Can progressive accumulation of H_2O_2 be the major factor responsible for degenerative diseases?

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Cu, Zn superoxide dismutase (Sod1), which is widely distributed and comprises 90% of the total SOD, has great physiological significance. Mutations in the *SOD1* gene cause a familial form of amyotrophic lateral sclerosis among other disorders associated with the aging process. In the present study, using *Saccharomyces cerevisiae* cells as an experimental model of eukaryotic organism, we investigated the role of Cu-Zn superoxide dismutase (Sod1) in the maintenance of chronological lifespan. Cells growing under caloric restriction, an intervention used to slow aging progress, increased cell longevity of both wild type (wt) and *sod1* mutant strains. However, after 48 hours the mutant strain showed lower viability and higher levels of intracellular oxidation, lipid peroxidation, protein oxidation and mitochondrial mutagenesis than the wt strain, suggesting increased production of H_2O_2. It is known that in the reaction catalyzed by Sod, one molecule of H_2O_2 is produced from two superoxide ions; in the non-catalyzed reaction, two superoxide ions yield two molecules of peroxide. This could explain why in the absence of this enzyme cells would suffer an increase in the formation of hydrogen peroxide accumulated during the aging process, causing oxidative damages. Through a comparative proteomic analysis between the wt and mutant strains, alterations in the expression of some proteins that will be further identified were observed, which might help us to better understand the mechanisms by which mutant *sod1* causes degenerative diseases.