

A New Superfamily of Protein Kinases

Background

There is one well characterized superfamily of eukaryotic protein kinases called the serine/threonine/tyrosine family of kinases. All members of this superfamily share a similar structural organization in their catalytic domains. These kinases phosphorylate amino acid residues located in the loops or turns of their substrates. In prokaryotes, the histidine kinase superfamily is involved in signal transduction acting as sensor components. Several eukaryotic protein kinases showing structural homology to this superfamily have recently been described. Recently, several protein kinases lacking homology with either the eukaryotic or prokaryotic superfamily of kinases have also been reported.

The eukaryotic elongation factor-2 kinase (eEF-2) is specific for the phosphorylation of elongation factor 2 and shows no homology to any of the known superfamily of kinases. However, the myosin heavy chain kinase A shows a strong homology with eEF-2 indicating that these two kinases represent a novel superfamily of kinases. Preliminary evidence suggests that eEF-2 kinase is upregulated in human cancers. Thus, the unique structure of eEF-2 kinase makes it an ideal target for the development of protein kinase inhibitors having the potential for use as therapeutic agents.

The present invention discloses additional members of a novel superfamily of eukaryotic protein kinases that is not related to any of the known protein kinases. The discovery and characterization of this superfamily of kinases has both therapeutic and diagnostic implications for diseases associated with cell cycle progression and malignant transformation.

Description of the Technology

UMDNJ researchers have discovered a new superfamily of protein kinases related to eEF-2 kinase. The protein kinases of this new superfamily have a strong sequence homology to eEF-2 kinase but not to the protein kinases of either serine/threonine/tyrosine kinase or histidine kinase superfamily. The new superfamily of protein kinases phosphorylates α -helical regions of proteins instead of β -turns.

Additionally, using a novel α -helical 16-amino acid peptide derived from the myosin heavy chain protein as a phosphorylation substrate, an assay has been developed that can be used in the high-throughput screening of inhibitors of protein kinases. These inhibitors can be used for the therapy of malignant transformations, including, but not limited to, breast cancers.

Advantages:

- The family of protein kinases disclosed in the present invention have a unique structure
- The protein kinases of the present invention have no homology to any of the known protein kinases making them ideal targets in the design of high throughput screening assays for inhibitors of specific protein kinases

Applications

- High-throughput screening of compounds capable of inhibiting the protein kinases

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- For the design and development of diagnostic and therapeutic formulations that can inhibit eEF-2 kinase activity
- Sequences complementary to eEF-2 kinase can be used as antisense drugs or in gene therapy

Deliverables:

- Cloned gene encoding eEF-2 kinase
- Gene encoding heart, melanoma, ch4 protein kinases
- Assays for screening inhibitors of protein kinases

Patent Status

- United States Patent issued on February 12, 2002
- Patent Number: US 6,346,406 B1

Licensing Opportunity

- This technology is available for exclusive license.

Contact

Peter Golikov, MS, MBA
Director, Ventures and Licensing
University of Medicine and Dentistry of New Jersey
335 George Street
New Brunswick, NJ 08901
Direct Phone: (732)-235-9355
Main Office Phone: (732)-235-9350
Facsimile: (732)-235-9358
golikope@umdnj.edu

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