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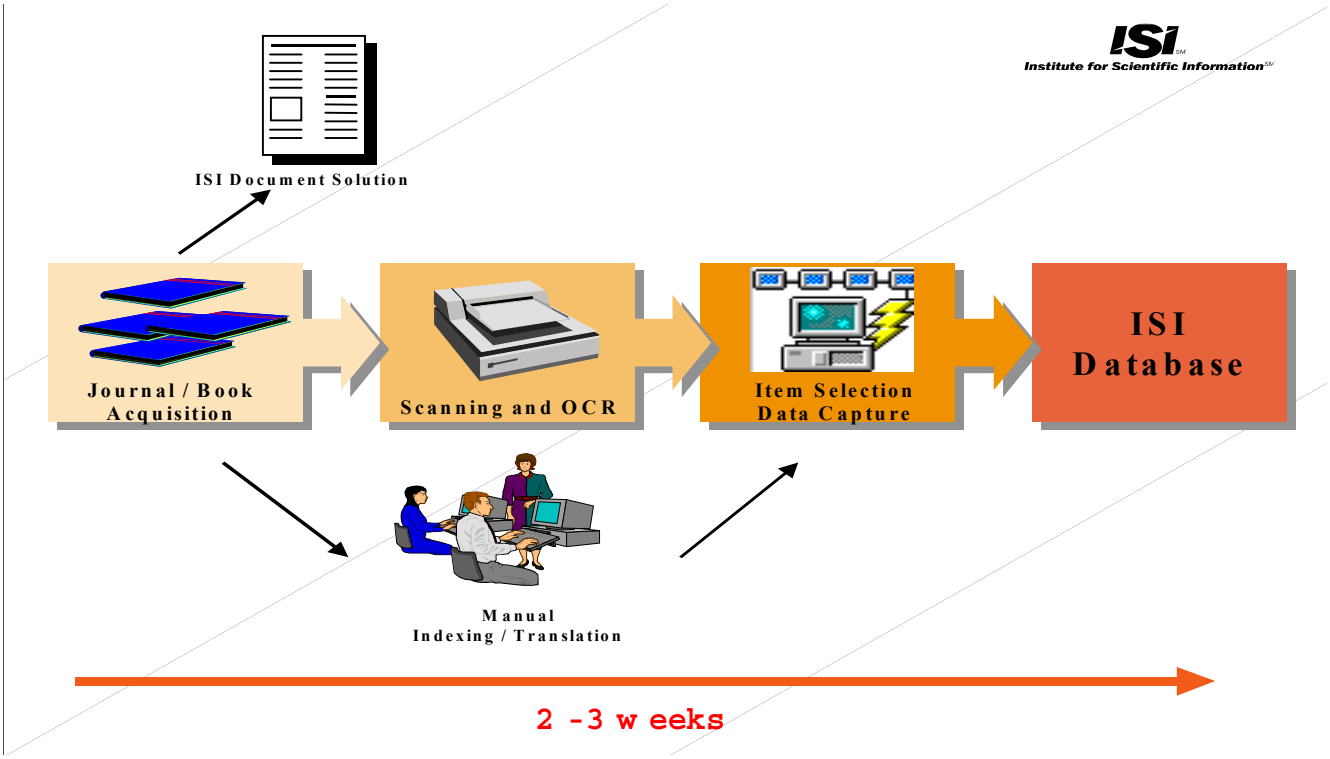

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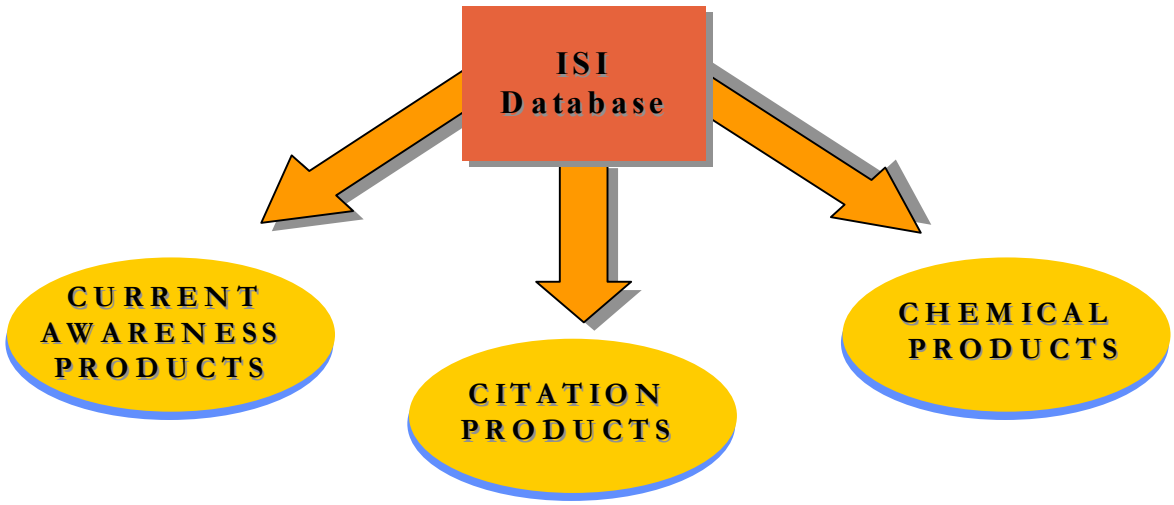

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Proc. Natl. Acad. Sci. USA
Vol. 96, pp. 2042–2047, March 1999
Biophysics

Copper binding to the prion protein: Structural implications of four identical cooperative binding sites

(octarepeat peptides/nuclear magnetic resonance/circular dichroism/electron spin resonance)

JOHN H. VILES*, FRED E. COHEN†‡§¶, STANLEY B. PRUSINER¶‖, DAVID B. GOODIN*, PETER E. WRIGHT*,**††, AND H. JANE DYSON*††

Department of *Molecular Biology and **Skaggs Institute for Chemical Biology, Scripps Research Institute, La Jolla, CA 90237; and Departments of ‖Neurology, †Pharmaceutical Chemistry, ‡Cellular and Molecular Pharmacology, §Medicine, and ¶Biochemistry and Biophysics, University of California, San Francisco, CA 94143

Contributed by Stanley B. Prusiner, December 29, 1998

ABSTRACT **Evidence is growing to support a functional role for the prion protein (PrP) in copper metabolism. Copper ions appear to bind to the protein in a highly conserved octapeptide repeat region (sequence PHGGGWGQ) near the N terminus. To delineate the site and mode of binding of Cu(II) to the PrP, the copper-binding properties of peptides of varying lengths corresponding to 2-, 3-, and 4-octarepeat sequences have been probed by using various spectroscopic techniques. A two-octarepeat peptide binds a single Cu(II) ion with $K_d \approx 6$ μM whereas a four-octarepeat peptide cooperatively binds four Cu(II) ions. Circular dichroism spectra indicate a distinctive structuring of the octarepeat region on Cu(II) binding. Visible absorption, visible circular dichroism, and electron spin resonance spectra suggest that the coordination sphere of the copper is identical for 2, 3, or 4 octarepeats, consisting of a square-planar geometry with three nitrogen ligands and one oxygen ligand. Consistent with the pH dependence of Cu(II) binding, proton NMR spectroscopy indicates that the histidine residues in each octarepeat are coordinated to the Cu(II) ion. Our working model for the structure of the complex shows the histidine residues in successive octarepeats bridged between two copper ions, with both the Nε2 and Nδ1 imidazole nitrogen of each histidine residue coordinated and the remaining coordination sites occupied by a backbone amide nitrogen and a water molecule. This arrangement accounts for the cooperative nature of complex formation and for the apparent evolutionary requirement for four octarepeats in the PrP.**

Prion diseases are a novel class of neurodegenerative diseases, including scrapie in sheep, bovine spongiform encephalopathy in cattle, and Creutzfeldt-Jacob disease in humans (1). A new variant form of Creutzfeldt-Jacob disease has been reported that is thought to be caused by the ingestion of infected beef (2, 3). A variety of biochemical, biophysical, cell biologic, and transgenetic experiments have indicated that the critical pathogenic event in prion disease is the misfolding of a benign cellular prion protein (PrP^C) to form the infectious disease-causing isoform, the scrapie isoform of PrP (4–7).

Until recently, little has been known about the normal function of PrP^C in the brain. There is now a body of evidence to indicate a role for PrP^C in copper metabolism. Mice deficient in PrP^C showed a >10-fold reduction of copper in a microsomal fraction from brain relative to wild-type mice and a reduction in activity of Cu/Zn superoxide dismutase (8). It also has been shown that cerebellar cells from mice deficient in PrP^C are more sensitive to copper toxicity and oxidative stress (9).

Mature Syrian hamster PrP^C is a glycoprotein containing two N-linked carbohydrates and one disulfide bridge. Post-translational processing results in the cleavage of a 22-residue leader sequence and the C-terminal tail after the attachment of a glycosylphosphatidylinositol anchor to serine 231. The solution structures of the mouse prion protein fragment, PrP(121–231) (10, 11), and of Syrian hamster PrP(90–231) (12) have been reported. The sequence of PrP(90–231) corresponds to the protease-resistant core of the scrapie isoform of PrP (PrP27–30), which can mediate prion disease.

The secondary structure of the full length Syrian hamster PrP(29–231) has been determined, and the dynamic properties of the protein backbone have been measured (13). The secondary structural elements of the full length apo PrP(29–231) are identical to those of PrP(90–231). The N-terminal half of the apoprotein, residues 29–124, is unstructured, with considerable backbone flexibility (13). Residues 51–91 contain an unusual glycine-rich repeat every eight residues; this sequence is termed the octarepeat region. Residues 60–91 consist of four octarepeat sequences $(PHGGGWGQ)_4$, and residues 51–59 have a homologous sequence but lack the histidine residue

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Copper binding **to the prion protein: Structural implications of four identical cooperative binding sites**

Viles JH, Cohen FE, Prusiner SB, Goodin DB, Wright PE, Dyson HJ

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA
96: (5) 2042-2047 MAR 2 1999

Document type: Article **Language:** English **Cited References:** 34 **Times Cited:** 15

Abstract:
Evidence is growing to support a functional role for the prion protein (PrP) in copper metabolism. Copper ions appear to bind to the protein in a highly conserved octapeptide repeat region (sequence PHGGGWGQ) near the N terminus. To delineate the site and made of binding of Cu(II) to the PrP, the copper-binding properties of peptides of varying lengths corresponding to 2-, 3-, and 4-octarepeat sequences have been probed by using various spectroscopic techniques. A two-octarepeat peptide binds a single Cu(II) ion with K-d approximate to 6 mu M whereas a four-octarepeat peptide cooperatively binds four Cu(II) ions. Circular dichroism spectra indicate a distinctive structuring of the octarepeat region on Cu(II) binding. Visible absorption, visible circular dichroism, and electron spin resonance spectra suggest that the coordination sphere of the copper is identical for 2, 3, or 4 octarepeats, consisting of a square-planar geometry with three nitrogen ligands and one oxygen ligand. Consistent with the pH dependence of Cu(II) binding, proton NMR spectroscopy indicates that the histidine residues in each octarepeat are coordinated to the Cu(II) ion. Our working model for the structure of the complex shows the histidine residues in successive octarepeats bridged between two copper ions, with both the N epsilon 2 and N delta 1 imidazole nitrogen of each histidine residue coordinated and the remaining coordination sites occupied by a backbone amide nitrogen and a water molecule. This arrangement accounts for the cooperative nature of complex formation and for the apparent evolutionary requirement for four octarepeats in the PrP.

Author Keywords:
octarepeat peptides, nuclear magnetic resonance, circular dichroism, electron spin resonance

KeyWords Plus:
CREUTZFELDT-JAKOB-DISEASE, NMR STRUCTURE, SCRAPIE, COMPLEX, SPECTROSCOPY, CONVERSION, HISTIDINE, VARIANT, REGION, BRAIN

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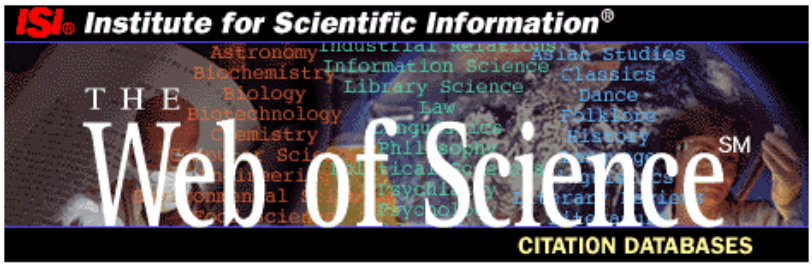

