



**STN Workshops**

# Biotechnology Searching on STN

April 2002

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Printed in the USA

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## **At the end of this workshop, you will be able to**

- Identify relevant biotechnology files on STN
- Develop precise, yet comprehensive text-based search queries
- Use file-specific features, such as online thesauri, to develop search queries
- Use substance description based queries in REGISTRY and DGENE to complement the results of text-based queries

## **Before you begin**

This workshop is designed for searchers with a basic knowledge of STN search techniques.

*Prerequisite:* STN Basics, Introduction to Online Searching for Chemistry, or equivalent online experience

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# BIOTECHNOLOGY FILES

**In this section, you will learn**

- STN databases containing biotechnology information
- Unique database features and/or content

# Overview

Biotechnology is a rapidly growing sci-tech area, covering subjects such as

- Identifying, cloning, and expressing genes encoding important target proteins related to a disease or activity, and potential antibodies or ligands to these proteins
- Genetic polymorphism, including single nucleotide polymorphism (SNP) or haplotypes and the effect of this genetic variability on protein targets of candidate drugs
- Screening methods used to identify lead molecules for target proteins, enzymes, or receptors

# Biotechnology Databases on STN

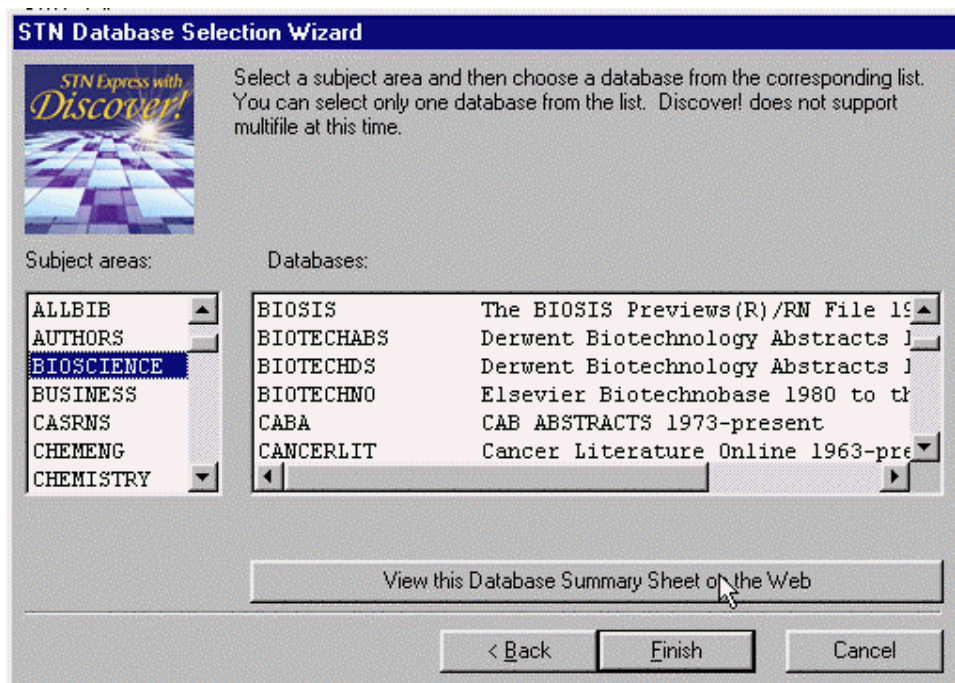
STN contains a wealth of information about biotechnology: Some files cover biotechnology exclusively, while others cover biotechnology aspects as they pertain to the subject matter of the file.

All files that cover some aspects of biotechnology are included in the “Bioscience” file cluster. The specific files may be displayed on STN using either

- A display command

```
=> D CLUSTER BIOSCIENCES
```

- The STN Database Selection wizard



# Substance-Based Biotechnology Files

Substance-based files may be searched directly or indirectly by sequences, e.g., a BLAST protein or nucleic acid search.

File	Sequence Content	Unique Features
REGISTRY	<ul style="list-style-type: none"><li>■ Nucleic acids</li><li>■ Proteins</li></ul>	<ul style="list-style-type: none"><li>■ CAS RNs</li><li>■ Sequence description and patent source in the Chemical Name field (/CN)</li><li>■ Note field (/NTE) describing modified or non-natural sequences</li></ul>
GENBANK	Nucleic acids	<ul style="list-style-type: none"><li>■ Referenced and unreferenced sequences</li><li>■ CAS RNs</li><li>■ CANs for referenced sequences in the Other Sources field (/OS)</li><li>■ Sequence identifying information (/CI, /ST, /ORGN, /FEAT)</li></ul>
DGENE	<ul style="list-style-type: none"><li>■ Nucleic acids</li><li>■ Proteins</li></ul>	<ul style="list-style-type: none"><li>■ Abstract text</li><li>■ Sequence identifying information (/DESC) and keywords (/KW)</li><li>■ Patent information (/BIB)</li></ul>

## Text-Based Biotechnology Files

File	Unique Features
CAplus	<ul style="list-style-type: none"><li>■ Currency – daily updates</li><li>■ Journal and patent sources</li><li>■ CA Lexicon</li><li>■ CAS RNs</li></ul>
BIOSIS	<ul style="list-style-type: none"><li>■ Meeting abstracts</li><li>■ Thesauri for Biosystematic codes, controlled terms, and organisms</li><li>■ Gene name field (/GEN)</li><li>■ CAS RNs</li></ul>
MEDLINE	<ul style="list-style-type: none"><li>■ MeSH thesaurus</li><li>■ OLDMEDLINE</li><li>■ CAS RNs</li></ul>
EMBASE	<ul style="list-style-type: none"><li>■ EMTREE thesaurus</li><li>■ International coverage</li><li>■ CAS RNs</li></ul>
BIOTECHABS	<ul style="list-style-type: none"><li>■ 30% of the file is patents</li><li>■ Controlled term thesaurus</li></ul>
BIOTECHNO	<ul style="list-style-type: none"><li>■ CAS RNs</li><li>■ Trade names</li></ul>

### *note*

→ The CAplus file is identical in content with the HCAplus file. For a query with many search terms, consider using HCAplus: Its charges are based on connect hour, with no search term charges.

# TEXT-BASED SEARCH STRATEGIES

**In this section, you will learn how to**

- Use STN system features to overcome the challenges in biotechnology text searches
- Develop search strategies using online thesauri
- Conduct a multiframe search using file-specific search strategies

# Biotechnology Search Challenges

In many ways, developing an effective biotechnology search strategy is similar to that for any other subject area. However, several challenges may greet the searcher; fortunately, each with potential solutions.

Challenge	Solution
Keeping current with a very active area of research	Files with frequent updates
Identifying terminology	<ul style="list-style-type: none"><li>■ Web based support sites</li><li>■ Online thesauri, including the CA Lexicon</li></ul>
Locating new disclosures	<ul style="list-style-type: none"><li>■ Patent-containing files</li><li>■ Value-added indexing to capture the science, disclosed in the language of the scientist</li><li>■ Online classification thesauri, international and U.S. patent classifications</li></ul>
Identifying relevant files	INDEX command to explore content of multiple files, including a cluster

# Identifying Useful Search Terms

There are a number of ways to identify useful search terms for text-based searches:

- STN search techniques
- Web resources

## STN Search Techniques

Search Technique	Results	Advantages
Free-text, "quick and dirty" search, followed by results review with D SCAN	<ul style="list-style-type: none"><li>■ Controlled terminology</li><li>■ Synonyms</li></ul>	<ul style="list-style-type: none"><li>■ Quick</li><li>■ No-cost display</li></ul>
EXPAND in CT field	<ul style="list-style-type: none"><li>■ Controlled terminology</li><li>■ Synonyms</li></ul>	Detailed exploration of database producer controlled terminology
ANALYZE CT or classification indexing, e.g. IC, NCL, MC	Highly posted classification indexing terms	Identifies unfamiliar terms

## Web Resources

Web resources are available to help identify the terminology of biotechnology:

- Glossary of genetic terms: <http://www.nhgri.nih.gov/DIR/VIP/Glossary/index.html> ✱
- Molecular biology learning tools and problem sets: [http://www.biology.arizona.edu/molecular\\_bio/molecular\\_bio.html](http://www.biology.arizona.edu/molecular_bio/molecular_bio.html) ✱
- Graphics gallery for biotechnology: <http://www.accessexcellence.org/AB/GG/> ✱
- Taxonomy: <http://www.ncbi.nlm.nih.gov/Taxonomy/taxonomyhome.html/> ✱
- Additional biotechnology links: <http://biochemlinks.com/bclinks/biotech.cfm> ✱

# Multifile Searching

For comprehensive searching it is usually necessary to search more than one file. Several features of the STN system facilitate multifile searching:

- A search may be run in multiple files at the same time
- A search may be run in separate files sequentially
- The query underlying an L-numbered answer set can usually be re-searched by searching that L-number directly
- An L-numbered answer set is always available even when switching to a different file

In many cases, sequential file searching provides greater flexibility in developing a relevant search strategy for each file. It is the approach taken here.

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***Search Question:**      What recent literature, including patents, describes the study of single nucleotide polymorphisms in potential genes associated with the predisposition, treatment, or complications of diabetes?*

---

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## **Background (see the patent WO200190128):**

Genetic variability within a population may explain why different patients react differently to drug regimens, or are susceptible to specific diseases. Subtle alterations in nucleotide sequences that encode a pharmaceutically significant protein may lead to a variation in expression, structure and/or the function of the protein. Drugs interacting with these proteins may exhibit differing efficacy, or pharmacodynamics.

If desired this search could be expanded to research on the ordered combination of polymorphisms in the various forms of the gene, known as a haplotypes.

## Important Search Concepts:

*Major concepts — must be present for relevance*

- SNP, or single nucleotide polymorphisms
- Genetic variation, variability or variants
- Diabetes

*Minor concepts — may be used for refinement*

Genes

## Search Strategy

To conduct a multfile biotech text-based search

- Step 1 Select relevant files.
- Step 2 Develop a search strategy in the primary file.
- Step 3 Search additional files using the same, or a modified, search strategy.
- Step 4 Remove duplicate records.
- Step 5 Display results.

## Step 1. Select relevant files

Files, in most cases, are selected on past search experience and search results. Lacking that experience initially, a cluster of files, e.g. BIOSCIENCES, can be searched. Since many clusters may include >20 files, the best approach is to use the INDEX command.

INDEX scans the selected files and determines how many answers would be retrieved from each of the files in the cluster, IF you actually entered that file to conduct the search.

```
=> INDEX BIOSCIENCE
```

```
INDEX 'ADISALERTS, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,  
      BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS,  
      BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI,  
      CROPB, CROPU, DDFB, DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG,...'
```

```
=> S SINGLE NUCLEOTIDE POLYMORPHISM
```

```
      1  FILE ADISALERTS  
     26  FILE AGRICOLA  
      8  FILE ANABSTR  
      2  FILE BIOBUSINESS  
     70  FILE BIOCOMMERCE  
    1152  FILE BIOSIS  
     107  FILE BIOTECHABS  
     107  FILE BIOTECHDS  
    1072  FILE BIOTECHNO  
      55  FILE CABA  
      69  FILE CANCERLIT  
    1014  FILE CAPLUS
```

```
●  
●  
●
```

```
42 FILES HAVE ONE OR MORE ANSWERS, 61 FILES SEARCHED IN STNINDEX
```

```
L1  QUE SINGLE NUCLEOTIDE POLYMORPHISM
```

```
=> D RANK
```

```
F1      435788  DGENE  
F2      2961   GENBANK  
F3      1271   EMBASE  
F4      1152   BIOSIS  
F5      1072   BIOTECHNO  
F6      1014   CAPLUS  
F7      695    SCISEARCH  
F8      486    MEDLINE  
F9      463    ESBIODASE  
F10     401    PROMT
```

```
●  
●  
●
```

---

## Helpful HINT

More information about the INDEX command, and all STN commands, is available at:

<http://www.cas.org/training/stncommands/stncommands.html> 

---

### Step 2. Develop a search strategy in the primary file

Most strategies are developed using an iterative search → evaluate → modify approach, until a good balance of precision and recall is achieved.

*Conduct a “quick and dirty” search in HCAplus:*

```
=> FILE HCAPLUS

=> SET ABBREV ON PERM

=> SET PLURALS ON PERM

=> S SINGLE NUCLEOTIDE POLYMORPHISM AND DIABETES

    973074 SINGLE
      2407 SINGLES
    975132 SINGLE
          (SINGLE OR SINGLES)
    279110 NUCLEOTIDE
      98096 NUCLEOTIDES
    327203 NUCLEOTIDE
          (NUCLEOTIDE OR NUCLEOTIDES)
      71591 POLYMORPHISM
      17106 POLYMORPHISMS
      75330 POLYMORPHISM
          (POLYMORPHISM OR POLYMORPHISMS)
      1962 SINGLE NUCLEOTIDE POLYMORPHISM
          (SINGLE(W)NUCLEOTIDE(W)POLYMORPHISM)
      67626 DIABETES
L1      100 SINGLE NUCLEOTIDE POLYMORPHISM AND DIABETES
```

**Identify additional terminology using the no-cost display:**

=> D SCAN

L1 100 ANSWERS HCAPLUS COPYRIGHT 2002 ACS  
CC 14-8 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 3  
TI Mutation screening of the hepatocyte nuclear factor (HNF)-6 gene in Japanese subjects with **diabetes** mellitus  
ST hepatocyte nuclear factor 6 gene mutation **diabetes** Japan  
IT Gene, animal  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(HNF-6-encoding; mutation screening of hepatocyte nuclear factor gene in Japanese subjects with **diabetes** mellitus)  
IT **Diabetes** mellitus  
(MODY (maturity-onset **diabetes** of the young); mutation screening of hepatocyte nuclear factor gene in Japanese subjects with **diabetes** mellitus)  
IT Transcription factors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(hepatocyte nuclear factors, 6; mutation screening of hepatocyte nuclear factor gene in Japanese subjects with **diabetes** mellitus)  
IT Human  
Human groups  
Population genetics  
Susceptibility (genetic)  
(mutation screening of hepatocyte nuclear factor gene in Japanese subjects with **diabetes** mellitus)  
IT Genetic polymorphism  
(single nucleotide; mutation screening of hepatocyte nuclear factor gene in Japanese subjects with **diabetes** mellitus)

Note CAS indexing:

- Gene, animal
- Genetic polymorphism linked to single nucleotide

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L1 100 ANSWERS HCAPLUS COPYRIGHT 2002 ACS  
CC 14-8 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 2, 3  
TI Genetic variation in aldosterone synthase predicts plasma glucose levels  
ST genetic variation aldosterone synthase plasma glucose diabetic  
IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(CYP11B2; genetic variation in aldosterone synthase predicts fasting plasma glucose levels in population of Chinese and Japanese origin in relation to **diabetes**)  
IT Human groups  
(Chinese; genetic variation in aldosterone synthase predicts fasting plasma glucose levels in population of Chinese and Japanese origin in relation to diabetes)

Note the free-text "genetic variation" terminology.

- 
- 
-

**Explore terms in the CA Lexicon:**

Having seen additional possible search terms and controlled terminology indexing, several of these terms may be explored in the CA Lexicon for further leads. The CA Lexicon is a thesaurus of controlled indexing terms used in the CA files. The CA Lexicon is accessed in the Controlled Term (/CT) field.

If you wish to...	Enter this command:
Determine if a term is a controlled indexing term	=> <b>E TERM/CT</b>
Explore all hierarchical entries for a valid term	=> <b>E TERM+ALL/CT</b> or => <b>E E-number+ALL</b> (+ALL is one of many Relationship Codes available)
Search a term and its older, newer, or "use for" terms	=> <b>S E-number+PFT</b>
Search a term and its narrower terms in the hierarchy	=> <b>S E-number+NT</b>

```

=> SET EXPAND CONTINOUS PERM

=> E SINGLE NUCLEOTIDE POLYMORPHISM/CT

```

E#	FREQUENCY	AT	TERM
E1	0	2	SINGLE MOLECULE ANALYSIS/CT
E2	26	4	SINGLE MOLECULE DETECTION/CT
E3	0	2	--> SINGLE NUCLEOTIDE POLYMORPHISM/CT
E4	0	2	SINGLE RADIAL IMMUNODIFFU
E5	0	2	SINGLE RADIAL IMMUNODIFFU
E6	0	2	SINGLE RADIAL IMMUNODIFFU
E7	0	2	SINGLE RADIAL IMMUNODIFFU
E8	469	2	ANALYSIS/CT
E9	0	2	SINGLE STRANDED DNA/CT
E10	0	1	SINGLE STRANDED DNA BINDING PROTEIN SSB/CT
E11	0	1	SINGLE-BASE/CT
E12	0	2	SINGLE-BASE PROPELLANTS/CT
E13	0	1	SINGLE-BATH/CT

```

=> E E3+ALL

E13      0      -->  Single nucleotide polymorphism/CT
E14      0      USE   Genetic polymorphism (L) single nucleotide/CT
*****  END  *****

```

*The AT column indicates the number of Associated Terms in the thesaurus.*

*"Single nucleotide polymorphism" is not a valid CT. However, an entry is available in the Lexicon.*

*E14 may be used directly as a search term.*

**note**

If this search were to be broadened to include the “haplotype” concept, the CA Lexicon can again be used to explore possible additional terms:

**=> E HAPLOTYPES/CT**

E#	FREQUENCY	AT	TERM
--	-----	--	----
E15	1	7	HAPLOTROPIS
E16	0	2	HAPLOTYPE/CT
E17	2184	12	--> HAPLOTYPES/CT

*“Haplotypes” is a valid entry. However, the AT column indicates additional terms may be of interest, in this case, narrower terms.*

**=> E E17+ALL**

E27	9744	BT1	Genotypes/CT
E28	2184	-->	Haplotypes/CT
	HN		Valid heading during volume 126 (1997) to present.
E29		UF	Haplotype/CT
E30		NT1	Antigens (L) H-2D/CT
E31		NT1	Antigens (L) H-2K/CT
E32		NT1	Antigens (L) H-2a/CT
E33		NT1	Antigens (L) H-2b/CT
E34		NT1	Antigens (L) H-2q/CT
E35		NT1	Histocompatibility antigens (L) H-2a/CT
E36		NT1	Histocompatibility antigens (L) H-2b/CT
E37		NT1	Histocompatibility antigens (L) H-2q/CT
E38		NT1	Histocompatibility antigens (L) H-2s/CT
***** END *****			

**=> S HAPLOTYPES+NT/CT (OR => S E28+NT)**

**=> E GENE, ANIMAL/CT**

E#	FREQUENCY	AT	TERM
--	-----	--	----
E124	0	2	GENE ZFY PROTEINS/CT
E125	0	2	GENE ZIF/268 PROTEINS/CT
E126	154304	547	--> GENE, ANIMAL/CT
E127	0	7	GENE, ANIMAL (L) .ALPHA./
E128	0	5	GENE, ANIMAL (L) 1/CT
E129	0	5	GENE, ANIMAL (L) 2/CT
E130	0	6	GENE, ANIMAL (L) A/CT
E131	0	7	GENE, ANIMAL (L) A-MYB/CT
E132	0	8	GENE, ANIMAL (L) ABDOMINAL-A/CT
E133	0	7	GENE, ANIMAL (L) ABDOMINAL-B/CT
E134	0	6	GENE, ANIMAL (L) ABO/CT
E135	0	6	GENE, ANIMAL (L) ACE/CT

*“Gene, animal” is a valid controlled term, with hundreds of associated terms. In this case most are to specific genes, indexed as “Gene, animal” linked to the specific gene designation.*

From the free-text observed in the titles and indexing (D SCAN) and controlled terms identified in the CA Lexicon, a search query can be developed for a comprehensive, yet reasonably precise answer set.

***Search the refined query:***

```
=> S E14 OR SNP OR SINGLE NUCLEOTIDE POLYMORPHISM OR GENETIC VARIA?

    33124 GENETIC POLYMORPHISM/CT
    113814 SINGLE/IT
        114 SINGLES/IT
    113916 SINGLE/IT
            ((SINGLE OR SINGLES)/IT)
    194423 NUCLEOTIDE/IT
    48458 NUCLEOTIDES/IT
    230882 NUCLEOTIDE/IT
            ((NUCLEOTIDE OR NUCLEOTIDES)/IT)
    1484 "GENETIC POLYMORPHISM (L) SINGLE NUCLEOTIDE"/CT
    3365 SNP
    876 SNPS
    3772 SNP
            (SNP OR SNPS)
    973074 SINGLE
    2407 SINGLES
    975132 SINGLE
            (SINGLE OR SINGLES)
    279110 NUCLEOTIDE
    98096 NUCLEOTIDES
    327203 NUCLEOTIDE
            (NUCLEOTIDE OR NUCLEOTIDES)
    71591 POLYMORPHISM
    17106 POLYMORPHISMS
    75330 POLYMORPHISM
            (POLYMORPHISM OR POLYMORPHISMS)
    1962 SINGLE NUCLEOTIDE POLYMORPHISM
            (SINGLE(W)NUCLEOTIDE(W)POLYMORPHISM)
    486867 GENETIC
    71309 GENETICS
    518835 GENETIC
            (GENETIC OR GENETICS)
    863535 VARIA?
    10269 GENETIC VARIA?
            (GENETIC(W)VARIA?)
L2    15119 "GENETIC POLYMORPHISM (L) SINGLE NUCLEOTIDE"/CT OR SNP OR
        SINGLE NUCLEOTIDE POLYMORPHISM OR GENETIC VARIA?

=> S DIABETES

L3    67626 DIABETES

=> S L2 AND L3

L4    349 L2 AND L3

=> S L4 AND PY>1999

    2057503 PY>1999
L5    197 L4 AND PY>1999
```

*Recall that E14 represents the controlled term for single nucleotide polymorphism.*

*The final query utilizes both free-text and controlled indexing.*

---

## Helpful HINT

HCAplus is updated daily with new records. Indexing for these records may not be available initially. The combination of a controlled indexing query and free-text query assures retrieval of both indexed and newly added records to the HCAplus file.

---

When conducting a search with many text terms, it may be advantageous to rearrange the answers into relevance order. On STN the FOCUS command uses sophisticated algorithms based on search term occurrence, proximity, and fields.

*Use FOCUS to place most relevant answers first:*

=> D TI 1-5

L5 ANSWER 1 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
TI Endothelin-1 promoter polymorphism

*Compare the titles of the first 5 records before and after using the FOCUS command.*

L5 ANSWER 2 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
TI Variations in insulin secretion in carriers of gene variants in IRS-1 and -2

L5 ANSWER 3 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
TI KIR6.2 polymorphism predisposes to type 2 **diabetes** by inducing overactivity of pancreatic  $\beta$ -cell ATP-sensitive K<sup>+</sup> channels

L5 ANSWER 4 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
TI Systematic search for **single nucleotide polymorphisms** in the resistin gene: the absence of evidence for the association of three identified **single nucleotide polymorphisms** with Japanese type 2 **diabetes**

L5 ANSWER 5 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
TI Human resistin gene, obesity, and type 2 **diabetes**: mutation analysis and population study

=> FOCUS L5

PROCESSING COMPLETED FOR L5  
L6 197 FOCUS L5 1-

=> D TI 1-5

L6 ANSWER 1 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
TI Isolation and characterization of the human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and their lack of association with Type II **diabetes**

*(continued on next page)*

L6 ANSWER 2 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
TI Systematic search for **single nucleotide polymorphisms** in the resistin gene: the absence of evidence for the association of three identified **single nucleotide polymorphisms** with Japanese type 2 **diabetes**

L6 ANSWER 3 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
TI Detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases

L6 ANSWER 4 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
TI Detection of **single nucleotide polymorphisms** of the TGF- $\beta$ 1 promoter and uses in prediction of genetic susceptibility to diseases

L6 ANSWER 5 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
TI Genetics of platelet receptor **single-nucleotide polymorphisms**: clinical implications in thrombosis

=> D IBIB ABS HITIND 1-3

L6 ANSWER 1 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:467865 HCAPLUS [Full-text](#)  
DOCUMENT NUMBER: 136:181742  
TITLE: Isolation and characterization of the human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and their lack of association with Type II **diabetes**  
AUTHOR(S): Matsubara, A.; Wasson, J. C.; Donelan, S. S.; Welling, C. M.; Glaser, B.; Permutt, M. A.  
CORPORATE SOURCE: Division of Metabolism, Endocrinology and Diabetes, Washington University School of Medicine, St. Louis, MO, USA  
SOURCE: Diabetologia (2001), 44(7), 910-913  
CODEN: DBTGJ; ISSN: 0012-186X  
PUBLISHER: Springer-Verlag  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Aims/hypothesis. AKT1, a serine/threonine protein kinase, is an important downstream target of the insulin-signaling pathway, with both anti-apoptotic and peripheral metabolic effects. Because impaired insulin signaling is a major hallmark of Type II (non-insulin-dependent) **diabetes** mellitus, the authors considered whether the AKT1 gene could be a candidate gene involved in susceptibility of this condition. To test this possibility, the authors isolated and characterized the human AKT1 gene. The authors also looked for **single nucleotide polymorphisms** in the gene and examined their association with Type II **diabetes** mellitus in the Ashkenazi Jewish population. Methods. Human BAC/Pl genomic libraries were screened to isolate the AKT1 gene. To obtain structural information and the sequences of the exon-intron boundaries, BAC/Pl clones were directly sequenced. Identification of **single nucleotide polymorphisms** was done by polymerase chain reaction of each exon, followed by denaturing high performance liquid chromatog. Six **single nucleotide**

(continued on next page)

**polymorphisms** were genotyped in Ashkenazi Jewish patients with Type II **diabetes** mellitus and in control subjects. Results. The human AKT1 gene was at least 24.6 kb in length and comprised 14 exons. Altogether 13 putative intragenic **single nucleotide polymorphisms**, with minor-allele frequencies ranging from 0.011 to 0.354, were identified. The allelic and the genotypic frequencies of 6 **single nucleotide polymorphisms** were the same in diabetic patients and in control subjects. Conclusion/interpretation. The results of the authors' studies show that the AKT1 gene is not a major contributor to susceptibility to Type II **diabetes** mellitus in Ashkenazi Jews.

