CALIFORNIA STATE SCIENCE FAIR
2012 PROJECT SUMMARY

Name(s)

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Project Number

S1206

Project Title

Mild Carbon Monoxide Exposure as a Therapeutic Agent in the Mouse Inner Ear

Abstract

Objectives/Goals

We tested the hypothesis that low levels of CO exposure upregulates deense mechanisms that ameliorate oxidative stress which contributes to inner ear deterioration in the MRI/lpr mouse model. The MRL/lpr mouse strain is one of the best studied models of spontaneous systemic lupus erythematosus (SLE). In autoimmunie diseases there is an attenuation of defense mechanism against oxidative stress. SLE in humans is a chronic, inflammatory, autoimmune disorder that may affect the skin, joints, kidneys, and other organs such as the inner ear. Carbon monoxide (CO) produced endogenously has emerged as a signaling molecule involved in the physiology of the nervous, cardiovascular, renal, and gastroenterological systems. Therapeutic upregulation of CO tissue levels can be achieved via exogenous application of CO, for instance by direct inhalation of CO gas. To date there are no studies on the expression of oxidative stress markers or functional and structural proteins after mild CO exposure in the MRL/lpr mouse inner ear. The mechanisms that account for inner ear protection by CO exposure were investigated in this project.

Methods/Materials

MRL/lpr mouse pups were exposed to CO (25 ppm) or air (control) from post-natal day 5 to 20. The concentrations of CO we tested were below the upper levels set by most regulatory agencies. It was hypothesized that mild CO exposure could result in prevention of the deterioration of the cochlea of the MRL/lpr mice after CO exposure, when compared with MRL/lpr mice exposed to air. Changes in the MRL/lpr cochlea were studied by the application of immunocytochemistry, and supported with the use of mRNA expression and tandem mass spectroscopy applied to proteomics.

Results

By immunocytochemistry we detected an upregulation in several protective proteins including heme oxygenase-1 (HO-1) and antioxidant enzymes, superoxide dismutase (SOD-1 and SOD-2). There was also upregulation at the mRNA genes related to oxidative stress using specific gene assays. By proteomics we detected the expression of proteins involved in protein degradation (Ubiquitin system).

Conclusions/Discussion

Our results suggest that mild CO exposure could be used to prevent cochlear deterioration after noise-induced hearing loss and ototoxic treatments with antibiotics or cisplatin in which oxidative stress is present.

Summary Statement

Current project investigates the correlation between low levels of CO exposure and upregulation of defense mechanisms in the inner ear of MRL/lpr mouse model.

Help Received

Dr. Lopez taught lab techniques (Immunohistochemical staining and fluorescence microscopy), guided and mentored this project; let me use all lab supplies. Work done in the Department of Head and Neck Surgery, David Geffen School of Medicine, UCLA.