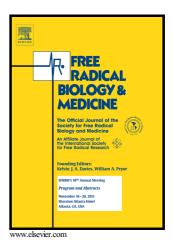
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Abstract

The free radical theory of ageing provided an intellectual framework for many laboratories working on ageing. However, experimental and clinical evidence showing that high doses of antioxidants do not have an effect on ageing or on age-associated diseases, cast doubts on the validity of this theory.

Data from our own laboratory show that oxidative damage does not correlate with age, especially in the geriatric population, but rather with the frailty state. This has led us to postulate the free radical theory of frailty that proposes that oxidative damage is associated with frailty, but not with chronological age itself. Superoxide dismutase deficient mice are more frail than controls. But more importantly, we have observed that animals that are protected against oxidative damage by overexpression of antioxidant enzymes, delay the onset of frailty and are more vigorous than controls.

In this review, we describe results from both, experimental animals and human cohorts, that lead us to the formulate this free radical theory of frailty.

Graphical abstract

PHYSIOLOGICAL OXIDATIVE STRESS

HEALTHY AGING ROBUSTNESS

OXIDATIVE STRESS

CHRONOLOGICAL AGE

OXIDATIVE DAMAGE

FREE RADICAL-INDUCED FRAILTY DISABILITY OXIDATIVE DAMAGE

Fig 1. Graphical abstract. Intensity scales ranging from physiological oxidative stress to a toxic oxidative burden. Healthy aging is achieved through the maintenance of a redox homeostasis as we age. However, frailty and disability result from an increase in oxidative damage during aging.

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