CC 14-8 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 3, 7, 13

ST AKT1 gene sequence human polymorphism type II **diabetes**; **single nucleotide polymorphism** AKT1 gene type II **diabetes**

IT Gene, animal  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(AKT1; isolation and characterization of human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and lack of association with type II **diabetes** in Ashkenazi Jewish population)

IT Human groups  
(Ashkenazi Jewish; isolation and characterization of human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and lack of association with type II **diabetes** in Ashkenazi Jewish population)


IT Genetic element  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(exon; isolation and characterization of human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and lack of association with type II **diabetes** in Ashkenazi Jewish population)

IT Genetic element  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(intron; isolation and characterization of human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and lack of association with type II **diabetes** in Ashkenazi Jewish population)

IT Allele frequency  
DNA sequences  
Genotypes  
Human  
Population genetics  
Protein sequences  
Susceptibility (genetic)  
(isolation and characterization of human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and lack of association with type II **diabetes** in Ashkenazi Jewish population)

IT **Diabetes** mellitus  
(non-insulin-dependent; isolation and characterization of human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and lack of association with type II **diabetes** in Ashkenazi Jewish population)

*(continued on next page)*

IT **Genetic polymorphism**  Controlled term indexing.  
 (single nucleotide; isolation and characterization of human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and lack of association with type II **diabetes** in Ashkenazi Jewish population)

IT 399106-12-8  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (amino acid sequence; isolation and characterization of human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and lack of association with type II **diabetes** in Ashkenazi Jewish population)

IT 148640-14-6, Protein kinase Akt  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (isolation and characterization of human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and lack of association with type II **diabetes** in Ashkenazi Jewish population)

IT 381882-29-7, GenBank AF283818 381882-30-0, GenBank AF283819  
 381882-31-1, GenBank AF283820 381882-32-2, GenBank AF283821  
 381882-33-3, GenBank AF283822 381882-34-4, GenBank AF283823  
 381882-35-5, GenBank AF283824 381882-36-6, GenBank AF283825  
 381882-37-7, GenBank AF283826 381882-38-8, GenBank AF283827  
 381882-39-9, GenBank AF283828 381882-40-2, GenBank AF283829  
 381882-41-3, GenBank AF283830  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (nucleotide sequence; isolation and characterization of human AKT1 gene, identification of 13 **single nucleotide polymorphisms (SNPs)**, and lack of association with type II **diabetes** in Ashkenazi Jewish population)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 197 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:210348 HCAPLUS [Full-text](#)  
 TITLE: Systematic search for **single nucleotide polymorphisms** in the resistin gene: the absence of evidence for the association of three identified **single nucleotide polymorphisms** with Japanese type 2 **diabetes**

AUTHOR(S): Osawa, Haruhiko; Onuma, Hiroshi; Murakami, Akiko; Ochi, Masaaki; Nishimiya, Tatsuya; Kato, Kenichi; Shimizu, Ikki; Fujii, Yasuhisa; Ohashi, Jun; Makino, Hideichi

CORPORATE SOURCE: Department of Laboratory Medicine, Ehime University  
 School of Medicine, Ehime University

SOURCE: Diabetes (2002), 51(3) Note that indexing is not yet available for this record. It was retrieved with the free-text query.  
 CODEN: DIAEAZ; ISSN: 0012-186X

PUBLISHER: American Diabetes Association

DOCUMENT TYPE: Journal

LANGUAGE: English

(continued on next page)

AB Resistin is a novel polypeptide specifically secreted from adipocytes, and its serum levels are increased in obese diabetic mice. Resistin antagonizes insulin and could account for insulin resistance. To determine whether there are **single nucleotide polymorphisms (SNPs)** in the resistin gene associated with type 2 **diabetes**, sequences for 24 Japanese type 2 diabetic patients were initially analyzed using PCR direct sequencing. Three **SNPs** were found in the introns, but none were present in the coding regions. The allele frequencies of genomic -167C>T, +157C>T, and +299G>A in 99 Japanese control subjects were determined to be 3.5, 6.6, and 39.4%, resp. In each pair of these **SNPs**, linkage disequil. were found between either -167C>T and +299G>A or +157C>T and +299G>A. A linkage disequil. was also detected among -167C>T, +157C>T, and +299G>A, and only four of the eight possible haplotypes defined by these **SNPs** were found. A comparison of the frequencies of these **SNPs** and haplotypes between 99 type 2 **diabetes** and 99 control subjects revealed no evidence for any association. These identified **SNPs**, which were in linkage disequil., represent potentially useful tools for searching for their association with specific phenotypes of **diabetes**.

CC 14 (Mammalian Pathological Biochemistry)

L6 ANSWER 3 OF 197 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:123275 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 136:162394

TITLE: Detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases

INVENTOR(S): Moskowitz, David W.

PATENT ASSIGNEE(S): Dzgenes, LLC, USA

SOURCE: PCT Int. Appl., 79 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

*A fully indexed Feb 14 patent publication.*

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012567	A1	20020214	WO 2001-US24985	20010809 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2000-224084P P 20000809

AB The invention discloses the **single nucleotide polymorphisms (SNPs)** at positions 520 and 638 on the human von Hippel-Lindau syndrome tumor suppressor gene promoter and detection of individuals at risk

*(continued on next page)*

for pathol. conditions based on the **SNPs**. In particular, the invention discloses that a **single nucleotide polymorphism (SNP)** associated with colon cancer, hypertension, atherosclerotic peripheral vascular disease due to hypertension, cerebrovascular accident due to hypertension, cataracts due to hypertension, hypertensive cardiomyopathy, myocardial infarction due to hypertension, end stage renal disease due to hypertension, non-insulin dependent **diabetes** mellitus, atherosclerotic peripheral vascular disease due to non-insulin dependent **diabetes** mellitus, cerebrovascular accident due to non-insulin dependent **diabetes** mellitus, ischemic cardiomyopathy, ischemic cardiomyopathy with non-insulin dependent **diabetes** mellitus, myocardial infarction due to non-insulin dependent **diabetes** mellitus, atrial fibrillation without valvular disease, alc. abuse, alc. cirrhosis, anxiety, asthma, chronic obstructive pulmonary disease, cholecystectomy, degenerative joint disease, end stage renal disease and frequent de-clots, end stage renal disease due to focal segmental glomerular sclerosis, end stage renal disease due to insulin dependent **diabetes** mellitus, end stage renal disease due to non-insulin dependent **diabetes** mellitus, and seizure disorder. The invention also discloses methods for using the **SNP** to determine susceptibility to these diseases; nucleotide sequences containing the **SNP**; kits for determining the presence of the **SNP**; and methods of treatment or prophylaxis based on the presence of the **SNP**.

- IC ICM C12Q001-68
- ICS C07H021-02
- CC 3-3 (Biochemical Genetics)
- Section cross-reference(s): 1, 14
- ST **single nucleotide polymorphism** human vHL  
gene promoter diagnosis; von Hippel Lindau syndrome tumor suppressor  
gene promoter polymorphism
- IT Cirrhosis  
(alc.; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)
- IT PCR (polymerase chain reaction)  
(allele specific; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)
- IT Fluorescent substances  
(as label; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)
- IT Antibodies
- Antigens
- Enzymes, biological studies
- Peptides, biological studies
- Radionuclides
- Steroids, biological studies
- Vitamins

*(continued on next page)*

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(as label; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)



- IT **Diabetes** mellitus  
(insulin-dependent; **single nucleotide polymorphisms** of the vHL gene promoter and uses in diagnosis of diseases)
- IT DNA sequence analysis  
(mini; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)
- IT **Diabetes** mellitus  
(non-insulin-dependent; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)
- IT DNA sequences  
(of gene vHL promoter of human; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)
- IT Atherosclerosis  
(of peripheral vascular disease due to hypertension or non-insulin dependent **diabetes** mellitus; **single nucleotide polymorphisms** of the vHL gene promoter and uses in diagnosis of diseases)
- IT Promoter (genetic element)  
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(of von Hippel-Lindau syndrome tumor suppressor gene; **single nucleotide polymorphisms** of the vHL gene promoter and uses in diagnosis of diseases)
- IT Genetic methods  
(oligonucleotide ligation anal.; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)
- IT Blood vessel, disease  
(peripheral, due to hypertension or **diabetes** mellitus type II; **single nucleotide polymorphisms** of the vHL gene promoter and uses in diagnosis of diseases)
- IT Genetic methods  
(restriction fragment anal.; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)

(continued on next page)

IT **Genetic polymorphism**  
 (**single nucleotide**; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)

IT Brain, disease  
 (stroke, due to hypertension or **diabetes** mellitus type II; **single nucleotide polymorphisms** of the vHL gene promoter and uses in diagnosis of diseases)

IT 37332-03-9, Fluorochrome  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (as label; detection of **single nucleotide polymorphisms** of the TGF- $\beta$ 1 promoter and uses in prediction of genetic susceptibility to diseases)

IT 395912-99-9  
 RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (nucleotide sequence; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)

IT 395915-41-0 395915-42-1 395915-43-2 395915-44-3 395915-45-4  
 395915-46-5 395915-47-6 395915-48-7  
 RL: PRP (Properties)  
 (unclaimed nucleotide sequence; detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

### Step 3. Search additional files

Terms identified from the primary file may be searched in additional files; however, the controlled terminology will most likely require modification, based on individual database producer indexing systems.

A search strategy, represented by an L-number, may be reused in any additional files when appropriate.

#### *Extend the search in BIOSIS:*

=> FILE BIOSIS			
=> E SINGLE NUCLEOTIDE POLYMORPHISM/CT			
E#	FREQUENCY	AT	TERM
--	-----	--	----
E39	2		SINGLE NUCLEOTIDE POLYMORPHIC MARKERS/CT
E40	1		SINGLE NUCLEOTIDE POLYMORPHIC SITES/CT
E41	211	-->	SINGLE NUCLEOTIDE POLYMORPHISM/CT
E42	4		SINGLE NUCLEOTIDE POLYMORPHISM (SNP)/CT
E43	1		SINGLE NUCLEOTIDE POLYMORPHISM 63/CT
E44	1		SINGLE NUCLEOTIDE POLYMORPHISM ALLELE RESOLUTION/CT
E45	1		SINGLE NUCLEOTIDE POLYMORPHISM ALLELES/CT
E46	1		SINGLE NUCLEOTIDE POLYMORPHISM ANALYSIS/CT
E47	1		SINGLE NUCLEOTIDE POLYMORPHISM CHIP/CT
E48	1		SINGLE NUCLEOTIDE POLYMORPHISM COMPARISONS/CT
E49	1		SINGLE NUCLEOTIDE POLYMORPHISM COSEGREGATION/CT
E50	1		SINGLE NUCLEOTIDE POLYMORPHISM DETECTION/CT

*Note: Many controlled indexing phrases start with “single nucleotide polymorphism”.*

---

## Helpful HINT

Recall that all individual words of the controlled term indexing (/CT) are part of the Basic Index (/BI). In this example, the free-text query for “single nucleotide polymorphism” will search both the indexing terms and text within the title and abstract.

BIOSIS now contains a field for gene names (/GEN) which is also part of the Basic Index. Its content will enhance this search.

---

**Conduct a free-text query in BIOSIS:**

```
=> S SNP OR SINGLE NUCLEOTIDE POLYMORPHISM OR GENETIC VARIA?

    3107 SNP
    755 SNPS
    3527 SNP
      (SNP OR SNPS)
    498870 SINGLE
    480 SINGLES
    499163 SINGLE
      (SINGLE OR SINGLES)
    178428 NUCLEOTIDE
    50677 NUCLEOTIDES
    208801 NUCLEOTIDE
      (NUCLEOTIDE OR NUCLEOTIDES)
    72805 POLYMORPHISM
    23321 POLYMORPHISMS
    84574 POLYMORPHISM
      (POLYMORPHISM OR POLYMORPHISMS)
    2031 SINGLE NUCLEOTIDE POLYMORPHISM
      (SINGLE(W)NUCLEOTIDE(W)POLYMORPHISM)
    399930 GENETIC
    891815 GENETICS
    1085299 GENETIC
      (GENETIC OR GENETICS)
    686324 VARIA?
    25802 GENETIC VARIA?
      (GENETIC(W)VARIA?)
L7    30135 SNP OR SINGLE NUCLEOTIDE POLYMORPHISM OR GENETIC VARIA?
```

**=> S DIABETES**

```
    135224 DIABETES
    1 DIABETESES
L8    135224 DIABETES
      (DIABETES OR DIABETESES)
```


**=> S L7 AND L8**

```
L9    385 L7 AND L8
```

**=> S L9 AND PY>1999**

```
    1090352 PY>1999
L10   197 L9 AND PY>1999
```

**=> D SCAN**

```
L10  197 ANSWERS BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI    Genetic variation in the matrix metalloproteinase 9
      gene, MMP9, in Type 2 diabetes patients with renal disease.
IT    Miscellaneous Descriptors
      Meeting Abstract; Meeting Poster 
```

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

*Coverage of meetings and conferences is a strength of BIOSIS.*

*(continued on next page)*

L10 197 ANSWERS BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
TI Association of calpain 10 genetic polymorphisms with type 2  
**diabetes** and insulin response in non-diabetic Chinese.  
IT Methods & Equipment  
HOMA-beta: evaluation method; OGTT [oral glucose tolerance test]:  
diagnostic method  
IT Miscellaneous Descriptors  
**SNP [single nucleotide  
polymorphism]**; allelic frequency; genotype; glucose tolerance;  
insulin response; risk assessment; Meeting Abstract; Meeting  
Poster

=> D IBIB ABS 1-2, 11

L10 ANSWER 1 OF 197 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2002:203582 BIOSIS [Full-text](#)  
DOCUMENT NUMBER: PREV200200203582  
TITLE: Mutation screening of the urocortin gene:  
Identification of new **single nucleotide  
polymorphisms** and association studies with obesity  
in French Caucasians.  
AUTHOR(S): Delplanque, J.; Vasseur, F.; Durand, E.;  
Abderrahmani, A.; Dina, C.; Waeber, G.; Guy-Grand,  
B.; Clement, K.; Weill, J.; Boutin, P.; Froguel, P.  
(1)  
CORPORATE SOURCE: (1) Centre National de la Recherche Scientifique  
8090, Institut Pasteur de Lille, 1 rue Calmette,  
F-59019, Lille Cedex: [froguel@mail-good.pasteur-lille.fr](mailto:froguel@mail-good.pasteur-lille.fr) France  
SOURCE: Journal of Clinical Endocrinology & Metabolism, (  
**February, 2002**) Vol. 87, No. 2, pp. 867-869.  
<http://jcem.endojournals.org>. print.  
ISSN: 0021-972X.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
AB A linkage between obesity-related phenotypes and the 2p21-23 locus  
has been reported previously. The urocortin (UCN) gene resides at  
this interval, and its protein decreases appetite behavior,  
suggesting that UCN may be candidate gene for susceptibility to  
obesity. We localized the UCN gene by radiation hybrid mapping, and  
the surrounding markers were genotyped in a collection of French  
families. Evidence for linkage was shown between the marker D2S165  
and leptin levels (LOD score, 1.34; P = 0.006) and between D2S2247  
and the z-score of body mass index (LOD score, 1.829; P = 0.0019).  
The gene was screened for **SNPs** in 96 obese patients. Four new  
variants were established. Two **single nucleotide polymorphisms** were  
located in the promoter (-535 A fwdarw G, -286 G fwdarw A), one in  
intron 1 (+31 C fwdarw G), and one in the 3'-untranslated region  
(+34 C fwdarw T). Association studies in cohorts of 722 unrelated  
obese and 381 control subjects and transmission disequilibrium  
tests, performed for the two frequent promoter polymorphisms, in 120  
families (894 individuals) showed that no association was present  
between these variants and obesity, obesity-related phenotypes, and  
**diabetes**. Thus, our analyses of the **genetic variations** of the UCN  
gene suggest that, at least in French Caucasians, they do not  
represent a major cause of obesity.

(continued on next page)

L10 ANSWER 2 OF 197 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:203560 BIOSIS [Full-text](#)

DOCUMENT NUMBER: PREV200200203560

TITLE: A **single nucleotide polymorphism** in protein tyrosine phosphatase PTP-1B is associated with protection from **diabetes** or impaired glucose tolerance in Oji-Cree.

AUTHOR(S): Mok, Andrea; Cao, Henian; Zinman, Bernard; Hanley, Anthony J. G.; Harris, Stewart B.; Kennedy, Brian P.; Hegele, Robert A. (1)

CORPORATE SOURCE: (1) Blackburn Cardiovascular Genetics Laboratory, Robarts Research Institute, 406-100 Perth Drive, London, Ontario, N6A 5K8: robert.hegele@rri.on.ca Canada

SOURCE: Journal of Clinical Endocrinology & Metabolism, (February, 2002) Vol. 87, No. 2, pp. 724-727.

<http://jcem.endojournals.org>. print.

ISSN: 0021-972X.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Several lines of evidence support a role for protein tyrosine phosphatase 1B (PTP-1B) in metabolism, and specifically in insulin sensitivity and obesity. We report the development of reagents for the amplification and sequencing of the PTP-1B gene, which has resulted in the identification of a novel **single nucleotide polymorphism** ( **SNP**), designated 981Cfwdarw T. We found a significant association between this **SNP** and the risk of either impaired glucose tolerance (IGT) or type 2 **diabetes** in the Oji-Cree of Sandy Lake, Ontario, Canada. Six hundred and fifty-three subjects were genotyped using PCR amplification of exon 8, followed by digestion with the restriction enzyme AvaI. Sixty-eight subjects were heterozygotes, and none was a homozygote. Thus, the overall frequencies of the C allele and the T allele were 0.948 and 0.052, respectively. Subjects with the PTP-1B 981T/981C genotype were approximately 40% less likely to have IGT or **diabetes** as subjects with the 981C/981C genotype (P = 0.040). There was no difference in quantitative traits among subjects grouped according to the PTP-1B 981Cfwdarw T **SNP** genotype. These very preliminary findings suggest that genomic variation in PTP-1B is associated with a reduced risk of **diabetes** and are consistent with the idea that this protein is important in metabolism.

L10 ANSWER 11 OF 197 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:140998 BIOSIS [Full-text](#)

DOCUMENT NUMBER: PREV200200140998

TITLE: **Single nucleotide polymorphisms (SNPs)** associated with genetic susceptibility to NASH/NAFLD and ALD: Same again please.

AUTHOR(S): Jacob, John (1); Saksena, Sushma (1); Leathart, Julian B. (1); James, Oliver (1); Daly, Ann K. (1); Day, Christopher P. (1)

CORPORATE SOURCE: (1) Univ of Newcastle upon Tyne, Newcastle upon Tyne UK

*(continued on next page)*

SOURCE: Hepatology, (October, 2001) Vol. 34, No. 4 Pt. 2, pp. 460A.  
<http://hepatology.aasldjournals.org/scripts/om.dll/serve?action=searchDB&searchDBfor=home&id=jhep.print>.  
 Meeting Info.: 52nd Annual Meeting and Postgraduate Courses of the American Association for the Study of Liver Diseases  
 Dallas, Texas, USA November 09-13, 2001  
 ISSN: 0270-9139.

DOCUMENT TYPE: Conference  
 LANGUAGE: English

***Extend the search into BIOTECHNO:***

=> FILE BIOTECHNO

=> S L10

753 SNP  
 515 SNPS  
 1020 SNP  
 (SNP OR SNPS)  
 130102 SINGLE  
 32 SINGLES  
 130125 SINGLE  
 (SINGLE OR SINGLES)  
 118911 NUCLEOTIDE  
 20812 NUCLEOTIDES  
 128368 NUCLEOTIDE  
 (NUCLEOTIDE OR NUCLEOTIDES)  
 43082 POLYMORPHISM  
 12081 POLYMORPHISMS  
 45542 POLYMORPHISM  
 (POLYMORPHISM OR POLYMORPHISMS)  
 1333 SINGLE NUCLEOTIDE POLYMORPHISM  
 (SINGLE(W)NUCLEOTIDE(W)POLYMORPHISM)  
 231500 GENETIC  
 35306 GENETICS  
 247893 GENETIC  
 (GENETIC OR GENETICS)  
 120121 VARIA?  
 13363 GENETIC VARIA?  
 (GENETIC(W)VARIA?)  
 12928 DIABETES  
 250665 PY>1999  
 L11 123 L9 AND PY>1999

*Note: The complete multi-step query developed in BIOSIS can be re-searched here.*

=> D TRIAL 1-2

L11 ANSWER 1 OF 123 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
 AN 2002:34177889 BIOTECHNO  
 TI The mechanisms of action of PPARs

*BIOTECHNO use the D TRIAL format for strategy evaluation.*

*(continued on next page)*

CT \*receptor intrinsic activity; \*peroxisome proliferator activated receptor; **diabetes** mellitus; dyslipidemia; gene expression regulation; DNA responsive element; promoter region; transcription initiation; lipid metabolism; atherosclerosis; inflammation; cancer; infertility; demyelination; molecular mechanics; protein structure; dimerization; drug receptor binding; assay; drug effect; treatment outcome; molecular cloning; protein analysis; insulin sensitivity; in vivo study; hypertension; **genetic variability**; insulin resistance; fertility; central nervous system; crystal structure; human; nonhuman; review; priority journal; peroxisome proliferator activated receptor alpha; peroxisome proliferator activated receptor gamma; peroxisome proliferator activated receptor delta; transcription factor; ligand; retinoid X receptor; fatty acid; icosanoid; fibric acid derivative; 2,4 thiazolidinedione derivative; peroxisome proliferator activated receptor agonist; rosiglitazone; pioglitazone; englitazone; ciglitazone; antilipemic agent; 2 chloro 3 [4 (2 methyl 2 phenylpropoxy)phenyl]propionic acid ethyl ester; 5 (2,4 dioxo 5 thiazolidinylmethyl) 2 methoxy n [4 (trifluoromethyl)benzyl]benzamide; phenylacetic acid derivative; 1 796449; 1 805645; gw 2570; nonsteroid antiinflammatory agent; indometacin; fenoprofen; ibuprofen; gw 0072; clofibrate; unindexed drug; unclassified drug

L11 ANSWER 2 OF 123 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
AN 2001:34177630 BIOTECHNO

TI Analysis of linkage disequilibrium between polymorphisms in the KCNJ9 gene with type 2 **diabetes** mellitus in Pima Indians

CT \*non insulin dependent **diabetes** mellitus; \*nucleotide sequence; genetic analysis; genetic linkage; genetic polymorphism; race difference; potassium channel; chromosome 1; genotype; disease predisposition; genetic predisposition; **single nucleotide polymorphism**; high risk population; gene linkage disequilibrium; human; major clinical study; controlled study; adult; article; priority journal; G protein coupled receptor

**note**

Though BIOTECHNO is heavily indexed, it does not contain an online thesaurus.

**=> E GENETIC POLYMORPHISM/CT**

E51	1	GENETIC POLARIZATION/CT
E52	1	GENETIC POLLUTION/CT
E53	10247 -->	GENETIC POLYMORPHISM/CT
E54	1860	GENETIC PREDISPOSITION/CT
E55	1	GENETIC PRINCIPLES/CT
E56	900	GENETIC PROCEDURES/CT
E57	12	GENETIC PURITY/CT
E58	8839	GENETIC RECOMBINATION/CT
E59	1	GENETIC RECONSTRUCTION/CT
E60	4	GENETIC REGISTRY/CT
E61	4074	GENETIC REGULATION/CT
E62	528	GENETIC RELATIONSHIP/CT

**=> D IALL 2**

L11 ANSWER 2 OF 123 BIOTECHNO COPYRIGHT 2002 E  
ACCESSION NUMBER: 2001:34177630 BIOTECHNO  
TITLE: Analysis of linkage disequilibrium and  
polymorphisms in the KCNJ9 gene with type 2  
**diabetes** mellitus in Pima Indians  
AUTHOR: Wolford J.K.; Hanson R.L.; Kobes S.; Bogardus  
C.; Prochazka M.  
CORPORATE SOURCE: J.K. Wolford, Phoenix Epidemiol. and Res.  
Branch, N. Inst. Diabet./Digest./Kidney Dis.,  
National Institutes of Health, 4212 North 16th  
Street, Phoenix, AZ 85016, United States.  
E-mail: jwolford@exchange.nih.gov  
SOURCE: Molecular Genetics and Metabolism, (2001),  
73/1 (97-103), 21 reference(s)  
CODEN: MGMEFF ISSN: 1096-7192  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ABSTRACT: The KCNJ9 gene encodes a G-protein-coupled inwardly rectifying  
potassium channel and is located within a region on human  
chromosome 1 that has been linked with type 2 **diabetes**  
mellitus in Pima Indians and Caucasians. To assess the  
potential contribution of genetic alterations within KCNJ9 to  
**diabetes** susceptibility in the Pimas, we have genotyped 11  
**single nucleotide polymorphisms (SNPs)** in 50 Pimas with  
**diabetes** and 50 Pimas over the age of 45 without **diabetes** and  
in 51 sib pairs, discordant for the disease, who were

*Since the indexing portion of  
the record is relatively  
concise, the IALL format may  
be preferred in this file.*

*(continued on next page)*

characterized by decreased allele sharing at the chromosomal location of the maximum LOD score. We detected three **SNP** clusters exhibiting distinct linkage disequilibria. Polymorphisms in intron 2, exon 3, and the 3'-UTR were in statistically significant linkage disequilibrium with **diabetes** in the case-control group (P = 0.006), but not the sibling pairs (P = 0.097). A weak association with **diabetes** was also found in the original linkage set comprising 1150 Pimas (odds ratio = 0.64/P = 0.079 for a dominant model and OR = 0.67/P = 0.005 for a recessive model). However, no effect on linkage was detected following adjustment for one of the most strongly associated **SNPs** in the entire original linkage set. Our results indicate that variants in **KCNJ9** are associated with **diabetes** in Pimas but do not account for the linkage of 1q with **diabetes** in this population. .COPYRGT. 2001 Academic Press.

CONTROLLED TERM: \*non insulin dependent **diabetes** mellitus;  
\*nucleotide sequence; genetic analysis; genetic linkage; genetic polymorphism; race difference; potassium channel; chromosome 1; genotype; disease predisposition; genetic predisposition; **single nucleotide polymorphism**; high risk population; gene linkage disequilibrium; human; major clinical study; controlled study; adult; article; priority journal; G protein coupled receptor

GENE NUMBER: GENBANK AF193615 submitted number; GENBANK AL121987 submitted number

## Step 4. Remove duplicate records

Duplicate journal literature may be present among the HCAplus, BIOSIS, and BIOTECHNO abstracts. Several options are available for merging the answer sets, removing duplicates, and arranging the records.

If you wish to...	Use these STN commands:
Simply remove duplicate records	<p>=&gt; <b>DUP REMOVE L# L# L#</b>            where the L#'s are the individual files answer sets</p>
Merge multiple answer sets together, keeping all records	<p>=&gt; <b>DUP IDENTIFY L# L# L#</b></p>
<ol style="list-style-type: none"> <li>1. Merge multiple answer sets</li> <li>2. Group patent records by invention family</li> </ol>	<p>=&gt; <b>DUP IDENTIFY L# L# L#</b>            =&gt; <b>FSORT L#</b> (the one created by DUP IDE)</p>
Rearrange the records based on relevance	<p>=&gt; <b>FOCUS L#</b>            the L# created by DUP REM or DUP IDE</p>
Maintain the answers in file order instead of chronological order	<p>=&gt; <b>SET DUPORDER FILE</b>            issued before the DUP command</p>

### *Remove duplicate records:*

```
=> SET DUPORDER FILE
SET COMMAND COMPLETED
```

```
=> DUP REM L5 L10 L11
```

```
PROCESSING COMPLETED FOR L5
PROCESSING COMPLETED FOR L10
PROCESSING COMPLETED FOR L11
```

```
L12      346 DUP REM L5 L10 L11 (171 DUPLICATES REMOVED)
          ANSWERS '1-197' FROM FILE HCAPLUS
          ANSWERS '198-297' FROM FILE BIOSIS
          ANSWERS '298-346' FROM FILE BIOTECHNO
```

*The order of the L-numbers indicates your preference in file selection for the retained record.*

*Note: We know which answers come from which file.*

## **note**

The SET DUPORDER FILE option allows selective displays, with unique display formats, from each file.

However, this “merged” answer set may also be rearranged in relevance order using the FOCUS command.

=> FOCUS L12

PROCESSING COMPLETED FOR L12  
L13            346 FOCUS L12 1-

*The same 346  
records in relevance  
order.*

## **Helpful HINT**

The order of the L-numbers in a DUP REM command indicates your preference in file selection for the retained record. This preference may be based on record content or display cost.

### **Step 5. Display records**

Any display format consistent across all files may be used.

