

## **P21-ACTIVATED KINASE (PAK I) AND RELATED PEPTIDES**

University of California scientists have purified p21-activated protein kinase (PAK I), a unique inhibitor of cell division, cleavage, and programmed death (apoptosis), physiological processes that are associated with several important diseases. PAK I is cleaved during the onset of apoptosis, playing a key role in the regulation of cell death and possibly in the maintenance of cells in their non-dividing state (cytostasis). PAK I activation requires two autophosphorylation steps, the first one involving a regulatory domain and the second one involving a catalytic domain. Since the regulatory domain can interact with a number of different compounds, PAK I can be activated under several different conditions.

The UC scientists have obtained PAK I's DNA coding sequences, and have also developed a synthetic peptide that mimics the recognition/phosphorylation site of PAK I. The synthetic peptide is preferentially phosphorylated by PAK I relative to other major protein kinases (e.g. cAMP-dependent protein kinase and protein kinase C), so its interaction with the PAK I regulatory domain is both sensitive and highly specific. This allows the assay of PAK I activity in cell extracts or with partially purified enzyme in the presence of other protein kinases.

With apoptosis playing an important role in the suppression of cancer, autoimmunity, and viral infections, the detection of PAK I activity using the synthetic peptide may be of considerable importance. Such detection techniques might be useful for the elucidation of apoptosis induction, the characterization of disorders associated with such apoptosis-induction mechanisms, and the formulation and screening of agents for preventing or treating these major medical disorders. Likewise, the cytostatic properties of PAK I itself may make it useful as a drug-design target. PAK I can be produced using physiological and recombinant DNA techniques, which could potentially be combined with various drug-delivery procedures or gene therapy to help treat patients with PAK-related disorders.

**PATENT STATUS:** US Patent No. [6,228,989](#) issued May 8, 2001