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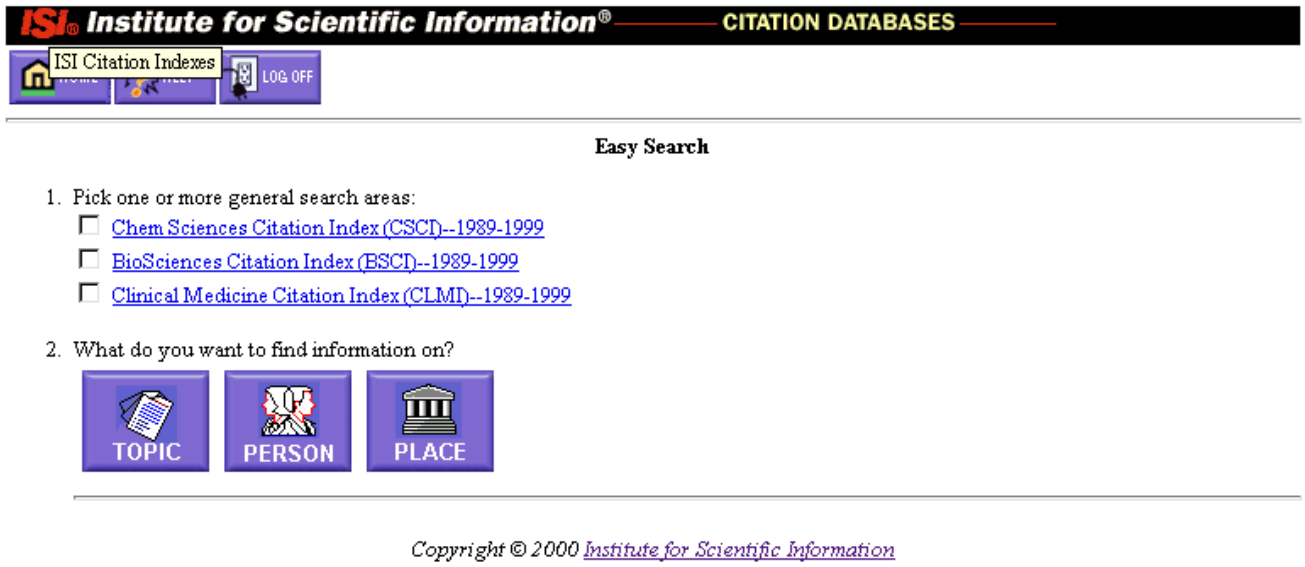

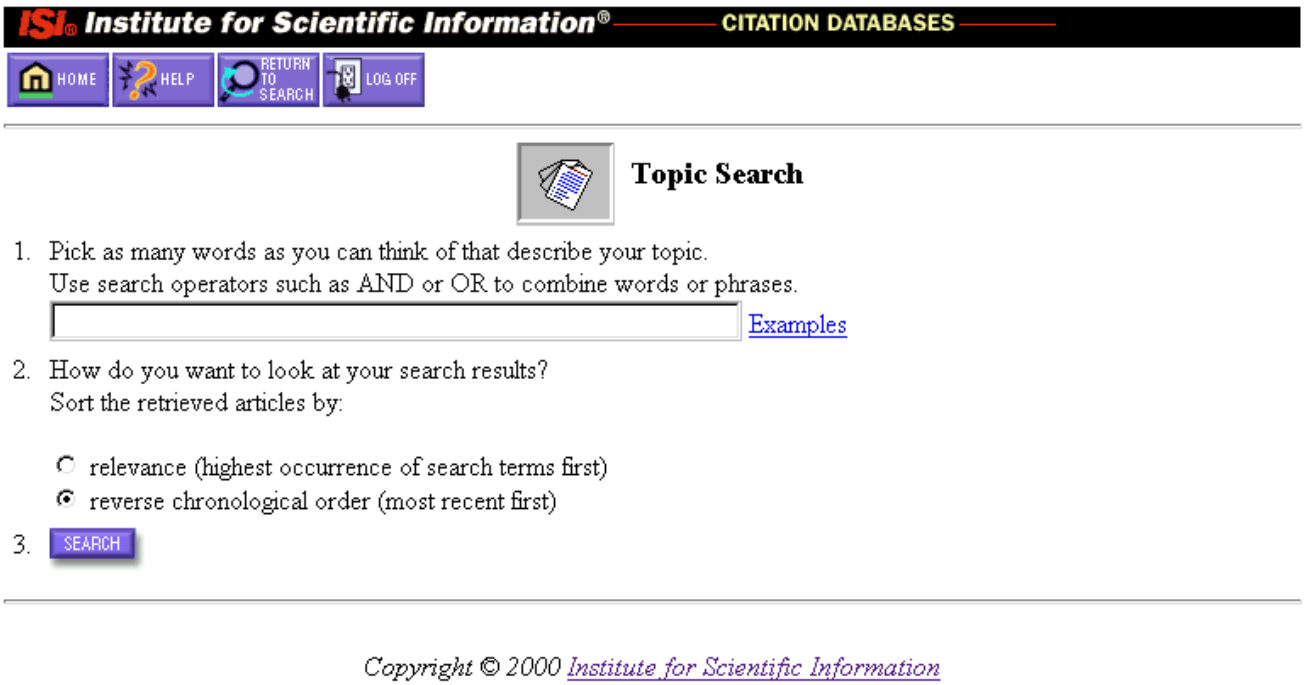

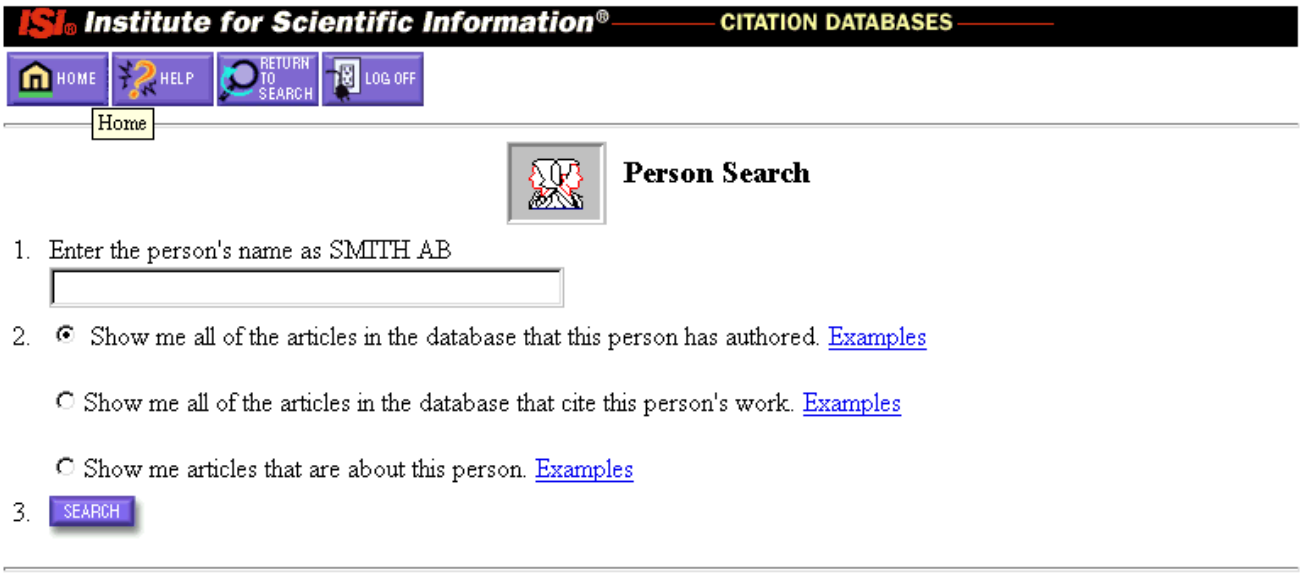

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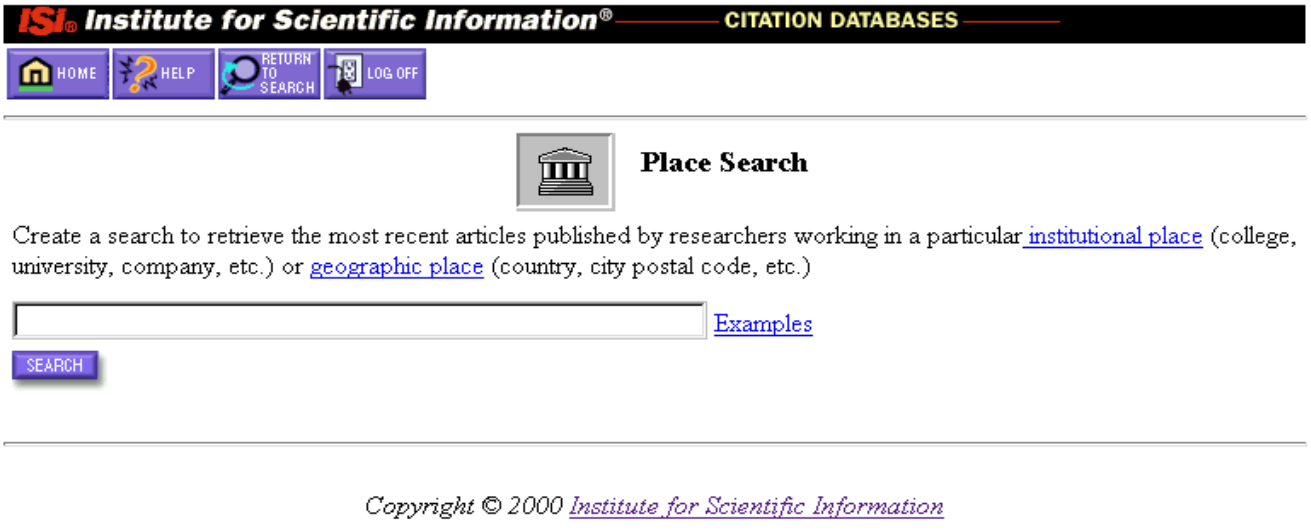

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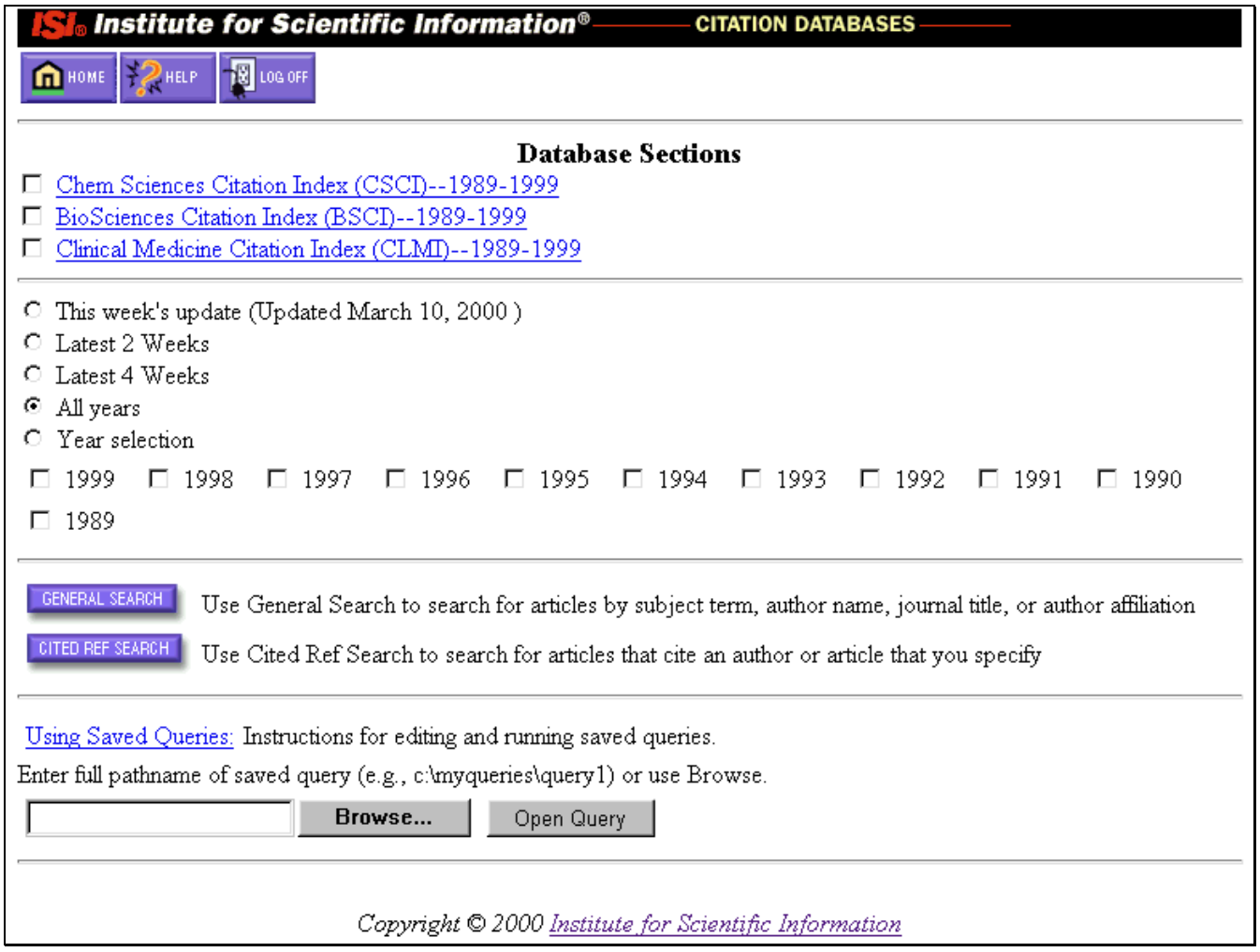

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☐ Zhou L, Song ZW, Tittel J, et al.
HAC-1, a Drosophila homolog of APAF-1 and CED-4 functions in developmental and radiation-induced **apoptosis**
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☐ Haining WN, Carboy-Newcomb C, Wei CL, et al.
The proapoptotic function of Drosophila Hid is conserved in mammalian cells
P NATL ACAD SCI USA 96: (9) 4936-4941 APR 27 1999

☐ Bergmann A, Agapite J, **Steller H**
Mechanisms and control of programmed **cell death** in invertebrates
ONCOGENE 17: (25) 3215-3223 DEC 24 1998

☐ Goswami J, Sinskey AJ, **Steller H**, et al.
Apoptosis in batch cultures of Chinese Hamster Ovary cells
BIOTECHNOL BIOENG 62: (6) 632-640 MAR 20 1999

☐ Bergmann A, Agapite J, McCall K, et al.
The Drosophila gene hid is a direct molecular target of Ras-dependent survival signaling
CELL 95: (3) 331-341 OCT 30 1998

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Control of **apoptosis** in Drosophila.
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Bergmann A, Agapite J, **Steller H**
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17: (25) 3215-3223 DEC 24 1998

Document type: Review **Language:** English **Cited References:** 130 **Times Cited:** 6

Abstract:
Apoptosis is a morphologically distinct form of programmed **cell death** that plays important roles in development, tissue homeostasis and a wide variety of diseases, including cancer, AIDS, stroke, myopathies and various neurodegenerative disorders (see Thompson (1995) for review). It is now clear that **apoptosis** occurs by activating an intrinsic **cell suicide** program which is constitutively expressed in most animal cells, and that key components of this program have been conserved in evolution from worms to insects to man. Genetic studies of programmed **cell death** in experimentally highly accessible invertebrate model systems have provided important clues about the molecular nature of the death program, and the intracellular mechanisms that control its activation. This review summarizes some of the key findings in this area, but also touches on some of the many unresolved questions and challenges that remain.

