Sequence, Structure and Function of Microtubule Affinity-Regulating Kinase: An Enzyme Plays Potential Role in Cell Division

Farha Naz, Faizan Ahmad and Md. Imtaiyaz Hassan

Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, Jamia Nagar, New Delhi 110025, India

Address for correspondence:
E-mail: imtiyaz.hassan@gmail.com

Microtubule affinity-regulating kinase (MARK) is a Ser/Thr kinase, which phosphorylates tubulin binding domain (KXGS motifs in the repeat domain) of MAPs, this result in the detachment of MAPS from microtubules and regulates microtubule dynamics. MARK-related kinases occurs in various organisms and are involved in establishing and maintaining cell polarity and actively participates in the differentiation and outgrowth of cell processes from neuroblastoma and other cell models. MARK4 is recently discovered and considered as a most suitable target for cancer because of its direct involvement in the cell division. The MARK4 is 82,520 Da, contains 752 amino acids, which is divided into three distinct domains, i. 252 residues long protein kinase (59–310), ii. 45 residues long UBA (324 – 368) and iii. 50 residues long kinase association domain (703 – 752). The residues 65–73 are considered for ATP binding domain. The Lys88 is considered as ATP binding site. The active site of this enzyme was proposed as Asp181. MARK4 is activated by phosphorylation on Thr-214 and catalyzes the reaction: ATP + a protein = ADP + a phosphoprotein. There are several biological functions are associated to MARK4 including microtubule bundle formation, nervous system development and positive regulation of programmed cell death. Therefore MARK4 is considered as a best suitable target for structure based rational drug design. Our sequence, structure and function based analysis will be helpful for better understanding of mechanism of regulation of microtubule dynamics and associated diseases by MARK4.