionally broad. It can apply to the assessment of specific genes, proteins, products of cellular processes, a series of biological processes or even the response of cells or tissues to therapeutic strategies.

In fact, some biomarkers may have the additional benefit to function as a surrogate marker to be able to be used to predict clinical outcome in some cases. For example, biomarkers such as estrogen levels may predict the onset of postmenopausal breast cancer and a poor clinical outcome. Yet, reliance on any single biomarker can become an imperfect science, since a number of other pathways that occur in combination with a particular biomarker may have a significant role. In the case of breast cancer, new work suggests that the release of androgens, cytokines or even changes in body mass and exercise can influence outcome as well as alter the predictability of a specific biomarker. For these reasons, assessment of multiple biomarkers may have greater clinical utility for the formulation of a diagnosis and the process of following disease outcome and therapeutic options.

In this regard, biomarkers have a critical utility in multiple disease processes especially those impacted by oxidative stress. In this issue of *Oxidative Medicine and Cellular Longevity*, our articles highlight some of the potential novel biomarkers to be considered in a variety of disorders and how these genes or proteins may ultimately alter oxidative stress and disease outcome. During both normal physiological conditions and cellular stress, microparticles that consist of cell fragments can be released and may be indicative of tissue injury. Vince et al. show that vascular adhesion molecule-1 (VCAM-1) positive microparticle and S100A12, a calcium binding protein belonging to the S100 family, may function as biomarkers for endothelial dysfunction and neutrophil activity during oxidative stress. These proteins may provide important targets for early hypoxic injury since they become elevated following hypoxia in individuals. Interestingly, the effects of enhanced oxygen levels on endothelial cells also may stimulate different pathways that can serve as biomarkers but also

alter vascular function. In their paper, Xu et. al. demonstrate that endothelial nitric oxide synthase (eNOS) mRNA and protein can become up-regulated in endothelial cells during hyperbaric oxygen exposure. However, this can be a delayed response that may or may not alter vascular tone but may function as a signal for other vascular pathways that have a role during disorders such as epilepsy. In disorders such as thrombophilia, it appears that reactive oxygen species consisting of hydrogen peroxide are involved and that the generation of hydrogen peroxide sets into play the activation of an antioxidant defense system. The authors of this study, Pristiv et al., suggest that screening of the level of ascorbyl radical, which may be used to determine the oxidative status of amniotic fluid during pregnancy, could become an early biomarker for diseases such as thrombophilia.

Also in this issue of *Oxidative Medicine and Cellular Longevity*, novel studies illustrate potential therapeutic strategies directed against oxidative stress cellular injury. Bloomer and Fisher-Wellman link diets with high fat content to the release of excess free radicals in the body. Elevated free radical release in the body has been tied to a number of disorders such as heart disease, diabetes and Alzheimer's disease. The study, which was confined to women, demonstrated that women who were obese were more likely to have higher and prolonged release of free radicals in the body when compared to non-obese counterparts. These findings shed significant light on the almost immediate role diet can play in relation to the development of long-term disorders in the body and provide vital information to design therapies for a number of diseases caused by oxidative stress. Work by Yanagida et al. identify a unique role for the astrocytic protein DJ-1 during oxidative stress and illustrate through gene silencing studies and magnetic resonance imaging the neuroprotective capacity of DJ-1 when released from non-neuronal astrocytic cells. Other work by Helal et al. suggest that metallothionein induction by ZnSO<sub>4</sub> can possibly preserve memory function through the prevention of hippocampal neuronal cell loss in the brain and reduce markers of oxidative stress during administration of the chemotherapy agent carmustine that results in learning and memory impairment. These original studies complement the review articles in this issue by Fisher-Wellman et al. that discusses the potential antioxidant pathways associated with exercise during cardiac and metabolic disorders as well as the work by Kovacic and Somanathan that outlines unique pathways tied to memory formation during administration of the hypnotic Zolpidem. For this issue of *Oxidative Medicine and Cellular Longevity*, we offer exciting new insights for our readers in regards to biomarkers and treatment strategies that affect multiple disease pathways, and more importantly, clinical outcome.

Correspondence to: Kenneth Maiese; Professor and Director, Division of Cellular and Molecular Cerebral Ischemia; Departments of Neurology and Anatomy & Cell Biology; Centers for Molecular Medicine and Institute for Environmental Health Sciences; Wayne State University School of Medicine; Detroit, Michigan 48201 USA

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