Author Keywords:
C-elegans, Drosophila, **apoptosis**, programmed **cell death**, ced genes

KeyWords Plus:
APOPTOSIS INHIBITORY PROTEIN, DROSOPHILA EYE DEVELOPMENT, CAENORHABDITIS-ELEGANS, CYTOCHROME-C, TYROSINE KINASE, GENETIC-CONTROL, NERVOUS-SYSTEM, BCL-2, REAPER, CED-4

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Mechanisms and control of programmed cell death in invertebrates

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CHEN P	GENE DEV	10	1773	1996
CHEN P	J BIOL CHEM	247	25735	1996
CHINNAIYAN AM	J BIOL CHEM	271	4573	1996
CHINNAIYAN AM	SCIENCE	275	1122	1997
CHU ZL	P NATL ACAD SCI USA	94	10057	1997
CLEARY ML	CELL	47	19	1986
CLEM RJ	MOL CELL BIOL	14	5212	1994
CONRADT B	CELL	93	519	1998
CROOK NE	J VIROL	67	2168	1993
DAVIDSON FF	NATURE	391	587	1998
DAVIE EW	BIOCHEMISTRY-US	30	10363	1991
DEVERAUX QL	EMBO J	17	2215	1998
DEVERAUX QL	NATURE	388	300	1997
DICKSON BJ	GENETICS	142	163	1996
DOWNWARD J	CURR OPIN GENET DEV	8	49	1998
DUCKETT CS	EMBO J	15	2685	1996
ELLIS HM	CELL	44	817	1986

A reference that also occurs in any of the three databases as a source record is underlined as a hot link. Clicking a reference's hot link displays the cited reference as a source record, as illustrated on the next page.

CITED REFERENCE LINK TO SOURCE

ISI Institute for Scientific Information® — CITATION DATABASES

HOME | HELP | GENERAL SEARCH | CITED REF SEARCH | MARK | SEARCH RESULTS | LOG OFF

Cited References--Full Record

Article 1 of 1 RELATED RECORDS

SURVIVAL OF PHOTORECEPTOR NEURONS IN THE COMPOUND EYE OF DROSOPHILA DEPENDS ON CONNECTIONS WITH THE OPTIC GANGLIA

CAMPOS AR, FISCHBACH KF, STELLER H

DEVELOPMENT

114: (2) 355-366 FEB 1992

Document type: Article **Language:** English **Cited References:** 55 **Times Cited:** 32

Abstract:
The importance of retinal innervation for the normal development of the optic ganglia in Drosophila is well documented. However, little is known about retrograde effects of the optic lobe on the adult photoreceptor cells (R-cells). We addressed this question by examining the survival of R-cells in mutant flies where R-cells do not connect to the brain. Although imaginal R-cells develop normally in the absence of connections to the optic lobes, we find that their continued survival requires these connections. Genetic mosaic studies with the disconnected (disco) mutation demonstrate that survival of R-cells does not depend on the genotype of the eye, but is correlated with the presence of connections to the optic ganglia. These results suggest the existence of retrograde interactions in the Drosophila visual system reminiscent of trophic interactions found in vertebrates.

Author Keywords:
TROPHIC INTERACTIONS, VISUAL SYSTEM, CELL DEATH, RETINAL DEGENERATION, DROSOPHILA

KeyWords Plus:
POST-EMBRYONIC DEVELOPMENT, CRAYFISH GIANT-AXONS, NINAE OPSIN GENE, VISUAL-SYSTEM, SCHISTOCERCA-GREGARIA, TROPHIC DEPENDENCIES, MELANOGASTER, PROJECTIONS, LOCUST, GROWTH

Addresses:
CAMPOS AR, MIT, HOWARD HUGHES MED INST, DEPT BRAIN & COGNIT SCI, CAMBRIDGE, MA 02139.
MIT, DEPT BIOL, CAMBRIDGE, MA 02139.
INST BIOL 3, W-7800 FREIBURG, GERMANY.

Publisher:
COMPANY OF BIOLOGISTS LTD, CAMBRIDGE

IDS Number:
HJ331

ISSN:
0950-1991

RELATED RECORDS

Clicking RELATED RECORDS on a Full Record or Cited References display retrieves articles that cite one or more of the same papers cited by the displayed record, sorted by relevance.

Related Records--Summary

These documents in the database are related to parent record:
Bergmann A. **Mechanisms and control of programmed** cell death **in invertebrates**

Page 1 (Articles 1 -- 10): MARK ALL SUBMIT

[1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10]

☐ Cryns V, Yuan JY
Proteases to die for
GENE DEV 12: (11) 1551-1570 JUN 1 1998

☐ Rathmell JC, Thompson CB
The central effectors of cell death in the immune system
ANNU REV IMMUNOL 17: 781-828 1999

☐ Dbaibo GS, Hannun YA
Signal transduction and the regulation of apoptosis: roles of ceramide
APOPTOSIS 3: (5) 317-334 OCT 1998

☐ Strasser A, Huang DCS, Vaux DL
The role of the bcl-2/ced-9 gene family in cancer and general implications of defects in cell death control for tumourigenesis and resistance to chemotherapy
BBA-REV CANCER 1333: (2) F151-F178 OCT 24 1997

☐ Zhou L, Song ZW, Tittel J, et al.
HAC-1, a Drosophila homolog of APAF-1 and CED-4 functions in developmental and radiation-induced apoptosis
MOL CELL 4: (5) 745-755 NOV 1999

☐ Earnshaw WC, Martins LM, Kaufmann SH
Mammalian caspases: Structure, activation, substrates, and functions during apoptosis
ANNU REV BIOCHEM 68: 383-424 1999

☐ Kidd VJ
Proteolytic activities that mediate apoptosis
ANNU REV PHYSIOL 60: 533-573 1998

☐ Pettmann B, Henderson CE
Neuronal cell death
NEURON 20: (4) 633-647 APR 1998

☐ Salvesen GS
Programmed cell death and the caspases
APMIS 107: (1) 73-79 JAN 1999

☐ Slee EA, Martin SJ
Regulation of caspase activation in apoptosis: implications for transformation and drug resistance
CYTOTECHNOLOGY 27: (1-3) 309-320 1998

Page 1 (Articles 1 -- 10): MARK ALL SUBMIT

[1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10]

19686 documents in the database are related to parent record. (500 shown)

Related Records are a fast and effective method of expanding a search without having to modify or replace the original query.

Related Records are from all years and all databases no matter what databases and years have been selected for the original search.

The Related Records list is sorted by number of shared references. The first record on the list shares the greatest number of references with the parent record.

As more records are added to the database, the number of Related Records for a given article may increase.

TIMES CITED

Clicking the Times Cited link on a full record displays all the papers that cite the displayed record. The citing papers are from all databases and all data years available.

As more records are added to the databases, the Times Cited count may increase.

Citing Articles--Summary

Mechanisms and control of programmed cell death **in invertebrates**
Bergmann A, Agapite J, **Steller H**
ONCOGENE
17: (25) 3215-3223 DEC 24 1998

These documents in the database cite the above article:

Page 1 (Articles 1 -- 8): MARK ALL SUBMIT

[1]

☐ Lockshin RA, Osborne B, Zakeri Z
Cell death in the third millennium
CELL DEATH DIFFER 7: (1) 2-7 JAN 2000

☐ Vaquero M
Apoptosis: To be or not to be, that is the question
MED CLIN-BARCELONA 114: (4) 144-156 FEB 5 2000

☐ Hozak RR, Manji GA, Friesen PD
The BIR motifs mediate dominant interference and oligomerization of inhibitor of apoptosis Op-IAP
MOL CELL BIOL 20: (5) 1877-1885 MAR 2000

☐ Lisi S, Mazzon I, White K
Diverse domains of THREAD/DIAP1 are required to inhibit apoptosis induced by REAPER and HID in drosophila
GENETICS 154: (2) 669-678 FEB 2000

☐ Bonini NM, Fortini ME
Surviving Drosophila eye development: integrating cell death with differentiation during formation of a neural structure
BIOESSAYS 21: (12) 991-1003 DEC 1999

☐ Zhou L, Song ZW, Tittel J, et al.
HAC-1, a Drosophila homolog of APAF-1 and CED-4 functions in developmental and radiation-induced apoptosis
MOL CELL 4: (5) 745-755 NOV 1999

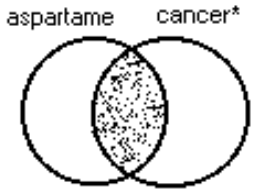
• • •

TRUNCATION / WILDCARD SYMBOLS

Truncation and wildcard symbols are useful to retrieve variants of words. These may be used within and at the end of search terms.

METHOD	SYMBOL	EXAMPLE	RETRIEVES
Any number	*	pharmac*	pharmacy pharmacology pharmaceutics pharmaceutical
		sul*ur	sulphur sulfur
		bure*t*	buret burets burette burettes bureaucrat bureaucratic
Single character	?	wom?n	woman women womyn
		en?oblast	endoblast entoblast
		colo?r	colour *not color*
Wildcard & Right-end Truncation	? *	ch?mi*	chemist chemistry chimia chimica chemie

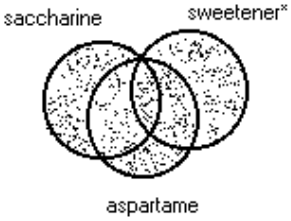
BOOLEAN OPERATORS



AND

All search terms must occur to be retrieved.

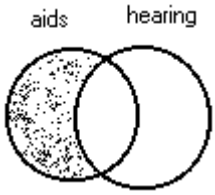
TOPIC: aspartame AND cancer*
Retrieves documents that contain both *aspartame* and *cancer**.



OR

Any one of the search terms must occur to be retrieved. Use when searching variants and synonyms.

TOPIC: aspartame OR saccharine OR sweetener*
Retrieves documents that contain one of the terms.



NOT

Excludes records that contain a given search term.

TOPIC: aids NOT hearing

Retrieves documents with *aids,* excluding any which also contain *hearing*.

PROXIMITY OPERATORS

Implied Adjacency

By default, searching a phrase retrieves records that contain the adjacent terms in the same order.

TOPIC: balloon angioplasty

Abstract:
...is a new therapeutic approach targeted at the revention of restenosis after coronary **balloon angioplasty**. Several mostly...

SAME SENT

Terms must occur within the same sentence (where "sentence" is understood to be a period-delimited string), in any order.

TOPIC: hepatitis SAME treatment
TOPIC: hepatitis SENT treatment

Abstract:
We describe herein the operative **treatment** of a single subglissonian HCC of segment III in a child, HCV (**hepatitis** C virus)-related cirrhosis.

TOPIC SEARCH

Fields searched in the Topic Index:

	Clinical Medicine (CLMI)	BioSciences (BSCI)	Chem Sciences (CSCI)
Source title words	All Years	All Years	All Years
Author keywords	1991 →	1991 →	1991 →
KeyWords Plus	1991 →	1991 →	1991 →
Author abstracts	1991 →	1991 →	1991→

Develop synonyms (natural language, acronyms, jargon); connect with OR operator.

Treat all Topic Index searching as term-indexed.

Apply the SAME or SENT operators.

Avoid using the AND operator to combine concepts; use more specific proximity operators.

Search variants of all terms.

TOPIC: (honey bee* or honeybee* or apis mellif*) same danc*

Truncate for plural and derivative forms.

TOPIC: enzym*
Retrieves *enzyme,enzymes, enzymatic, enzymology*

Punctuation marks are searched as a space, but do display.

TOPIC: 2 4 dinitrotoluene is equivalent to **TOPIC: 2,4-dinitrotoluene**.

Title:
Aerobic biodegradation of **2,4-dinitrotoluene**, aminonitrotoluene isomers, and 2,4-diaminotoluene

Abstract:
2,4-Dinitrotoluene (DNT) is widely used in industry, including the manufacture of propellants. **2,4-Diaminotoluene** (DAT), 2-amino-4-nitrotoluene (2A4NT), and 4-amino-2-nitrotoluene...

Use the SAME operator to search for phrases containing a possessive.

TOPIC: kaposi* same sarcom*
Retrieves *Kaposi sarcoma, Kaposis-sarcoma, Kaposis sarcoma, Kaposi's sarcoma*

Search hyphenated words with a hyphen (or a space) and fused as one word, without a hyphen.

TOPIC: x-ray* or xray*
or **TOPIC: x ray* or xray***
Retrieves *X-ray or X-rays or Xray or Xrays or X-rayed…*

Spell out Greek letters and other special characters.

To retrieve an article whose title appears as:
Electroabsorption spectroscopy of β-carotene and α,ω-bis(1,1-dimethylheptyl)-1,3,5,7,9,11,13,15-hexadecaoctaene

TOPIC: (beta carotene and alpha omega) ☒ Title only

Personal names may be inverted in all subject fields except abstracts.
Use the SAME operator:

TOPIC: salk same (jonas or j)

CONQUERORS OF POLIOMYELITIS – ENDERS JOHN F., SALK, JONAS E. AND SABIN, ALBERT B.
SHAFRIR E
ISRAEL JOURNAL OF MEDICAL SCIENCES
31: (8) 525-526 AUG 1995

Document type: Editorial Material Language: English Cited References: 0 Times Cited: 0

EDITORIAL RULES -TITLES

Non-English titles are translated into U.S. English, when no translation is provided by the journal.

