



Novel Bi-Functional Alpha-Kinases: Protein Kinases Linked to Ion Channels (Alexey G. Ryazanov, RWJ 00-08) Therapeutic Target

Background

A superfamily of protein kinases (serine/threonine/tyrosine protein kinases) that phosphorylate amino acid residues located in the loops or turns of their substrates is most well-characterized. Several other protein kinases have been documented that lack homology to this superfamily of kinases. Recently a new class of kinases, alpha kinases, lacking homology to the serine/threonine/tyrosine protein kinase superfamily has been identified. Eukaryotic Elongation Factor 2 Kinase (eEF-2) belongs to this second family of kinase. The alpha kinases differ from serine/threonine/tyrosine protein kinases in that they phosphorylate a threonine amino acid residue located in the alpha helical region of the substrate. The present invention relates to the discovery and characterization of additional members of the family of the alpha kinases that are related to the eEF-2 kinase but possess certain unique characteristics. The characterization of additional members has both therapeutic and diagnostic implications for diseases associated with cell cycle progression and malignant transformation.

Summary of Invention

Genes for tissue specific alpha kinases such as melanoma alpha kinase, heart alpha kinase, skeletal muscle alpha kinase and lymphocyte alpha kinase have been identified, cloned and sequenced. These kinases lack sequence homology to the well-characterized serine/threonine/tyrosine superfamily with partial homology to eEF-2 alpha kinases. In addition, a subfamily of bifunctional alpha kinases was discovered and found to contain an ion channel covalently linked to the catalytic domain of the protein kinase. The presence of an ion channel linked to the kinase molecule is indicative of self-regulation of the molecule and suggests a phosphorylation mechanism that is distinctive from previously characterized mechanisms. The present technology provides vectors encoding and expressing the channel kinases.

Applications

- To generate antibodies (monoclonal or polyclonal) to the kinases
- To develop novel drug for cancer and other malignancies
- To diagnose and treat medical conditions requiring modulations of alpha kinase activities

Patent Status

United States CIP application filed.

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