

## Extracellular Superoxide Dismutase Protein in Diabetes

Mohammed El-Lakany

Egypt

Diabetes is characterized by chronic hyperglycaemia, which can increase reactive oxygen species (ROS) production by the mitochondrial electron transport chain. The formation of ROS induces oxidative stress and activates oxidative damage-inducing genes in cells. No research has been published on oxidative damage-related extracellular superoxide dismutase (EC-SOD) protein levels in human diabetic skin. We investigated the expression of EC-SOD in diabetic skin compared with normal skin tissue *in vivo*. The expression of EC-SOD protein was evaluated by western blotting in 6 diabetic skin tissue samples and 6 normal skin samples. Immunohistochemical staining was also carried out to confirm the EC-SOD expression level in the 6 diabetic skin tissue samples. Diabetes is a critical disease prevalent throughout the world's population. The damage it causes arises from a number of pathologic mechanisms including oxidative stress. Oxidative stress is caused by a cascade of reactive oxygen species (ROS) released from the mitochondria, a process related to type 1 diabetes, which is induced by apoptosis of pancreatic beta-cells, and type 2 diabetes, which is induced by insulin resistance. ROS and the resulting oxidative damage are closely correlated with the pathogenesis and complications of diabetes. Physiologically balanced ROS levels are involved in cell signalling and protection from various pathogens. A dysregulated ROS concentration may contribute to the development of a wide range of human diseases, such as diabetes, cancer, hypertension, atherosclerosis, and premature aging. The evidence indicates the crucial role of oxidative stress in diabetes-related tissue injury. The increased insulin resistance and reduced insulin secretory response induce an impaired glucose tolerance, leading to oxidative stress by the production of higher levels of ROS. ROS play an important role in the activation of stress responsive signalling pathways regulating the expression of genes responsible for cellular damage. While cells have a wide range of defence mechanisms against free radicals, free radicals bypass defence systems and attack and modify subcellular components, including proteins, lipids, and nucleic acids. Proteins are a prominent target of oxygen free radicals and other reactive species. Superoxide dismutases (SOD) are the first and most important major line of antioxidant defense systems against ROS, particularly superoxide anion radicals. Among the SOD isoenzymes, extracellular superoxide dismutase (EC-SOD) was most recently discovered and is the principal defense mechanism against superoxide-mediated damage to both the

cell surface and the extracellular matrix proteins. Kimura et al. reported a positive correlation between serum EC-SOD levels and the severity of vascular complications in diabetes. However, little is known about the role of EC-SOD in the diabetic skin *in vivo*. The aim of this study was to investigate the expression of EC-SOD *in vivo*. We hypothesized that EC-SOD protein expression will be lower in diabetic skin tissue than in normal skin tissue. We studied the expression of EC-SOD in normal skin tissues and diabetic skin tissues by using western blot and immunochemistry. The Institutional Review Board of a university hospital in Seoul, Korea reviewed and approved this research protocol involving the use of tissue samples. A total of 6 normal skin tissue samples and 6 diabetic skin samples were obtained from patients who underwent surgery between December 2012 and January 2013 in the Department of Plastic and Reconstructive Surgery at the same university hospital. Informed consent was obtained from the patients before surgery. The normal skin tissues were collected from the back of 6 women who had breast reconstruction using the latissimus dorsi flap procedure. Diabetic skin samples were obtained from patients undergoing amputation surgery. A portion of the specimens were frozen in liquid nitrogen immediately after resection for western blot analysis, and stored at -80°C. For the immunohistochemical studies, the stored formalin-fixed, paraffin-embedded samples, including the 6 diabetic skin tissues and 6 normal skin tissues, were used. The Institutional Review Board of a university hospital in Seoul, Korea reviewed and approved this research protocol involving the use of tissue samples. A total of 6 normal skin tissue samples and 6 diabetic skin samples were obtained from patients who underwent surgery between December 2012 and January 2013 in the Department of Plastic and Reconstructive Surgery at the same university hospital. Informed consent was obtained from the patients before surgery. The normal skin tissues were collected from the back of 6 women who had breast reconstruction using the latissimus dorsi flap procedure. Diabetic skin samples were obtained from patients undergoing amputation surgery. A portion of the specimens were frozen in liquid nitrogen immediately after resection for western blot analysis, and stored at -80°C. For the immunohistochemical studies, the stored formalin-fixed, paraffin-embedded samples, including the 6 diabetic skin tissues and 6 normal skin tissues, were used. The relative abundance of the protein expression of each sample was analyzed by Phosphor-Imager software.