Enterovirus in human pathology revisited
Pozzetto B, Bourlet T
ANNALES DE BIOLOGIE CLINIQUE
55: (3) 183-188 MAY-JUN 1997

Document Type: Review **Language: French** Cited References: 43 Times Cited: 0

BOOK REVIEW SEARCH

Book reviews are indexed from *Science* and *Nature*.

The names of all authors, editors, translators and commentators are included in the TITLE field.

ISI creates a cited reference to the author and book being reviewed.

TOPIC: ants and bourke
Restrict search to a specific language or document type: **All Languages** **Book Review**

Social evolution in ants - Bourke,**AFG, Franks,NR**
Crozier RH
SCIENCE
271: (5256) 1682-1682 MAR 22 1996

Document type: Book Review **Language:** English Cited References: 1 **Times Cited:** 0

Addresses:
Crozier RH, LA TROBE UNIV, SCH GENET & HUMAN VARIAT, BUNDOORA, VIC 3083, AUSTRALIA.

Cited Author	Cited Work	Volume	Page	Year
☑ BOURKE AFG	SOCIAL EVOLUTION ANT			1995

If the original language of the book is not in English, the language will be given in the TITLE field.

TITLE: jelly fish
Restrict search to a specific language or document type: **German** **Book Review**

Algae, jellyfish, water fleas - The world of plankton - German - **Sommer,U**
Harms J
ETHOLOGY
103: (10) 881-881 OCT 1997

Document type: Book Review **Language:** German Cited References: 1 **Times Cited:** 0

KeyWords Plus® Creation Cycle

SAMPLE SOURCE RECORD

Title: Respiratory and immunological findings in brewery workers
Author(s): GodnicCvar J; Zuskin E; Mustajbegovic J; Schachter EN (REPRINT);
Kanceljak B; Macan J; Ilic Z; Ebling Z
Journal: AMERICAN JOURNAL OF INDUSTRIAL MEDICINE, 1999, V35, N1 (JAN), P 68-75
Author Keywords: brewery workers ; respiratory symptoms ; lung function ; immunology

Selected Cited References: (39 total, 14 shown for demonstration)
*WHO, 1986, P39, EARL DET OCC LUNG DI
BLASKI CA, 1996, V154, P334, AM J RESP CRIT CARE
HUY T, 1991, V144, P1314, AM REV RESPIR DIS
IVERSEN M, 1990, V20, P211, CLIN EXP ALLERGY
KORTEKANGASSAVO.O, 1993, V48, P147, ALLERGY
KORTEKANGASSAVO.O, 1994, V24, P836, CLIN EXP ALLERGY
MAESTRELLI P, 1992, V22, P103, CLIN EXP ALLERGY
MALMBERG P, 1986, V10, P316, AM J IND MED
MCCARTHY PE, 1985, V42, P106, BRIT J IND MED
MEZNAR B, 1989, P148, 14 INT C EUR AC ALL
REVSBECH P, 1990, V45, P204, ALLERGY
SHELDON JM, 1957, P507, MANUAL CLIN ALLERGY
SMID T, 1994, V25, P877, AM J IND MED
VIDAL C, 1995, V75, P121, ANN ALLERG ASTHMA IM

KeyWord Plus(R): ATOPIC-DERMATITIS PATIENTS; LUNG-FUNCTION;
GRAIN DUST; OCCUPATIONAL ASTHMA; MITE ALLERGY; STORAGE MITE; EXPOSURE;
HYPERSENSITIVITY; SYMPTOMS; DISEASE

ISI SOURCE DATABASE (1970-PRESENT)

No title available

The role of atopy in **grain dust**-induced airway **disease**

GRAIN DUST AND **LUNG-FUNCTION** - DOSE-RESPONSE RELATIONSHIPS

MITE ALLERGY AND **EXPOSURE** TO **STORAGE MITES** AND HOUSE DUST MITES IN FARMERS

SKIN PRICK TEST REACTIONS TO BREWERS-YEAST (SACCHAROMYCES-CEREVISIAE) IN ADULT **ATOPIC-DERMATITIS PATIENTS**

IMMEDIATE **HYPERSENSITIVITY** TO BAKERY, BREWERY AND WINE PRODUCTS IN YEAST-SENSITIVE **ATOPIC-DERMATITIS PATIENTS**

GUIDELINES FOR THE DIAGNOSIS OF **OCCUPATIONAL ASTHMA**

RELATIONSHIP BETWEEN **SYMPTOMS** AND **EXPOSURE** TO MOLD DUST IN SWEDISH FARMERS

LUNG-FUNCTION AFTER **EXPOSURE** TO BARLEY DUST

No title available

STORAGE MITE ALLERGY AMONG BAKERS

No title available

DUST-RELATED AND ENDOTOXIN-RELATED ACUTE **LUNG-FUNCTION** CHANGES AND WORK-RELATED **SYMPTOMS** IN WORKERS IN THE ANIMAL FEED-INDUSTRY

FOOD-INDUCED AND **OCCUPATIONAL ASTHMA** DUE TO BARLEY FLOUR

FREQUENTLY OCCURRING TITLE WORDS

ATOPIC-DERMATITIS PATIENTS
LUNG-FUNCTION
GRAIN DUST
OCCUPATIONAL ASTHMA
MITE ALLERGY
STORAGE MITE
EXPOSURE
HYPERSENSITIVITY
SYMPTOMS
DISEASE

SEARCH STRATEGY WORKSHEET

INQUIRY

_____

_____

CONCEPT 1		CONCEPT 2		CONCEPT 3
	SAME SENT AND		SAME SENT AND	
	|		|	
OR	|		|	
OR	|		|	
OR	|		|	
	|		|	

SUBJECT FIELDS TO BE SEARCHED (CIRCLE AT LEAST ONE):

TOPIC INDEX TITLE ONLY

Search Statements:_____

_____

SEARCHING BY SOURCE AUTHOR

ISI captures ALL authors, and all authors can be searched, displayed, printed and/or exported.

Enter the surname, followed by a space and up to 5 initials.

Source Document	ISI Database	Search by:	
Alan Boyd C.D.E. Smith	Smith ABCDE	AUTHOR:	smith abcde
		AUTHOR:	smith a*

Search for variations on names where the family name may not be the last name.

Source Document	ISI Database	Search by:	
Shi-Wa Yen	Yen SW Shi WY	AUTHOR:	(yen sw or shi wy)
Uzonyi Kiss Sandor	Uzonyi KS Sandor UK Kiss SU	AUTHOR:	(uzonyi ks or sandor uk or kiss su)

For all ISI databases, compound names were fused from 1972-1997. For complete retrieval in Web of Science-Corporate Editions, search them in fused and compound forms

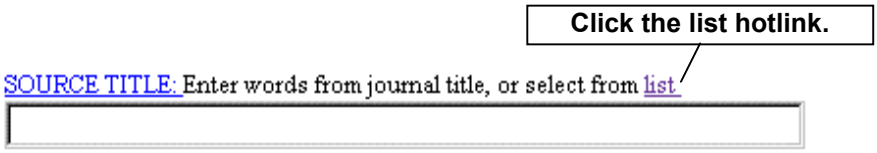
Source Document	ISI Database	Search by:	
D. Lagadic-Gossmann	Lagadic Gossmann D LagadicGossmann D	AUTHOR:	lagadic gossmann d* or lagadicgossmann d*
Geraldo Felipe de la Fuente	de la Fuente GF delaFuente GF	AUTHOR:	de la fuente g* or delafuente g*
J. O'Brien	O Brien J OBrien J	AUTHOR:	o brien j* or obrien j*

Titles of rank, generational designations, such as Junior or Senior, and academic degrees are dropped.

Source Document	ISI Database	Search by:	
Lord Duvall Edwards	Edwards D	AUTHOR:	edwards d*
W. Brumfitt, Jr.	Brumfitt W	AUTHOR:	brumfitt w*

SEARCHING BY SOURCE TITLE (JOURNAL NAME)

The SOURCE TITLE field is phrase-indexed. Select title(s) from the Full Journal Title list or enter the title in full or truncate it from the right.



SOURCE TITLE: *biochemical and biophys**
Retrieves:
BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS
Does not retrieve:
JOURNAL OF BIOCHEMICAL OR BIOPHYSICAL METHODS

SOURCE TITLE: *science*
Retrieves only:
SCIENCE

SOURCE TITLE: *science**
Retrieves:
SCIENCE
SCIENCE PROGRESS
But does not retrieve:
SOCIAL SCIENCE & MEDICINE

Internal punctuation and ampersands may be entered and will display, but will be searched as a space.

SOURCE TITLE: blood coagulation & fibrinolysis
Retrieves:
BLOOD COAGULATION & FIBRINOLYSIS

SOURCE TITLE: *a + u-architecture and urbanism*
Retrieves:
A + U-ARCHITECTURE AND URBANISM

Search our master journal list, including a one-year rolling file of journal coverage changes at this address:

www.isinet.com/journals/journals.html

SEARCHING BY ADDRESS

ISI captures ALL author addresses and all addresses can be searched, displayed, printed, and/or exported.

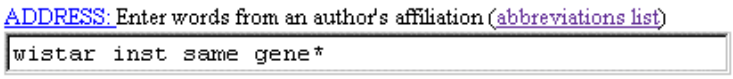
Reprint authors are shown. Other addresses are *not* paired with authors.

ISI applies standard abbreviations for common address terms. Click the abbreviations list hypertext link to the "Address Abbreviations" Help page to identify abbreviated terms. Truncate abbreviations for complete retrieval.

ISI also abbreviates some corporate and institution names and state/country names. To view these abbreviations, click the corporate and institution names and state/country names hot links located on the "Address Abbreviations" Help page.

Some abbreviations occur in addresses so frequently that they may *only* be searched with other significant address terms. Refer to the hypertext link disallowed words in the Address section of the General Search Help page.

Use the most significant address terms and adjacency.



Addresses:
Chirmule N, Univ Penn, Inst Human **Gene** Therapy, Dept Mol & Cellular Engn, 204 **Wistar Inst**, 3601 Spruce St, Philadelphia, PA 19104 USA.
Univ Penn, Inst Human Gene Therapy, Dept Mol & Cellular Engn, Philadelphia, PA 19104 USA.
Univ Penn, Inst Human Gene Therapy, Dept Med, Philadelphia, PA 19104 USA.
Wistar Inst, Philadelphia, PA 19104 USA.

Addresses are searchable by institution, department, street, city, state, province, country, postal code, or any combination of these components.

ADDRESS: Enter words from an author's affiliation (abbreviations list)

```
usa and japan and france
```

Addresses:
Zeman J, MPI FKF, Grenoble High Magnet Field Lab, 25 Av Martyrs, F-38042 Grenoble 9, **France**.
MPI FKF, Grenoble High Magnet Field Lab, F-38042 Grenoble 9, **France**.
Univ Calif Berkeley, Dept Phys, Berkeley, CA 94720 **USA**.
Lawrence Berkeley Lab, Div Sci Mat, Berkeley, CA 94720 **USA**.
Univ Electrocommun, Dept Commun & Syst, Tokyo, **Japan**.

ADDRESS: Enter words from an author's affiliation (abbreviations list)

```
N-0407
```

Addresses:
Spandow O, Ulleval Hosp, Dept Otorhinolaryngol, **N-0407** Oslo, Norway.
Univ Umea Hosp, Dept Otorhinolaryngol, S-90185 Umea, Sweden.

To retrieve records that contain two or more terms in the same address, use the SAME operator.

ADDRESS: Enter words from an author's affiliation (abbreviations list)

```
univ colorado and boulder
```

General Search Results--Summary
Address=univ colorado and boulder; DocType=All document types; Language=All languages; Databases=SCI-EXPANDED, SSCI, A&HCI; Timespan=All Years; (sorted by latest date)

38963 of 22075292 documents matched the query. (500 shown)

Addresses:
Schmitz S, Inst Behav Genet, Campus Box 447, **Boulder**, CO 80309 USA.
Inst Behav Genet, **Boulder**, CO 80309 USA.
Univ Colorado, Hlth Sci Ctr, Dept Psychiat, Denver, CO 80262 USA.
Univ London, Inst Psychiat, Genet & Dev Psychiat Res Ctr, London, England.

Address terms joined with AND may occur in different addresses.

ADDRESS: Enter words from an author's affiliation (abbreviations list)

```
univ colorado same boulder
```

General Search Results--Summary
Address=univ colorado same boulder; DocType=All document types; Language=All languages; Databases=SCI-EXPANDED, SSCI, A&HCI; Timespan=All Years; (sorted by latest date)

38836 of 22075292 documents matched the query. (500 shown)

Address terms joined with SAME must occur in the same address.

Addresses:
Wang XT, Univ Colorado, Dept Chem, Campus Box 194, POB 173364, Denver, CO 80217 USA.
Univ Colorado, Dept Chem, Denver, CO 80217 USA.
Univ Colorado, Dept Chem & Biochem, **Boulder**, CO 80309 USA.

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PRINCIPLES & USES OF CITATION SEARCHING

Citation indexing uses the cited references in published articles as index terms or entries. It exploits the formal linkages between papers established by the authors themselves. Citation searching offers the unique capability of finding new, unknown information based on older, known information.

