

**EXECUTIVE SUMMARY [NON-CONFIDENTIAL, NON-TECHNICAL ABSTRACT FOR PUBLIC INFORMATION OR PROGRAM PROMOTION]:** State 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.

Atherosclerosis is a disease where fatty substances and cholesterol deposit in the inner lining of an artery, forming a plaque. This is facilitated by the accumulation and death of fat-loaded macrophage cells, which increases plaque size and advances the disease. Macrophage death within the plaque occurs via a suicidal process known as apoptosis, which involves precise changes in the expression of key genes. Recent studies in rabbits have demonstrated that lesions containing apoptotic macrophage cells are rich in a specific protein called BTG1, the product of the *BTG1* gene that belongs to a family of anti-proliferative genes. We hypothesize that BTG1 over expression may alter the properties of macrophages such that they exhibit increased expression of those genes that promote the uptake of cholesterol and fat. We will test our hypothesis by introducing *BTG1* in the human monocyte-macrophage cell line, THP-1, and study its effect on genes known to promote fat accumulation and subsequent atherosclerosis. We will also evaluate whether BTG1 over-expression might be a consequence of fat-loading in macrophages, thereby committing them to apoptosis. This project will provide valuable insight into the mechanism of macrophage apoptosis, and over the long term, contribute towards the development of strategies to retard plaque progression, and improve the quality of life for individuals suffering from atherosclerosis.