=> D IBIB ABS 1-3

L13 ANSWER 1 OF 346 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER:            2001:467865 HCAPLUS [Full-text](#)  
DOCUMENT NUMBER:            136:181742  
TITLE:                        Isolation and characterization of the human AKT1  
gene, identification of 13 **single nucleotide  
polymorphisms (SNPs)**, and their lack of  
association with Type II **diabetes**  
AUTHOR(S):                    Matsubara, A.; Wasson, J. C.; Donelan, S. S.;  
Welling, C. M.; Glaser, B.; Permutt, M. A.  
CORPORATE SOURCE:            Division of Metabolism, Endocrinology and  
Diabetes, Washington University School of  
Medicine, St. Louis, MO, USA  
SOURCE:                        Diabetologia (**2001**), 44(7), 910-913  
CODEN: DBTGJ; ISSN: 0012-186X  
PUBLISHER:                    Springer-Verlag  
DOCUMENT TYPE:                Journal  
LANGUAGE:                      English

*(continued on next page)*

AB Aims/hypothesis. AKT1, a serine/threonine protein kinase, is an important downstream target of the insulin-signaling pathway, with both anti-apoptotic and peripheral metabolic effects. Because impaired insulin signaling is a major hallmark of Type II (non-insulin-dependent) **diabetes** mellitus, the authors considered whether the AKT1 gene could be a candidate gene involved in susceptibility of this condition. To test this possibility, the authors isolated and characterized the human AKT1 gene. The authors also looked for **single nucleotide polymorphisms** in the gene and examined their association with Type II **diabetes** mellitus in the Ashkenazi Jewish population. Methods. Human BAC/Pl genomic libraries were screened to isolate the AKT1 gene. To obtain structural information and the sequences of the exon-intron boundaries, BAC/Pl clones were directly sequenced. Identification of **single nucleotide polymorphisms** was done by polymerase chain reaction of each exon, followed by denaturing high performance liquid chromatog. Six **single nucleotide polymorphisms** were genotyped in Ashkenazi Jewish patients with Type II **diabetes** mellitus and in control subjects. Results. The human AKT1 gene was at least 24.6 kb in length and comprised 14 exons. Altogether 13 putative intragenic **single nucleotide polymorphisms**, with minor-allele frequencies ranging from 0.011 to 0.354, were identified. The allelic and the genotypic frequencies of 6 **single nucleotide polymorphisms** were the same in diabetic patients and in control subjects. Conclusion/interpretation. The results of the authors' studies show that the AKT1 gene is not a major contributor to susceptibility to Type II **diabetes** mellitus in Ashkenazi Jews.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 346 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:210348 HCAPLUS [Full-text](#)  
TITLE: Systematic search for **single nucleotide polymorphisms** in the resistin gene: the absence of evidence for the association of three identified **single nucleotide polymorphisms** with Japanese type 2 **diabetes**  
AUTHOR(S): Osawa, Haruhiko; Onuma, Hiroshi; Murakami, Akiko; Ochi, Masaaki; Nishimiya, Tatsuya; Kato, Kenichi; Shimizu, Ikki; Fujii, Yasuhisa; Ohashi, Jun; Makino, Hideichi  
CORPORATE SOURCE: Department of Laboratory Medicine, Ehime University School of Medicine, Ehime, 791-0295, Japan  
SOURCE: Diabetes (2002), 51(3), 863-866  
CODEN: DIAEAZ; ISSN: 0012-1797  
PUBLISHER: American Diabetes Association  
DOCUMENT TYPE: Journal  
LANGUAGE: English

(continued on next page)

AB Resistin is a novel polypeptide specifically secreted from adipocytes, and its serum levels are increased in obese diabetic mice. Resistin antagonizes insulin and could account for insulin resistance. To determine whether there are **single nucleotide polymorphisms (SNPs)** in the resistin gene associated with type 2 **diabetes**, sequences for 24 Japanese type 2 diabetic patients were initially analyzed using PCR direct sequencing. Three **SNPs** were found in the introns, but none were present in the coding regions. The allele frequencies of genomic -167C>T, +157C>T, and +299G>A in 99 Japanese control subjects were determined to be 3.5, 6.6, and 39.4%, resp. In each pair of these **SNPs**, linkage disequil. were found between either -167C>T and +299G>A or +157C>T and +299G>A. A linkage disequil. was also detected among -167C>T, +157C>T, and +299G>A, and only four of the eight possible haplotypes defined by these **SNPs** were found. A comparison of the frequencies of these **SNPs** and haplotypes between 99 type 2 **diabetes** and 99 control subjects revealed no evidence for any association. These identified **SNPs**, which were in linkage disequil., represent potentially useful tools for searching for their association with specific phenotypes of **diabetes**.

L13 ANSWER 3 OF 346 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:123275 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 136:162394  
 TITLE: Detection of **single nucleotide polymorphisms** of the human von Hippel-Lindau syndrome tumor suppressor (vHL) gene promoter and uses in prediction of genetic susceptibility to diseases  
 INVENTOR(S): Moskowitz, David W.  
 PATENT ASSIGNEE(S): Dzgenes, LLC, USA  
 SOURCE: PCT Int. Appl., 79 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
-----		-----	-----	-----	
WO 2002012567	A1	20020214	WO 2001-US24985	20010809	<--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-224084P	P	20000809

(continued on next page)

AB The invention discloses the **single nucleotide polymorphisms (SNPs)** at positions 520 and 638 on the human von Hippel-Lindau syndrome tumor suppressor gene promoter and detection of individuals at risk for pathol. conditions based on the **SNPs**. In particular, the invention discloses that a **single nucleotide polymorphism (SNP)** associated with colon cancer, hypertension, atherosclerotic peripheral vascular disease due to hypertension, cerebrovascular accident due to hypertension, cataracts due to hypertension, hypertensive cardiomyopathy, myocardial infarction due to hypertension, end stage renal disease due to hypertension, non-insulin dependent **diabetes** mellitus, atherosclerotic peripheral vascular disease due to non-insulin dependent **diabetes** mellitus, cerebrovascular accident due to non-insulin dependent **diabetes** mellitus, ischemic cardiomyopathy, ischemic cardiomyopathy with non-insulin dependent **diabetes** mellitus, myocardial infarction due to non-insulin dependent **diabetes** mellitus, atrial fibrillation without valvular disease, alc. abuse, alc. cirrhosis, anxiety, asthma, chronic obstructive pulmonary disease, cholecystectomy, degenerative joint disease, end stage renal disease and frequent de-clots, end stage renal disease due to focal segmental glomerular sclerosis, end stage renal disease due to insulin dependent **diabetes** mellitus, end stage renal disease due to non-insulin dependent **diabetes** mellitus, and seizure disorder. The invention also discloses methods for using the **SNP** to determine susceptibility to these diseases; nucleotide sequences containing the **SNP**; kits for determining the presence of the **SNP**; and methods of treatment or prophylaxis based on the presence of the **SNP**.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> SAVE L13 SNPS/A

ANSWER SET L13 HAS BEEN SAVED AS 'SNPS/A'

=> LOG Y

---

## Helpful HINT

An answer set may be saved for further use at a later time. For information on saving and later reactivating answer sets, see the segments on the SAVE and ACTIVATE commands in

<http://www.cas.org/training/stncommands/stncommands.html> 

## Skills Practice

1. How has MALDI mass spectrometry been used in the identification or determination of genetic markers?

2. Retrieve literature on genetic engineering applied to developing tomatoes with increased freeze protection.

*Note: A Chemical and Engineering News article referred to the concept of “antifreeze proteins”.*

3. Retrieve literature describing DNA or nucleic acid probes for low-density lipoproteins and their use in assessing the risk of atherosclerosis.

# BIOMOLECULE SEARCH STRATEGIES

**In this section, you will learn how to**

- Locate biomolecule information using text terms and sequence description terms
- Enhance biomolecule search results using classification indexing

# Searching for Biomolecules

Substance retrieval of biomolecules may be accomplished several ways on STN:

- Similarity sequence searching, e.g., BLAST or FASTA
- Code match sequence searching, e.g. /SQSN or /SQSP in the REGISTRY or DGENE files
- Searching sequence description of biomolecule names

## *note*

Similarity sequence searching is taught in the companion workshop Sequence Searching on STN.

## Biomolecule Naming System

With small molecules, very specific rules of nomenclature are applied to create a unique substance name. With larger biomolecules, such as nucleic acids and proteins, a more descriptive naming system is used. Biomolecule names may include information on the source organism, clone, gene, strain, function, substrate, ligands, etc.

### *Illustration – biomolecule name:*

```
DNA (mouse clone FSH-R1 follicle-stimulating hormone receptor cDNA)
```

## *note*

Unclaimed sequences from patents do not receive a descriptive name on entry to the REGISTRY file.

## Searching Biomolecule Names

The descriptive information used in biomolecule names may also be used to index the subject matter of the original publication.

In many cases, the best approach for searching for information about biomolecules requires searches of both text-based files and substance-based files. This is especially true for classes of sequences which may be described by both

- Controlled term indexing
- Specific sequence

### Search strategy

The combination text-based search and substance-based search is accomplished by doing the following:

1. Search the sequence description of the biomolecule name in the text-based file. Identify relevant controlled-term indexing.
2. Formulate a query using sequence description. Search this query in a substance-based file, e.g. REGISTRY, DGENE, or GENBANK.

### Descriptive information in substance files

Within the substance-based files, biomolecule name (or descriptive) information appears in the following fields. The Basic Index (/BI) of these files includes the single words appearing in these descriptive fields and usually represents the best search field.

File	Representative Sequence Description	Display Field
REGISTRY	DNA (mouse clone FSH-R1 follicle-stimulating hormone receptor cDNA)	CN
DGENE	Follicle stimulating hormone receptor; FSH receptor; ovarian dysgenesis; hypergonadotropic hypogonadism; diagnosis	DESC, KW
GENBANK	Mus musculus adult male testis cDNA, RIKEN full-length enriched library, clone:4933403I07:follicle stimulating hormone receptor, full insert sequence	DEF

## Search strategies in substance files — overview

Each record in REGISTRY, DGENE, and GENBANK represents one substance. To retrieve literature indexed to these substances, the following strategies are recommended:

From this file	Transfer this data	Example
REGISTRY <sup>1</sup>	CAS RNs represented by an L#	=> FILE HCAPLUS => S L# from REGISTRY
DGENE <sup>2</sup>	PN or OS	=> FILE WPINDEX => TRANSFER L# PN
GENBANK <sup>3</sup>	RN to REGISTRY or OS to HCAPLUS	=> FILE REGISTRY => TRANSFER L# RN or => FILE HCAPLUS => TRANSFER OS /AN

<sup>1</sup> CAS RNs from REGISTRY may be searched in any STN file containing CAS RN indexing, e.g., MEDLINE, BIOSIS, etc.

<sup>2</sup> DGENE contains a sequence abstract and bibliographic information for the patent. More comprehensive information for the invention is included in the WPINDEX record.

<sup>3</sup> GENBANK may include bibliographic information for the source of sequence information, although many sequences are unpublished. The /OS field provides a link to HCAPLUS for the source information, if available.

# Classes of Substances

Classes of nucleic acids or peptides, e.g., G-protein coupled receptors, may be described using

- Controlled term subject indexing
- Specific sequences

For comprehensive retrieval of relevant information, this requires a search of text-based records, as well as substance-based records.

---

---

*Search Question:*      *Retrieve journal and patent literature describing FSH-like receptors.*

---

---

## Background (see the patent WO2001088127):

FSH, or follicle stimulating hormone, receptors represent one type of cell-surface receptors known as G-protein coupled receptors (GPCRs). It has been estimated that there are <50 types of GPCRs. GPCRs are good therapeutic targets.

Subclasses of GPCRs have been classified based on the structure of the GPCR. Members of this family respond to a wide range of ligands; however, a specific receptor type such as follicle-stimulating hormone receptor may be very selective for selected ligands. These ligands may provide models for development of agonists or antagonists for this receptor.

FSH-like GPCRs may be used to identify possible candidate compounds as agonists or antagonists or to develop antibodies that may block the receptor, preventing binding by an endogenous ligand.

Medline's definition for an FSH receptor is as follows: Cell surface proteins that bind FOLLICLE STIMULATING HORMONE with high affinity and trigger intracellular changes influencing the behavior of cells.

## Important search concepts:

### *Major concepts — must be present for relevance*

- FSH receptors
- Follicle-stimulating hormone receptors
- GPCR or G-protein coupled receptors (may be too broad, depending on client needs)

### *Minor concepts — may be used for refinement*

- Agonist
- Antagonist
- Antibody
- Ligand

## Search Strategy

### To retrieve literature on a class of biomolecules

#### Stage 1: Searching Text-Based Files

- Step 1 Identify sequence description terms for the class of biomolecules in subject indexing thesauri.
- Step 2 Retrieve literature describing the class of biomolecules.
- Step 3 Enhance results using classification indexing.

#### Stage 2: Searching Substance-Based Files

- Step 4 Evaluate the sequence description terms for biomolecules in the substance-based file.
- Step 5 Conduct a free-text name segment search.
- Step 6 Retrieve literature indexed to specific sequences.

# Searching Text-Based Files

## Step 1. Identify sequence description terms in a thesaurus

Online thesauri such as the CA Lexicon in CAPLUS or MeSH in MEDLINE may provide information on a class of biomolecules.

*Explore FSH receptors in the CA Lexicon:*

```
=> FILE HCAPLUS
```

```
=> SET EXPAND CONTINUOUS
```

```
=> SET ABBREV ON; SET PLURALS ON
```

```
=> E FSH RECEPTORS/CT
```

E#	FREQUENCY	AT	TERM
--	-----	--	----
E1	0	1	FSE/CT
E2	0	1	FSH/CT
E3	321	16 -->	FSH RECEPTORS/CT
E4	0	1	FSH-FORMING/CT
E5	0	2	FSH-FORMING CELL ANTERIOR LOBE PITUITARY GLAND/CT
E6	0	1	FSH-PRODUCING/CT
E7	0	2	FSH-PRODUCING CELL ANTERIOR LOBE PITUITARY GLAND/CT
E8	0	1	FSH-SECRETING/CT
E9	0	2	FSH-SECRETING CELL ANTERIOR LOBE PITUITARY GLAND/CT
E10	0	1	FSL/CT
E11	0	4	FSL 300/CT
E12	0	1	FSM/CT

```
=> E E3+ALL
```

E13	486417	BT3	Proteins/CT
E14	226733	BT2	Receptors/CT
E15	2698	BT1	G protein-coupled r
E16	486417	BT4	Proteins/CT
E17	226733	BT3	Receptors/CT
E18	2698	BT2	G protein-coupled r
E19	486417	BT4	Proteins/CT
E20	226733	BT3	Receptors/CT
E21	2210	BT2	Protein receptors/C
E22	878	BT1	Gonadotropin recep
E23	486417	BT3	Proteins/CT
E24	226733	BT2	Receptors/CT
E25	2210	BT1	Protein receptors/CT
E26	321	-->	FSH receptors/CT
		HN	Valid heading during volume 126 (1997) to present.
E27		OLD	Receptors (L) FSH/CT
E28		UF	Follitropin receptors/CT

\*\*\*\*\* END\*\*\*

*FSH Receptors has been a valid controlled term since 1997. Its use will result in precise search results.*

*If broader retrieval is desired, terms such as the following can be used:*

- Protein receptors
- Gonadotropin receptors
- G protein-coupled receptors

**note**

Controlled terminology may lag behind an evolving area of research. A controlled indexing term may not be created until the concept has made a significant appearance in the literature.

**Exploring broader terms:**

A search of broader terminology may retrieve additional records where the FSH concept was not of major emphasis and the record was only indexed to a broad class term.

**=> E G PROTEIN COUPLED RECEPTORS/CT**

E#	FREQUENCY	AT	TERM
---	-----	--	----
E29	0	2	G PERIOD/CT
E30	0	2	G PHASE/CT
E31	0		--> G PROTEIN COUPLED RECEPTORS/CT
E32	0	8	G PROTEIN-COUPLED RECEPTOR KINASE/CT
E33	2698	124	G PROTEIN-COUPLED RECEPTORS/CT
E34	0	6	G PROTEIN-COUPLED RECEPTORS (L) CRLR (CALCITONIN RECEPTOR-LIKE RECEPTOR)/CT
E35	0	8	G PROTEIN-COUPLED RECEPTORS (L) GLUCAGON-LIKE PEPTIDE-2/CT

*Punctuation (e.g., hyphens) can be important in controlled terminology phrases.*

●  
●  
●

**=> E E33+ALL**

E41	486417	BT2	Proteins/CT
E42	226733	BT1	Receptors/CT
E43	2698		--> G protein-coupled receptors/CT HN Valid heading during volume 126 (1997) to present.
E44		OLD	Receptors (L) G protein-coupled/CT
E45	130	NT1	ACTH receptors/CT
E46	123	NT1	Bombesin receptors/CT
E47	163	NT2	Gastrin-releasing peptide receptors/CT
E48		NT2	Receptors (L) gastrin-releasing peptide/CT
E49		NT2	Receptors (L) neuromedin B/CT
E50	366	NT1	Calcitonin gene-related peptide receptors/CT
E51		NT2	Receptors (L) CGRP1 (calcitonin gene-related peptide 1)/CT
E52	190	NT1	Calcitonin receptors/CT
E53	558	NT1	Corticotropin releasing factor receptors/CT
E54		NT2	Receptors (L) ACTH-releasing factor, type I/CT
E55		NT2	Receptors (L) ACTH-releasing factor, type II/CT

*(continued on next page)*

E56	321	NT1	FSH receptors/CT
E57	218	NT1	Galanin receptors/CT
E58	163	NT1	Gastrin-releasing peptide
E59	142	NT1	Glucagon receptors/CT
E60	147	NT1	Glucagon-like peptide-1 r
E61	878	NT1	Gonadotropin receptors/CT
E62	321	NT2	FSH receptors/CT
E63		NT2	Receptors (L) FSH/CT
E64		NT2	Receptors (L) gonadotropin, complexes/CT
E65		NT2	Receptors (L) pituitary gonadotropin I/CT
E66		NT2	Receptors (L) pituitary gonadotropin II/CT
E67		NT2	Receptors (L) pituitary gonadotropin type I/CT

*FSH receptors is also a narrower term under Gonadotropin receptors.*

•  
•  
•

## Step 2. Retrieve literature describing the class of biomolecules

The CPlus file is updated daily with new records, indexing for which may not be added for several weeks. This has implications for search strategy:

- To retrieve indexed records, a search using controlled terminology results in a precise answer set.
- To retrieve non-indexed records, a free-text query should be run. Some loss of precision may occur, but the gains of currency are significant.

### Search for indexed records:

```
=> S E26+PFT
```

```
L1          915 "FSH RECEPTORS"+PFT/CT (3 TERMS)
```

*The PFT relationship code is used to search for OLD, NEW and UF terms.*

### Search for non-indexed records:

```
=> S FSHR OR (FOLLICLE STIMULAT? OR FSH OR FOLLITROPIN) (3A) RECEPTOR
```

```
L2          1614 FSHR OR (FOLLICLE STIMULAT? OR FSH OR FOLLITROPIN) (3A)
              RECEPTOR
```

```
=> S L2 NOT L1
```

```
L3          738 L2 NOT L1
```

*(3A) proximity ensures that search terms are closely associated with one another, in either order.*

*(continued on next page)*

```
=> S L3 AND NONINDEXED/FS
      881955 NONINDEXED/FS
L4      32 L3 AND NONINDEXED/FS
```

```
=> D SCAN
```

```
L4  32 ANSWERS  HCAPLUS  COPYRIGHT 2002 ACS
CC  3 (Biochemical Genetics)
TI  Stability of human follicle-stimulating hormone
receptor mRNA in stably transfected cells
```

```
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
```

```
L4  32 ANSWERS  HCAPLUS  COPYRIGHT 2002 ACS
CC  3 (Biochemical Genetics)
TI  Stage-dependent expression of androgen receptor and FSH
receptor in adult rat testis
ST  androgen receptor cellular localization expression pattern; FSH
receptor testis testosterone spermatogenesis
```

```
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0
```

```
=> S L1 OR L4
```

```
L5      947 L1 OR L4
```

```
=> S L5 AND PY>1999
```


```
      2084384 PY>1999
L6      172 L5 AND PY>1999
```

*Some of these records will be of marginal interest. But some, especially those from the non-indexed portion of the file may be very relevant. The File Segment index (/FS) clearly differentiates records that are indexed from those that are not.*

### Step 3. Enhance results using classification indexing

One way to enhance retrieval is to evaluate the indexing of the answer set to identify most often posted terms. Some of these terms may make good search terms.

To evaluate indexing for a set of records, use the STN ANALYZE command. Key features of the command include

- Up to five fields of data may be analyzed with one command
- Each extracted field of data may be displayed separately
- While there is a flat fee associated with ANALYZE, all displays of the data are no-cost
- For further details: <http://www.cas.org/training/stncommands/stncommands.html> 

***ANALYZE the answer set for highly posted terms:***

- CT = controlled terminology
- IC = international patent class

=> ANALYZE L6 1- CT IC NCL

L7 ANALYZE L6 1- CT IC NCL : 889 TERMS

=> D CT TOP20 DOC

L7 ANALYZE L6 1- CT IC NCL : 889

*The display code TOP20 shows the top 20 controlled indexing terms from the answer set. Results confirm that the majority of retrieved records do have FSH Receptors as a controlled term.*

TERM #	# OCC	# DOC	% DOC	CT IC NCL
1	142	141	83.43	FSH RECEPTORS
2	76	53	31.36	OVARY
3	51	51	30.18	GONADOTROPIN RECEPTORS
4	34	33	19.53	SIGNAL TRANSDUCTION, BIOLOGICAL
5	454	31	18.34	GENE, ANIMAL
6	29	26	15.38	TESTIS
7	19	18	10.65	CELL PROLIFERATION
8	18	17	10.06	MRNA
9	23	16	9.47	MUTATION
10	18	16	9.47	STRUCTURE-ACTIVITY RELATIONSHIP
11	18	15	8.88	FERTILITY
12	14	13	7.69	PROTEIN MOTIFS
13	13	13	7.69	THYROTROPIN RECEPTORS
14	279	12	7.10	PROTEINS, SPECIFIC OR CLASS
15	95	12	7.10	TRANSCRIPTION FACTORS
16	62	12	7.10	RECEPTORS
17	17	11	6.51	ANTIBODIES
18	14	11	6.51	GENETIC ELEMENT
19	11	11	6.51	CELL DIFFERENTIATION
20	11	11	6.51	PROTEIN SEQUENCES

=> D IC DGT2

L7 ANALYZE L6 1- CT IC NCL : 889 TERMS

TERM #	# OCC	# DOC	% DOC	CT IC NCL
68	6	6	3.55	C12N005-10
69	6	6	3.55	C12Q001-68
100	5	5	2.96	C12N015-12
134	4	4	2.37	C07K014-705
135	4	4	2.37	C07K014-72
178	3	3	1.78	A61K038-24
179	3	3	1.78	A61K048-00
192	3	3	1.78	C12N015-62

*The top international patent classes appearing on 3 or more patent documents.*

*The display code DGT2 shows answers with document counts >2. Any number may be used here.*

## Helpful HINT

To determine the meaning of the international patent classification codes, use the IC thesaurus in the CPlus file.

=> E C12N005-10/IC + TI

E9	140	BT5	C/IC SECTION C - CHEMISTRY; METALLURGY
E10	0	BT4	C0/IC CHEMISTRY
E11	1	BT3	C12/IC BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING
E12	66721	BT2	C12N/IC MICRO-ORGANISMS OR ENZYMES; COMPOSITIONS THEREOF (biocides, pest repellants or attractants, or plant growth regulators containing micro- organisms, viruses, microbial fungi, enzymes, fermentates, or substances produced by, or extracted from, micro-organisms or animal material A01N063-00; food compositions A21, A23; medicinal preparations A61K; chemical aspects of, or use of materials for, bandages, dressings, absorbent pads or surgical articles A61L; fertilisers C05); PROPAGATING, PRESERVING, OR MAINTAINING MICRO-ORGANISMS (preservation of living parts of humans or animals A01N001-02); MUTATION OR GENETIC ENGINEERING; CULTURE MEDIA (microbiological testing media C12Q) (3)
E13	3973	BT1	C12N005-00/IC Undifferentiated human, animal or plant cells, e.g. cell lines; Tissues; Cultivation or maintenance thereof; Culture media therefor (plant reproduction by tissue culture techniques A01H004-00) (3, 5)
E14	6866	-->	( IPC EDITION: 3-6 ) C12N005-10/IC . Cells modified by introduction of foreign genetic material, e.g. virus-transformed cells (5) ( IPC EDITION: 5-6 )

\*\*\*\*\* END\*\*\*

**IC summary:**

<b>IC</b>	<b>Title</b>	<b>No. of records in answer set</b>
C12N005-10	Cells modified by introduction of foreign genetic material, e.g. virus-transformed cells	6
C12Q001-68	Measuring or testing processes involving enzymes or micro-organisms . involving nucleic acids	6
C12N015-12	Genes encoding animal proteins	5
C07K014-705	Receptors; Cell surface antigens; Cell surface determinants	4
C07K014-72	Receptors; Cell surface antigens; Cell surface determinants .. for hormones	4
A61K038-24	Follicle-stimulating hormone (FSH); Chorionic gonadotropins, e.g. HCG; Luteinising hormone (LH); Thyroid-stimulating hormone	3
A61K048-00	Medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases; Gene therapy	3
C12N015-62	DNA sequences coding for fusion proteins	3

**Expand search to include “receptor” IC classes:**

```
=> S (C07K014-705/IC OR C07K014-72/IC) AND (FSH OR FOLLICLE STIMULAT? OR FOLLITROPIN)
```

```
L8          11 (C07K014-705/IC OR C07K014-72/IC) AND (FSH OR FOLLICLE STIMULAT? OR FOLLITROPIN)
```

**Expand search to include "FSH" IC class:**

```
=> S A61K038-24/IC AND RECEPTOR
L9          15 A61K038-24/IC AND RECEPTOR
=> S (L8 OR L9) AND PY>1999
          2084384 PY>1999
L10        20 (L8 OR L9) AND PY>1999
```

**Isolate unique records:**

```
=> S L10 NOT L6
L11        11 L10 NOT L6
=> D SCAN
L11 11 ANSWERS HCAPLUS COPYRIGHT 2002 ACS
IC ICM C12N015-62
ICS C07K019-00; C07K014-59; A61K038-24; C07K016-26; C12N015-85;
C12N005-10
CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 3
TI Single-chain bifunctional glycoprotein hormones and their use as
agonists and antagonists
ST TSH FSH LH chorionic gonadotrophin single chain
IT Chimeric genes
RL: BUU (Biological use, unclassified); BIOL (Biological study);
USES
(Uses)
(for bifunctional hormones; single-chain bifunctional
glycoprotein hormones and their use as agonists and antagonists)
IT Molecular cloning
(of chimeric genes for bifunctional hormones; single-chain
bifunctional glycoprotein hormones and their use as agonists and
antagonists)
IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES
(Uses)
(to bifunctional hormones; single-chain bifunctional glycoprotein
hormones and their use as agonists and antagonists)
IT 9002-61-3P, Chorionic gonadotrophin 9002-67-9P, LH 9002-68-0P,
FSH 9002-71-5P, TSH
RL: BAC (Biological activity or effector, except adverse); BPN
(Biosynthetic preparation); BPR (Biological process); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
(Process); USES
(Uses)
(single-chain bifunctional glycoprotein hormones and their use as
agonists and antagonists)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0
```

*11 additional patent records  
of possible interest.*

**Combine results:**

```
=> S L6 OR L11  
L12          180 L6 OR L11
```

**note**

The search for FSH receptors could be enhanced by exploring other files as well, similar to the first search example:

```
=> FILE MEDLINE  
  
=> E RECEPTORS, FSH+ALL/CT  
  
●  
●  
●  
E148      34587   BT3   Receptors, Cell Surface/CT  
E149      1258   BT2   Receptors, Peptide/CT  
E150       626   BT1   Receptors, Neuropeptide/CT  
E151       756   -->  Receptors, FSH/CT  
E152       756   MN    D12.776.543.750.720.600.370./CT  
E153       756   MN    D12.776.543.750.750.555.370./CT  
E154       756   MN    D12.776.543.750.750.660.350.300./CT  
          DC    an INDEX MEDICUS major descriptor  
          NOTE  Cell surface proteins that bind  
                FOLLICLE STIMULATING HORMONE with  
                high affinity and trigger  
                intracellular changes influencing  
                the behavior of cells.  
          INDX  DF: RECEPT FSH  
          AQ    AD AG AI AN BI BL CH CL DE DF  
                GE HI IM IP ME PH RE TU UL  
          PNTE  FSH (1966-1986)  
  
●  
●  
●  
*****      END***  
  
=> FILE USPATFULL  
  
=> S (FSHR OR (FOLLICLE STIMULAT? OR FSH OR FOLLITROPIN) (S)  
    RECEPTOR)/TI,AB,CLM  
  
L16          33 (FSHR OR (FOLLICLE STIMULAT? OR FSH OR  
                FOLLITROPIN) (S)RECEPTOR)/TI,AB,CLM
```

## Searching Substance-Based Files

The first stage of the search found literature indexed to controlled terms describing biomolecules. There may also be specific peptide clones, analogs, and/or homologs of these receptors developed for identifying drug targets and nucleic acids encoding for them.