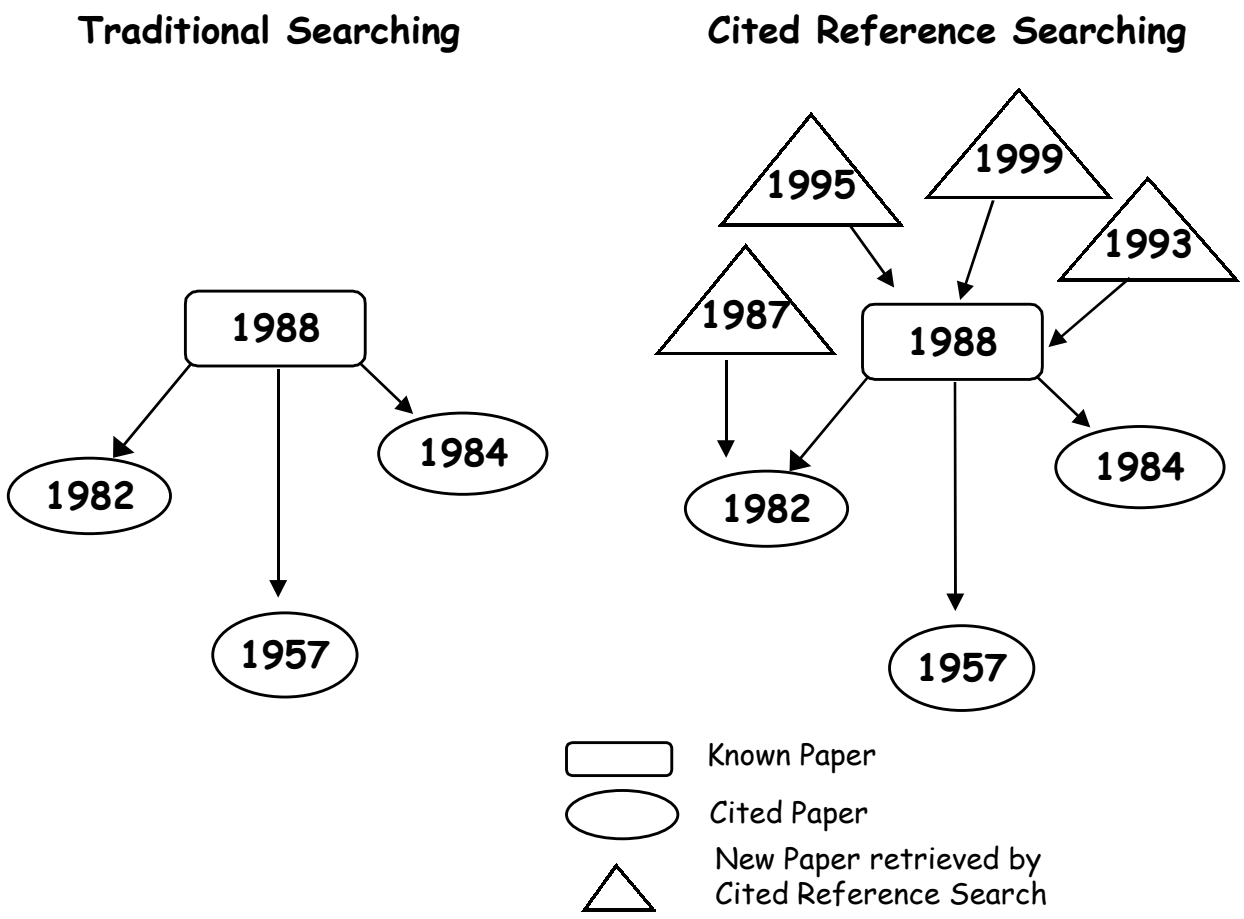
Examples of the many ways you can use ISI citation information:

- Discover who is citing your research and how your research is influencing newer research.
- Uncover the directions in which research is progressing based on an earlier study.
- Track the work of a research colleague or noted authority. ISI products allow you to focus your search on new work in which the author cites a particular paper from his/her earlier research.
- Verify the accuracy of a cited reference as included in a paper's list of references.
- Identify the sources of information that competitors, either domestic or international, are consulting for their research.
- Justify your journal acquisition policies by determining the usage of each title by your staff or the larger research community.
- Construct an objective history of a field of study, significant invention or discovery. Citation indexing tracks the scholarly links that map scientific impact and influence.

Cited Reference Searching: An Introduction
http://www.isinet.com/training/jobaids/citrefpr/prim1.html

Cited Reference Variations
http://www.isinet.com/training/jobaids/citrefpr/variat/variat2.html

Cited Reference Searching



Proc. Natl. Acad. Sci. USA
Vol. 96, pp. 2042–2047, March 1999
Biophysics

Copper binding to the prion protein: Structural implications of four identical cooperative binding sites

(octarepeat peptides/nuclear magnetic resonance/circular dichroism/electron spin resonance)

JOHN H. VILES*, FRED E. COHEN†‡§¶, STANLEY B. PRUSINER¶‖, DAVID B. GOODIN*, PETER E. WRIGHT*,**††, AND H. JANE DYSON*††

Department of *Molecular Biology and **Skaggs Institute for Chemical Biology, Scripps Research Institute, La Jolla, CA 90237; and Departments of ‖Neurology, †Pharmaceutical Chemistry, ‡Cellular and Molecular Pharmacology, §Medicine, and ¶Biochemistry and Biophysics, University of California, San Francisco, CA 94143

Contributed by Stanley B. Prusiner, December 29, 1998

ABSTRACT **Evidence is growing to support a functional role for the prion protein (PrP) in copper metabolism. Copper ions appear to bind to the protein in a highly conserved octapeptide repeat region (sequence PHGGGWGQ) near the N terminus. To delineate the site and mode of binding of Cu(II) to the PrP, the copper-binding properties of peptides of varying lengths corresponding to 2-, 3-, and 4-octarepeat sequences have been probed by using various spectroscopic techniques. A two-octarepeat peptide binds a single Cu(II) ion with $K_d \approx 6$ μM whereas a four-octarepeat peptide cooperatively binds four Cu(II) ions. Circular dichroism spectra indicate a distinctive structuring of the octarepeat region on Cu(II) binding. Visible absorption, visible circular dichroism, and electron spin resonance spectra suggest that the coordination sphere of the copper is identical for 2, 3, or 4 octarepeats, consisting of a square-planar geometry with three nitrogen ligands and one oxygen ligand. Consistent with the pH dependence of Cu(II) binding, proton NMR spectroscopy indicates that the histidine residues in each octarepeat are coordinated to the Cu(II) ion. Our working model for the structure of the complex shows the histidine residues in successive octarepeats bridged between two copper ions, with both the Nε2 and Nδ1 imidazole nitrogen of each histidine residue coordinated and the remaining coordination sites occupied by a backbone amide nitrogen and a water molecule. This arrangement accounts for the cooperative nature of complex formation and for the apparent evolutionary requirement for four octarepeats in the PrP.**

Prion diseases are a novel class of neurodegenerative diseases, including scrapie in sheep, bovine spongiform encephalopathy in cattle, and Creutzfeldt-Jacob disease in humans (1). A new variant form of Creutzfeldt-Jacob disease has been reported that is thought to be caused by the ingestion of infected beef (2, 3). A variety of biochemical, biophysical, cell biologic, and transgenetic experiments have indicated that the critical pathogenic event in prion disease is the misfolding of a benign cellular prion protein (PrP^C) to form the infectious disease-causing isoform, the scrapie isoform of PrP (4–7).

Until recently, little has been known about the normal function of PrP^C in the brain. There is now a body of evidence to indicate a role for PrP^C in copper metabolism. Mice deficient in PrP^C showed a >10-fold reduction of copper in a microsomal fraction from brain relative to wild-type mice and a reduction in activity of Cu/Zn superoxide dismutase (8). It also has been shown that cerebellar cells from mice deficient in PrP^C are more sensitive to copper toxicity and oxidative stress (9).

Mature Syrian hamster PrP^C is a glycoprotein containing two N-linked carbohydrates and one disulfide bridge. Post-translational processing results in the cleavage of a 22-residue leader sequence and the C-terminal tail after the attachment of a glycosylphosphatidylinositol anchor to serine 231. The solution structures of the mouse prion protein fragment, PrP(121–231) (10, 11), and of Syrian hamster PrP(90–231) (12) have been reported. The sequence of PrP(90–231) corresponds to the protease-resistant core of the scrapie isoform of PrP (PrP27–30), which can mediate prion disease.

The secondary structure of the full length Syrian hamster PrP(29–231) has been determined, and the dynamic properties of the protein backbone have been measured (13). The secondary structural elements of the full length apo PrP(29–231) are identical to those of PrP(90–231). The N-terminal half of the apoprotein, residues 29–124, is unstructured, with considerable backbone flexibility (13). Residues 51–91 contain an unusual glycine-rich repeat every eight residues; this sequence is termed the octarepeat region. Residues 60–91 consist of four octarepeat sequences $(PHGGGWGQ)_4$, and residues 51–59 have a homologous sequence but lack the histidine residue

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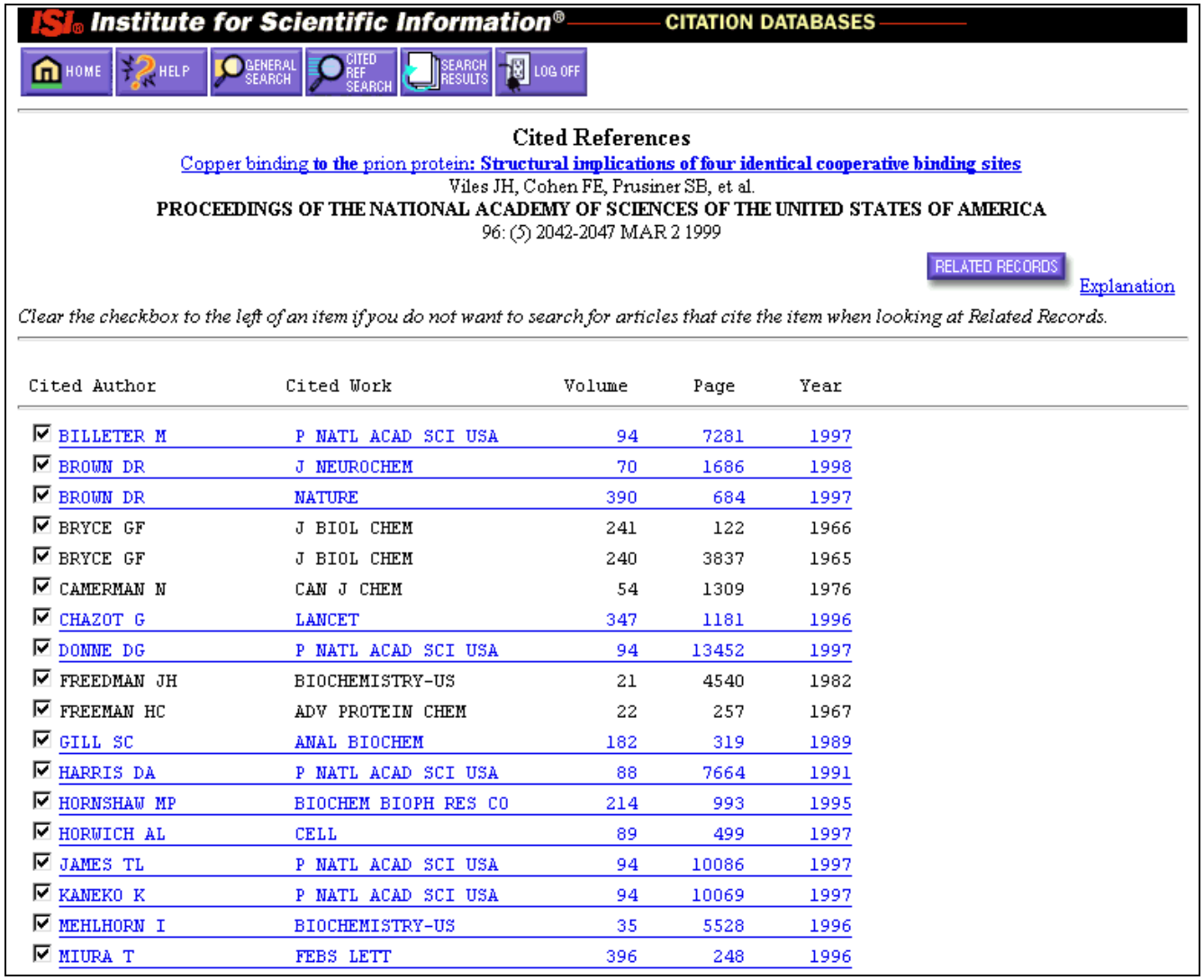

