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HUMAN SERUM ALBUMIN-THIOREDOXIN FUSION PROTEIN WITH LONG BLOOD RETENTION PROPERTY IS EFFECTIVE IN SUPPRESSING LUNG INJURY

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ABSTRACT

Thioredoxin (Trx) is a redox-active protein with anti-inflammatory effects but with a short half life of 1 hour. Genetic fusion of Trx to human serum albumin (HSA) extended its half life without causing significant loss of its biological activities. HSA-Trx caused a decrease in the number of cells in brochoalveolar lavage fluid, the wet/dry ratio and the inflammation at the respiratory tract of the ovalbumin (OVA) induced lungs injury model mouse. Three intraperitoneal doses of Trx alone produced the same extent of suppression of those three detrimental effects of OVA as one intravenous dose of HSA-Trx. Inhibition experiments confirmed that reactive oxygen species (ROS) and reactive nitrogen species (RNS) involved in the progression of the injury. HSA-Trx inhibited the production of ROS as confirmed in the EPR experiment, but lungs tissue staining suggested that induced nitrogen oxide synthase (iNOS) was not suppressed by the fusion protein. Instead, the production of nitrotyrosine, 8-nitro-cGMP, and 8-hydroxy-2'-deoxyguanosine downstream to the iNOS has been inhibited. This suggested that HSA-Trx produced lungs protection effect via inhibition of ROS and RNS and their reactant, peroxynitrite. HSA-Trx sustained the superior redox properties of Trx thus has great potential in treating oxidative stress related diseases.