These sequences may be retrieved in the substance files REGISTRY and DGENE. Nucleic acids encoding for FSH receptors may be retrieved from the GENBANK file.

### Step 4. Evaluate biomolecule names

The same terminology identified in the controlled indexing terms of CPlus using the CA Lexicon may be used as search terms in substance-based files.

Specific chemical names are searched in the Chemical Name index (/CN) of the REGISTRY database.

#### *Test exact matches on biomolecule names:*

```
=> FILE REGISTRY
```

```
=> SET EXPAND CONTINUOUS
```

```
=> E FSH RECEPTORS/CN
```

```
E165      1      FSH RECEPTOR (SHEEP CLONE S3352A 670-AMINO ACID
RESIDUE ISOFORM PRECURSOR)/CN
E166      1      FSH RECEPTOR (THALARCTOS MARITIMUS)/CN
E167      0 --> FSH RECEPTORS/CN
E168      1      FSH-BI/CN
E169      1      FSH-BINDING INHIBITOR/CN
E170      1      FSH-P/CN
E171      1      FSH-RELEASING FACTOR/CN
E172      1      FSH-RELEASING HORMONE/CN
E173      1      FSH-RH/CN
E174      1      FSH36/CN
E175      1      FSII/CN
E176      1      FSJ-III/CN
```

*Note the complexity of chemical names for most biological compounds.*

#### **note**

A search in the Chemical Name index results in the following:

```
=> S FSH RECEPTOR?/CN
```

```
L1          12 FSH RECEPTOR?/CN
```

### ***Test for broader matches on biomolecule names:***

Similar to the construction of the Basic Index of biographic files, each word of a chemical name is considered a Basic Index entry. Therefore, simple text-based search queries may be conducted in the Basic Index of REGISTRY to retrieve the desired substances.

#### **=> E FOLLITROPIN**

E177	168	FOLLISTATIN/BI
E178	1	FOLLISTREL/BI
E179	4 -->	FOLLITROPIN/BI
E180	1	FOLLORMON/BI
E181	6	FOLLOWING/BI
E182	1	FOLLTROPIN/BI
E183	1	FOLLUTEIN/BI
E184	1	FOLNIT/BI
E185	1	FOLOBUS/BI
E186	1	FOLOGE/BI
E187	1	FOLOGENON/BI
E188	6	FOLONE/BI

#### **=> E FSH**

E189	1	FSGSH/BI
E190	2	FSGTP1/BI
E191	111 -->	FSH/BI
E192	4	FSH $\beta$ /BI
E193	3	FSH05/BI
E194	1	FSH1/BI
E195	1	FSH15W6/BI
E196	2	FSH16/BI
E197	1	FSH2/BI
E198	2	FSH22/BI
E199	8	FSH23/BI
E200	2	FSH24/BI

### **Step 5. Conduct a free-text name segment search**

*Note: (L) proximity is used to ensure that name segments appear in the same name.*

**=> S FSHR OR (FSH OR FOLLITROPIN OR FOLLICLE STIMULAT?) (L) RECEPTOR**

L13	126	FSHR OR (FSH OR FOLLITROPIN OR FOLLICLE STIMULAT?) (L) RECEPTOR
-----	-----	---

## *D SCAN to review specific biomolecules:*

```
=> D SCAN

L13 126 ANSWERS   REGISTRY   COPYRIGHT 2002 ACS
IN   DNA (Cynops pyrrhogaster FSH receptor cDNA plus flanks) (9CI)
SQL  3075
MF   Unspecified
CI   MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L13 126 ANSWERS   REGISTRY   COPYRIGHT 2002 ACS
IN   DNA (synthetic ovarian dysgenesis-correlated FSH receptor gene
mutant PCR primer 10f) (9CI)
SQL  62
MF   Unspecified
CI   MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L13 126 ANSWERS   REGISTRY   COPYRIGHT 2002 ACS
IN   DNA (human FSH receptor gene exon 6 plus flanks) (9CI)
SQL  88
MF   Unspecified
CI   MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0
```

## Step 6. Retrieve literature indexed to specific substances

```
=> FILE HCAPLUS

=> S L13 AND PY>1999

          47 L13
          2084384 PY>1999
L14      15 L13 AND PY>1999
```

### Combining results of text- and substance-based searches:

```
=> S L14 OR L12
L15          183 L14 OR L12
```

### Isolating unique records from the substance search:

```
=> S L14 NOT L12
L16          3 L18 NOT L15
```

*3 additional records were retrieved.  
In many cases even more dramatic  
enhanced retrieval is observed.*

```
=> D IBIB ABS IND
```

```
L16 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:528537 HCAPLUS
DOCUMENT NUMBER: 115:128537
TITLE: Purification and cloning of glycoprotein hormone
receptor molecules for diagnosis and therapy
INVENTOR(S): Nikolics, Karoly; McFarland, Keith C.; Segaloff,
Deborah L.; Seeburg, Peter H.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
```

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9013643	A2	19901115	WO 1990-US2488	19900504
WO 9013643	A3	19910110		
W: AU, CA, HU, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9057321	A1	19901129	AU 1990-57321	19900504
EP 471030	A1	19920219	EP 1990-908349	19900504
EP 471030	B1	19941214		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04505103	T2	19920910	JP 1990-508176	19900504
EP 614975	A1	19940914	EP 1994-104166	19900504
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
ES 2068388	T3	19950416	ES 1990-908349	19900504
US 6261800	B1	20010717	US 1994-207814	19940307 <--
PRIORITY APPLN. INFO.:				US 1989-347683 A2 19890505
				EP 1990-908349 A3 19900504
				WO 1990-US2488 A 19900504
				US 1991-781153 B1 19911031

*(continued on next page)*

AB Receptors for LH, chorionic gonadotropin (CG), FSH, and TSH are purified and cloned. The receptors are useful in diagnosis and therapy. Pharmaceutical compns. contain therapeutically effective amts. of the receptors. The receptors are also useful in assays for their resp. hormones. The LH/CG receptor was purified from pseudopregnant rat ovaries, partial sequences were obtained and used to make oligonucleotide primers, the primers were used in a polymerase chain reaction (PCR) to prepare a product containing part of the LH/CG receptor coding sequence, and the PCR product was used to screen a rat luteal cDNA library. The nucleotide and predicted amino acid sequence of the rat LH/CG receptor cDNA with 43 nucleotides of 5' flanking and 759 nucleotides of 3' flanking sequence are shown as are the sequences for FSH receptor cDNA. The sequences were compared to each other and to others, especially to sequences of G protein-coupled receptors.

IC ICM C12N015-12  
ICS A61K037-02; G01N033-76; C12P021-08; C12N001-21; C12N005-10

CC 2-10 (Mammalian Hormones)  
Section cross-reference(s): 3, 6, 9, 63

ST receptor glycoprotein hormone; cloning LH chorionic gonadotropin receptor; nucleotide sequence LH chorionic gonadotropin receptor

IT Rat  
(LH/chorionic gonadotropin and FSH receptors of, nucleotide and protein sequences of)

IT Ovary, composition  
(LH/chorionic gonadotropin receptor of)

IT Mammal  
(cloning in cell of, of LH/chorionic gonadotropin receptor-encoding DNA)

IT Bacteria  
Escherichia coli  
Eukaryote  
Prokaryote  
Yeast  
(cloning in, of LH/chorionic gonadotropin receptor-encoding DNA)

IT Gene and Genetic element, animal  
RL: BIOL (Biological study)  
(for glycoprotein hormone receptors, cloning)

IT Receptors  
RL: BIOL (Biological study)  
(for glycoprotein hormones, for diagnosis and therapy)

IT Neoplasm inhibitors  
(glycoprotein hormone receptors)

IT Hormones  
RL: BIOL (Biological study)  
(glycoprotein, receptors for, for diagnosis and therapy)

IT Protein sequences  
(of FSH receptor, of rat)

IT Protein sequences  
(of LH/chorionic gonadotropin receptor, of rat)

IT Molecular cloning  
(of glycoprotein hormone receptor DNA)

IT Pharmaceutical dosage forms  
(of glycoprotein hormone receptors)

*This record is indexed to a broader concept "receptors".*

*(continued on next page)*

- IT Plasmid and Episome  
(pCFSH-R, FSH receptor cDNA on, expression of, in 293 animal cells)
- IT Plasmid and Episome  
(pCLHR, LH/chorionic gonadotropin receptor cDNA on, expression of, in 293 animal cells)
- IT Nucleic acid hybridization  
(to DNA encoding FSH or LH/chorionic gonadotropin receptors)
- IT Antibodies  
RL: BIOL (Biological study)  
(to glycoprotein hormone receptor)
- IT Graves' disease  
Hypothyroidism  
Thyroid gland, neoplasm  
(treatment of, with TSH hormone receptor)
- IT Fertility  
Osteoporosis  
(treatment of, with glycoprotein hormone receptor)
- IT Animal cell line  
(293, LH/chorionic gonadotropin receptor cDNA expression in)
- IT Deoxyribonucleic acid sequences  
(FSH receptor-specifying, of rat)
- IT Deoxyribonucleic acid sequences  
(LH receptor-specifying, of rat)
- IT Prostate gland  
(disease, benign hyperplasia, treatment of, with glycoprotein hormone receptor)

*Note the wealth of "genetic engineering" indexing concepts added to this record.*

- 
- 
-

## Option: Extending the search to DGENE/WPINDEX

The DGENE file, from Derwent, includes records for individual sequences indexed from the patent records that are also added to the WPINDEX record. Each sequence record provides more detail about the sequence itself, whereas the WPINDEX file includes more information about the invention.

The sequence information is indexed into three fields in DGENE:

This field ...	Contains the following information:
KW	Non-controlled indexing describing the content of the patent
DESC	One-line description of the sequence
FEAT	Additional information indicating positions of known features of the sequence, e.g., coding regions

Once the sequences of interest are retrieved, the patent numbers may be readily transferred to WPINDEX for additional information about the invention.

Similar to the earlier search in REGISTRY and HCAPLUS, a search of DGENE for specific substances will be augmented with a subject search in the text-based file, WPINDEX, for records where the substances of interest are described with subject terms.

### *Conducting a free-text name segment search:*

```
=> FILE DGENE
```

```
=> S (FSHR OR (FSH OR FOLLITROPIN OR FOLLICLE STIMULAT?) (L) RECEPTOR)
  /FEAT, KW, DESC
```

```
L17      117 (FSHR OR (FSH OR FOLLITROPIN OR FOLLICLE STIMULAT?) (L)
          RECEPTOR)/FEAT,KW,DESC
```

```
=> D TRIAL 1-2
```

```
L17      ANSWER 1 OF 117  DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
AN       AAM47959  Protein          DGENE
TI       New polynucleotide, useful for treating Alzheimer's disease,
         Parkinson's disease, Huntington's chorea, diabetes and tumours,
         comprises isolated polynucleotide encoding human follicle
         stimulating hormone-like G-protein coupled receptor -
DESC    Lymnaea stagnalis GPCR GRL101 precursor protein SEQ ID NO 3.
```

*(continued on next page)*

```

KW      Human; follicle stimulating hormone-like G protein-coupled
receptor; FHS-like GPCR; cytostatic; antidiabetic; osteopathic;
antimigraine; nootropic; neuroprotective; antiparkinsonian;
antitumour, antiasthmatic; antiulcer; antiallergic; antigout;
cerebroprotective; antifertility; contraceptive; anorectic;
antianginal; tranquillizer; hypotensive; antidepressant;
neuroleptic; antiemetic; anticonvulsant; cardiant; analgesic;
depilatory; gene; receptor; urinary incontinence; cancer; diabetes;
osteoporosis; neurodegenerative disorder; Alzheimer's disease;
Parkinson's disease; Huntington's chorea; contraceptive; stroke;
great pond snail; GRL101; SwissProt Accession Number P46023.

SQL    1115


L17    ANSWER 2 OF 117  DGENE COPYRIGHT 2002 DERWENT INFORMATION LTD
AN     AAM47958  Protein          DGENE
TI     New polynucleotide, useful for treating Alzheimer's disease,
Parkinson's disease, Huntington's chorea, diabetes and tumours,
comprises isolated polynucleotide encoding human follicle
stimulating hormone-like G-protein coupled receptor -
DESC   Human FSH-like GPCR SEQ ID NO 2.
KW     Human; follicle stimulating hormone-like G protein-coupled
receptor; FHS-like GPCR; cytostatic; antidiabetic; osteopathic;
antimigraine; nootropic; neuroprotective; antiparkinsonian;
antitumour, antiasthmatic; antiulcer; antiallergic; antigout;
cerebroprotective; antifertility; contraceptive; anorectic;
antianginal; tranquillizer; hypotensive; antidepressant;
neuroleptic; antiemetic; anticonvulsant; cardiant; analgesic;
depilatory; gene; receptor; urinary incontinence; cancer; diabetes;
osteoporosis; neurodegenerative disorder; Alzheimer's disease;
Parkinson's disease; Huntington's chorea; contraceptive; stroke.

SQL    191

```

### *Locating patents indexed to specific sequences:*

The STN TRANSFER command may be used to take selected information, e.g. the patent numbers from these sequence records, and re-search this information in the target file, WPINDEX. Additional features of the command include

- More than one field of data may be transferred, however using only PN suffices here
- It is an automated process initiated in the target file, WPINDEX in this example
- For further details: <http://www.cas.org/training/stncommands/stncommands.html> 

=> FILE WPINDEX

=> TRANSFER L17 PN

ENTER ANSWER NUMBERS, RANGES (1-), OR ?:1-  
L18 TRANSFER L17 1- PN : 12 TERMS  
L19 12 L18

*The TRANSFER command selected 12 PN terms. This implies that the 117 sequences were described in 12 patents.*

=> S L19 AND PY.B>1999

1262084 PY.B>1999  
(PY.B>1999)  
L20 3 L19 AND PY.B>1999

=> D IBIB 3

L20 ANSWER 3 OF 3 WPINDEX COPYRIGHT 2002 DERWENT INFORMATION LTD  
ACCESSION NUMBER: 2001-091069 [10] WPINDEX  
DOC. NO. CPI: C2001-026721  
TITLE: New composition for regulating fertility, and for chemoprevention and chemotherapy of cancer, comprises an antisense oligonucleotide that is complementary to a **NUCLEOTIDE SEQUENCE OF A FOLLICLE-STIMULATING HORMONE RECEPTOR.**  
DERWENT CLASS: A96 B04 D16  
INVENTOR(S): LABARBERA, A R; WANG, Y; ZHU, C  
PATENT ASSIGNEE(S): (UYCI-N) UNIV CINCINNATI  
COUNTRY COUNT: 92  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000073416	A1	20001207	(200110)*	EN	89 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000051379	A	20001218	(200118)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000073416	A1	WO 2000-US13488	20000516
AU 2000051379	A	AU 2000-51379	20000516

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000051379	A Based on	WO 200073416

PRIORITY APPLN. INFO: US 1999-158612P 19991008; US 1999-136489P  
19990528

While in WPINDEX the free-text query developed for HCAplus can also be searched here. For Derwent subscribers additional search approaches may be available, e.g. Derwent Manual Code classification.

*Note: (3A) proximity is used to ensure search terms are closely associated with one another, in either order.*

**Search by free-text in WPINDEX:**

=> S FSHR OR (FSH OR FOLLITROPIN OR FOLLICLE STIMULAT?) (3A) RECEPTOR

L22 27 FSHR OR (FSH OR FOLLITROPIN OR FOLLICLE STIMULAT?) (3A) RECEPTOR

=> S L22 AND PY.B>1999

1262084 PY.B>1999  
(PY.B>1999)

L23 11 L22 AND PY.B>1999

=> S L21 OR L23

L24 11 L21 OR L23

=> D IBIB

L24 ANSWER 1 OF 11 WPINDEX COPYRIGHT 2002 DERWENT INFORMATION LTD  
 ACCESSION NUMBER: 2002-049533 [06] WPINDEX  
 DOC. NO. NON-CPI: N2002-036590  
 DOC. NO. CPI: C2002-014019  
 TITLE: New polynucleotide, useful for treating Alzheimer's disease, Parkinson's disease, Huntington's chorea, diabetes and tumors, comprises isolated polynucleotide encoding human follicle stimulating hormone-like G-protein coupled receptor.  
 DERWENT CLASS: B04 D16 S03  
 INVENTOR(S): RAMAKRISHNAN, S  
 PATENT ASSIGNEE(S): (FARB) BAYER AG  
 COUNTRY COUNT: 94  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001088127	A2	20011122	(200206)*	EN	98 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC					
MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE					
DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG					
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ					
PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN					
YU ZA ZW					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001088127	A2	WO 2001-EP5613	20010517

PRIORITY APPLN. INFO: US 2000-205057P 20000518

Many of these inventions may also be included in the answer set from HCAplus. However, a unique invention may be included here. Again, the TRANSFER command can readily extract and search the patent numbers in CAplus.

**TRANSFER PNs from WPINDEX to HCAplus:**

=> TRANSFER L24 1- PN

L25 TRANSFER L24 1- PN : 29 TERMS  
L26 11 L25

=> S L26 NOT L15

L27 3 L26 NOT L15

=> D SCAN

L27 3 ANSWERS HCAPLUS COPYRIGHT 2002 ACS

IC ICM G01N033-52

ICS C07H021-04; C07K014-00; C12N015-12

CC 2-1 (Mammalian Hormones)

Section cross-reference(s): 1, 3

TI Enzyme-based G protein-coupled receptor assay for monitoring GPCR activity and protein/protein interactions in GPCR signaling and for screening ligands

ST enzyme assay G protein coupled receptor signaling ligand screening; ICAST assay G protein coupled receptor signaling ligand screening

IT Animal cell line

(A431, cells expressing fusion proteins containing <SYM98>-galactosidase mutants, a GPCR and another interacting protein; enzyme-based G protein-coupled receptor assay for monitoring GPCR signaling and for screening ligands)

IT Adenosine receptors

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)

(A2; enzyme-based G protein-coupled receptor assay for monitoring GPCR activity and protein/protein interactions in GPCR signaling and for screening ligands)

- 
- 
- 

IT G protein-coupled receptors

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)

(enzyme-based G protein-coupled receptor assay for monitoring GPCR activity or screening ligands)

- 
- 
- 

IT 355171-82-3

RL: PRP (Properties)

(unclaimed protein sequence; enzyme-based G protein-coupled receptor assay for monitoring GPCR activity and protein/protein interactions in GPCR signaling and for screening ligands)

=> S L15 OR L26

L28 183 L15 OR L26

*This record appears to be indexed more broadly to G protein coupled receptors. Highlights the value of multifile searching.*

*Recall L15 is the original HCAplus answer set of 183 records.*

## Option: Extending the search to GENBANK

The GENBANK file is the largest integrated database of nucleic acid sequences, both referenced in the literature and un-referenced. Unique to GENBANK on STN is the addition of CAS RNs and in many cases a link to the HCAplus record for the source reference.

Similar to DGENE, sequence description information is best searched in these fields:

This field ...	Contains the following information:
DEF	One-line description of the sequence
FEAT	Additional information indicating positions of known features of the sequence, e.g., coding regions

### Conducting a free-text name segment search:

Searching “translation” in the FEAT search field may retrieve a nucleic acid record that includes translation information for a specific peptide.

```
=> FILE GENBANK
```

```
=> S (FSHR OR (FSH OR FOLLITROPIN OR FOLLICLE STIMULAT?) (L)
RECEPTOR)/DEF,FEAT
```

```
L29          75 (FSHR OR (FSH OR FOLLITROPIN OR FOLLICLE
STIMULAT?) (L)RECEPTOR)/DEF,FEAT
```

```
=> S L29 AND TRANSLATION/FEAT
```

```
589881 TRANSLATION/FEAT
L30          55 L29 AND TRANSLATION/FEAT
```

```
=> D ALL
```

```
L30 ANSWER 1 OF 55          GENBANK@ COPYRIGHT 2002
```

```
LOCUS (LOC):          AF436883          GenBank (R)
GenBank ACC. NO. (GBN): AF436883
CAS REGISTRY NO. (RN): 370552-29-7
SEQUENCE LENGTH (SQL): 529
MOLECULE TYPE (CI):   mRNA; linear
DIVISION CODE (CI):   Other vertebrates
DATE (DATE):          14 Nov 2001
DEFINITION (DEF):     Salmo salar putative follicle-
stimulating hormone receptor mRNA,
partial cds.
```

*55 of the nucleic acid records include translation information for the encoded protein.*

*(continued on next page)*

SOURCE: Atlantic salmon.  
 ORGANISM (ORGN): Salmo salar  
 Eukaryota; Metazoa; Vertebrata; Euteleostomi; Neopterygii; Teleostei; Protacanthopterygii; Salmo

NUCLEIC ACID COUNT (NA): 108 a 168 c 121

REFERENCE: 1 (bases 1 to 529)  
 AUTHOR (AU): Andersson, E.; Kumar, R.S.; Trant, J.M.; Ackers, J.A.; Stefansson, S.O.  
 TITLE (TI): Isolation of putative FSH receptor cDNA from Atlantic salmon gonads  
 JOURNAL (SO): Unpublished

REFERENCE: 2 (bases 1 to 529)  
 AUTHOR (AU): Ackers, J.A.; Kumar, R.S.; Trant, J.M.  
 TITLE (TI): Direct Submission  
 JOURNAL (SO): Submitted (22-OCT-2001) Center of Marine Biotechnology, University of Maryland Biotechnology Institute, 701 East Pratt Street, Baltimore, MD 21202, USA

FEATURES (FEAT):

Feature Key	Location	Qualifier
source	1..529	/organism="Salmo salar" /db-xref="taxon:8030" /tissue-type="ovary"
CDS	<1..>529	/codon-start=2 /product="putative follicle-stimulating hormone receptor" /protein-id="AAL31634.1" /db-xref="GI:16923915" /translation="HKLFILMGNLQLSHMHNNSEFK GAEGPGFLDISRTALSSLPESVLG EVEHLSAVSVFSLRALPPLSLFTKLRQANLTYPS HCCAFHKHQQRNRTFRMNSACFKPG AQDNLHFFMDFCLNWTSVACSPAPDAFNPCE DIMGSAPLRVLIWIIISVLALLGNTIVL LVLLGSRKMTVPRFL"

SEQUENCE (SEQ):

```

1 acacaaactg tttctcatg gcaacctgca actttctcat atgcataata attccttcaa
61 aggagcagag gggccggggt tcttagacat ctctcgtaga gcgctgagtt ccctgccaga
121 gtcagtgctg ggtgaagttag agcatctgtc cgctgtctcg gtgttctcac tcagagcgct
181 gcctcccctg tccctattca caaagctacg acaggctaac ctcacctacc catctcactg
241 ctgcgccttc cataaacacc agaggaacag gaccttccgg atgaactccg cgtgctttaa
301 acccggggct caggacaacc tccacttctt catggacttc tgtttaaatt ggacgtctgt
361 ggctgtagt cccgcccccg atgccttcaa cccctgtgaa gacatcatgg gctccgcccc
421 tctacgtgtc ctcatctgga tcatctctgt gctcgactg ttaggcaaca ccatctgtct
481 gcttgtgttg ctaggcagcc gagcgaagat gacggtgcca cgcttctctg
  
```

*This was a direct submission – there is no literature reference given. Perhaps the CAS RN could be used to retrieve literature in HCAplus.*

*Note the translated protein.*



## Skills Practice

1. Retrieve literature that discusses genetic vectors used in the recombinant preparation of tumor necrosis factor receptor or receptor-like proteins.

*Note:* There are many types of genetic vectors — explore the CA Lexicon to identify sequence description terms. Use REGISTRY to locate specific receptor proteins, limiting to protein/FS.

# **BIOTECHNOLOGY SEARCHING ON STN**

## **SUGGESTED SOLUTIONS TO SKILLS PRACTICE PROBLEMS**

**APRIL 2002**

The solutions presented here are solutions that can be attained using techniques and search tools presented in the accompanying workbook.

## Skills Practice (page 40):

**Question 1:** How has MALDI mass spectrometry been used in the identification or determination of genetic markers?

```
=> FILE HCAPLUS
```

```
=> E MALDI/CT
```

E#	FREQUENCY	AT	TERM
E1	1	6	MALDANE SARSI/CT
E2	1		MALDANIDAE/CT
E3	0	3	--> MALDI/CT
E4	0	3	MALDI MASS SPECTROMETRY/CT
E5	0	1	MALE/CT
E6	0	2	MALE ACCESSORY GLAND/CT
E7	0	2	MALE ACCESSORY GLAND REPRODUCTIVE ORGAN/CT
E8	0	2	MALE ACCESSORY REPRODUCTIVE GLAND/CT
E9	84	2	MALE ACCESSORY REPRODUCTIVE ORGAN/CT
E10	0	2	MALE ACCESSORY SEX ORGAN/CT
E11	0	2	MALE CASTRATION/CT
E12	33	2	MALE CONTRACEPTIVES/CT

```
=> E E4+ALL
```

```
E13      0  --> MALDI mass spectrometry/CT
E14      USE Laser desorption mass spectrometry (L)
           photoionization, matrix-assisted laser
E15      USE Laser ionization mass spectrometry (L)
           photodesorption, matrix-assisted/CT
```

*MALDI mass spectrometry is not a controlled vocabulary indexing term.*

```
***** END***
```

```
=> E E15+ALL
```

```
E16      26307 BT3 Analysis/CT
E17      1500  BT3 Measurement/CT
E18      19964 BT2 Mass spectrometry/CT
E19      1240  BT1 Laser ionization mass spectrometry/CT
E20      --> Laser ionization mass spectrometry (L)
           photodesorption, matrix-assisted/CT
E21      UF   MALDI/CT
E22      UF   MALDI mass spectrometry/CT
E23      UF   Matrix-assisted laser desorption ionization
           mass spectrometry/CT
```

```
***** END***
```

*(continued on next page)*

=&gt; S E20+PFT

L1 1768 "LASER IONIZATION MASS SPECTROMETRY (L) PHOTODESORPTION,  
MATRIX-ASSISTED"+PFT/CT (4 TERMS)

=&gt; S MALDI OR MATRIX ASSISTED(S)DESORPTION(S)IONIZATION

=&gt; S L1 OR L2

L3 6402 L1 OR L2

=&gt; E GENETIC MARKERS/CT

E#	FREQUENCY	AT	TERM
--	-----	--	----
E24	0	5	GENETIC MAPS/CT
E25	1035	2	GENETIC MARKER/CT
E26	5802	16	--> GENETIC MARKERS/CT
E27	9767	84	GENETIC METHODS/CT
E28	0	2	GENETIC METHODS (L) DNA FINGERPRINTING/CT
E29	0	3	GENETIC METHODS (L) GENE DISCOVERY/CT
E30	0	2	GENETIC METHODS (L) GENOTYPING/CT
E31	0	2	GENETIC METHODS (L) NASBA (NUCLEIC ACID SEQUENCE-BASED AMPLIFICATION)/CT
E32	0	2	GENETIC METHODS (L) SELEX/CT
E33	0	3	GENETIC METHODS (L) TWO-HYBRID SCREENING/CT
E34	0	2	GENETIC OBESITY/CT
E35	0	2	GENETIC OPERATOR/CT

=&gt; E E26+ALL

E36	5436	BT1	Biomarkers (biological responses)/CT
E37	9767	BT2	Genetic methods/CT
E38	32308	BT1	Genetic mapping/CT
E39	5802	-->	Genetic markers/CT
		HN	Valid heading during volume 126 (1997) to present.
E40	1035	OLD	Genetic marker/CT
E41		UF	Arbitrary DNA segment/CT
E42		UF	Chromosome markers/CT
E43		UF	DNA markers/CT
E44		UF	Gene marker/CT
E45		UF	Markers/CT
E46		UF	Markers (genetic)/CT
E47	1657	NT1	EST (expressed sequence tag)/CT
E48		NT1	Genetic element (L) EST (expressed sequence tag)/CT
E49		NT1	Genetic element (L) STS (sequence-tagged site)/CT
E50	500	NT1	STS (sequence-tagged site)/CT
E51	980	RT	QTL (quantitative trait loci)/CT
*****	END***		

(continued on next page)

=> S E39+PFT,NT

L4 8797 "GENETIC MARKERS"+PFT,NT/CT (12 TERMS)

=> S (DNA OR GENETIC OR GENE)(S)MARKER OR EST OR STS OR SEQUENCE TAG?