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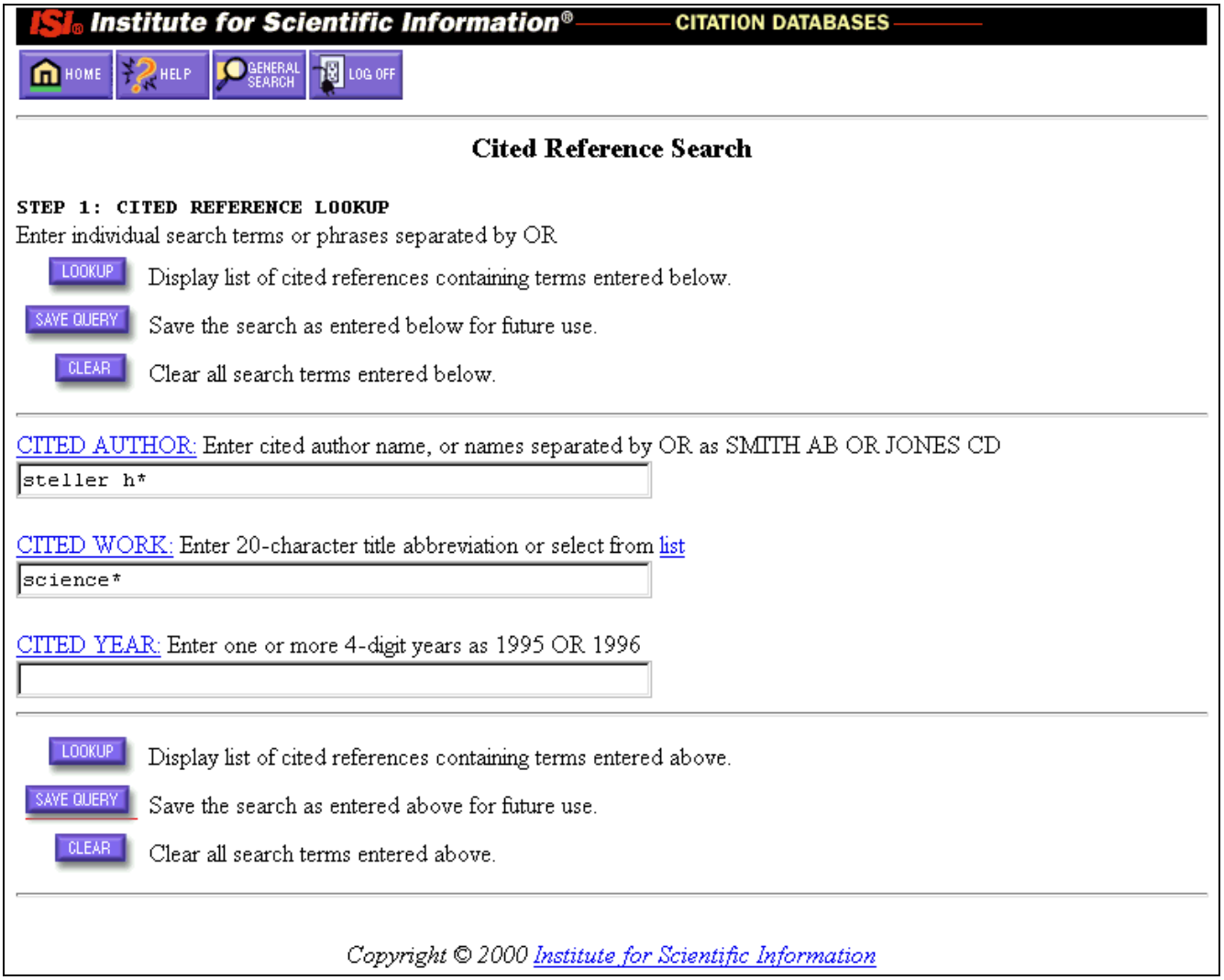

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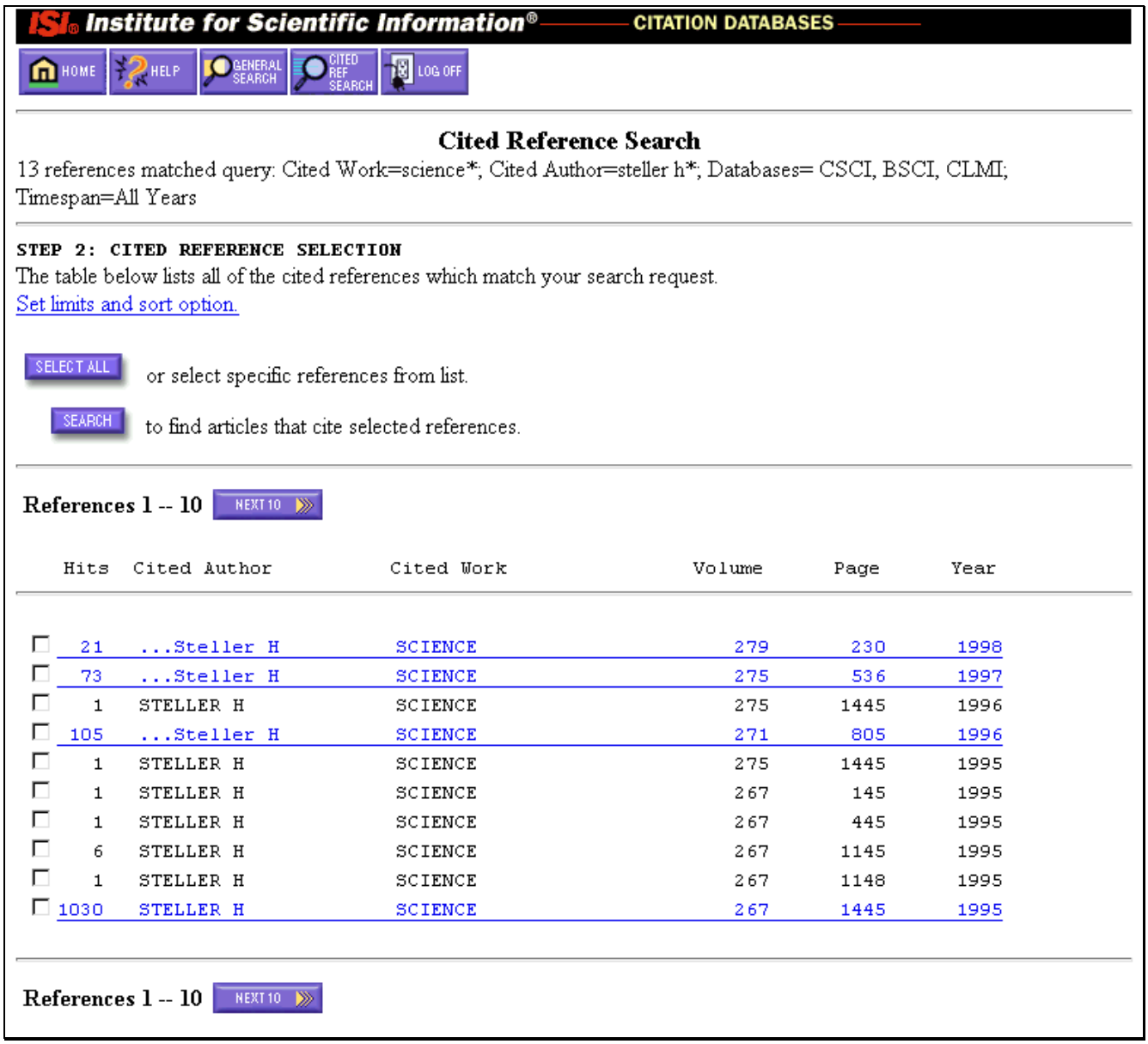

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Search Results--Full Record

Article 5 of 1043 PREVIOUS NEXT SUMMARY RELATED RECORDS

Effect of brief exposure to mitomycin C on cultured human nasal mucosa fibroblasts

Hu D, Sires BS, Tong DC, Royack GA, Oda D

OPHTHALMIC PLASTIC AND RECONSTRUCTIVE SURGERY

16: (2) 119-125 MAR 2000

Document type: Article **Language:** English **Cited References:** 20 **Times Cited:** 0

Abstract:

Purpose: To observe the effect of mitomycin C (MMC) on cultured human nasal mucosa fibroblasts.

Methods: Cultured human nasal mucosa fibroblasts were exposed to MMC (0.1-0.4 mg/ml) for 1 to 5 minutes. The viability of the fibroblasts was determined by MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide) assay; DNA fragmentation (apoptosis) by terminal deoxynucleotldyl transferase-mediated dUTP nick-end labeling (TUNEL); apoptotic percentage by flow cytometry; and morphology by light microscopy.

Results: A portion of the fibroblasts survived the mitomycin treatment and showed evidence of regrowth within 2 to 3 days. These cells reached confluence in 5 to 7 days. The inhibition rates by MTT assay of 0.4 mg/ml MMC for 5-minute exposures was 31.3%. Dose-response effect was noted with the lower concentrations and shorter exposure times where the inhibition rates were lower (but not significantly so). DNA fragmentation was observed in fibroblasts 24 hours after MMC exposure (0.4 mg/ml) for 5 minutes compared with normal control. The apoptotic rate of fibroblasts treated by 0.4 mg/ml MMC was significantly higher than the control ($p < 0.05$).

Conclusions: Short MMC exposure times have a variable cytotoxic effect and inhibit proliferation of cultured nasal mucosa fibroblasts. MMC also can induce apoptosis with a 5-minute exposure time. Therefore, it is possible that MMC has a complex effect in dacryocystorhinostomy.

KeyWords Plus:

TENONS CAPSULE FIBROBLASTS, RAPID COLORIMETRIC ASSAY, FLOW-CYTOMETRY, APOPTOSIS, CELLS, DACRYOCYSTORHINOSTOMY, PROLIFERATION, SURGERY, GROWTH, IDENTIFICATION

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Hu D, Sires BS, Tong DC, et al.

OPHTHALMIC PLASTIC AND RECONSTRUCTIVE SURGERY

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☑ HOPPENREIJS VPT	CORNEA	15	386	1996
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☑ JAVATE RM	OPHTHALMIC PLAST REC	11	54	1995
☑ KAO SCS	OPHTHALMOLOGY	104	86	1997
☑ KHAW PT	EYE	8	188	1994
☑ MOSMANN T	J IMMUNOL METHODS	65	55	1983
☑ POOT M	CYTOMETRY	27	358	1997
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☑ UGURBAS SH	OPHTHALMIC SURG LAS	28	300	1997
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☐	1	STELLER H	SCIENCE	275	1445	1996
☐	105	...Steller H	SCIENCE	271	805	1996
☐	1	STELLER H	SCIENCE	275	1445	1995
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1	GOULD SJ	HENS TEETH HORSES TO			1990
1	GOULD SJ	HENS TEETH HORSES TO		177	1987
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Page 1 (Articles 1 -- 10): MARK ALL SUBMIT

[1 | 2 . . .

☐ Fujikawa T, Idei K, Ebihara T, et al.
Aromatic hydrogenation of distillates over SiO2-Al2O3-supported noble metal catalysts
APPL CATAL A-GEN 192: (2) 253-261 FEB 14 2000

☐ Macleod N, Fryer JR, Stirling D, et al.
Deactivation of bi- and multimetallic reforming catalysts: influence of alloy formation on catalyst activity
CATAL TODAY 46: (1) 37-54 NOV 2 1998

☐ Dumas JM, Rmili S, Barbier J
Preparation of Pt-Cu/SiO2 by surface redox reaction
J CHIM PHYS PCB 95: (7) 1650-1665 JUL-AUG 1998

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☑	2	...Steller H	BIOTECHNOL BIOENG	62	632	1999
☑	43	...Steller H	CELL	95	331	1998
☑	1	STELLER H	CELL	50	139	1987
☑	1	STELLER H	CELL	50	1136	1987
☑	110	STELLER H	CELL	50	1139	1987
☑	1	STELLER H	CELLULAR INTERACTION			1993
☑	1	STELLER H	CELLULAR INTERACTION		77	1993
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Page 1 (Articles 1 -- 10): UNMARK ALL SUBMIT

[1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10]

☑ Le Gall M, Chambard JC, Breittmayer JP, et al.
The p42/p44 MAP kinase pathway prevents apoptosis induced by anchorage and serum removal
MOL BIOL CELL 11: (3) 1103-1112 MAR 2000

☑ Consoulas C
Remodeling of the leg sensory system during metamorphosis of the hawkmoth, Manduca sexta
J COMP NEUROL 419: (2) 154-174 APR 3 2000

☑ Kazemi-Esfarjani P, Benzer S
Genetic suppression of polyglutamine toxicity in Drosophila
SCIENCE 287: (5459) 1837-1840 MAR 10 2000

☑ Prober DA, Edgar BA
Ras1 promotes cellular growth in the Drosophila wing
CELL 100: (4) 435-446 FEB 18 2000

☑ Shimamura A, Ballif BA, Richards SA, et al.
Rsk1 mediates a MEK-MAP kinase cell survival signal
CURR BIOL 10: (3) 127-135 FEB 10 2000

☑ Goyal L, McCall K, Agapite J, et al.
Induction of apoptosis by Drosophila reaper, hid and grim through inhibition of IAP function
EMBO J 19: (4) 589-597 FEB 15 2000

☑ Miller DT, Read R, Rusconi J, et al.
The Drosophila primo locus encodes two low-molecular-weight tyrosine phosphatases
GENE 243: (1-2) 1-9 FEB 8 2000

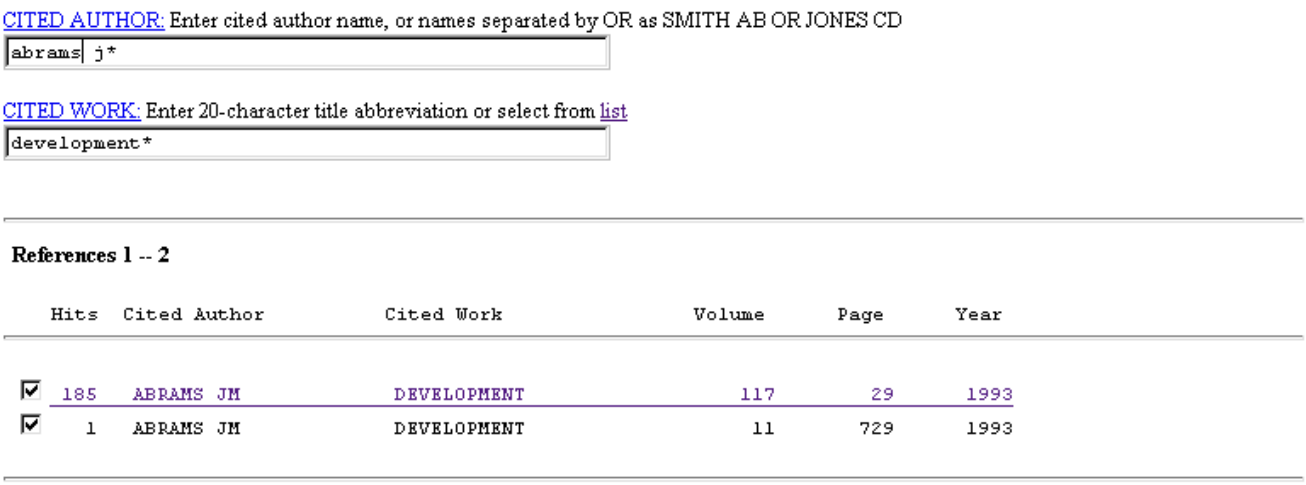
☑ Bausenwein BS, Schmidt M, Mielke B, et al.
In vivo functional analysis of the Daughter of Sevenless protein in receptor tyrosine kinase signaling
MECH DEVELOP 90: (2) 205-215 FEB 2000

