SUPEROXIDE AND AGE-DEPENDENT DNA DAMAGE

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Aging is the major risk factor for human cancers. However, the mechanisms responsible for the effect of aging on tumor incidence are poorly understood, in part because few model systems are available to study age-dependent genomic instability. My laboratory has studied the role of superoxide in aging and age-dependent macromolecular damage. Using the simple S. cerevisiae chronological life span model system, we characterized age-dependent DNA damage with focus on mutations caused by superoxide and other toxic oxygen species. We also describe the role of the Sch9/Akt, Ras and Tor aging regulatory pathways in the age-dependent genomic instability in both wild type cells and cells with increased oxidative stress. Finally, we describe the paradoxic role of error-prone DNA repair proteins in age-dependent DNA mutations with focus on those caused by oxidants. We propose that chronologically aging S. cerevisiae can serve as a valuable model to identify and characterize genes that regulate genomic instability and understand the mechanisms responsible for age-dependent DNA mutations and cancer in mammals.

Keywords: S. cerevisiae, aging, superoxide, DNA damage, mutations