Superoxide, O2●–, is formed in all living organisms that come in contact with air, and, depending upon its biological context, it may act as a signaling agent, a toxic species, or a harmless intermediate that decomposes spontaneously. Its levels are limited in vivo by two different types of enzymes, superoxide reductase (SOR) and superoxide dismutase (SOD). Although superoxide has long been an important factor in evolution, it was not so when life first emerged on Earth at least 3.5 billion years ago. At that time, the early biosphere was highly reducing and lacking in any significant concentrations of dioxygen (O2), very different from what it is today. Consequently, there was little or no O2●– and therefore no reason for SOR or SOD enzymes to evolve. Instead, the history of biological O2●– probably commences somewhere around 2.4 billion years ago, when the biosphere started to experience what has been termed the “Great Oxidation Event”, a transformation driven by the increase in O2 levels, formed by cyanobacteria as a product of oxygenic photosynthesis. (1) The rise of O2 on Earth caused a reshaping of existing metabolic pathways, and it triggered the development of new ones. (2) Its appearance led to the formation of the so−called “reactive oxygen species” (ROS), for example, superoxide, hydrogen peroxide, and hydroxyl radical, and to a need for antioxidant enzymes and other antioxidant systems to protect against the growing levels of oxidative damage to living systems.