

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

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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

Kanazawa University Graduate School of Medical Science

## Principal Investigator

**HIGUCHI Yoshihiro** Kanazawa Univ., Grad.Sch.Med.Sci., Res Assoc, 医学系研究科, 助手 (10019630)

## Co-Investigator(Kenkyū-buntansha)

MURAKAMI Takashi Kanazawa Univ., Grad.Sch.Med.Sci., Assoc Prof., 医学系研究科, 助教授 (40210009)

TANII Hideji Kanazawa Univ., Grad.Sch.Med.Sci., Assoc Prof., 医学系研究科, 助教授 (90110618)

## Project Period (FY)

2003 - 2005

## Keywords

Glutamate / Glia / Apoptosis / Necrosis / Glutathione / Ultraviolet / Giant DNA fragmentation / Lipid peroxidation

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

