Molecular Mechanisms of Neural Cell Death

2004 Fiscal Year Final Research Report Summary

Molecular Mechanisms of Neural Cell Death

Research Project

Project/Area Number

15500256

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Neurochemistry/Neuropharmacology

Research Institution

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Keywords

Necdin / MAGE-D1 / Msx / E2F1 / p53 / p75NTR / TrkA / NGF

Research Abstract

Necdin is a 325-amino acid protein encoded in a cDNA clone isolated from a subtraction library of neurally differentiated mouse embryonal carcinoma cells. The mouse necdin gene is expressed predominantly in postmitotic cells such as neuron and skeletal muscle. The human necdin gene is mapped to chromosome 15q11-q12, a region deleted in Prader-Willi syndrome (PWS). Disruption of the mouse necdin gene results in early postnatal lethality, reduction in specific groups of hypothalamic neurons, and be-havioral alterations, which are characteristics of the PWS phenotype. Necdin shows a significant homology to MAGE family proteins, the remarkable feature of which is a large central region termed MAGE homology domain (MHD). We tested the interactions of necdin and MAGE-D1 (a MAGE family protein) with p75NTR (a neurotrophin receptor) by co-immunoprecipitation assay. Both of necdin and MAGE-D1 bound to the intracellular domain of p75NTR. Necdin protects the E2F1-induced cell death using N1E-115 neuroblastoma cells. While MACE-D1 enhances the p75NTR-induced cell death, co-expression of p75NTR significantly abrogated the necdin induced suppression

of cell death through the dissociation of the binding between necdin and E2F1. Furthermore, MAGE-D1 dissociated the interaction of TrkA and p75NTR, necdin enhanced the binding. We next investigated the direct interaction of necdin and MAGE-D1. Necdin bound to MACE-D1 through the MAGE homology domain by pull-down assay in vitro and co-immunoprecipitation analysis in vivo. We also demonstrated that necdin interacted with Msx homeoprotein via MAGE-D1. These findings suggest that necdin and MAGE-D1 regulate the neural cell death via the interaction with neurotrophin receptors.

Research Products (6 results)

All | 2005 | 2004

All | Journal Article

[Journal Article] Functional domains of necdin for protein-protein unteractions, nuclear natrix targeting and cell growth suppression — 2005

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[Journal Article] Necdin interacts with the Msx2 homeodomain protein via MAGE-D1 to promote myogenic differentiation of C2C12 cells — 2004

[Journal Article] Necdin-related MAGE proteins differentially interact with the E2F1 transcription factor and the p75 neurotrophin receptor — 2004

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