

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.

A healthy human immune system is capable of identifying early tumor cells and inducing their death. The flip side of cell death is cell survival. Cell survival involves recruitment of factors and expression of genetically encoded instructions that promote inflammation, wound healing, and defense against infection. Like cell death, cell survival is necessary for the maintenance of human health. However, cell survival can be a bad thing if not properly regulated. If unchecked it can lead to chronic inflammatory diseases such as arthritis, asthma, and colitis. Furthermore, these sites of chronic inflammation have been shown to function as hotbeds for tumor formation and growth as these environments naturally inhibit cell death. One key element of cell survival is the transcription factor NF- κ B signal transduction pathway. Within this chain of communicating factors, the enzyme complex known as I κ B kinase (IKK) regulates NF- κ B-dependent cell survival. We have recently succeeded in purifying human IKK beta subunit as well as its related protein in fruit flies. Interestingly, although the two factors exhibit many similar biological functions and structural characteristics, the chemistry that they perform differs significantly. We propose to compare the activities of these two related IKK proteins in order to identify the mechanism of IKK-induced cell survival. This project will lay the groundwork for the design of small molecular IKK inhibitors and modulators which could serve to better regulate cell survival in the future.