L5 199700 (DNA OR GENETIC OR GENE)(S)MARKER OR EST OR STS OR SEQUENCE TAG?

=> S L4 OR L5

L6 199700 L4 OR L5

=> S L3 AND L6

L7 112 L3 AND L6

=> D IBIB ABS HITIND 1-4

L7 ANSWER 1 OF 112 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:195073 HCAPLUS [Full-text](#)

TITLE: **Maldi**-tof mass spectrometry of bacteria

AUTHOR(S): Lay, Jackson O., Jr.

CORPORATE SOURCE: Division of Chemistry, National Center for

Toxicological Research, Food and Drug

Administration, Jefferson, AR, 72079, USA

SOURCE: Mass Spectrometry Reviews (2002), Volume Date

2001, 20(4), 172-194

CODEN: MSRVD3; ISSN: 0277-7037

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The development of **MALDI**-TOF mass spectrometry methods for the characterization of bacteria is reviewed and discussed. The general use of **MALDI** for the characterization of large biomols. led directly to obvious applications involving the anal. of isolated bacterial proteins. More surprising was the observation that **MALDI**-TOF mass spectrometry could be applied directly to crude cellular fractions or cellular suspensions and that the resulting data from such complex mixts. could provide evidence for chemotaxonomic classification. Versatility and the rapidity of anal. led to the rapid development of a number of **MALDI**-TOF methods involving bacteria. Examples of some of the applications covered in this review are the anal. of bacterial RNA and **DNA**, the detection of recombinant proteins, the characterization of targeted or unknown proteins, bacterial proteomics, the detection of virulence **markers**, and the very rapid characterization of bacteria at the genus, species, and strain level. The demonstrated capability of taxonomic classification at the strain level, using unprocessed cells, opens the possibility that **MALDI**-TOF and similar mass spectrometry approaches may contribute significantly to fulfilling emerging needs for the development of near real-time methods for the characterization of bacteria.

CC 9 (Biochemical Methods)

(continued on next page)

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 112 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:79731 HCAPLUS [Full-text](#)  
TITLE: A Trypanosoma brucei protein complex that binds G-overhangs and co-purifies with telomerase activity  
AUTHOR(S): Cano, Maria Isabel N.; Blake, Julie Johnson; Blackburn, Elizabeth H.; Agabian, Nina  
CORPORATE SOURCE: Departments of Stomatology, Microbiology and Immunology, University of California, San Francisco, CA, 94143-0422, USA  
SOURCE: Journal of Biological Chemistry (2002), 277(2), 896-906  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The chromosomal ends of Trypanosoma brucei, like those of most eukaryotes, contain conserved 5'-TTAGGG-3' repeated sequences and are maintained by the action of telomerase. Fractionated T. brucei cell exts. with telomerase activity were used as a source of potential regulatory factors or telomerase-associated components that might interact with T. brucei telomeres. Electrophoretic mobility shift assays and UV crosslinking were used to detect possible single-stranded telomeric protein·DNA complexes and to **estimate** the approx. size of the protein constituents. Three single-stranded telomeric protein·DNA complexes were observed. Complex C3 was highly specific for the G-strand telomeric repeat sequence and shares biochem. characteristics with G-rich, single-stranded telomeric binding proteins and with components of the telomerase holoenzyme described in yeast, ciliates, and humans. Susceptibility to RNase A or chem. nuclease (hydroxyl radical) pre-treatment showed that complex C3 was tightly associated with an RNA component. **Matrix-assisted laser desorption /ionization**-time of flight mass spectrometry was used to **estimate** the mol. mass of the peptides obtained by in-gel Lys-C digestion of low abundance C3-associated proteins. The mol. masses of the peptides showed no homologies with other proteins from trypanosomes or with any protein in the databases screened.

CC 7-3 (Enzymes)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 112 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:40647 HCAPLUS [Full-text](#)  
TITLE: Characterisation of global protein expression by two-dimensional electrophoresis and mass spectrometry: proteomics of Toxoplasma gondii

(continued on next page)

AUTHOR(S): Cohen, A. M.; Rumpel, K.; Coombs, G. H.;  
Wastling, J. M.

CORPORATE SOURCE: Division of Infection & Immunity, Institute of  
Biomedical and Life Sciences, University of  
Glasgow, Glasgow, G12 8QQ, UK

SOURCE: International Journal for Parasitology (2002),  
32(1), 39-51  
CODEN: IJPYBT; ISSN: 0020-7519

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The development of tools for the anal. of global gene expression is  
vital for the optimal exploitation of the data on parasite genomes  
that are now being generated in abundance. Recent advances in two-  
dimensional electrophoresis (2-DE), mass spectrometry and  
bioinformatics have greatly enhanced the possibilities for mapping  
and characterization of protein populations. We have employed these  
developments in a proteomics approach for the anal. of proteins  
expressed in the tachyzoite stage of *Toxoplasma gondii*. Over 1000  
polypeptides were reproducibly separated by high-resolution 2-DE  
using the pH ranges 4-7 and 6-11. Further sepns. using narrow range  
gels suggest that at least 3000-4000 polypeptides should be  
resolvable by 2-DE using multiple single pH unit gels. Mass  
spectrometry was used to characterize a variety of protein spots on  
the 2-DE gels. Peptide mass fingerprints, acquired by matrix-  
assisted laser desorption/ionisation-( **MALDI**) mass spectrometry,  
enabled unambiguous protein identifications to be made where full  
gene sequence information was available. However, interpretation of  
peptide mass fingerprint data using the *T. gondii* expressed **sequence  
tag (EST)** database was less reliable. Peptide fragmentation data,  
acquired by post-source decay mass spectrometry, proved a more  
successful strategy for the putative identification of proteins  
using the *T. gondii* **EST** database and protein databases from other  
organisms. In some instances, several protein spots appeared to be  
encoded by the same gene, indicating that post-translational  
modification and/or alternative splicing events may be a common  
feature of functional gene expression in *T. gondii*. The data  
demonstrate that proteomic analyses are now viable for *T. gondii* and  
other protozoa for which there are good **EST** databases, even in the  
absence of complete genome sequence. Moreover, proteomics is of  
great value in interpreting and annotating **EST** databases.

CC 10 (Microbial, Algal, and Fungal Biochemistry)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L7 ANSWER 4 OF 112 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:27248 HCAPLUS [Full-text](#)

TITLE: Demonstration of Dimethylnonanoyl-CoA  
Thioesterase Activity in Rat Liver Peroxisomes  
Followed by Purification and Molecular Cloning  
of the Thioesterase Involved

AUTHOR(S): Ofman, R.; el Mrabet, L.; Dacremont, G.; Spijer,  
D.; Wanders, R. J. A.

(continued on next page)

CORPORATE SOURCE: Department of Clinical Chemistry, University of  
Amsterdam, Amsterdam, 1100 DE, Neth.  
SOURCE: Biochemical and Biophysical Research  
Communications (2002), 290(2), 629-634  
CODEN: BBRCA9; ISSN: 0006-291X  
PUBLISHER: Academic Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Peroxisomes play an indispensable role in cellular fatty acid oxidation in higher eukaryotes by catalyzing the chain shortening of a distinct set of fatty acids and fatty acid derivs. including pristanic acid (2,6,10,14-tetramethylpentadecanoic acid). Earlier studies have shown that pristanic acid undergoes three cycles of  $\beta$ -oxidation in peroxisomes to produce 4,8-dimethylnonanoyl-CoA (DMN-CoA) which is then transported to the mitochondria for full oxidation to CO<sub>2</sub> and H<sub>2</sub>O. In principle, this can be done via two different mechanisms in which DMN-CoA is either converted into the corresponding carnitine ester or hydrolyzed to 4,8-dimethylnonanoic acid plus CoASH. The latter pathway can only be operational if peroxisomes contain 4,8-dimethylnonanoyl-CoA thioesterase activity. In this paper we show that rat liver peroxisomes indeed contain 4,8-dimethylnonanoyl-CoA thioesterase activity. We have partially purified the enzyme involved from peroxisomes and identified the protein as the rat ortholog of a known human thioesterase using **MALDI** -TOF mass spectrometry in combination with the rat **EST** database. Heterologous expression studies in Escherichia coli established that the enzyme hydrolyzes not only DMN-CoA but also other branched-chain acyl-CoAs as well as straight-chain acyl-CoA-esters. Our data provide convincing evidence for the existence of the second pathway of acyl-CoA transport from peroxisomes to mitochondria by hydrolysis of the CoA-ester in peroxisomes followed by transport of the free acid to mitochondria, reactivation to its CoA-ester, and oxidation to CO<sub>2</sub> and H<sub>2</sub>O. (c) 2002 Academic Press.

CC 7 (Enzymes)  
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D IBIB ABS HITIND 110-112

L7 ANSWER 110 OF 112 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1995:591743 HCAPLUS [Full-text](#)  
DOCUMENT NUMBER: 122:315550  
TITLE: Characterization of Polymers by **Matrix-Assisted Laser Desorption Ionization**-Time of Flight Mass Spectrometry. End Group Determination and Molecular Weight Estimates in Poly(ethylene glycols)  
AUTHOR(S): Montaudou, Giorgio; Montaudou, Maurizio S.; Puglisi, Concetto; Samperi, Filippo  
CORPORATE SOURCE: Dipartimento di Scienze Chimiche, Universita di Catania, Catania, 95125, Italy

(continued on next page)

SOURCE: Macromolecules (1995), 28(13), 4562-9  
 CODEN: MAMOBX; ISSN: 0024-9297

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB **Matrix-assisted** laser **desorption ionization**-time of flight mass spectrometry (**MALDI**-TOF MS) allows mass measurements of large mols. such as those present in synthetic and natural macromols. We have used a self-calibrating method for the **MALDI**-TOF spectra of polymers, with 2-(4- hydroxyphenylazo)benzoic acid as matrix, enabling us to obtain accurate mass values. Polyethylene glycol (PEG) samples having two different kinds of end groups were used in our work: (i) anionic PEG, H-(CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-H; (ii) cationic PEG, H-(CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>n</sub>-OH. The **MALDI**-TOF spectra recorded in reflected mode allowed unambiguous identification of the end groups present in these PEG samples. Five anionic PEG samples with very narrow mol. weight distributions (MWD) were studied. The **MALDI**-TOF spectra of PEGs were recorded in both linear and reflected modes. Due to the high sensitivity and the highly linear response of HIMAS (a microchannel detector equipped with a photomultiplier), measurements of **MALDI**-TOF spectra were used in our work to **estimate** the MW and MWD of the PEG samples. Our results show that the mol. weight **ests.** provided by **MALDI**-TOF measurements agree with the values obtained by conventional techniques such as GPC, osmometry, and viscometry.

CC 36-4 (Physical Properties of Synthetic High Polymers)

L7 ANSWER 111 OF 112 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:526012 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 122:266525  
 TITLE: Characterization of polymers by **matrix-assisted** laser **desorption/ionization** time-of-flight mass spectrometry: molecular weight estimates in samples of varying polydispersity

AUTHOR(S): Montaudou, Giorgio; Montaudou, Maurizio S.; Puglisi, Concetto; Samperi, Filippo  
 CORPORATE SOURCE: Dipartimento di Scienze Chimiche, Universita di Catania, Catania, 95125, Italy  
 SOURCE: Rapid Commun. Mass Spectrom. (1995), 9(5), 453-60  
 CODEN: RCMSEF; ISSN: 0951-4198

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB **Matrix-assisted** laser **desorption/ionization** time-of-flight mass spectrometry (**MALDI**-TOF MS) was used to **estimate** mol. weight distributions (MWD) of PMMA, polystyrene, and poly(ethylene glycol), nylon 6, polycarbonate, and polyester. The mol. weight **ests.** provided by **MALDI**-TOF measurements agree with the values obtained by conventional techniques, such as gel-permeation chromatog. (GPC), only in the case of polymer samples with very narrow MWD. However, when the polydispersity reaches values around 1.10 the difference between the MW measured by GPC and measured by **MALDI** may amount to up to about 20%. At higher dispersions, the **MALDI** spectra fail to yield reliable MW values.

CC 36-4 (Physical Properties of Synthetic High Polymers)  
 Section cross-reference(s): 73

(continued on next page)

IT Molecular weight  
(distribution; of polymers evaporating by **matrix-assisted**  
laser **desorption/ionization** time-of-flight mass  
spectrometry)

IT Polycarbonates, properties  
Polyesters, properties  
Polymers, properties  
RL: PRP (Properties)  
(mol. weight distribution of polymers evaporating by **matrix-**  
**assisted** laser **desorption/ionization**  
time-of-flight mass spectrometry)

IT 9003-53-6, Polystyrene 9011-14-7, PMMA 24936-97-8, Adipic  
acid-butanediol copolymer, sru 24980-41-4,  $\epsilon$ -Caprolactone  
homopolymer 25038-54-4, Nylon 6, properties 25038-54-4D, Nylon  
6, functionalized 25103-87-1, Adipic acid-butanediol copolymer  
25248-42-4,  $\epsilon$ -Caprolactone homopolymer, sru 25322-68-3,  
Poly(ethylene glycol)  
RL: PRP (Properties)  
(mol. weight distribution of polymers evaporating by **matrix-**  
**assisted** laser **desorption/ionization**  
time-of-flight mass spectrometry)

L7 ANSWER 112 OF 112 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1995:269471 HCAPLUS [Full-text](#)  
DOCUMENT NUMBER: 122:177400  
TITLE: Models for matrix-assisted desorption by a  
laser-pulse  
AUTHOR(S): Johnson, R. E.  
CORPORATE SOURCE: Engineering Physics, Thornton Hall B103  
University of Virginia, Charlottesville, VA,  
22903, USA  
SOURCE: Int. J. Mass Spectrom. Ion Processes (1994),  
139, 25-38  
CODEN: IJMPDN; ISSN: 0168-1176  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Although there is no complete quant. description of matrix-assisted  
desorption of biomols., the qual. picture given by most workers is  
roughly the same. Based on such a picture, progress on a quant.  
description can be made using a framework in which specific phys.  
quantities can be extracted Such a framework is given here for the  
total (ablation) yield and for the matrix or analyte mol. ion  
yields, and the effect of averaging over a Gaussian laser profile is  
evaluated. The dependence of the yield on fluence near threshold  
can be used to distinguish between ejection models, and the incident  
angle dependence of the yield can be used to determine whether  
ejection occurs in response to the initial energy d. distribution or  
whether a transport process affects the ejection efficiency. Also  
the shift in value of the threshold fluence between matrix mol.  
ejection and ion ejection is due to the difference in the energy  
barriers to ejection. This shift is used to **estimate** the energy per  
ion for matrix ion formation and ejection to be  $\approx 1.5$  to 2eV.  
Finally, the relation between the depth of origin of the analyte  
ions and the threshold dependence of the yield is considered. In  
the appendix the relations of the excitation and ejection parameters  
to those phys. quantities determining the plume are described, as is  
a simple phys. model for **MALDI**.

CC 80-6 (Organic Analytical Chemistry)  
Section cross-reference(s): 9, 26, 73

=> **FOCUS L7**

*Use FOCUS to reorder  
the records by relevance.*

PROCESSING COMPLETED FOR L7  
L8 112 FOCUS L7 1-

=> **D TI 1-5**

L8 ANSWER 1 OF 112 HCAPLUS COPYRIGHT 2002 ACS  
TI Detection of single nucleotide polymorphisms and cytosine methylations in chemically modified genomic DNA for diagnosis and prognosis of genetic disorders

L8 ANSWER 2 OF 112 HCAPLUS COPYRIGHT 2002 ACS  
TI High-throughput development and characterization of a genomewide collection of **gene**-based single nucleotide polymorphism **markers** by chip-based **matrix-assisted** laser **desorption/ionization** time-of-flight mass spectrometry

L8 ANSWER 3 OF 112 HCAPLUS COPYRIGHT 2002 ACS  
TI Use of **matrix-assisted** laser **desorption/ionization** time-of-flight mass mapping and nanospray liquid chromatography/electrospray **ionization** tandem mass spectrometry **sequence tag** analysis for high sensitivity identification of yeast proteins separated by two-dimensional gel electrophoresis

L8 ANSWER 4 OF 112 HCAPLUS COPYRIGHT 2002 ACS  
TI Identifying Proteins Using **Matrix-Assisted** Laser **Desorption/Ionization** In-Source Fragmentation Data Combined with Database Searching

L8 ANSWER 5 OF 112 HCAPLUS COPYRIGHT 2002 ACS  
TI Structural analysis and identification of gel-purified proteins, available in the femtomole range, using a novel computer program for peptide sequence assignment, by **matrix-assisted** laser **desorption ionization**-reflectron time-of-flight-mass spectrometry

=> **FILE BIOSIS**

=> **E GENETIC MARKERS/CT**

E#	FREQUENCY	AT	TERM
--	-----	--	----
E52	1		GENETIC MARKER PROTEINS/CT
E53	1		GENETIC MARKER SEARCH/CT
E54	149	-->	GENETIC MARKERS/CT
E55	2		GENETIC MARKING/CT
E56	15		GENETIC MATERIAL/CT
E57	1		GENETIC MATERIAL DELIVERY PHARMACEUTICAL COMPOSITIONS/CT
E58	2		GENETIC MATERIAL INTERACTION/CT

(continued on next page)

```
E59          1          GENETIC MATERIAL TRANSFER SYSTEM/CT
E60          11         GENETIC MECHANISM/CT
E61          23         GENETIC MECHANISMS/CT
E62          1          GENETIC MECHANISMS OF RESISTANCE/CT
E63          3          GENETIC MEDIATION/CT
```

=> D HIS

(FILE 'HCAPLUS' ENTERED AT 15:21:05 ON 27 MAR 2002)

```
DEL HIS
DEL SEL
```

FILE 'HCAPLUS' ENTERED AT 16:12:03 ON 27 MAR 2002

```
E MALDI/CT
E E4+ALL
E E15+ALL
L1          1768 S E20+PFT
L2          6251 S MALDI OR MATRIX ASSISTED(S) DESORPTION(S) IONIZATION
L3          6402 S L1 OR L2
E GENETIC MARKERS/CT
E E26+ALL
L4          8797 S E39+PFT,NT
L5          199700 S (DNA OR GENETIC OR GENE)(S) MARKER OR EST OR STS OR
SEQUENCE T
L6          199700 S L4 OR L5
L7          112 S L3 AND L6
L8          112 FOCUS L7 1-
```

FILE 'BIOSIS' ENTERED AT 16:21:38 ON 27 MAR 2002

```
E GENETIC MARKERS/CT
```

=> S L2 AND L5

```
L9          51 L2 AND L5
```

*Directly use L-numbers  
from HCAPLUS to re-  
search the query in BIOSIS.*

=> D SCAN

```
L9          51 ANSWERS BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI          Demonstration of dimethylnonanoyl-CoA thioesterase activity in rat
liver peroxisomes followed by purification and molecular cloning of
the thioesterase involved.
IT          Miscellaneous Descriptors
oxidation
```

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

```
L9          51 ANSWERS BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
TI          Fine mapping and single nucleotide polymorphism association results
of candidate genes for asthma and related phenotypes.
IT          Methods & Equipment
MALDI-TOF MS: analytical method; fine mapping: molecular
genetic method; genotyping: molecular genetic method; single
nucleotide polymorphism analysis: molecular genetic method
IT          Miscellaneous Descriptors
phenotype; single nucleotide polymorphism
```

(continued on next page)

L9 51 ANSWERS BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
TI The proteome of maize leaves: Use of gene sequences and expressed  
**sequence tag** data for identification of proteins with  
peptide mass fingerprints.  
IT Methods & Equipment  
Voyager-DE PRO mass spectrometer: PerSeptive Biosystems,  
laboratory equipment; **matrix assisted laser desorption**  
**/ionization**-time of flight mass spectrometer: analytical  
method, spectroscopic techniques: CB; two-dimensional  
electrophoresis: analytical method, gel electrophoresis  
IT Miscellaneous Descriptors  
expressed **sequence tag** data; gene sequences; genome  
sequence information; proteome

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> DUP REM L8 L9

FILE 'HCAPLUS' ENTERED AT 16:23:11 ON 27 MAR 2002

FILE 'BIOSIS' ENTERED AT 16:23:11 ON 27 MAR 2002

PROCESSING COMPLETED FOR L8

PROCESSING COMPLETED FOR L9

L10 115 DUP REM L8 L9 (48 DUPLICATES REMOVED)

ANSWERS '1-99' FROM FILE HCAPLUS

ANSWERS '100-115' FROM FILE BIOSIS

=> FOCUS L10

*FOCUS may be used with a  
multifile answer set as well.*

PROCESSING COMPLETED FOR L10

L11 115 FOCUS L10 1-

=> D TI 1-5

L11 ANSWER 1 OF 115 HCAPLUS COPYRIGHT 2002 ACS

TI High-throughput development and characterization of a genomewide  
collection of **gene**-based single nucleotide polymorphism  
**markers** by chip-based **matrix-assisted laser**  
**desorption/ionization** time-of-flight mass spectrometry

L11 ANSWER 2 OF 115 HCAPLUS COPYRIGHT 2002 ACS

TI Use of **matrix-assisted laser desorption/**  
**ionization** time-of-flight mass mapping and nanospray liquid  
chromatography/electrospray **ionization** tandem mass spectrometry  
**sequence tag** analysis for high sensitivity  
identification of yeast proteins separated by two-dimensional gel  
electrophoresis

L11 ANSWER 3 OF 115 HCAPLUS COPYRIGHT 2002 ACS

TI Identifying Proteins Using **Matrix-Assisted Laser**  
**Desorption/Ionization** In-Source Fragmentation Data  
Combined with Database Searching

(continued on next page)

L11 ANSWER 4 OF 115 HCAPLUS COPYRIGHT 2002 ACS  
TI Structural analysis and identification of gel-purified proteins, available in the femtomole range, using a novel computer program for peptide sequence assignment, by **matrix-assisted laser desorption ionization**-reflectron time-of-flight-mass spectrometry

L11 ANSWER 5 OF 115 HCAPLUS COPYRIGHT 2002 ACS  
TI Protein identification based on **matrix assisted laser desorption/ionization**-post source decay-mass spectrometry

=> D IBIB ABS HITIND

L11 ANSWER 1 OF 115 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:77638 HCAPLUS [Full-text](#)  
DOCUMENT NUMBER: 135:163086  
TITLE: High-throughput development and characterization of a genomewide collection of **gene**-based single nucleotide polymorphism **markers** by chip-based **matrix-assisted laser desorption/ionization** time-of-flight mass spectrometry  
AUTHOR(S): Buetow, Kenneth H.; Edmonson, Michael; MacDonald, Richard; Clifford, Robert; Yip, Ping; Kelley, Jenny; Little, Daniel P.; Strausberg, Robert; Koester, Hubert; Cantor, Charles R.; Braun, Andreas  
CORPORATE SOURCE: Laboratory of Population Genetics, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, 20892-5060, USA  
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(2), 581-584  
CODEN: PNASA6; ISSN: 0027-8424  
PUBLISHER: National Academy of Sciences  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB We describe here a system for the rapid identification, assay development, and characterization of gene-based single nucleotide polymorphisms (SNPs). This system couples informatics tools that mine candidate SNPs from public expressed **sequence tag** resources and automatically designs assay reagents with detection by a chip-based **matrix-assisted laser desorption/ionization** time-of-flight mass spectrometry platform. As a proof of concept of this system, a genomewide collection of reagents for 9,115 **gene**-based SNP **genetic markers** was rapidly developed and validated. These data provide preliminary insights into patterns of polymorphism in a genomewide collection of gene-based polymorphisms.  
CC 3-1 (Biochemical Genetics)  
Section cross-reference(s): 9  
ST genome SNP polymorphism marker **MALDI** TOF mass spectrometry

(continued on next page)

IT Time-of-flight mass spectrometry  
(**MALDI-**; high-throughput development and characterization of a genomewide collection of **gene**-based single nucleotide polymorphism **markers** by chip-based **matrix-assisted laser desorption/ionization** time-of-flight mass spectrometry)

IT Biosensors  
(chip; high-throughput development and characterization of a genomewide collection of **gene**-based single nucleotide polymorphism **markers** by chip-based **matrix-assisted laser desorption/ionization** time-of-flight mass spectrometry)

IT Genome  
(high-throughput development and characterization of a genomewide collection of **gene**-based single nucleotide polymorphism **markers** by chip-based **matrix-assisted laser desorption/ionization** time-of-flight mass spectrometry)

IT **Gene**  
RL: ANT (Analyte); ANST (Analytical study)  
(high-throughput development and characterization of a genomewide collection of **gene**-based single nucleotide polymorphism **markers** by chip-based **matrix-assisted laser desorption/ionization** time-of-flight mass spectrometry)

IT **Laser ionization mass spectrometry**  
(**photodesorption, matrix-assisted,** time-of-flight; high-throughput development and characterization of a genomewide collection of **gene**-based single nucleotide polymorphism **markers** by chip-based **matrix-assisted laser desorption/ionization** time-of-flight mass spectrometry)

IT Laser **desorption** mass spectrometry  
(photoionization, **matrix-assisted,** time-of-flight; high-throughput development and characterization of a genomewide collection of **gene**-based single nucleotide polymorphism **markers** by chip-based **matrix-assisted laser desorption/ionization** time-of-flight mass spectrometry)

IT **Genetic** polymorphism  
(single nucleotide; high-throughput development and characterization of a genomewide collection of **gene**-based single nucleotide polymorphism **markers** by chip-based **matrix-assisted laser desorption/ionization** time-of-flight mass spectrometry)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

## Skills Practice (page 40):

**Question 2:** Retrieve literature on genetic engineering applied to developing tomatoes with increased freeze protection.

