

脂質メディエーターの過酸化を介する神経系細胞死誘導機構の解明

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2005 Fiscal Year Final Research Report Summary

The study on the glutamate-induced glial cell death mechanism for modulation of apoptosis to necrosis by arachidonic acid-mediated lipid peroxidation

Research Project

Project/Area Number

15590268

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Pathological medical chemistry

Research Institution

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Keywords

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Research Abstract

Glutamate induced glutathione (GSH) depletion leading to cell death in C6 rat glioma cells through accumulation of reactive oxygen species (ROS) or hydroperoxides. A significant increase of 12-lipoxygenase activities was observed in the presence of arachidonic acid (AA) under the GSH depletion. AA promoted the glutamate-induced cell death reducing caspase-3 activity and diminishing internucleosomal DNA fragmentation observed in apoptosis. Furthermore, AA diminished intracellular NAD, ATP and

membrane potential revealing a dysfunction of mitochondrial membrane. Ac-DEVD, a caspase inhibitor, did not suppress the glutamate-induced cytolysis. These results suggest that AA promotes cell death by inducing to necrosis from caspase-3 independent apoptosis through lipid peroxidation initiated by ROS or lipid hydroperoxides generated during the GSH depletion in C6 cells.

Next, we studied the effect of AA on UV-induced cell death. At lethal dose, UV-C (254 nm) radiation induces cell dysfunction leading to apoptosis or necrosis. During the cell death of T-24 human bladder carcinoma cells, 1-2 Mbp giant DNA fragmentation was observed and consequently the DNA fragmentation was proceeded into high molecular weight 100-800 kbp DNA fragmentation followed by ladder-like inter-nucleosomal DNA fragmentation. Reactive lipid peroxides or oxygen species were not produced. In contrast, increase of caspase-3 and reduction of intracellular NAD and poly (ADP-ribose) polymerase were observed. UV-C radiation induces giant DNA fragmentation leading to apoptosis associated without producing DCFH detectable reactive oxygen species and with activation of caspase-3 and internucleosomal DNA fragmentation in T-24 carcinoma cells.

Research Products (19 results)

All	2006	2005	2004	2003
All	Journal Article			

[Journal Article] The role of lipid peroxidation in chromosomal DNA frag-mentation associated with cell death induced by glutathione depletion.	2006 ▾
[Journal Article] (Review) Antitumor and biological effects of Streptococcus pyogenes	2006 ▾
[Journal Article] (Review) The role of endonucleases in chromosomal DNA fragmentation associated with apoptosis and necrosis.	2006 ▾
[Journal Article] (Review) The role of endonucleases in chromosomal DNA fragmentation associated with apoptosis and necrosis.	2006 ▾
[Journal Article] (Review) Pathological changes induced by allylnitrile and crotononitrile: relationship with behavioral abnormalities.	2005 ▾
[Journal Article] Sulindac activates nuclear translocation of DFF40 and Endonuclease G but not induces oligonucleosomal DNA fragmentation in HT-29 cells.	2005 ▾
[Journal Article] Induction of detoxication enzymes in mice by naturally occurring allyl nitrile.	2005 ▾
[Journal Article] (Review) The role of lipid peroxidation in chromosomal DN frag-mentation associated with cell death induced by glutathione depletion.	2005 ▾
[Journal Article] Induction of detoxication enzymes in mice by naturally occurring allylnitrile.	2005 ▾
[Journal Article] (Review) Antitumor and biological effects of Streptococcus pyogenes	2005 ▾
[Journal Article] (Review) Glutathione depletion-induced chromosomal DNA frag-mentation associated with apoptosis and necrosis.	2004 ▾
[Journal Article] Promoting effect of polyunsaturated fatty acids on chromosomal giant DNA fragmentation associated with cell death induced by glitathione depletion.	2004 ▾
[Journal Article] Promoting effect of polyunsaturated fatty acids on chromosomal giant DNA fragmentation associated with cell death induced by glutathione depletion.	2004 ▾
[Journal Article] (Review) Glutathione depletion-induced chromosomal DNA fragmentation associated with apoptosis and necrosis.	2004 ▾
[Journal Article] (Review) Pathological changes induced by allylnitrile and crotononitrile : relationship with behavioral abnormalities.	2004 ▾
[Journal Article] (Review) Chromosomal DNA fragmentation in apoptosis and necrosis induced by oxidative stress.	2003 ▾
[Journal Article] Ultraviolet ray induces chromosomal giant DNA fragmentation followed by internucleosomal DNA fragmentation associated with apoptosis in rat glioma cells	2003 ▾
[Journal Article] (Review) Chromosomal DNA fragmentation in apoptosis and necrosis induced by oxidative stress.	2003 ▾
[Journal Article] Ultraviolet ray induces chromosomal giant DNA fragmentation followed by inter-nucleosomal DNA fragmentation associated with apoptosis in rat glioma cells.	2003 ▾

