Molecular cloning of a new kinesin superfamily member interacting with a NF-kappaB inhibitor

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Research Project

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06454217

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Allocation Type

Single-year Grants

Research Field

Immunology

Research Institution

Kanazawa University

Principal Investigator

YAMAMOTO Ken-ichi Kanazawa Uni., Cancer Res. Inst., Professor, がん研究所, 教授 (60115285)

Co-Investigator(Kenkyū-buntansha)

SHIMIZU Hiroko Kanazawa Uni., Cancer Res. Inst., Assi. Prof, がん研究所, 助手 (20126585)
YOSHIOKA Katuji Kanazawa Uni., Cancer Res. Inst., Asso. Prof, がん研究所, 助教授 (60200937)

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T Cells / Growth / Apoptosis / NF-kappaB / NF-kappaB Inhibitors / Proteolysis / Kinesin Superfamily / Microtubules

Research Abstract

NF-kappaB is aninducible transcription factor which plays an essential role in the activation of various immune genes, such as genes for interleukin-2 (IL-2) IL-2 receptor alpha chain, IL-6 and MHC molecules. The results of recent studies indicate that NF-kappaB and its family members play an

important role in the activation, growth, differentiation and apoptosis of various lymphoid cells. To study roles of NF-kappaB family members in the immune system, we studied how the activation of NF-kappaB family members is regulated and what cellular factors are involved. An unique feature of NF-kappaB is that it pre-exists in the cytoplasm in an inactive form complexed with inhibitory proteins. One of these inhibitors is p105 which is a precursor for one of subunits (p50) of the NF-kappaB transcription factor and the proteolytic processing of its inhibitory C-terminal region is required for generation of active NF-kappaB.We found that the p105 C-terminal region is phosphorylated in vivo on Ser- 894 and Ser-908, which are potential phosphorylation sites in vitro for proline-directed serine/threonine kinase such as cyclin-dependent kinase. Furthermore, the mutation of these in vivo phosphorylation sites retards p105 processing/degradation in vivo, suggesting that p105 processing/degradation is regulated in phosphorylation-dependent manners. To further identify cellular factors involved in p105 phosphorylation and processing, we carried out Far-Western and two-hybrid cloning using the p105 C-terminal region as a bait. One of several cDNA cloned found to encode a new member of the kinesin superfamily : the N-terminal portion of the predicted amino acid sequence contained ATP and microtubules binding motifs which are hallmarks of motor proteins and are well conserved in the kinesin superfamily. Interestingly, the expression of the gene encoding this new kinesin superfamily member which interacts with the C-terminal region of p105 in vitro was confined to thymus and testis. We are currently studing what roles this new kinesin superfamily member plays in the regulation of NF-kappaB activation.▲ Less

Research Products (14 results)

All | Other

All | Publications (14 results)

[Publications] Mitomo,K.,et al.: "Two different celluar redox systems regulate the DNA binding activity of the _P50 subunit of NF-κB in vitro." Gene. 145. 197-203 (1994)

[Publications] Shimizu,H.,et al.: "NF-κB and C/EBP transcription factor families synergistically function in mouse serum amyloid A gene expression induced by inflammatory cytokines." Gene. 149. 305-310 (1994)

[Publications] Mori,N.et al.: "Transactivation of the interleukin-6 promoter by human T-cell leukemia virus type I tax is mediated by NF-κB." Blood. 84. 2904-2911 (1994)

[Publications] Fujimoto,K.,et al.: "A role for phosphorylation in the proteolytic processing/degradation of the NF-κB precursor." Gene. 165. 183-189 (1995)

[Publications] Sun,X.,et al.: "Identification of a novel _P53 promoter cis-element involved in genotoxic stress-inducible _P53 gene expression." Mol.Cell.Biol.15. 4489-4496 (1995)

[Publications] Mitomo, K., et al.: "Two different redox systems regulate the DNA binding activity of the p50 subunit of NF-kappaB in vitro" Gene. 145. 197-203 (1994)

[Publications] Shimizu, H., et al.: "NF-kappaB and C/EBP transcription factor families synergistically function in mouse serum amyloid A gene expression induced by inflammatory cytokines" Gene. 149. 305-310 (1994)

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[Publications] Fujimoto, K., et al.: "A role for phosphorylation in the proteolytic processing/degradation of the NF-kappaB precursor" Gene. 165. 183-193 (1995)

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[Publications] Muraoka, K., et al.: "Immunosuppressant FK506 induces interleukin-6 production through the activation of transcription factor NF-kappaB : implications for FK506 nephropathy" J.Clin. Invest.(in press). (1996)

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