*Note: A Chemical and Engineering News article referred to the concept of “antifreeze proteins”.*

=> FILE HCAPLUS

=> S TOMATO AND FREEZING

=> D SCAN

L1 141 ANSWERS HCAPLUS COPYRIGHT 2002 ACS  
CC 17 (Foods)  
TI Determination of hydrogen cyanide on greenhouse **tomatoes**  
ST hydrogen cyanide **tomatoes**; cyanide hydrogen **tomatoes**;  
**tomatoes** hydrogen cyanide  
IT **Tomatoes**  
(hydrogen cyanide determination on)  
IT 74-90-8  
RL: ANT (Analyte); ANST (Analytical study)  
(determination of, on greenhouse **tomatoes**)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L1 141 ANSWERS HCAPLUS COPYRIGHT 2002 ACS  
CC 17-10 (Food and Feed Chemistry)  
Section cross-reference(s): 11  
TI Content of potentially anticarcinogenic flavonoids of 28 vegetables  
and 9 fruits commonly consumed in the Netherlands  
ST flavonoid fruit vegetable; season leafy vegetable flavonoid;  
quercetin fruit vegetable; kaempferol fruit vegetable; myricetin  
fruit vegetable; luteolin fruit vegetable; anticarcinogen flavonoid  
food  
IT Grape  
(black, myricetin of, season in relation to)  
IT Neoplasm inhibitors  
(flavonoids of fruits and vegetables in relation to)  
IT Turnip  
(flavonoids of tops of, season in relation to)  
IT Apricot  
Bean  
Broad bean  
Kale


*(continued on next page)*

Pea  
Peach  
Spinach  
    (flavonoids of, processing and season in relation to)  
IT Mushroom  
    (flavonoids of, processing in relation to)  
IT Brassica oleracea sabellica  
    Broccoli  
    Brussels sprout  
    Cauliflower  
    Chicory  
    Cucumber  
    Endive  
    Leek  
    Lettuce  
    Onion  
    Plum  
    Portulaca oleracea  
    Radish  
    Rutabaga  
    Sauerkraut  
    Strawberry  
    **Tomato**  
    (flavonoids of, season in relation to)  
IT Apple  
    Pear  
    (kaempferol and quercetin of, season and variety in relation to)  
IT Carrot  
    (luteolin of, processing in relation to)  
IT Canning  
    **Freezing** ← *Freezing as a method of food processing is not what we seek!*  
(of fruits and vegetables, flavonoids response to)  
IT Flavonoids  
    RL: BIOL (Biological study)  
    (of fruits and vegetables, processing and anticarcinogenic activity in relation to)  
    •  
    •  
    •  
  
L1 141 ANSWERS HCAPLUS COPYRIGHT 2002 ACS  
IC ICM C12N015-00  
CC 3-3 (Biochemical Genetics)  
Section cross-reference(s): 6, 11  
TI Transcription factor stress-related proteins and methods of use in Plants  
ST transcription factor stress related protein cDNA sequence; stress tolerance transgenic plant TFSRP gene expression  
IT mRNA  
    RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
    (APS-2, ZF-2, ZF-3, ZF-4, ZF-5, MYB-1, CABF-3 and SFL-1;  
    transcription factor stress-related proteins and methods of use in plants)

(continued on next page)

- IT Gene, animal  
Proteins, specific or class  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(APS-2; transcription factor stress-related proteins and methods of use in plants)
- IT Transcription factors  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(CABF-3 (CCAAT box-binding protein 3); transcription factor stress-related proteins and methods of use in plants)
- IT Gene, animal  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(CABF-3; transcription factor stress-related proteins and methods of use in plants)
- IT Proteins, specific or class  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(DNA-binding, zinc finger-containing, ZF-2; transcription factor stress-related proteins and methods of use in plants)
- IT Proteins, specific or class  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(DNA-binding, zinc finger-containing, ZF-3; transcription factor stress-related proteins and methods of use in plants)
- IT Proteins, specific or class  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(DNA-binding, zinc finger-containing, ZF-4; transcription factor stress-related proteins and methods of use in plants)
- IT Proteins, specific or class  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(DNA-binding, zinc finger-containing, ZF-5; transcription factor stress-related proteins and methods of use in plants)
- IT Gene, animal  
Proteins, specific or class  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(MYB-1; transcription factor stress-related proteins and methods of use in plants)

*(continued on next page)*

- IT Gene, animal  
Transcription factors  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(SFL-1; transcription factor stress-related proteins and methods of use in plants)
- IT Gene, plant  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(TFSRP; transcription factor stress-related proteins and methods of use in plants)
- IT Gene, animal  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(ZF-2; transcription factor stress-related proteins and methods of use in plants)
- IT Gene, animal  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(ZF-3; transcription factor stress-related proteins and methods of use in plants)
- IT Gene, animal  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(ZF-4; transcription factor stress-related proteins and methods of use in plants)
- IT Gene, animal  
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(ZF-5; transcription factor stress-related proteins and methods of use in plants)
- IT Stress, plant  
(environmental, tolerance to; transcription factor stress-related proteins and methods of use in plants)
- IT Stress, plant  This looks more relevant.  
(freezing; transcription factor stress-related proteins and methods of use in plants)
- IT Grass (Poaceae)  
(perennial; transcription factor stress-related proteins and methods of use in plants)
- IT Stress, plant  
(salinity; transcription factor stress-related proteins and methods of use in plants)
- 
- 
- 

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

(continued on next page)

## =&gt; E ANTIFREEZE PROTEINS/CT

E#	FREQUENCY	AT	TERM
--	-----	--	----
E1	401	8	ANTIFREEZE/CT
E2	0	2	ANTIFREEZE GLYCOPROTEINS/CT
E3	111	2	--> ANTIFREEZE PROTEINS/CT
E4	1098	2	ANTIFREEZE SUBSTANCES/CT
E5	0	1	ANTIFREEZING/CT
E6	0	2	ANTIFREEZING AGENTS/CT
E7	0	1	ANTIFRICTION/CT
E8	0	2	ANTIFRICTION ABRASION-RESISTANT COATING MATERIALS/CT
E9	0	3	ANTIFRICTION ABRASION-RESISTANT MATERIALS/CT
E10	0	2	ANTIFRICTION AGENTS/CT
E11	166	2	ANTIFRICTION COATINGS/CT
E12	0	2	ANTIFRICTION LUBRICATING OIL ADDITIVES/CT

## =&gt; E E3+ALL

E13 111 --> Antifreeze proteins/CT  
E14 USE Proteins (L) antifreeze/CT  
\*\*\*\*\* END\*\*\*

## =&gt; E E14+ALL

E15 485431 BT1 Proteins/CT  
E16 --> Proteins (L) antifreeze/CT  
E17 OLD Proteins, specific or class (L) antifreeze/CT  
E18 UF Antifreeze proteins/CT  
E19 UF THP proteins/CT  
E20 UF Thermal hysteresis proteins/CT  
\*\*\*\*\* END\*\*\*

## =&gt; S ANTIFREEZE(S)(PROTEIN OR GENE OR THP OR THERMAL HYSTERESIS)

L2 729 ANTIFREEZE(S)(PROTEIN OR GENE OR  
HYSTERESIS)

*Develop a free-text query from the controlled indexing terms.*

## =&gt; E TOMATO/CT

E#	FREQUENCY	AT	TERM
--	-----	--	----
E21	0	1	TOMATE/CT
E22	0	2	TOMATILLO/CT
E23	16630	89	--> TOMATO/CT
E24	0	16	TOMATO (L) CANNED/CT
E25	0	16	TOMATO (L) DISEASE/CT
E26	0	16	TOMATO (L) DISEASE, EARLY BLIGHT/CT
E27	0	17	TOMATO (L) DISEASE, LATE BLIGHT/CT
E28	0	16	TOMATO (L) DISEASE, WILT/CT
E29	0	16	TOMATO (L) DWARF/CT
E30	0	16	TOMATO (L) FROZEN/CT
E31	0	2	TOMATO (L) L. CHEESMANII/CT
E32	0	2	TOMATO (L) L. CHEESMANII MINOR/CT

(continued on next page)

## =&gt; E E23+ALL

E33	3118	BT6 Eukaryote (Eukaryotae)/CT
E34	11634	BT5 Plant (Embryophyta)/CT
E35	274	BT4 Angiosperm (Magnoliophyta)/CT
E36	604	BT3 Dicotyledon (Magnoliopsida)/CT
E37	1	BT2 Solanales/CT
E38	495	BT1 Solanaceae/CT
E39	43461	BT3 Food/CT
E40	0	BT2 Plant-derived food (non-CA heading)/CT
E41	3118	BT5 Eukaryote (Eukaryotae)/CT
E42	11634	BT4 Plant (Embryophyta)/CT
E43	274	BT3 Angiosperm (Magnoliophyta)/CT
E44	0	BT2 Unassigned angiosperms (non-CA heading)/CT
E45	10079	BT1 Vegetable/CT
E46	16630	--> Tomato/CT
		HN Valid heading during volume 76 (1972) to present.
		NOTE Lycopersicon esculentum can be assumed unless other information is stated in the index entry.
E47	1253	OLD Tomatoes/CT
E48		UF L. esculentum Tomato/CT
E49		UF Lycopersicon/CT
E50		UF Lycopersicon esculentum/CT
E51		UF Lycopersicon lycopersicum/CT
E52		UF Lycopersicum/CT
E53		UF Lycopersicum esculenta/CT
E54		UF Solanum lycopersicum/CT
E55	2	NT1 Lycopersicum peruvianum/CT
E56		NT1 Tomato (L) L. cheesmanii/CT
E57		NT1 Tomato (L) L. chilense/CT
E58		NT1 Tomato (L) L. chmielewskii/CT
E59		NT1 Tomato (L) L. esculentum cerasiforme/CT
E60		NT1 Tomato (L) L. esculentum flacca/CT
E61		NT1 Tomato (L) L. esculentum oogatah/CT
E62		NT1 Tomato (L) L. esculentum pimpinellifolium/CT
E63		NT1 Tomato (L) L. glandulosum/CT
E64		NT1 Tomato (L) L. hirsutum/CT
E65		NT1 Tomato (L) L. parviflorum/CT
E66		NT1 Tomato (L) L. pennellii/CT
E67		NT1 Tomato (L) L. peruvianum/CT
E68		NT1 Tomato (L) L. pimpinellifolium/CT
E69		NT1 Tomato (L) L. racemigerum/CT
E70		NT1 Tomato (L) Lycopersicon cheesmanii/CT
E71		NT1 Tomato (L) Lycopersicon chilense/CT
E72		NT1 Tomato (L) Lycopersicon chmielewskii/CT
E73		NT1 Tomato (L) Lycopersicon esculentum cerasiforme/CT
E74		NT1 Tomato (L) Lycopersicon esculentum flacca/CT

(continued on next page)

E75		NT1	Tomato (L) Lycopersicon esculentum oogatah/CT
E76		NT1	Tomato (L) Lycopersicon esculentum pimpinellifolium/CT
E77		NT1	Tomato (L) Lycopersicon glandulosum/CT
E78		NT1	Tomato (L) Lycopersicon hirsutum/CT
E79		NT1	Tomato (L) Lycopersicon parviflorum/CT
E80		NT1	Tomato (L) Lycopersicon pennellii/CT
E81		NT1	Tomato (L) Lycopersicon peruvianum/CT
E82		NT1	Tomato (L) Lycopersicon pimpinellifolium/CT
E83		NT1	Tomato (L) Lycopersicon racemigerum/CT
E84	7	NT1	Tomato (Lycopersicon cheesmanii)/CT
E85		NT2	Tomato (L) L. cheesmanii minor/CT
E86		NT2	Tomato (L) Lycopersicon cheesmanii minor/CT
E87	1	NT2	Tomato (Lycopersicon cheesmanii minor)/CT
E88	18	NT1	Tomato (Lycopersicon chilense)/CT
E89	4	NT1	Tomato (Lycopersicon chmielewskii)/CT
E90	19	NT1	Tomato (Lycopersicon esculentum cerasiforme)/CT
E91	0	NT1	Tomato (Lycopersicon esculentum flacca)/CT
E92	0	NT1	Tomato (Lycopersicon esculentum oogatah)/CT
E93	0	NT1	Tomato (Lycopersicon esculentum pimpinellifolium)/CT
E94	0	NT1	Tomato (Lycopersicon glandulosum)/CT
E95	28	NT1	Tomato (Lycopersicon hirsutum)/CT
E96		NT2	Tomato (L) L. glabratum/CT
E97		NT2	Tomato (L) L. hirsutum glabratum/CT
E98		NT2	Tomato (L) L. hirsutum hirsutum/CT
E99		NT2	Tomato (L) Lycopersicon glabratum/CT
E100		NT2	Tomato (L) Lycopersicon hirsutum glabratum/CT
E101		NT2	Tomato (L) Lycopersicon hirsutum hirsutum/CT
E102		NT2	Tomato (L) Lycopersicon hirsutum typicum/CT
E103	8	NT2	Tomato (Lycopersicon hirsutum glabratum)/CT
E104	1	NT2	Tomato (Lycopersicon hirsutum hirsutum)/CT
E105	6	NT2	Tomato (Lycopersicon hirsutum typicum)/CT
E106	2	NT1	Tomato (Lycopersicon parviflorum)/CT
E107	55	NT1	Tomato (Lycopersicon pennellii)/CT
E108		NT2	Tomato (L) Lycopersicon pennellii puberulum/CT

(continued on next page)

E109 0 NT2 Tomato (Lycopersicon pennellii  
puberulum)/CT  
E110 75 NT1 Tomato (Lycopersicon peruvianum)/CT  
E111 NT2 Tomato (L) L. peruvianum  
dentatum/CT  
E112 NT2 Tomato (L) L. peruvianum  
glandulosum/CT  
E113 NT2 Tomato (L) Lycopersicon peruvianum  
dentatum/CT  
E114 NT2 Tomato (L) Lycopersicon peruvianum  
glandulosum/CT  
E115 2 NT2 Tomato (Lycopersicon peruvianum  
dentatum)/CT  
E116 0 NT2 Tomato (Lycopersicon peruvianum  
glandulosum)/CT  
E117 38 NT1 Tomato (Lycopersicon  
pimpinellifolium)/CT  
E118 1 NT1 Tomato (Lycopersicon racemigerum)/CT  
E119 748 RT Tomato juice/CT  
E120 216 RT Tomato products/CT  
E121 RTCS Lycopene/CT  
\*\*\*\*\* END\*\*\*

=> S E46-E55

L3 17886 (TOMATO/CT OR TOMATOES/CT OR "L. ESCULENTUM TOMATO"/CT OR  
LYCOPERSICON/CT OR "LYCOPERSICON ESCULENTUM"/CT OR  
"LYCOPERSICON LYCOPERSICUM"/CT OR LYCOPERSICUM/CT OR  
"LYCOPERSICUM ESCULENTA"/CT OR "SOLANUM LYCOPERSICUM"/CT OR  
"LYCOPERSICUM PERUVIANUM"/CT)

=> S L2 AND L3

L4 3 L2 AND L3

=> D IBIB ABS HITIND 1-3

L4 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1997:687812 HCAPLUS [Full-text](#)  
DOCUMENT NUMBER: 128:3163  
TITLE: The research on introducing flounder  
**antifreeze protein gene**  
(afp) into tomato  
AUTHOR(S): Huang, Yong-Fen; Wang, Qing-Yin; Fu, Gui-Yong;  
Zhao, Xiao-Xiang; Yang, Zhi-Xing  
CORPORATE SOURCE: Department Biology, Harbin Normal University,  
Harbin, 150080, Peop. Rep. China  
SOURCE: Shengwu Huaxue Zazhi (1997), 13(4), 418-422  
CODEN: SHZAE4; ISSN: 1000-8543  
PUBLISHER: Zhongguo Shengwu Huaxue Yu Fenzi Shengwu Xuehui  
DOCUMENT TYPE: Journal  
LANGUAGE: Chinese

(continued on next page)

AB **Antifreeze protein gene** (afp) which is integrated into the Ti plasmid pMon322, was introduced into tomato via the pollen-tube pathway and ovary injection. The transgenic plants of D1 and D2 generation produced afp DNA on Southern blot. The assay of cold resistance in the field showed that transgenic plants could grow better than control under the average temperature that is 4.4°C below normal year in earlier spring, meanwhile the fatal temperature dropped 2°C. Thus, AFP gene has been integrated into the transgenic plants genome and expressed.

CC 17-10 (Food and Feed Chemistry)

ST flounder **antifreeze protein gene** tomato

IT Plasmids  
 (pMon322; research on introducing flounder **antifreeze protein gene** (afp) into tomato)

IT Flounder  
 Pollen tube  
 Temperature effects (biological)  
**Tomato**  
 (research on introducing flounder **antifreeze protein gene** (afp) into tomato)

IT **Genes** (animal)  
 RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)  
 (research on introducing flounder **antifreeze protein gene** (afp) into tomato)

IT **Antifreeze proteins**  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (research on introducing flounder **antifreeze protein gene** (afp) into tomato)

IT DNA  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (research on introducing flounder **antifreeze protein gene** (afp) into tomato)

=> E STRESS, PLANT/CT

E#	FREQUENCY	AT	TERM
--	-----	--	----
E122	0	3	STRESS, MICROBIAL (L) OSMOTIC/CT
E123	0	4	STRESS, MICROBIAL (L) TOXIC/CT
E124	4095	60 -->	STRESS, PLANT/CT
E125	0	4	STRESS, PLANT (L) ACIDITY/CT
E126	0	4	STRESS, PLANT (L) ALUMINUM/CT
E127	0	4	STRESS, PLANT (L) ALUMINUM EXCESS/CT
E128	0	4	STRESS, PLANT (L) AMMONIUM EXCESS/CT
E129	0	4	STRESS, PLANT (L) ANAEROBIC/CT
E130	0	4	STRESS, PLANT (L) BORON DEFICIENCY/CT
E131	0	4	STRESS, PLANT (L) BORON EXCESS/CT
E132	0	4	STRESS, PLANT (L) CHEM./CT
E133	0	5	STRESS, PLANT (L) COLD/CT

(continued on next page)

=&gt; E E124+ALL

E134	4095	-->	Stress, plant/CT
		HN	Valid heading during volume 131 (July 1999) to present.
E135	8427	OLD	Plant stress/CT
E136	2515	OLD	Plant stress and adaptation/CT
E137		UF	Biol. stress/CT
E138		UF	Biological stress/CT
E139		UF	Environmental stress/CT
E140	110	NT1	Hypoxia, plant/CT
E141		NT1	Plant stress (L) UV B/CT
E142		NT1	Plant stress (L) acidity/CT
E143		NT1	Plant stress (L) aluminum/CT
E144		NT1	Plant stress (L) aluminum excess/CT
E145		NT1	Plant stress (L) ammonium excess/CT
E146		NT1	Plant stress (L) anaerobic/CT
E147		NT1	Plant stress (L) boron deficiency/CT
E148		NT1	Plant stress (L) boron excess/CT
E149		NT1	Plant stress (L) chem./CT
E150		NT1	Plant stress (L) cold/CT
E151		NT1	Plant stress (L) copper excess/CT
E152		NT1	Plant stress (L) darkness/CT
E153		NT1	Plant stress (L) defoliation/CT
E154		NT1	Plant stress (L) environmental/CT
E155		NT1	Plant stress (L) freezing/CT
E156		NT1	Plant stress (L) frost/CT
E157		NT1	Plant stress (L) heat/CT
E158		NT1	Plant stress (L) hypoxic/CT
E159		NT1	Plant stress (L) infection/CT
E160		NT1	Plant stress (L) iron excess/CT
E161		NT1	Plant stress (L) light/CT
E162		NT1	Plant stress (L) light deficiency/CT
E163		NT1	Plant stress (L) light excess/CT
E164		NT1	Plant stress (L) manganese deficiency/CT
E165		NT1	Plant stress (L) manganese excess/CT
E166		NT1	Plant stress (L) mech./CT
E167		NT1	Plant stress (L) nitrogen deficiency/CT
E168		NT1	Plant stress (L) nutrient/CT
E169		NT1	Plant stress (L) nutrient deficiency/CT
E170		NT1	Plant stress (L) osmotic/CT
E171		NT1	Plant stress (L) phosphorus deficiency/CT
E172		NT1	Plant stress (L) potassium deficiency/CT
E173		NT1	Plant stress (L) salinity/CT
E174		NT1	Plant stress (L) shading/CT
E175		NT1	Plant stress (L) sodicity/CT
E176		NT1	Plant stress (L) sulfur deficiency/CT
E177		NT1	Plant stress (L) water/CT
E178		NT1	Plant stress (L) water deficiency/CT
E179		NT1	Plant stress (L) water excess/CT
E180		NT1	Plant stress (L) wounding/CT
E181		NT1	Plant stress (L) zinc deficiency/CT
E182		NT1	Plant stress (L) zinc excess/CT
E183		NT1	Plant stress and adaptation (L) water/CT

(continued on next page)




## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
WO 2002015675	A1	20020228	WO 2001-US26189	20010822
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			US 2000-227439P	P 20000822
			US 2000-713994	A 20001116
			US 2001-837944	A 20010416
AB	The invention relates to 232 Arabidopsis plant transcription factor polypeptides, polynucleotides that encode them, homologs from a variety of plant species, and methods of using the polynucleotides and polypeptides to produce <b>transgenic</b> plants having advantageous properties compared to a reference plant. Exemplary polynucleotides encoding the polypeptides of the invention were identified in the A. thaliana GenBank database using publicly available sequence anal. programs and parameters. Sequences initially identified were then further characterized to identify sequences comprising specified sequence strings corresponding to sequence motifs present in families of known transcription factors. Polynucleotide sequences meeting such criteria were confirmed as transcription factors. Further polynucleotides of the invention were identified by screening A. thaliana and/or other plant cDNA libraries with probes corresponding to known transcription factors under low stringency hybridization conditions. Addnl. sequences, including full-length coding sequences, were subsequently recovered by the rapid amplification of cDNA ends (RACE) procedure. The polynucleotides can be or were ectopically expressed in overexpressor or knockout plants and the changes in the characteristic(s) or trait(s) of the plant observed			
IC	ICM A01H005-00			
	ICS C12P021-00; C12N015-82			
CC	3-3 (Biochemical Genetics)			
	Section cross-reference(s): 5, 6, 11			
IT	Antioxidants			
	(alteration in level of; transcription factor <b>genes</b> from Arabidopsis thaliana and their use for modifying plant traits)			
IT	Amino acids, biological studies			
	Glucosinolates			
	Sterols			
	Tannins			
	Terpenes, biological studies			
	Tocopherols			
	Vitamins			

(continued on next page)

- Waxes  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(alteration in level of; transcription factor **genes** from  
Arabidopsis thaliana and their use for modifying plant traits)
- IT Carbohydrates, preparation  
Essential oils  
Fats and Glyceridic oils, preparation  
Proteins  
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP  
(Preparation)  
(alteration in production of; transcription factor **genes** from  
Arabidopsis thaliana and their use for modifying plant traits)
- IT Germination  
Growth and development, plant  
Leaf  
Leaf senescence  
Organ, plant  
Root  
Seed  
Stem  
Transpiration (plant)  
(alteration in; transcription factor **genes** from Arabidopsis  
thaliana and their use for modifying plant traits)
- IT Nucleic acids  
RL: AGR (Agricultural use); BUU (Biological use, unclassified); BIOL  
(Biological study); USES (Uses)  
(antisense; transcription factor **genes** from Arabidopsis  
thaliana and their use for modifying plant traits)
- IT Growth and development, plant  
(apical dominance, alteration in; transcription factor **genes**  
from Arabidopsis thaliana and their use for modifying plant  
traits)
- IT Melon (plant)  
(cantaloupe; transcription factor **genes** from Arabidopsis  
thaliana and their use for modifying plant traits)
- IT Stress, plant  
(cold, enhanced tolerance to; transcription factor **genes** from  
Arabidopsis thaliana and their use for modifying plant traits)
- IT Computer application  
(computer-readable medium and stored sequence information;  
transcription factor **genes** from Arabidopsis thaliana and  
their use for modifying plant traits)
- IT Fungi  
Microorganism  
Plant virus  
Radiation  
(enhanced tolerance to; transcription factor **genes** from  
Arabidopsis thaliana and their use for modifying plant traits)
- IT Heavy metals  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological  
study)  
(enhanced tolerance to; transcription factor **genes** from  
Arabidopsis thaliana and their use for modifying plant traits)

(continued on next page)

- IT Growth and development, plant  
(flowering, alteration in; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT **Stress, plant**  
(**freezing**, enhanced tolerance to; transcription factor **genes** from Arabidopsis thaliana and their use for modifying **plant** traits) 
- IT Root  
(hair, alteration in; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Stress, plant  
(heat, enhanced tolerance to; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Melon (plant)  
(honeydew; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Stem  
(internode, alteration in; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Growth and development, plant  
(lateral branching, alteration in; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Stress, plant  
(light deficiency, enhanced tolerance to; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Reproduction, plant  
(male sterility, alteration in; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Leaf abscission  
(petal, alteration in; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Lipids, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(prenyl-containing, alteration in level of; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Fruit  
(rosaceous; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Seed  
(testa, alteration in; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)
- IT Alfalfa (Medicago sativa)  
Arabidopsis thaliana  
Banana (Musa)  
Blackberry  
Blueberry  
Capsicum  
Carrot  
Cauliflower  
Coffee (Coffea)

(continued on next page)

Corn  
Cotton  
Cucumber (Cucumis sativus)  
Disease resistance, plant  
Eggplant (Solanum melongena)  
Grape  
Herbicide resistance  
Lettuce (Lactuca sativa)  
Mango (Mangifera indica)  
Melon (plant)  
Mint  
Onion (Allium cepa)  
Papaya (Carica papaya)  
Pea  
Pineapple (Ananas comosus)  
Plant (Embryophyta)  
Potato (Solanum tuberosum)  
Protein sequences  
Rape (plant)  
Raspberry  
Rice (Oryza sativa)  
Sequence homology analysis  
Soybean (Glycine max)  
Spinach (Spinacia oleracea)  
Squash (Cucurbita)  
Strawberry  
Sugarcane  
Sunflower  
Sweet corn  
Tobacco  
    **Tomato**  
Transformation, **genetic**  
Turf  
Watermelon (Citrullus lanatus)  
Wheat  
cDNA sequences  
    (transcription factor **genes** from Arabidopsis thaliana and  
    their use for modifying plant traits)  
IT EST (expressed sequence tag)  
    **Gene**, plant  
Transcription factors  
cDNA  
RL: AGR (Agricultural use); BSU (Biological study, unclassified);  
    BUU (Biological use, unclassified); PRP (Properties); BIOL  
    (Biological study); USES (Uses)  
    (transcription factor **genes** from Arabidopsis thaliana and  
    their use for modifying plant traits)  
IT Organ, plant  
    (trichome, alteration in; transcription factor **genes** from  
    Arabidopsis thaliana and their use for modifying plant traits)  
IT Brassica  
    (vegetable; transcription factor **genes** from Arabidopsis  
    thaliana and their use for modifying plant traits)

(continued on next page)

IT Stress, plant  
(water deficiency, enhanced tolerance to; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)

IT Stress, plant  
(waterlogging, enhanced tolerance to; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)

IT 9004-34-6, Cellulose, biological studies 9005-53-2, Lignin, biological studies 33069-62-4, Taxol  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (alteration in level of; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)

IT 7727-37-9, Nitrogen, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (alteration in uptake of; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)

IT 9005-25-8, Starch, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (alteration in; transcription factor **genes** from Arabidopsis thaliana and their use for modifying plant traits)

•  
•  
•

=> D HIS

=> FILE BIOSIS

=> S L2

L9 643 ANTIFREEZE(S) (PROTEIN OR GENE OR THP OR THERMAL HYSTERESIS)

=> S E46-E55/BI



Note using the CT from HCAPLUS, represented by E46-E55, re-qualified to the Basic Index in BIOSIS.

L10 35005 (TOMATO/BI OR TOMATOES/BI OR "L. ESCULENTUM TOMATO"/BI OR LYCOPERSICON/BI OR "LYCOPERSICON ESCULENTUM"/BI OR "LYCOPERSICON LYCOPERSICUM"/BI OR LYCOPERSICUM/BI OR "LYCOPERSICUM ESCULENTA"/BI OR "SOLANUM LYCOPERSICUM"/BI OR "LYCOPERSICUM PERUVIANUM"/BI)

=> S L9 AND L10

L11 2 L9 AND L10

=> D IBIB ABS HITIND 1-2

L11 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 1993:371026 BIOSIS [Full-text](#)  
DOCUMENT NUMBER: PREV199396056701  
TITLE: Proteins accumulate in the apoplast of winter rye leaves during cold acclimation.  
AUTHOR(S): Marentes, Eduardo; Griffith, Marilyn (1); Mlynarz, Andrzej; Brush, Ruth Anne (1)

(continued on next page)

CORPORATE SOURCE: (1) Dep. Biol., Univ. Waterloo, 200 University Ave.  
West, Waterloo, ON N2L 3G1 Canada

SOURCE: Physiologia Plantarum, (1993) Vol. 87, No. 4, pp.  
499-507.  
ISSN: 0031-9317.

DOCUMENT TYPE: Article

LANGUAGE: English

AB During cold acclimation, winter rye (*Secale cereale* L.) plants develop the ability to tolerate freezing temperatures by forming ice in intercellular spaces and xylem vessels. In this study **proteins**, were extracted from the apoplast of rye leaves to determine their role in controlling extracellular ice formation. Several polypeptides in the 15 to 32 kDa range accumulated in the leaf apoplast during cold acclimation at 5 degree C and decreased during deacclimation at 20 degree C. A second group of polypeptides (63, 65 and 68 kDa) appeared only when the leaves were maximally frost tolerant. Ice nucleation activity, as well as the previously reported **antifreeze** activity, was higher in apoplastic extracts from cold-acclimated than from nonacclimated rye leaves. These results indicate that apoplastic **proteins** exert a direct influence on the growth of ice. In addition, freezing injury was greater in extracted cold-acclimated leaves than in unextracted cold-acclimated leaves, which suggests that the **proteins** present in the apoplast are an important component of the mechanism by which winter rye leaves tolerate ice formation.

