Targeting aging itself, rather than combating each age-related pathology individually, seems to be a promising new strategy.[5–7] The question of whether we should consider aging as a disease is now discussed.[8–10] Growing evidence also supports the hypothesis stating that aging of living organisms can be considered as a particular case of programmed death of an organism (slow phenoptosis),[7,11] and that switching off this deleterious program may slow down or even abolish aging.[11]

Despite the fact that aging is a highly diverse phenomenon across the variety of living organisms, there are a few cellular processes linked to aging that are conserved over a broad evolutionary distance, from yeast to humans: mitochondrial function, nutrient signaling, proteostasis,[12,13] and autophagy.[14] In this review we focus mainly on one aspect of mitochondrial function: the generation of reactive oxygen species (ROS), and application of the mitochondria-targeted rechargeable antioxidants as a tool to suppress this generation. Experiments on several animal models are reviewed, with a special focus on the data obtained on the fruit fly *Drosophila melanogaster*.

9.2 Mitochondria Malfunction and Aging

Mitochondrial malfunction is a feature inherent in the aging of living creatures. It is documented for yeast,[15,16] invertebrates[17–19] and mammals[20,21] (see ref. 22 and 23 for recent reviews). The stability of mitochondria during purification procedures also seems to decrease with age, as demonstrated by experiments with rat skeletal muscle.[24] Mitochondrial genetic diseases, including those caused by defects in mitochondrial DNA polymerase gamma that lead to frequent mutations in mitochondrial DNA (mutator mouse[25,26]), result in phenotypes that resemble premature aging.

Deletions and mutations in mitochondrial DNA accumulate with age and clonally expand in tissues, accompanied by the decline in the respiratory function. A causative role for mtDNA mutations in mammalian aging was suggested (evidence for this hypothesis is reviewed in ref. 27), but quantitative analysis of the data obtained on the mutator mouse does not support this suggestion. In homozygous mutator mice with mtDNA mutation load much higher than that detected in aged animals or elderly humans, the lifespan is shortened, but heterozygous animals have normal phenotype and lifespan, despite having an mtDNA mutation burden at birth 30 times higher than that of aged wild-type mice.[28] It is therefore likely that mtDNA mutations increase is just one of the manifestations of damage accumulation that accompany normal, physiological aging rather than the cause of the latter.[22]

In mammals, the consequences of age-dependent mitochondrial malfunction involve: (i) oxidative stress due to excess generation of mitochondrial reactive oxygen species (mROS); (ii) proteotoxicity caused by impaired mitochondrial unfolded protein response (UPR^{mt});[12,13] and (iii) inflammation.[14,29] In invertebrates, mitochondria functions also decline with aging. Surprisingly, there are examples when mitochondrial dysfunction results in life extension rather than shortening. For example, certain Mit mutants of the nematode *Caenorhabditis elegans* are long-lived. The first Mit mutant