☑ Mastrangelo AJ, Hardwick JM, Zou SF, et al.
Part II. Overexpression of bcl-2 family members enhances survival of mammalian cells in response to various culture insults
BIOTECHNOL BIOENG 67: (5) 555-564 MAR 5 2000

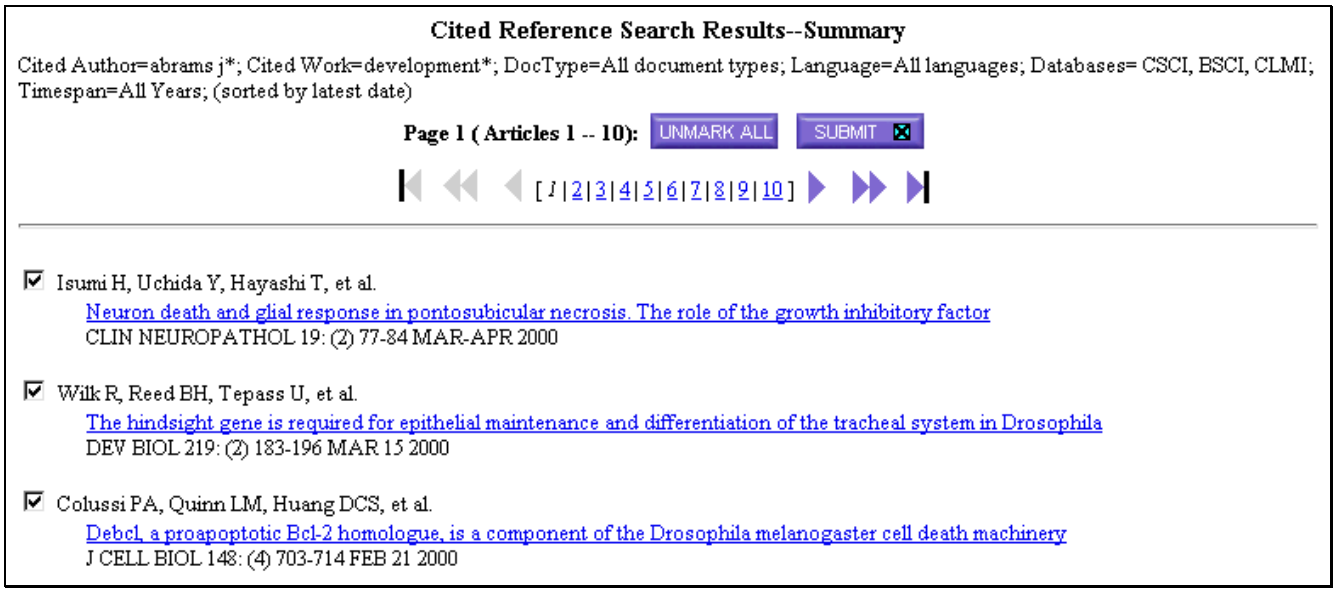
☑ Kazama H, Yonehara S
Oncogenic K-Ras and basic fibroblast growth factor prevent Fas-mediated apoptosis in fibroblasts through activation of mitogen-activated protein kinase
J CELL BIOL 148: (3) 557-566 FEB 7 2000

5. Perform Cited Reference search(es) for each co-author(s) that is a first listed author.

Author(s); ABRAMS JM, WHITE K, FESSLER LI, STELLER H
Title: PROGRAMMED CELL-DEATH DURING DROSOPHILA EMBRYOGENES
Source: DEVELOPMENT 117: (1) 29-43 JAN 1993



6. Mark records and submit them to the marked list.



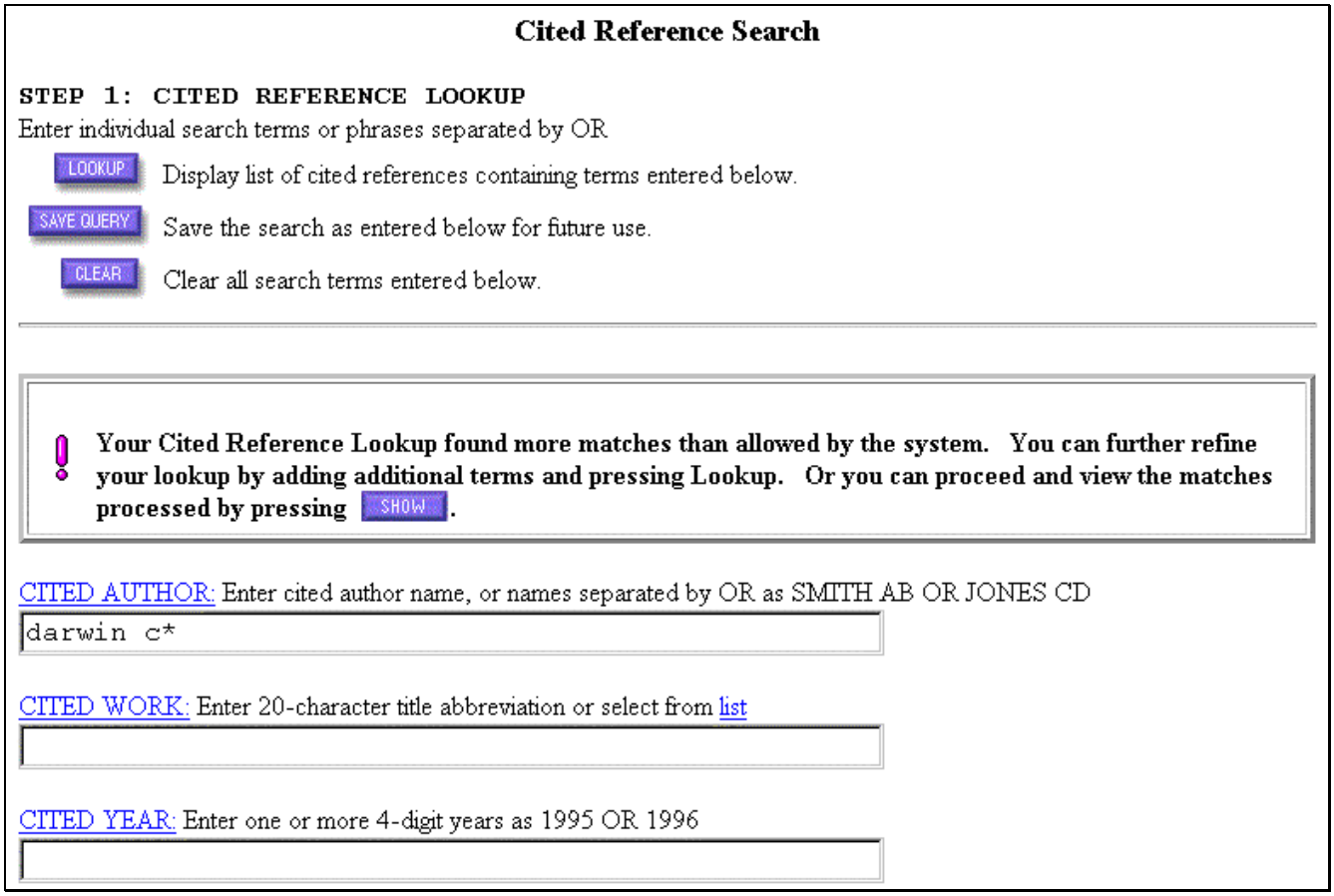
Repeat steps 4 and 5 for each first named co-author.

7. View your Marked List. Select a sort option and specify the fields you want to include, then print or save results.

Author(s):	Isumi H; Uchida Y; Hayashi T; Furukawa S; Takashima S
Title:	Neuron death and glial response in pontosubicular necrosis. The role of the growth inhibitory factor
Source:	CLINICAL NEUROPATHOLOGY 2000, Vol 19, Iss 2, pp 77-84
No. cited references:	26
Abstract:	Aim and methods: Fluorochrome and immunohistochemical studies were performed on neonates with pontosubicular necrosis (PSN), aged 26 - 42 weeks of gestation (GW), compared with preterm and term controls aged from 10 GW to 3 months of age. Results: A fluorochrome study using a confocal microscope revealed that nuclear DNA changes occurred earlier than cytoplasm degeneration with diminished RNA orange-red fluorescence. These changes were restricted to the small immature neurons in the pens and subiculum with PSN. On the other hand, although glial fibrillary acidic protein-positive reactive astrocytes were not increased in number, growth inhibitory factor-(GIF) immunoreactive glia with vesicular large nuclei were increased in number within the gray matter of the pens, subiculum, and cerebral cortex in the PSN group. The nuclei of GIF-containing astrocytes became round and vesicular, nearly twice in size and increased in number. Thus, the neuronal death began at the nuclei of selective neurons in specific areas in PSN, although GIF-containing astrocytes were increased in widespread areas. Conclusion: These facts suggest that immature neurons in the pontine nuclei and subiculum are selectively vulnerable to some insults such as hypocarbia and hyper-oxygenation, and PSN involves a possible apoptotic neuron death mechanism and a characteristic glial response.
Cited references:	ABRAMS JM-1993-DEVELOPMENT-V117-P29 AHDABBARMADA M-1980-PEDIATRICS-V66-P840 ANEZAKI T-1995-NEUROCHEM-INT-V271-P89 ARAI Y-1996-ACTA-NEUROPATHOL-V91-P396 BRUCK Y-1996-NEUROPATH-APPL-NEURO-V22-P23 CATHALA G-1983-DNA-J-MOLEC-CELL-BIO-V2-P329 FRIEDE RL-1972-ARCH-PATHOL-V94-P343 HASHIMOTO K-1991-BRAIN-DEV-JPN-V13-P155 KAGI JHR-1987-EXPERIENTIA-S-V52-P25 MITO T-1993-NEUROPEDIATRICS-V24-P204 MITO T-1985-NIHON-SHINSEIJI-GAKK-V21-P829 OOTSUKA N-UNPUB OZAWA H-1995-BRAIN-DEV-JPN-V17-P20 PALMITER RD-1992-P-NATL-ACAD-SCI-USA-V89-P6333 ROESSMANN U-1986-ACTA-NEUROPATHOL-V70-P302 ROTHSTEIN JD-1994-P-NATL-ACAD-SCI-USA-V91-P4155 SARNAT HB-1989-REV-NEUROL-V145-P127 SKULLERUD K-1986-ACTA-NEUROPATHOL-V70-P257 SOHMA O-1995-ACTA-NEUROPATHOL-BER-V90-P70 TAKASHIMA S-1990-P-11-INT-C-NEUR-P439 TOPALOGLU H-1989-ANAT-REC-V224-P88 TSUJI S-1992-EMBO-J-V13-P4843 UCHIDA Y-1988-BIOCHEM-BIOPH-RES-CO-V150-P1263 UCHIDA Y-1989-BRAIN-RES-V481-P190 UCHIDA Y-1991-NEURON-V7-P337 YAMADA M-1996-BRAIN-RES-V735-P257
Source item page count:	8
Publication Date:	MAR-APR
IDS No.:	295CU
29-char source abbrev:	CLIN NEUROPATHOL

MORE THAN FIVE HUNDRED CITED REFERENCES

If a Cited Reference Lookup retrieves more than 500 references you will receive a notice to refine the search.



Refine your search or click SHOW to view the references processed.

To refine a search either enter a value in more than one of the components of a cited reference or restrict your search to fewer data years at the outset.

SUMMARY OF CITED REFERENCE SEARCHING

ISI processes most formal cited references.

Only the *first* listed author of a cited reference is keyed.

Secondary cited authors can be searched if the document occurs as a source record in the loaded databases.

Variations of the same Cited References may appear in the databases.

There will be a hot link between a cited reference and its corresponding source record if the article referenced was covered by ISI, and if the source record is included in the loaded databases.

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SEARCH RESULTS

SEARCH RESULTS

The system returns a search summary of ten bibliographic records at a time.

Each title is linked to its Full Source Record.

Performing a Related Records search will replace the search results list.

To return to your original search results, click 

.

TOPIC: (mars or martian) same meteorit*

General Search Results--Summary

Topic=(mars or martian) same meteorit*; DocType=All document types; Language=All languages;
Databases=SCI-EXPANDED, SSCI, A&HCI; Timespan=All Years; (sorted by latest date)

Page 1 (Articles 1 -- 10): MARK ALL SUBMIT

[1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10]

☐ Farquhar J, Thiemens MH, Jackson T
Atmosphere-surface interactions on Mars: Delta O-17 measurements of carbonate from ALH 84001
SCIENCE 280: (5369) 1580-1582 JUN 5 1998

☑ McDonald GD, de Vanssay E, Buckley JR
Oxidation of organic macromolecules by hydrogen peroxide: Implications for stability of biomarkers on Mars
ICARUS 132: (1) 170-175 MAR 1998

☐ Spohn T, Sohl F, Breuer D
Mars
ASTRON ASTROPHYS REV 8: (3) 181-235 MAR 1998

☐ Posfai M, Buseck PR, Bazylinski DA, et al.
Reaction sequence of iron sulfide minerals in bacteria and their use as biomarkers
SCIENCE 280: (5365) 880-883 MAY 8 1998

☐ Taylor S, Lever JH, Harvey RP
Accretion rate of cosmic spherules measured at the South Pole
NATURE 392: (6679) 899-903 APR 30 1998

• • •

Page 1 (Articles 1 -- 10): MARK ALL SUBMIT

[1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10]

239 of 20936102 documents matched the query.

