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P16 Catalase Prevents Cardiomyocyte DNA Damage During Diabetes

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Oxidative stress-related cardiomyocyte damage in diabetes represents a major risk factor for heart disease. Reactive oxygen species triggers a series of deleterious stimuli that result in protein and DNA damage, cell dysfunction and cell death. Our previous study showed that the absence of cardiomyopathy in rats with streptozotocin (STZ)-induced diabetes is accompanied with significantly higher antioxidative activity of catalase (CAT), suggesting that CAT may be one of the key enzymes in heart protection during diabetes. To confirm this hypothesis we analysed oxidative status and extent of DNA damage in cardiomyocytes of diabetic rats with inhibited CAT activity. Diabetes was induced by intraperitoneal (i.p.) injection of STZ at 40 mg/kg/day for five consecutive days. Inhibition of CAT activity was established by daily i.p. administration of 1 mg/kg 3-amino-1,2,4 triazole throughout the 4 week period, starting from the 15^{th} day of STZ administration. Increased lipid peroxidation and H_2O_2 concentration in the heart of diabetic rats with inhibited CAT activity indicated higher level of oxidative stress when compared with diabetic ones. This is followed with decline of glutathione level, activity of glutathione peroxidase and total superoxide dismutase and increased activity of manganese superoxide dismutase whose overexpression could potentiate cardiac CAT activity. According to comet assay, impairment in antioxidant defense system led to significantly increased DNA damage in cardiomyocytes of rats with inhibited CAT activity in comparison with cardiomyocytes of diabetic rats. Also, Western immunoblot revealed that inhibition of CAT activity in diabetic heart was followed by twofold decrease in CAT expression as a result of the decrease in expression of Nrf2, the main transcription factor involved in CAT gene induction. These results suggest that CAT expression and activity is crucial in prevention of heart damage during diabetes.