

**EXECUTIVE SUMMARY [NON-CONFIDENTIAL, NON-TECHNICAL ABSTRACT FOR PUBLIC INFORMATION OR PROGRAM PROMOTION]:** State in layman's terms the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project relevant to California. Do not include proprietary or confidential information. This may be distributed before the funding decision has been finalized.

Copper exposure produces deficits in several stereotyped behaviors and in neuronal function in the aquatic annelid worm *Lumbriculus variegatus*. In all organisms, copper exposure causes the formation of reactive oxygen species (ROS), such as the hydroxyl radical. ROS formation also occurs in many other human diseases including neurodegenerative diseases, diabetes, heart attack and stroke. ROS react with all classes of biological molecules and cause damage to these molecules. The ways in which cells respond to this damage are shared by organisms as diverse as bacterial and humans. Cells protect their proteins from this oxidative damage by producing a number of protective proteins, of which, the heat shock proteins are one class. The research in this proposal seeks to protect animals from copper-induced oxidative damage via the pharmacological induction of heat shock proteins. The experiments in this proposal will use two species of animals, the aquatic worm *Lumbriculus variegatus* and the soil dwelling nematode *Caenorhabditis elegans*, based upon experimental advantages offered by each organism. Although these animals seem to be only distantly related to humans, the high degree of conservation of the protective mechanisms to ROS-induced damage means that the results of these studies are likely to have relevance to most organisms. This proposal contains three types of experiments. First, we will try to induce increased levels of heat shock proteins using drugs. Second, we will determine if these drugs can protect animals from copper-induced toxicity. Third, we will directly examine the ability of these drugs to alter the production of specific mRNAs, the molecules that direct synthesis of the heat shock proteins and their controlling factors.