CC Biochemical Studies - Proteins, Peptides and Amino Acids 10064  
External Effects - Temperature as a Primary Variable - Cold \*10616  
Metabolism - Proteins, Peptides and Amino Acids \*13012  
Temperature: Its Measurement, Effects and Regulation - Cryobiology \*23004  
Plant Physiology, Biochemistry and Biophysics - Temperature \*51503  
Plant Physiology, Biochemistry and Biophysics - Metabolism \*51519  
Plant Physiology, Biochemistry and Biophysics - Translocation, Accumulation \*51520

BC Gramineae \*25305

IT Major Concepts  
Metabolism; Physiology

IT Miscellaneous Descriptors  
LINOLENIC ACID; MEMBRANE PERMEABILITY; RIPENING

ORGN Super Taxa  
Gramineae: Monocotyledones, Angiospermae, Spermatophyta, Plantae;  
Solanaceae: Dicotyledones, Angiospermae, Spermatophyta, Plantae

ORGN Organism Name  
Gramineae (Gramineae); **Lycopersicon esculentum**  
(Solanaceae)

ORGN Organism Superterms  
angiosperms; dicots; monocots; plants; spermatophytes; vascular plants

(continued on next page)

L11 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1992:27792 BIOSIS [Full-text](#)

DOCUMENT NUMBER: BA93:17067

TITLE: EXPRESSION OF **ANTIFREEZE PROTEINS** IN  
TRANSGENIC PLANTS.

AUTHOR(S): HIGHTOWER R; BADEN C; PENZES E; LUND P; DUNSMUIR P

CORPORATE SOURCE: DNA PLANT TECHNOL. CORP., 6701 SAN PABLO AVE.,  
OAKLAND, CALIF. 94608, USA.

SOURCE: PLANT MOL BIOL, (1991) 17 (5), 1013-1022.

CODEN: PMBIDB. ISSN: 0167-4412.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Th quality of frozen fruits and vegetables can be compromised by the damaging effects of ice crystal growth within the frozen tissue. **Antifreeze proteins** in the blood of some polar fishes have been shown to inhibit ice recrystallization at low concentrations. In order to determine whether expression of **genes** of this type confers improved freezing properties to plant tissue, we have produced transgenic tobacco and **tomato** plants which express **genes** encoding **antifreeze proteins**. The afa3 **antifreeze gene** was expressed at high steady-state mRNA levels in leaves from transformed plants, but we did not detect inhibition of ice recrystallization in tissue extracts. However, both mRNA and fusion **proteins** were detectable in transgenic **tomato** tissue containing a chimeric **gene** encoding a fusion **protein** between truncated staphylococcal **protein A** and **antifreeze protein**. Furthermore, ice recrystallization inhibition was detected in this transgenic tissue.

CC Genetics and Cytogenetics - Plant \*03504

Biochemistry - Physiological Water Studies 10011

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

External Effects - Physical and Mechanical Effects \*10612

External Effects - Temperature as a Primary Variable - Cold \*10616

Metabolism - Proteins, Peptides and Amino Acids \*13012

Temperature: Its Measurement, Effects and Regulation - Cryobiology  
\*23004

Plant Physiology, Biochemistry and Biophysics - Water Relations  
\*51502

Plant Physiology, Biochemistry and Biophysics - Temperature \*51503

Plant Physiology, Biochemistry and Biophysics - Metabolism \*51519

BC Solanaceae 26775

IT Miscellaneous Descriptors

**TOMATO GENE EXPRESSION GENETIC TRANSFORMATION ICE  
RECRYSTALLIZATION INHIBITION ICE CRYSTAL DAMAGE TISSUE FREEZING**

## Skills Practice (page 40):

**Question 3:** Retrieve literature describing DNA or nucleic acid probes for low-density lipoproteins and their use in assessing the risk of atherosclerosis.

=> FILE HCAPLUS

=> S (DNA OR NUCLEIC ACID) (S) PROBE AND ATHEROSCLEROSIS AND LIPOPROTEIN

L1 20 (DNA OR NUCLEIC ACID) (S) PROBE AND ATHEROSCLEROSIS AND LIPOPROTEIN

=> D SCAN

L1 20 ANSWERS HCAPLUS COPYRIGHT 2002 ACS

CC 14-5 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 3

TI Familial apolipoprotein A-I, C-III, and A-IV deficiency and premature **atherosclerosis** due to deletion of a gene complex on chromosome 11

ST high density **lipoprotein** gene mutation **atherosclerosis**

IT Gene and Genetic element, animal

RL: PROC (Process)

(for high-d. **lipoprotein**-associated apolipoproteins, mutation of, in high-d. **lipoprotein** deficiency and premature **atherosclerosis** in human)

IT **Atherosclerosis**

(high-d. **lipoprotein**-associated apolipoprotein gene mutation associated with premature, in human)

IT **Lipoproteins**

RL: BIOL (Biological study)

(apo-, A-I, gene for, deletion of, in high-d. **lipoprotein** deficiency and premature **atherosclerosis** in human)

IT **Lipoproteins**

RL: BIOL (Biological study)

(apo-, A-IV, gene for, deletion of, in high-d. **lipoprotein** deficiency and premature **atherosclerosis** in human)

IT **Lipoproteins**

RL: BIOL (Biological study)

(apo-, C-III, gene for, deletion of, in high-d. **lipoprotein** deficiency and premature **atherosclerosis** in human)

IT Mutation

(deletion, of high-d. **lipoprotein**-associated apolipoprotein genes, in high-d. **lipoprotein** deficiency and premature **atherosclerosis** in human)

*(continued on next page)*

IT **Lipoproteins**  
 RL: BIOL (Biological study)  
 (high-d., deficiency of, mutation of associated with, in premature **atherosclerosis**)

IT Deoxyribonucleic acids  
 RL: PROC (Process)  
 (**lipoprotein** A-I-specifying, deletion of, in high-d. **lipoprotein** deficiency and premature **atherosclerosis** in human)

IT Deoxyribonucleic acids  
 RL: PROC (Process)  
 (**lipoprotein** A-IV-specifying, deletion of, in high-d. **lipoprotein** deficiency and premature **atherosclerosis** in human)

IT Deoxyribonucleic acids  
 RL: PROC (Process)  
 (**lipoprotein** C-III-specifying, deletion of, in high-d. **lipoprotein** deficiency and premature **atherosclerosis** in human)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L1 20 ANSWERS HCAPLUS COPYRIGHT 2002 ACS  
 IC ICM C12Q001-68  
 ICS C07K014-705  
 CC 14-14 (Mammalian Pathological Biochemistry)  
 Section cross-reference(s): 3, 9  
 TI Polymorphisms in a type I scavenger receptor gene and the diagnosis of obesity and cardiovascular disorders  
 ST scavenger receptor gene polymorphism obesity cardiovascular disease risk; LDL HDL scavenger receptor gene polymorphism  
 IT Genes (animal)  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (SR-BI, polymorphisms in; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)

IT Body (anatomical)  
 (body mass index, polymorphism in SR-BI gene and; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)

IT Primers (nucleic acid)  
**Probes (nucleic acid)** ←  
 RL: ARG (Analytical reagent use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (for detection of polymorphism in SR-BI gene; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)

IT Polymorphism (genetic)  
 SSCP (single-strand conformation polymorphism)  
 (in SR-BI gene of human; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)

*Lipoproteins” is the official controlled vocabulary term, with additional information “linked” to it: the text modification in parentheses and the CAS Role indexing.*

*Note the controlled term. The free-text query does pick this up.*

(continued on next page)

- IT Allele frequency  
(of alleles of SR-BI gene; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)
- IT High-density **lipoproteins**  
Low-density **lipoproteins**  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence) (polymorphism in SR-BI gene and plasma levels of; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)
- IT **Atherosclerosis**  
Cachexia  
Cardiovascular diseases  
Gallstones  
Obesity  
(polymorphism in SR-BI gene and susceptibility to; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)
- IT PCR (polymerase chain reaction)  
(polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)
- IT Intron (genetic element)  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (polymorphisms in, in SR-BI gene of human; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)
- IT Susceptibility (genetic)  
(to obesity and cardiovascular disease, polymorphism in SR-BI gene and; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)
- IT Scavenger receptors  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (type I, class B; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)
- IT 220133-92-6  
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (amino acid sequence; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)
- IT 220133-77-7 220133-78-8 220133-79-9 220133-80-2 220133-81-3  
220133-82-4 220141-45-7 220141-47-9 220141-49-1 220141-50-4  
220141-52-6 220141-54-8 220141-56-0  
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (nucleotide sequence; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)

(continued on next page)

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IT  220140-73-8  220140-74-9  220140-75-0  220140-76-1  220140-77-2
    220140-78-3  220140-79-4  220140-83-0  220140-85-2  220140-90-9
    220140-91-0  220140-92-1  220140-93-2  220140-94-3  220140-95-4
    220140-96-5  220141-00-4  220141-05-9  220141-09-3  220141-12-8
    220141-13-9  220141-19-5  220141-24-2  220141-25-3  220141-26-4
    220141-27-5  220141-28-6  220141-29-7  220141-31-1  220141-32-2

```

RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (primer for detection of polymorphism in SR-BI gene; polymorphism in type I scavenger receptor gene and diagnosis of obesity and cardiovascular disorders)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> E LOW DENSITY LIPOPROTEINS/CT

E#	FREQUENCY	AT	TERM
--	-----	--	----
E1	0	2	LOW BLOOD PRESSURE/CT
E2	0	7	LOW CARBON STEEL/CT
E3	0	-->	LOW DENSITY LIPOPROTEINS/CT
E4	0	2	LOW ERUCIC ACID RAPESEED OIL/CT
E5	0	1959	LOW G+C GRAM-POSITIVE BACTERIA/CT
E6	0	2	LOW GRAVITY/CT
E7	0	2	LOW HOP CLOVER/CT
E8	0	2	LOW MOL. WT. KININOGEN/CT
E9	0	2	LOW ODOR BASE SOLVENT/CT
E10	0	2	LOW ODOR PARAFFIN SOLVENT/CT
E11	0	2	LOW TEMP./CT
E12	0	1	LOW-AFFINITY/CT

=> E LOW-DENSITY LIPOPROTEINS/CT

E#	FREQUENCY	AT	TERM
--	-----	--	----
E13	0	2	LOW-DENSITY LIPOPROTEIN RECEPTOR-RELATED PROTEIN/CT
E14	0	2	LOW-DENSITY LIPOPROTEIN RECEPTORS/CT
E15	2753	2 -->	LOW-DENSITY LIPOPROTEINS/CT
E16	0	1	LOW-E/CT
E17	0	1	LOW-EMISSIVITY/CT
E18	0	1	LOW-ENERGY/CT
E19	0	2	LOW-ENERGY ELECTRON BEAM/CT
E20	0	2	LOW-ENERGY ELECTRON MICROSCOPY/CT
E21	0	2	LOW-ENERGY ELECTRON MICROSCOPY (LEEM)/CT
E22	0	2	LOW-ENERGY EXCITATIONS/CT
E23	0	2	LOW-ENERGY ION BEAMS/CT
E24	0	2	LOW-ENERGY QUASIPARTICLES/CT

=> E E15+ALL

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E25  2753  --> Low-density lipoproteins/CT
E26  USE  Lipoproteins (L) low-d./CT
*****  END***

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Confirms the use of "low-d" as text modification to the controlled vocabulary term, lipoproteins.

(continued on next page)

**=> E E26+ALL**

E27 485431 BT2 Proteins/CT  
 E28 49563 BT1 Lipoproteins/CT  
 E29 --> Lipoproteins (L) low-d./CT  
 E30 UF LDL/CT  
 E31 UF LDL (low-density lipoproteins)/CT  
 E32 UF Low-d. lipoprotein/CT  
 E33 UF Low-d. lipoproteins/CT  
 E34 UF Low-density lipoproteins/CT

\*\*\*\*\* END\*\*\*

**=> S LIPOPROTEIN (S) (LOW D OR LOW DENSITY OR LDL)**

L2 32221 LIPOPROTEIN (S) (LOW D OR LOW DENSITY OR LDL)

**=> E ATHEROSCLEROSIS/CT**

E#	FREQUENCY	AT	TERM
--	-----	--	----
E35	0	2	ATHEROGENIC DIET/CT
E36	183	2	ATHEROMA/CT
E37	15881	12	--> ATHEROSCLEROSIS/CT
E38	0	9	ATHEROSCLEROSIS (L) FATTY STREAK/CT
E39	0	2	ATHEROSCLEROSIS INHIBITORS/CT
E40	1	9	ATHEROSPERMA/CT
E41	5	8	ATHEROSPERMA MOSCHATUM/CT
E42	2	9	ATHEROSPERMA REPANDULUM/CT
E43	0	1	ATHERTON-TODD/CT
E44	0	2	ATHERTON-TODD PHOSPHORYLATION/CT
E45	0	2	ATHERTON-TODD REACTION/CT
E46	0	7	ATHERURUS/CT

**=> E E37+ALL**

E47 5703 BT5 Disease, animal/CT  
 E48 0 BT4 Diseases, by body part (non-CA heading)/CT  
 E49 4691 BT3 Blood vessel, disease/CT  
 E50 6781 BT2 Artery, disease/CT  
 E51 5983 BT1 Arteriosclerosis/CT  
 E52 15881 --> Atherosclerosis/CT  
     HN Valid heading during volumes 66-115  
        (1967-1991) and 126 (1997) to present.  
 E53 OLD Arteriosclerosis (L) atherosclerosis/CT  
 E54 1 OLD Atherogenesis/CT  
 E55 183 OLD Atheroma/CT  
 E56 RTCS 7 $\beta$ -Hydroxycholesterol/CT  
 E57 RTCS Cholesteryl linoleate/CT  
 E58 RTCS Lecithin-cholesterol acyltransferase/CT

\*\*\*\*\* END\*\*\*

*(continued on next page)*

=&gt; E E50+ALL

E59 5703 BT3 Disease, animal/CT  
 E60 0 BT2 Diseases, by body part (non-CA heading)/CT  
 E61 4691 BT1 Blood vessel, disease/CT  
 E62 6781 --> Artery, disease/CT  
     HN Valid heading during volumes 116-125  
         (1992-1996) and 131 (July 1999) to present.  
 E63 UF Arterial diseases/CT  
 E64 5983 NT1 Arteriosclerosis/CT  
 E65 1 NT2 Atherogenesis/CT  
 E66 183 NT2 Atheroma/CT  
 E67 15881 NT2 Atherosclerosis/CT  
 E68 NT2 Lung (L) arteriosclerosis/CT  
 E69 NT1 Artery (L) aorta, endothelium, injury/CT  
 E70 NT1 Artery (L) aorta, hypertrophy/CT  
 E71 NT1 Artery (L) aorta, injury/CT  
 E72 NT1 Artery (L) aorta, lesion/CT  
 E73 NT1 Artery (L) aorta, stenosis/CT  
 E74 NT1 Artery (L) arteritis/CT  
 E75 NT1 Artery (L) basilar, spasm/CT  
 E76 NT1 Artery (L) carotid, occlusion/CT  
 E77 NT1 Artery (L) coronary, endothelium, injury/CT  
 E78 NT1 Artery (L) coronary, occlusion/CT  
 E79 NT1 Artery (L) coronary, spasm/CT  
 E80 NT1 Artery (L) coronary, stenosis/CT  
 E81 NT1 Artery (L) endothelium, injury/CT  
 E82 NT1 Artery (L) hypertrophy/CT  
 E83 NT1 Artery (L) injury/CT  
 E84 NT1 Artery (L) intima, hyperplasia/CT  
 E85 NT1 Artery (L) occlusion/CT  
 E86 NT1 Artery (L) patent ductus arteriosus/CT  
 E87 NT1 Artery (L) periarteritis nodosa/CT  
 E88 NT1 Artery (L) peripheral, occlusion/CT  
 E89 NT1 Artery (L) renal, stenosis/CT  
 E90 NT1 Artery (L) spasm/CT  
 E91 NT1 Artery (L) stenosis/CT  
 E92 6 NT1 Artery, neoplasm/CT  
 E93 NT1 Claudication (L) intermittent/CT  
 E94 NT1 Heart (L) coronary/CT  
 E95 NT1 Heart (L) restenosis/CT  
 E96 NT1 Heart, disease (L) coronary/CT  
 E97 NT1 Heart, disease (L) restenosis/CT  
 E98 512 RT Aneurysm/CT  
 E99 48926 RT Artery/CT  
 \*\*\*\*\* END\*\*\*

=> S ATHEROSCLEROSIS OR ARTERIOSCLEROSIS OR ATHEROGENESIS OR ATHEROMA  
 OR CORONARY OR ARTERY OR ARTERIAL OR CARDIOVASCULAR

L3 218970 ATHEROSCLEROSIS OR ARTERIOSCLEROSIS OR ATHEROGENESIS OR  
 ATHEROMA OR CORONARY OR ARTERY OR ARTERIAL OR  
 CARDIOVASCULAR

(continued on next page)

## =&gt; E PROBES (NUCLEIC ACID)/CT

E#	FREQUENCY	AT	TERM
--	-----	--	----
E100	1	7	PROBERGROTHIUS SANGUINOLENS/CT
E101	0	1	PROBES/CT
E102	9647	19	--> PROBES (NUCLEIC ACID)/CT
E103	0	2	PROBES ELECTRODES/CT
E104	0	2	PROBES FLUORESCENT SUBSTANCES/CT
E105	0	2	PROBIOTIC/CT
E106	0	2	PROBIOTIC BACTERIA/CT
E107	0	2	PROBIOTICS/CT
E108	0	1	PROBLEM/CT
E109	0	1	PROBLEMATICUM/CT
E110	0	1	PROBLEMATICUS/CT
E111	0	9	PROBOLE/CT

## =&gt; E E102+ALL

E112	9771	BT1	Genetic methods/CT
E113	20864	BT2	Acids/CT
E114	29472	BT2	Organic compounds/CT
E115	36507	BT1	Nucleic acids/CT
E116	9647	-->	Probes (nucleic acid)/CT
		HN	Valid heading during volume 126 (1997) to present.
E117		OLD	Nucleotides (L) oligo-, deoxyribo-, probes/CT
E118		OLD	Nucleotides (L) oligo-, probes/CT
E119		OLD	Ribonucleic acids (L) probes/CT
E120		UF	Chromosomal probes/CT
E121		UF	DNA probes/CT
E122		UF	Nucleic acid probes/CT
E123		UF	Oligodeoxyribonucleotide probes/CT
E124		UF	Oligonucleotide probes/CT
E125		UF	Probe (nucleic acid)/CT
E126		UF	RNA probes/CT
E127	45919	RT	DNA/CT
E128	2824	RT	DNA microarray technology/CT
E129	17657	RT	Nucleic acid hybridization/CT
E130		RTCS	Cy5/CT
***** END***			

## =&gt; S (DNA OR OLIGONUCLEOTIDE OR NUCLEIC ACID) (S) PROBE

L4 40211 (DNA OR OLIGONUCLEOTIDE OR NUCLEIC ACID) (S) PROBE

## =&gt; D HIS

(FILE 'HOME' ENTERED AT 11:27:46 ON 28 MAR 2002)

FILE 'HCAPLUS' ENTERED AT 11:27:59 ON 28 MAR 2002

L1 20 S (DNA OR NUCLEIC ACID) (S) PROBE AND ATHEROSCLEROSIS AND LIPOP  
E LOW DENSITY LIPOPROTEINS/CT

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E LOW-DENSITY LIPOPROTEINS/CT
E E15+ALL
E E26+ALL
L2      32221 S LIPOPROTEIN (S) (LOW D OR LOW DENSITY OR LDL)
E ATHEROSCLEROSIS/CT
E E37+ALL
E E50+ALL
L3      218970 S ATHEROSCLEROSIS OR ARTERIOSCLEROSIS OR ATHEROGENESIS
OR ATHE
E PROBES (NUCLEIC ACID)/CT
E E102+ALL
L4      40211 S (DNA OR OLIGONUCLEOTIDE OR NUCLEIC ACID) (S) PROBE

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=> S L2 AND L3 AND L4

L5 19 L2 AND L3 AND L4

=> FOCUS L5

PROCESSING COMPLETED FOR L5

L6 19 FOCUS L5 1-

=> D KWIC 1-2

L6 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2002 ACS  
 AB A review with 117 refs. Apolipoprotein E plays a central role in clearance of **lipoprotein** remnants by serving as a ligand for **low-d. lipoprotein** and apolipoprotein E receptors. Three common alleles (apolipoprotein E2, E3 and E4) give rise to six phenotypes. Apolipoprotein E3 is. . . apolipoprotein E isoforms derive from nucleotide substitutions in codons 112 and 158. Resulting cysteine-arginine substitutions cause differences in: affinities for **low-d. lipoprotein** and apolipoprotein E receptors, **low-d. lipoprotein** receptor activities, distribution of apolipoprotein E among **lipoproteins**, **low-d. lipoprotein** formation rate, and cholesterol absorption. Accompanying changes in triglycerides, cholesterol and **low-d. lipoprotein** may promote **atherosclerosis** development. Over 90% of patients with familial dysbetalipoproteinemia have apolipoprotein E2/E2. Apolipoprotein E4 may promote **atherosclerosis** by its **low-d. lipoprotein** raising effect. Establishment of apolipoprotein E isoforms may be important for patients with diabetes mellitus and several non-atherosclerotic diseases. Apolipoprotein. . . enzyme-conjugated second antibody. Apolipoprotein E genotyping demonstrates underlying point mutations. Analyses of polymerase chain reaction products are done by allele-specific **oligonucleotide probes**, restriction fragment length polymorphism, single-stranded conformational polymorphism, the primer-guided nucleotide incorporation assay, or denaturing gradient gel electrophoresis. Detection with primers. . .

L6 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2002 ACS  
 TI Method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene

*While D SCAN is a no-cost format, at times the KWIC format may be more useful for evaluating records. E.g. the abstract is never shown in D SCAN, yet in a free-text query the search terms may be only appear there.*

(continued on next page)

- AB The invention provides a method for diagnosing an increased risk of developing **arteriosclerosis** or **coronary** disease which involves determining whether an individual carries a 68 base pair insertion at nucleotide 844 of the cystathionine  $\beta$ -synthase. . . . (homozygotic or heterozygotic nature) of this mutation. The method also includes testing for some of the risk factors associated with **coronary** disease, such as testing for diabetes mellitus or determining the levels of **low-d. lipoproteins (LDL)**, high-d. **lipoproteins (HDL)** and triglycerides. The invention claims homozygotic individuals exhibit higher increased risk of **arteriosclerosis** or **coronary** disease and homocysteine levels are similar in 844ins68 carriers and non-carriers. The invention further provides a diagnostic kit used for determining increased risk to **arteriosclerosis** which contains a **probe** specific for detecting **nucleic acid** mols. encoding the 844ins68 CBS gene and two primers specific for amplification of **nucleic acid** mols. Surrounding nucleotide 844 of the CBS gene. The invention specifically measured homocysteine levels, both basal and post-methionine loading (PM),. . . plasma folate, vitamins B6 and B12 in patients only. For heterozygous and homozygous carriers combined, the odds ratio (O.R.) for **cardiovascular** disease (CVD) was 1.7 (95 % CI 1.1-2.7). The O.R. for heterozygous carriers was 1.5 (95 % CI 0.9-2.3), whereas.
- ST **arteriosclerosis** risk cystathionine synthase gene 844ins68 mutation detection genotype; **coronary** disease risk CBS gene 844ins68 mutation detection genotype; kit probe **arteriosclerosis** risk CBS gene 844ins68 mutation detection; primer kit **arteriosclerosis** risk CBS gene amplification; insertion mutation 844ins68 CBS homozygous **coronary artery** disease risk; **cardiovascular** disease insertion mutation 844ins68 CBS gene risk factor
- IT **Artery, disease**  
(**coronary**; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Test kits  
(diagnostic kit used; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT **Cardiovascular** system  
(disease; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(for cystathionine  $\beta$ -synthase; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)

(continued on next page)

- IT Disease, animal  
(genetic, fatal or debilitating; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Genotypes  
(heterozygosity; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Lipoproteins  
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(high-d.; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence of insertion mutation 844ins68 in the CBS gene and testing for risk factors associated with **coronary** disease)
- IT Genotypes  
(homozygosity; individuals homozygous for the cystathionine  $\beta$ -synthase (CBS) gene insertion mutation 844ins68 exhibit higher increased risk of **arteriosclerosis** or **coronary** disease)
- IT Mutation  
(insertion, 844ins68, insertion of 68 bp at nucleotide 844; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT **Lipoproteins**  
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(low-d.; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence of insertion mutation 844ins68 in the CBS gene and testing for risk factors associated with **coronary** disease)
- IT **Arteriosclerosis**  
Genotyping (method)  
Nucleic acid hybridization  
PCR (polymerase chain reaction)  
Susceptibility (genetic)  
(method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Diabetes mellitus  
(method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence of insertion mutation 844ins68 in the CBS gene and testing for risk factors associated with **coronary** disease)

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- IT Glycerides, biological studies  
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence of insertion mutation 844ins68 in the CBS gene and testing for risk factors associated with **coronary** disease)
- IT Diagnosis  
(mol., of increased risk of **arteriosclerosis** or **coronary** disease; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Genotypes  
(of 844ins68 mutation; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT **Probes (nucleic acid)**  
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(used in detecting CBS gene 844ins68 mutation; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Primers (nucleic acid)  
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(used to amplify CBS gene around bp 844; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT 9023-99-8, Cystathionine  $\beta$ -synthase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT 6027-13-0, Homocysteine  
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(similar in 844ins68 carriers and non-carriers; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining presence of insertion mutation 844ins68 in CBS gene and testing for risk factors associated with **coronary** disease)

=> D IBIB ABS HITIND 2

L6 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:708949 HCAPLUS [Full-text](#)  
DOCUMENT NUMBER: 131:307664

(continued on next page)

TITLE: Method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene

INVENTOR(S): Franco, Rendrik Franca; Trip, Maria Dorothea; Reitsma, Pieter Hendrik

PATENT ASSIGNEE(S): Amsterdam Molecular Therapeutics B. V., Neth.

SOURCE: PCT Int. Appl., 17 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955909	A1	19991104	WO 1998-NL234	19980427
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9873505	A1	19991116	AU 1998-73505	19980427
PRIORITY APPLN. INFO.:			WO 1998-NL234	19980427

AB The invention provides a method for diagnosing an increased risk of developing **arteriosclerosis** or **coronary** disease which involves determining whether an individual carries a 68 base pair insertion at nucleotide 844 of the cystathionine  $\beta$ -synthase (CBS) gene (844ins68), followed by determining the genotype (homozygotic or heterozygotic nature) of this mutation. The method also includes testing for some of the risk factors associated with **coronary** disease, such as testing for diabetes mellitus or determining the levels of **low-d. lipoproteins (LDL)**, **high-d. lipoproteins (HDL)** and triglycerides. The invention claims homozygotic individuals exhibit higher increased risk of **arteriosclerosis** or **coronary** disease and homocysteine levels are similar in 844ins68 carriers and non-carriers. The invention further provides a diagnostic kit used for determining increased risk to **arteriosclerosis** which contains a **probe** specific for detecting **nucleic acid** mols. encoding the 844ins68 CBS gene and two primers specific for amplification of **nucleic acid** mols. surrounding nucleotide 844 of the CBS gene. The invention specifically measured homocysteine levels, both basal and post-methionine loading (PM), and levels of plasma folate, vitamins B6 and B12 in patients only. For heterozygous and homozygous carriers combined, the odds ratio (O.R.) for **cardiovascular** disease (CVD) was 1.7 (95 % CI 1.1-2.7). The O.R. for heterozygous carriers was 1.5 (95 % CI 0.9-2.3), whereas for homozygotes it accrued to 14.0 (95 % CI 1.7-115). Both fasting and PM homocysteine, and vitamin B6 and folate levels did not differ between carriers and

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non-carriers of the mutation. These results show that a common insertion in the CBS gene represents a novel risk factor for premature CVD, and exhibits a strong gene dosage effect.

- IC ICM C12Q001-68  
ICS G01N033-50; G01N033-92
- CC 3-1 (Biochemical Genetics)  
Section cross-reference(s): 13, 14
- ST **arteriosclerosis** risk cystathionine synthase gene 844ins68 mutation detection genotype; **coronary** disease risk CBS gene 844ins68 mutation detection genotype; kit probe **arteriosclerosis** risk CBS gene 844ins68 mutation detection; primer kit **arteriosclerosis** risk CBS gene amplification; insertion mutation 844ins68 CBS homozygous **coronary artery** disease risk; **cardiovascular** disease insertion mutation 844ins68 CBS gene risk factor
- IT **Artery**, disease  
(**coronary**; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Test kits  
(diagnostic kit used; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT **Cardiovascular** system  
(disease; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(for cystathionine  $\beta$ -synthase; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Disease, animal  
(genetic, fatal or debilitating; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Genotypes  
(heterozygosity; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)

(continued on next page)

- IT Lipoproteins  
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses) (high-d.; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence of insertion mutation 844ins68 in the CBS gene and testing for risk factors associated with **coronary** disease)
- IT Genotypes  
(homozygosity; individuals homozygous for the cystathionine  $\beta$ -synthase (CBS) gene insertion mutation 844ins68 exhibit higher increased risk of **arteriosclerosis** or **coronary** disease)
- IT Mutation  
(insertion, 844ins68, insertion of 68 bp at nucleotide 844; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT **Lipoproteins**  
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses) (low-d.; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence of insertion mutation 844ins68 in the CBS gene and testing for risk factors associated with **coronary** disease)
- IT **Arteriosclerosis**  
Genotyping (method)  
Nucleic acid hybridization  
PCR (polymerase chain reaction)  
Susceptibility (genetic)  
(method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)
- IT Diabetes mellitus  
(method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence of insertion mutation 844ins68 in the CBS gene and testing for risk factors associated with **coronary** disease)
- IT Glycerides, biological studies  
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses) (method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence of insertion mutation 844ins68 in the CBS gene and testing for risk factors associated with **coronary** disease)
- IT Diagnosis  
(mol., of increased risk of **arteriosclerosis** or **coronary** disease; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)

(continued on next page)

IT Genotypes  
(of 844ins68 mutation; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)

IT **Probes (nucleic acid)**  
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(used in detecting CBS gene 844ins68 mutation; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)

IT Primers (nucleic acid)  
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(used to amplify CBS gene around bp 844; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)

IT 9023-99-8, Cystathionine  $\beta$ -synthase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining the presence and genotype of insertion mutation 844ins68 in the cystathionine  $\beta$ -synthase (CBS) gene)

IT 6027-13-0, Homocysteine  
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(similar in 844ins68 carriers and non-carriers; method for determining increased risk for **arteriosclerosis** or **coronary** disease by determining presence of insertion mutation 844ins68 in CBS gene and testing for risk factors associated with **coronary** disease)

REFERENCE COUNT:                   6           THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

## Skills Practice (page 70):

**Question 1:** Retrieve literature that discusses genetic vectors used in the recombinant preparation of tumor necrosis factor receptor or receptor-like proteins.

*Note:* There are many types of genetic vectors — explore the CA Lexicon to identify sequence description terms. Use REGISTRY to locate specific receptor proteins, limiting to protein/FS.

