



Figure 8.1 The correlation between the reciprocal maximum life-span ($1/T$) and the ratio of specific metabolic rate to SOD (V/E) in brain for mammalian species: 1: house mouse; 2: deer mouse; 3: common tree shrew; 4: squirrel monkey; 5: bush baby; 6: moustache tamarin; 7: lemur; 8: African green monkey; 9: Rhesus monkey; 10: olive baboon; 11: gorilla; 12: chimpanzee; 13: orangutan; 14: man (data compiled from ref. 13).

By using the free coefficient D , it was estimated that the longevity of the human brain could reach 250 years should the reliability of the antioxidant SOD defense be absolutely perfect. By using the free coefficient D of the relevant equations for the heart and liver, the limit longevity values were estimated to be 100 and 200 years, respectively.^{11,12} Although these estimations are illustrative, they do emphasize the large role of ROS in the pathogenesis of the cardiovascular system.

It has long been known that free radical oxidation damages of DNA, proteins and lipids take place in cells and tissues (see ref. 24 and 26). However, biochemical mechanisms of toxicity of $O_2^{\cdot-}$ are not quite clear. The oxygen radical anion $O_2^{\cdot-}$ is not so much an oxidant but, on the contrary, it is a rather powerful reductant. It is noteworthy that tissues like the liver, kidney and adrenals with a high amount of reduced glutathione (GSH) are also characterized with a high level of activity of SOD. This positive correlation between the GSH amount and the SOD activity, first noted half a century ago,^{10,12} has been proved experimentally.³⁰ It suggests that the GSH pool is tracking the intensity of the $O_2^{\cdot-}$ fluxes, thereby regulating the SOD activity in cells and tissues.

Since then, a new protein family of NAD^+ -dependent protein deacetylases or the so-called sirtuins (Silent Information Regulators) has been discovered. The first from this protein family, Sir2, was discovered in yeast cells. In human and animal organisms, seven sirtuins (Sirt1–7) orthological to yeast cell Sir2 have now been found.^{31–37} They are localized in cell nuclei (Sirt1,