

EXECUTIVE SUMMARY [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.

Zinc fingers (ZnFs) are small protein motifs with one or more Zn^{2+} ions as a structural factor and conserved cysteine and/or histidine residues as ligands. ZnF-containing proteins participate in a variety of cellular processes, such as DNA replication, transcription, and repair, where Zn(II) is crucial for the function of the ZnF-containing protein mainly through maintaining protein structure. ZnFs have been proposed to be cellular targets for the carcinogenic and/or toxic metals having high affinities for sulfhydryl groups, e.g., Hg(II) and Cd(II). The Fpg protein is a ZnF containing DNA repair protein. The ZnF is essential for damaged DNA recognition in the Fpg protein. Previous studies have demonstrated that the activity of Fpg is inhibited in the presence of Cd(II) or Hg(II). In the proposed research, we will investigate the binding of the toxic metal ions, Hg(II) and Cd(II), to the Fpg protein and how the binding will affect the structure of the Fpg protein. Our long term goal is to determine the detailed structure basis of the interactions of toxic metal ions with ZnF-containing proteins. The investigation of the toxic metal-bound sites are crucial to understand the relationship between the altered structure upon metal binding and metal toxicology/carcinogenesis. This project will provide insight into the molecular mechanisms of metal toxicology/carcinogenesis and will provide interdisciplinary research training for students.