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Production of Human Keratinocyte 14 Promoter Driven EC-SOD Transgenic Mice

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Superoxide dismutases are key antioxidant enzymes in metabolism of reactive oxygen species. Three different isoforms of SOD exist in mammals. The extracellular SOD (EC-SOD) is the most recently discovered SOD family member. This isoform is a copper- and zinc-containing enzyme like Cu/Zn-SOD and a homotetrameric glycoprotein with a molecular weight of about 165 kDa in mouse. Unlike Cu/Zn- and Mn-SOD, EC-SOD has been found in the extracellular matrix of tissue and extracellular fluids, such as serum, cerebrospinal, ascite, and synovial fluids. It has been known that EC-SOD may play an important role in several diseases. However, EC-SOD is only present at low levels in extracellular fluids and it is difficult to obtain the purified protein, and thus, little is known about the physiological and biochemical properties of EC-SOD than other SODs. In the skin, many sources promote production of ROS and consequently, induce tissue damage by ROS. To study the prevention mechanisms of EC-SOD in the skin, we have generated the skin-specific EC-SOD over-expressed mice with keratin 14 promoter.

The tumor-preventing activity of EC-SOD in carcinogenesis was assessed using 7,12-dimethylbenz [a]anthracene (DMBA, 100 $\mu g/\mu \ell$). Topical application of DMBA followed by 12-O-tetradecanoylphorbol 13-acetate (TPA, 3 μg) treatment twice a week for 20 weeks resulted in the development of tumors in mice. At week 9, nearly 40% of wild-type mice developed tumors in the skin, in contrast to only 10% of EC-SOD over - expressed mice. No tumors were observed in wild-type and EC-SOD over - expressed mice that were administered TPA alone. Based on these results, we speculate that EC-SOD will play major roles in prevention of skin carcinogenesis.

Key words: ***Transgenic mouse, Extracellular Superoxide Dismutase, Carcinogen***