MARKING RECORDS

You can mark articles while viewing the Search Results - Summary or the Full Record.

From Search Results - Summary:

1. **Click the checkbox(es) to the left of each record to select individual records or click** 

to select the 10 records displayed.

2. **You must submit the selected records to the marked list by clicking** 

or the navigation buttons  .

From Search Results - Full Record display:

Click the MARK button to add the displayed record to the marked list.

The MARK button will toggle to an UNMARK button. To remove the displayed record from the marked list, click the UNMARK button.

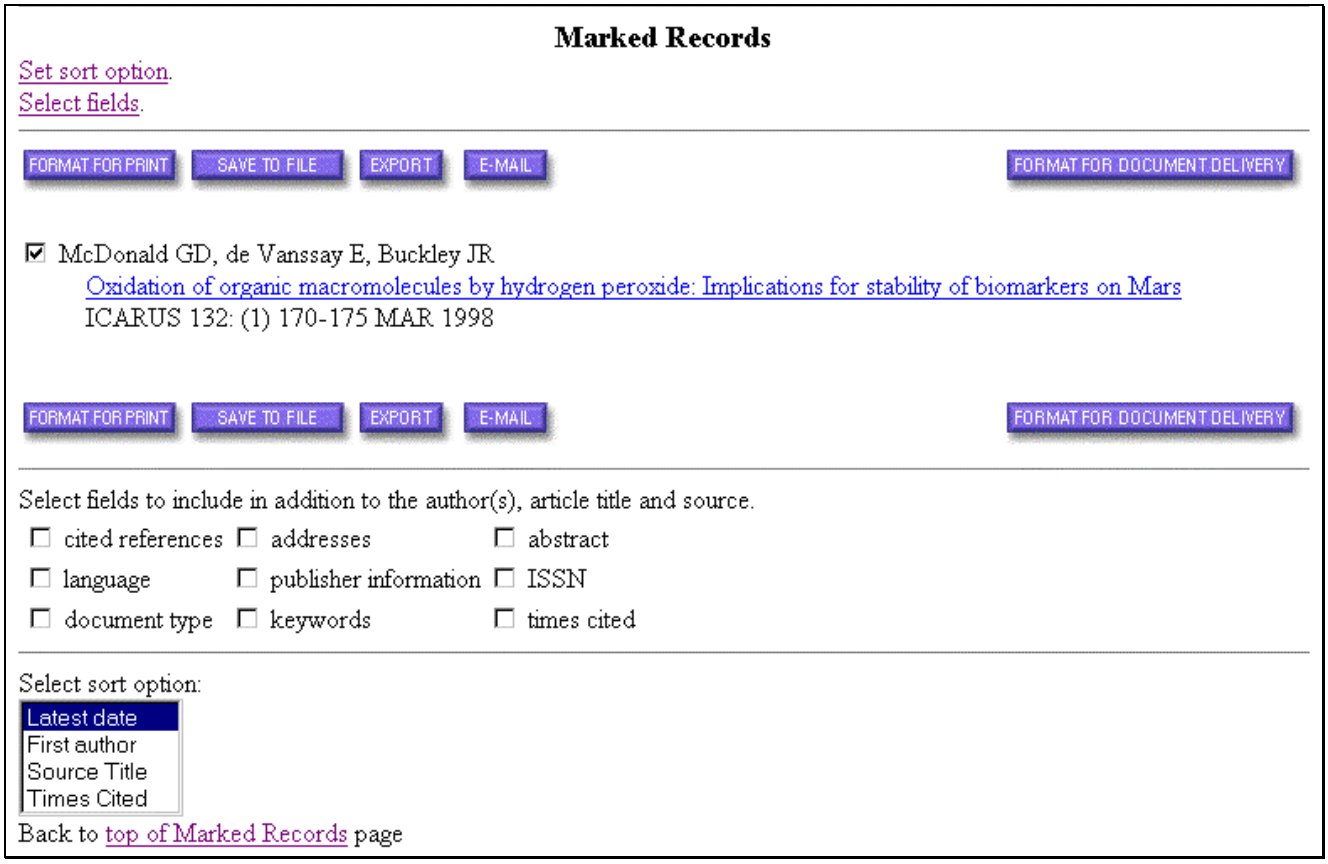
Note: If a record has been marked and then the Web browser's BACK button is clicked, the record reappears unmarked. This is a function of the browser only— the record is still marked.

When at least one record has been marked, the MARKED LIST button will become active.

MARKED LIST

Click the MARKED LIST button to:

- **Format records to print**
- **Save records to file**
- **Export records directly to ProCite or Reference Manager**
- **E-mail records with a note to a specified e-mail address**
- **Format records for document delivery requests**



To add fields other than the author(s), article title, and source fields to your output, click the desired fields' checkboxes.

Prior to exporting or printing, the records can be sorted by Latest Date, First Author, Source Title, or Times Cited.

PRINTING RECORDS

Using the Web browser's print option prints the graphics and text as they appear on the displayed Web page.

Instead, mark the articles of interest and view the Marked List. Then click FORMAT FOR PRINT. The records will be formatted in a plain text format with field labels.

Then use the print option in the Web browser to print the formatted records.

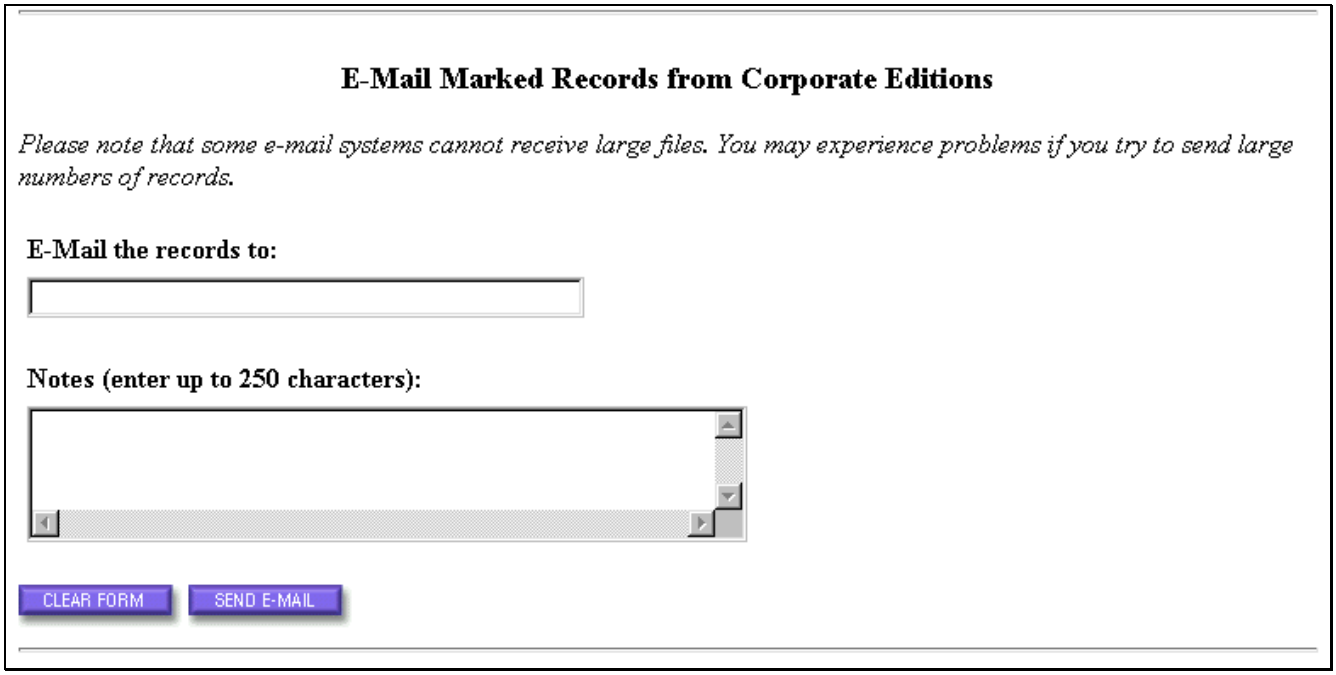
```
Record 1 of 1
Author(s):              McDonald GD; de Vanssay E; Buckley JR
Title:                  Oxidation of organic macromolecules by hydrogen
                        peroxide: Implications for stability of
                        biomarkers on Mars
Source:                 ICARUS 1998, Vol 132, Iss 1, pp 170-175
Document Type:          Article
Times Cited:            0
Source item page count: 6
Publication Date:       MAR
IDS No.:                ZP811
29-char source abbrev:  ICARUS

 ----------------------------------------------------------------------
```

E-MAILING RECORDS

From the Marked List, click to E-MAIL open an e-mail form in your browser.

Enter an e-mail address and a note to be included with your saved records. Then click SEND E-MAIL to send the saved records to the specified address.

Enter your name in the Notes field so that your receipient knows from whom the e-mail was sent.



ORDERING DOCUMENTS

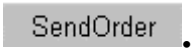
Your site's document delivery configuration, if enabled, will either:

- **Send requests to Electronic ISI Document Solution™ by e-mail**
- **Send requests to a designated e-mail address**
- **Link to a designated website**

ISI Document Solution™ (IDS) can provide tear sheet copies or photocopies of a desired article.

To order the full text of the article(s) from *ISI Document Solution* ™

1. **Click** 

on the Marked List page.
2. **Complete the Requester Information form.**
3. **Click** 

.

EXPORTING / SAVING RECORDS

1. **Click the MARKED LIST button to review records on your Marked List.**

2. **You may add fields other than the author(s), article title and source fields to your output by clicking the desired fields' checkboxes.**

3. **You may also sort records by Latest Date, First Author, Source Title, or Times Cited.**

4. **There are two options for saving / exporting records.**

To export records directly to ProCite or Reference Manager:

Click EXPORT. You must have ProCite or Reference Manager installed, along with the appropriate ISI/RIS Web Capture Utility. For instructions to download and install this utility, click the ISI/RIS Web Capture Utility hot link on the "Marked Records for Printing, Exporting, and Ordering" Help page.

To save records in an ISI tagged file format:

Click SAVE TO FILE. Specify a path and file name in the File / Save dialog box *e.g, File.txt.* A file will be saved containing the fields and records you specified, with fields identified by two-character tags. This format can be imported into a bibliographic management package.

SAVING AND RUNNING QUERIES

A General Search or Cited Reference Search query can be saved for later use.

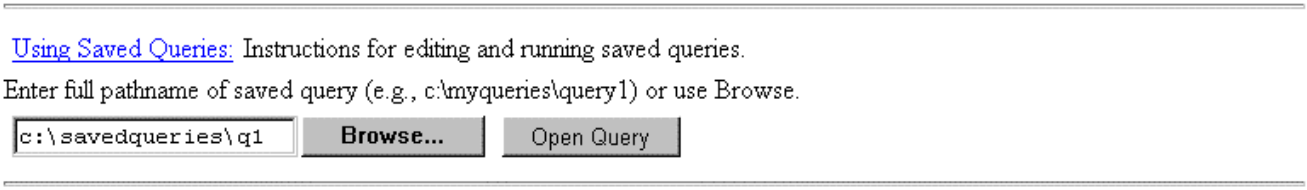
Queries can be saved either to the Client or to the Server depending on your site's configuration.

Only search parameters are saved, not the database and time span selections in effect at the time the query is saved. When run, this query runs against the current session's database and time span selections.

To Save a Query

1. **Enter your search query value(s) on the search screen.**
2. **Click** SAVE QUERY **.**
3. **Specify the file name with a *.htm or *.html extension. A Server save also requires a user name and password.**

To Run a Saved Query



1. **From the Full Search screen, you can enter the pathname for your saved query, or you can browse to select a saved query from your files.**
2. **When you have entered the pathname for the saved query, click OPEN QUERY to open the query in your browser.**
3. **Click the SEARCH or LOOKUP button to execute the search.**

SAVING CITED REFERENCE SEARCHES

Pressing the SAVE QUERY button in a Cited Reference Search will save the CITED AUTHOR, CITED WORK, and CITED YEAR entries.

It will NOT save the selections from the LOOKUP table.

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ISI 3501 Market Street Philadelphia, PA 19104 U.S.A.	Phone: 1-800-336-4474 ext. 1591 215-386-0100 ext. 1591 Fax: 215-386-6362 E-mail: help@isinet.com	Phone: 1-800-336-4474 ext. 1401 215-386-0100 ext. 1401 Fax: 215-386-6362 E-mail: educate@isinet.com
Latin America & Mexico 3501 Market Street Philadelphia, PA 19104 U.S.A.		
ISI Europe Brunel Science Park Uxbridge UB8 3PQ United Kingdom	Phone: +44-1895-270016 Fax: +44-1895-256710 E-mail: eurohelp@isinet.co.uk	Phone: +44-1895-270016 Fax: +44-1895-256710 E-mail: eurohelp@isinet.co.uk
ISI Japan Thompson Corporation K.K. Palaceside Building 5F 1-1-1 Hitotsubashi Chiyoda-ku Tokyo 100-0003 Japan	Phone: +81-3-5218-6530 Fax: +81-3-5218-6536 E-mail: jphelp@isinet.com	Phone: +81-3-5218-6530 Fax: +81-3-5222-1280 E-mail: jphelp@isinet.com
ISI Asia 60 Albert Street #15-01 Albert Complex Singapore 189969 Singapore	Phone: +65-338-7747 Fax: +65-338-9949 E-mail: asiahelp@isinet.com	Phone: +65-338-7747 Fax: +65-338-9949 E-mail: asiahelp@isinet.com

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