```
=> FILE HCAPLUS
```

```
=> E TUMOR NECROSIS FACTOR RECEPTORS/CT
```

E#	FREQUENCY	AT	TERM
--	-----	--	----
E1	0	2	TUMOR NECROSIS FACTOR RECEPTOR TYPE II/CT
E2	0	2	TUMOR NECROSIS FACTOR RECEPTOR-ASSOCD. FACTOR 2/CT
E3	1688	43	--> TUMOR NECROSIS FACTOR RECEPTORS/CT
E4	0	14	TUMOR NECROSIS FACTOR RECEPTORS (L) CAR1 (CYTOPATHIC A VIAN LEUKOSIS-SARCOMA VIRUS 1)/CT
E5	0	29	TUMOR NECROSIS FACTOR RECEPTORS (L) P55/CT
E6	0	14	TUMOR NECROSIS FACTOR RECEPTORS (L) P55, COMPLEXES/CT
E7	0	15	TUMOR NECROSIS FACTOR RECEPTORS (L) P55, FUSION PRODUCTS/CT
E8	0	17	TUMOR NECROSIS FACTOR RECEPTORS (L) P55, SOL./CT
E9	0	19	TUMOR NECROSIS FACTOR RECEPTORS (L) P60/CT
E10	0	28	TUMOR NECROSIS FACTOR RECEPTORS (L) P75/CT
E11	0	14	TUMOR NECROSIS FACTOR RECEPTORS (L) P75, COMPLEXES/CT
E12	0	14	TUMOR NECROSIS FACTOR RECEPTORS (L) P75, FUSION PRODUCTS/CT

```
=> E E3+ALL
```

E13	485268	BT4	Proteins/CT
E14	226682	BT3	Receptors/CT
E15	1175	BT2	Hormone receptors/CT
E16	2060	BT5	Body, anatomical/CT
E17	0	BT4	Organ systems (non-CA heading)/CT
E18	2085	BT3	Immune system/CT
E19	485268	BT4	Proteins/CT
E20	226682	BT3	Receptors/CT

*(continued on next page)*

E21	0	BT2 Immune receptors (non-	<i>Relatively new Controlled Indexing term, 1997 to present.</i>
E22	2095	BT1 Cytokine receptors/C	
E23	1688	--> Tumor necrosis factor receptors/CT	
		HN Valid heading during volume 126 (1997) to present.	
E24		OLD Lymphokine and cytokine receptors (L) tumor necrosis factor/CT	
E25		OLD Lymphokine and cytokine receptors (L) tumor necrosis factor- $\alpha$ /CT	
E26		OLD Receptors (L) tumor necrosis factor/CT	
E27		OLD Receptors (L) tumor necrosis factor- $\alpha$ /CT	
E28		UF Cachectin receptors/CT	
E29		UF TNF receptors/CT	
E30		UF Tumor necrosis factor- $\alpha$ receptors/CT	
E31		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor p55/CT	
E32		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor p55, complexes/CT	
E33		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor p55, fusion products/CT	
E34		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor p60/CT	
E35		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor p75/CT	
E36		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor p75, complexes/CT	
E37		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor p75, fusion products/CT	
E38		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor p80/CT	
E39		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor sol./CT	
E40		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor sol. p55/CT	
E41		NT1 Lymphokine and cytokine receptors (L) tumor necrosis factor sol. p75/CT	
E42		NT1 Proteins, specific or class (L) tumor necrosis factor-binding, 55,000-mol.-wt./CT	
E43		NT1 Proteins, specific or class (L) tumor necrosis factor-binding, p60/CT	
E44		NT1 Receptors (L) tumor necrosis factor p55/CT	
E45		NT1 Receptors (L) tumor necrosis factor p55, complexes/CT	
E46		NT1 Receptors (L) tumor necrosis factor p55, fusion products/CT	
E47		NT1 Receptors (L) tumor necrosis factor p75/CT	

(continued on next page)

```

E48          NT1  Receptors (L) tumor necrosis factor
              p75, complexes/CT
E49          NT1  Receptors (L) tumor necrosis factor
              p75, fusion product/CT
E50          NT1  Receptors (L) tumor necrosis factor
              sol. p55/CT
E51          NT1  Receptors (L) tumor necrosis factor
              sol. p75/CT
E52          NT1  Receptors (L) tumor necrosis factor,
              p60/CT
E53          NT1  Receptors (L) tumor necrosis factor,
              p80/CT
E54          NT1  Receptors (L) tumor necrosis factor,
              sol./CT
E55          13201 RT   Tumor necrosis factors/CT
*****      END***

```

=> S E23+PFT,NT

```
L1          3157 "TUMOR NECROSIS FACTOR RECEPTORS"+PFT,
```

*Recall the PFT relationship code searches for OLD and NEW terms, if used, as well as UF terms.*

=> E GENETIC VECTORS/CT

E#	FREQUENCY	AT	TERM
--	-----	--	----
E56	0	2	GENETIC TRANSLOCATION/CT
E57	0	2	GENETIC TYPING/CT
E58	11731	20 -->	GENETIC VECTORS/CT
E59	0	2	GENETIC VECTORS (L) COSMID/CT
E60	0	2	GENETIC VECTORS (L) PHAGEMID/CT
E61	0	2	GENETIC VECTORS (L) YAC/CT
E62	0	2	GENETIC X-LINKED HYDROCEPHALUS/CT
E63	44389	27	GENETICS/CT
E64	0	2	GENETICS (L) CYTO-/CT
E65	0	6	GENETICS (L) CYTOGENETICS/CT
E66	0	2	GENETICS (L) DISORDERS/CT
E67	0	5	GENETICS (L) EPIGENETICS/CT

=> E E58+ALL

```

E68          9767 BT1  Genetic methods/CT
E69          11731 --> Genetic vectors/CT
              HN   Valid heading during volume 116 (1992) to
              present.
E70          UF   Cloning vectors/CT
E71          UF   Expression vectors/CT
E72          UF   Shuttle vectors/CT
E73          17   NT1  Artificial chromosome/CT
E74          86   NT2  BAC (bacterial artificial chromosome)/CT
E75          9    NT3  PAC (P1-derived artificial chromosome)/CT
E76          NT2  Genetic vectors (L) YAC/CT
E77          556  NT2  YAC (yeast artificial chromosome)/CT
E78          355  NT1  Cosmids/CT

```

(continued on next page)

```

E79      173      NT1  Phagemids/CT
E80      7719     NT1  Plasmid vectors/CT
E81      6077     NT1  Virus vectors/CT
E82      2322     NT2  Retroviral vectors/CT
E83      556      NT2  Virus vectors, bacterial (L) lambda gt10/CT
E84      10222    RT   Genetic engineering/CT
E85      44389    RT   Genetics/CT
E86      7064     RT   Plasmids/CT
*****  END***
    
```

=> S E69+PFT,NT

L2 25005 "GENETIC VECTORS"+PFT,NT/CT (15 TERMS)

=> S L1 AND L2

L3 87 L1 AND L2

=> D SCAN TI HIT

```

L3      87 ANSWERS  HCAPLUS  COPYRIGHT 2002 ACS
TI      Albumin fusion proteins with therapeutic proteins for improved
shelf-life
IT      Cell adhesion molecules
        Cytokines
        Enzymes, biological studies
        Fusion proteins (chimeric proteins)
        Growth factors, animal
        Interferons
        Interleukin 2
        Synthetic gene
        Tumor necrosis factor receptors
RL:     BPN (Biosynthetic preparation); PRP (Properties); THU
        (Therapeutic use); BIOL (Biological study); PREP (Preparation);
        USES (Uses)
        (albumin fusion proteins with therapeutic proteins for improved
        shelf-life)
IT      Plasmid vectors ←
        (pC4:HSA, for mammalian cell expression; albumin fusion proteins
        with therapeutic proteins for improved shelf-life)
IT      Plasmid vectors
        (pPPC0005, for yeast expression; albumin fusion proteins with
        therapeutic proteins for improved shelf-life)
IT      Plasmid vectors
        (pScCHSA, for yeast expression; albumin fusion proteins with
        therapeutic proteins for improved shelf-life)
IT      Plasmid vectors
        (pScNHSA, for yeast expression; albumin fusion proteins with
        therapeutic proteins for improved shelf-life)
    
```

*Some biotechnology records have long indexing sections. Limiting D SCAN to the TI and HIT indexing allows quicker evaluation.*

*Note the narrower term "plasmid vectors"*

(continued on next page)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L3 87 ANSWERS HCAPLUS COPYRIGHT 2002 ACS

TI Blocking Sp1 transcription factor broadly inhibits extracellular matrix gene expression in vitro and in vivo: implications for the treatment of tissue fibrosis

IT **Tumor necrosis factor receptors**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(p55, gene encoding; blocking Sp1 transcription factor broadly inhibits extracellular matrix gene expression in vitro and in vivo and implications for treatment of tissue fibrosis)

IT **Genetic vectors**

(pRSV/ASSp1, for antisense oligonucleotide to Sp1; blocking Sp1 transcription factor broadly inhibits extracellular matrix gene expression in vitro and in vivo and implications for treatment of tissue fibrosis)

L3 87 ANSWERS HCAPLUS COPYRIGHT 2002 ACS

TI Adeno-associated virus production of soluble tumor necrosis factor receptor neutralizes tumor necrosis factor  $\alpha$  and reduces arthritis

IT Adeno-associated virus

Fibroblast

Gene therapy

Immunotherapy

Rheumatoid arthritis

Synovial membrane

**Virus vectors**

(adeno-associated virus production of soluble tumor necrosis factor receptor neutralizes tumor necrosis factor  $\alpha$  and reduces arthritis)

IT **Tumor necrosis factor receptors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(p55, soluble; adeno-associated virus production of soluble tumor necrosis factor receptor neutralizes tumor necrosis factor  $\alpha$  and reduces arthritis)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L3 87 ANSWERS HCAPLUS COPYRIGHT 2002 ACS

TI Novel molecules of the T129-related protein family and uses thereof

IT Apoptosis

Cell differentiation

Cell proliferation

**Genetic vectors**

Molecular cloning

Plasmids

Protein sequences

Test kits

cDNA sequences

(human T129 protein and related proteins and uses thereof)

(continued on next page)

IT **Tumor necrosis factor receptors**  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(superfamily; human T129 protein and related proteins and uses thereof)

L3 87 ANSWERS HCAPLUS COPYRIGHT 2002 ACS

TI Transfection of cells of multicellular organisms in vivo using low-voltage electrical pulses

IT CD4 (antigen)  
Cholinergic receptors  
Peptides, biological studies  
**Tumor necrosis factor receptors**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(genes for agonist or antagonist; transfection of cells of multicellular organisms in vivo using low-voltage elec. pulses)

IT Colon tumors  
Electric potential  
Fibrosarcoma  
Gene therapy  
Lung tumors  
Melanoma  
Plasmids  
Transformation (genetic)  
**YAC (yeast artificial chromosome)**  
(transfection of cells of multicellular organisms in vivo using low-voltage elec. pulses)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> S VECTOR OR PLASMID OR COSMID OR PHAGEMID OR YAC OR ARTIFICIAL CHROMOSOME

L4 221553 VECTOR OR PLASMID OR COSMID OR PHAGEMID OR YAC OR ARTIFICIAL CHROMOSOME

=> S TNFR OR (TUMOR NECROSIS FACTOR OR TNF)(L)RECEPTOR

L5 12210 TNFR OR (TUMOR NECROSIS FACTOR OR TNF)(L)RECEPTOR

=> S L4 AND L5

L6 485 L4 AND L5

=> D SCAN TI HIT

L6 485 ANSWERS HCAPLUS COPYRIGHT 2002 ACS

TI Interleukin-1 Hy2 materials and methods

*Expand the search to use a free-text query. Some of these records may still be in the process of being indexed.*

(continued on next page)

IT Alleles  
Alzheimer's disease  
Anemia (disease)  
Anti-inflammatory agents  
Autoimmune disease  
Culture media  
Cytotoxic agents  
DNA sequences  
Drug screening  
Epitopes  
Fever and Hyperthermia  
Genetic mapping  
Genetic polymorphism  
Genetic **vectors**  
Hybridoma  
Hypotension  
Immunosuppressants  
Inflammation  
Leukocytopenia  
Lung, disease  
Lupus erythematosus  
Molecular cloning  
Multiple organ failure  
Nucleic acid hybridization  
Osteoporosis  
PCR (polymerase chain reaction)  
Prognosis  
Protein sequences  
Rheumatoid arthritis  
Sepsis  
Susceptibility (genetic)  
Test kits  
Thrombosis  
(interleukin 1 receptor antagonist IL-1 Hy2, polynucleotides and antibodies for diagnosis, therapy and research)

IT **Tumor necrosis factors**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(interleukin 1 **receptor** antagonist IL-1 Hy2, polynucleotides and antibodies for diagnosis, therapy and research)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L6 485 ANSWERS HCAPLUS COPYRIGHT 2002 ACS

TI Monoclonal and humanized antibodies selective for **tumor necrosis factor**-related apoptosis-inducing ligand **receptor** DR5

TI Monoclonal and humanized antibodies selective for **tumor necrosis factor**-related apoptosis-inducing ligand **receptor** DR5

IT Adeno-associated virus  
Adenoviridae  
Herpesviridae  
Lentivirus  
(as **vector** for expression of antibodies to TRAIL receptors)

(continued on next page)

IT **Plasmid vectors**  
 Retroviral **vectors**  
 Virus **vectors**  
 (for expression of antibodies to TRAIL receptors)

IT 263325-86-6, 26: PN: EP990663 SEQID: 55 unclaimed DNA 263325-95-7, 35:  
 PN: EP990663 SEQID: 64 unclaimed DNA 372537-20-7 372537-21-8  
 372537-22-9 372537-23-0 372537-24-1 372537-25-2 372537-26-3  
 372537-27-4 372537-28-5 372537-29-6 372537-30-9 372537-31-0  
 372537-32-1 372537-33-2 372537-34-3 372537-35-4 372537-36-5  
 372537-37-6 372537-38-7 372537-39-8 372537-40-1 372537-41-2  
 372537-42-3 372537-43-4 372537-44-5 372537-45-6 372537-46-7  
 372537-47-8 372537-48-9 372537-49-0 372537-50-3 372537-51-4  
 372537-52-5 372537-53-6 372537-54-7 372537-55-8 372537-56-9  
 372537-57-0 372537-59-2 372537-60-5 372537-64-9 372537-65-0  
 372537-66-1 372537-67-2 372537-68-3 372537-69-4 372537-70-7  
 372537-71-8 372537-72-9 372537-78-5 372537-79-6 372537-80-9  
 372537-81-0 372537-82-1 372537-83-2 372537-84-3 372537-85-4  
 372537-86-5 372537-87-6 372537-88-7 372537-89-8 372537-90-1  
 372537-91-2 372537-92-3 372537-93-4 372537-94-5 372537-95-6  
 372537-96-7 372537-97-8 372537-98-9 372537-99-0 372538-00-6  
 372538-01-7 372538-02-8 372538-03-9

RL: PRP (Properties)  
 (unclaimed nucleotide sequence; monoclonal and humanized antibodies selective for **tumor necrosis factor** -related apoptosis-inducing ligand **receptor DR5**)

IT 372537-58-1 372537-61-6 372537-62-7 372537-63-8 372537-73-0  
 372537-74-1 372537-75-2 372537-76-3 372537-77-4

RL: PRP (Properties)  
 (unclaimed protein sequence; monoclonal and humanized antibodies selective for **tumor necrosis factor** -related apoptosis-inducing ligand **receptor DR5**)

IT 157147-95-0 372483-84-6 372483-85-7 372483-86-8 372483-87-9  
 372483-88-0 372483-89-1 372483-91-5

RL: PRP (Properties)  
 (unclaimed sequence; monoclonal and humanized antibodies selective for **tumor necrosis factor**-related apoptosis-inducing ligand **receptor DR5**)

L6 485 ANSWERS HCAPLUS COPYRIGHT 2002 ACS

TI Inhibition of TRAIL-induced apoptosis and forced internalization of TRAIL receptor 1 by adenovirus proteins

IT Proteins  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (TRAIL (**tumor necrosis factor**-related apoptosis-inducing ligand); inhibition of TRAIL-induced apoptosis and forced internalization of TRAIL **receptor 1** by adenovirus proteins)

(continued on next page)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L6 485 ANSWERS HCAPLUS COPYRIGHT 2002 ACS  
 TI Cytokine gene therapy for myocarditis by in vivo electroporation

L6 485 ANSWERS HCAPLUS COPYRIGHT 2002 ACS  
 TI Protein and cDNA sequences of a novel human cell cycle-related protein SRIK associated with protein kinase RIP3, and uses thereof in drug screening

IT Genetic **vectors**  
 (for expressing SRIK; protein and cDNA sequences of novel human cell cycle-related protein SRIK associated with protein kinase RIP3, and uses thereof in drug screening)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> **S L6 AND NONINDEXED/FS**

875062 NONINDEXED/FS  
 L7 18 L6 AND NONINDEXED/FS

=> **S L3 OR L7**

L8 104 L3 OR L7

=> **FILE REGISTRY**

=> **E TUMOR NECROSIS FACTOR RECEPTOR/CN**

E88	1	TUMOR NECROSIS FACTOR HOMOLOG DNA98853 (HUMAN CLONE ATCC203906)/CN
E89	1	TUMOR NECROSIS FACTOR LIGAND FHM (HUMAN)/CN
E90	0 -->	TUMOR NECROSIS FACTOR RECEPTOR/CN
E91	1	TUMOR NECROSIS FACTOR RECEPTOR (1-ASPARTIC ACID(HUMAN SOLUBLE TYPE I))/CN
E92	1	TUMOR NECROSIS FACTOR RECEPTOR (1-LEUCINE) (HUMAN SOLUBLE TYPE II)/CN
E93	1	TUMOR NECROSIS FACTOR RECEPTOR (108-ARGININE) (HUMAN ISOFORM P75)/CN
E94	1	TUMOR NECROSIS FACTOR RECEPTOR (108-ARGININE, 120-ARGININE) (HUMAN ISOFORM P75)/CN
E95	1	TUMOR NECROSIS FACTOR RECEPTOR (120-ARGININE) (HUMAN ISOFORM P75)/CN
E96	1	TUMOR NECROSIS FACTOR RECEPTOR (CAMELPOX VIRUS GENE CRME)/CN
E97	1	TUMOR NECROSIS FACTOR RECEPTOR (COWPOX VIRUS STRAIN BRIGHTON GENE CRMD)/CN
E98	1	TUMOR NECROSIS FACTOR RECEPTOR (COWPOX VIRUS STRAIN ELEPHANT POX GENE CRME)/CN
E99	1	TUMOR NECROSIS FACTOR RECEPTOR (COWPOX VIRUS STRAIN MUNICH-EP-2 GENE CRMD)/CN

(continued on next page)

=> S TUMOR NECROSIS FACTOR RECEPTOR?/CN

L9 102 TUMOR NECROSIS FACTOR RECEPTOR?/CN

*It may be best to use a free-text based name segment search for biomolecules.*

=> S TNFR OR (TUMOR NECROSIS FACTOR OR TNF)(L)RECEPTOR

L10 889 TNFR OR (TUMOR NECROSIS FACTOR OR TNF)(L)RECEPTOR

=> S L10 NOT L9

L11 787 L10 NOT L9

=> D SCAN

L11 787 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
IN DNA (human tumor necrosis factor receptor-associated factor HAUSP  
cDNA) (9CI)

SQL 639

MF Unspecified

CI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

\*\*\* USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE \*\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L11 787 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
IN DNA (human clone HELBP70R tumor necrosis factor receptor 5 gene  
fragment) (9CI)

SQL 340

MF Unspecified

CI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

\*\*\* USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE \*\*\*

L11 787 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
IN DNA (human tumor necrosis factor receptor 6α cDNA plus flanks)  
(9CI)

SQL 1077

MF Unspecified

CI MAN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

\*\*\* USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE \*\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> S L11 AND PROTEIN/FS

1306197 PROTEIN/FS

L12 380 L11 AND PROTEIN/FS

=> FILE HCAPLUS

*(continued on next page)*

=&gt; S L12

L13 306 L12

=&gt; D HIS

(FILE 'HCAPLUS' ENTERED AT 14:30:42 ON 27 MAR 2002)

DEL HISTORY

DEL SELECT

FILE 'HCAPLUS' ENTERED AT 14:50:52 ON 27 MAR 2002

E TUMOR NECROSIS FACTOR RECEPTOR/CT

E E1+ALL

DEL SEL

E TUMOR NECROSIS FACTOR RECEPTORS/CT

E E3+ALL

L1 3157 S E23+PFT,NT

E GENETIC VECTORS/CT

E E58+ALL

L2 25005 S E69+PFT,NT

L3 87 S L1 AND L2

L4 221553 S VECTOR OR PLASMID OR COSMID OR PHAGEMID OR YAC OR  
ARTIFICIAL

L5 12210 S TNFR OR (TUMOR NECROSIS FACTOR OR TNF)(L)RECEPTOR

L6 485 S L4 AND L5

L7 18 S L6 AND NONINDEXED/FS

L8 104 S L3 OR L7

FILE 'REGISTRY' ENTERED AT 14:59:38 ON 27 MAR 2002

E TUMOR NECROSIS FACTOR RECEPTOR/CN

L9 102 S TUMOR NECROSIS FACTOR RECEPTOR?/CN

L10 889 S TNFR OR (TUMOR NECROSIS FACTOR OR TNF)(L)RECEPTOR

L11 787 S L10 NOT L9

L12 380 S L11 AND PROTEIN/FS

FILE 'HCAPLUS' ENTERED AT 15:01:25 ON 27 MAR 2002

L13 306 S L12

=&gt; S L13 AND (L2 OR L4)

L14 74 L13 AND (L2 OR L4)

=&gt; D SCAN TI HIT

L14 74 ANSWERS HCAPLUS COPYRIGHT 2002 ACS

TI Adeno-associated virus expression **vectors** carrying genes for  
antagonists of tumor necrosis factor (TNF) for use in the treatment  
of TNF-associated disordersTI Adeno-associated virus expression **vectors** carrying genes for  
antagonists of tumor necrosis factor (TNF) for use in the treatment  
of TNF-associated disordersIT Adeno-associated virus  
(CMVrTNFR-Fc (recombinant), gene for soluble TNF receptor analog  
on; adeno-associated virus expression **vectors** carrying genes for  
antagonists of tumor necrosis factor (TNF) for use in treatment  
of TNF-associated disorders)

(continued on next page)

*Recall L2 and L4 are the "genetic vector" concept records. Many of these 74 records may only be indexed to a CAS RN for a specific biomolecule rather than a controlled term for the class of substances.*

- IT Immunoglobulins  
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(G1, fusion products with TNF receptor; adeno-associated virus expression **vectors** carrying genes for antagonists of tumor necrosis factor (TNF) for use in treatment of TNF-associated disorders)
- IT Tumor necrosis factors  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (adeno-associated virus expression **vectors** carrying genes for antagonists of tumor necrosis factor (TNF) for use in treatment of TNF-associated disorders)
- IT Cartilage  
Ligament  
Synovial membrane  
Tendon  
(administration of adeno-associated virus gene therapy **vector** to; adeno-associated virus expression **vectors** carrying genes for antagonists of tumor necrosis factor (TNF) for use in treatment of TNF-associated disorders)
- IT Interleukin 1  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (antagonists of, in treatment of inflammatory disease; adeno-associated virus expression **vectors** carrying genes for antagonists of tumor necrosis factor (TNF) for use in treatment of TNF-associated disorders)
- IT Adeno-associated virus  
(expression **vector**; adeno-associated virus expression **vectors** carrying genes for antagonists of tumor necrosis factor (TNF) for use in treatment of TNF-associated disorders)
- IT Connective tissue  
(gene therapy of inflammatory disease of; adeno-associated virus expression **vectors** carrying genes for antagonists of tumor necrosis factor (TNF) for use in treatment of TNF-associated disorders)
- IT Arthritis  
Inflammation  
(gene therapy of; adeno-associated virus expression **vectors** carrying genes for antagonists of tumor necrosis factor (TNF) for use in treatment of TNF-associated disorders)
- IT Gene therapy  
(of inflammatory disease; adeno-associated virus expression **vectors** carrying genes for antagonists of tumor necrosis factor (TNF) for use in treatment of TNF-associated disorders)
- IT Tumor necrosis factor receptors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(p80, fusion products; adeno-associated virus expression **vectors** carrying genes for antagonists of tumor necrosis factor (TNF) for use in treatment of TNF-associated disorders)
- IT Tumor necrosis factor receptors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(soluble analogs; adeno-associated virus expression **vectors** carrying genes for antagonists of tumor necrosis factor (TNF) for use in treatment of TNF-associated disorders)

(continued on next page)

IT Interleukin 1 receptors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(type II, as interleukin 1 antagonists; adeno-associated virus  
expression **vectors** carrying genes for antagonists of tumor  
necrosis factor (TNF) for use in treatment of TNF-associated  
disorders)

IT **156201-06-8** 224331-09-3 311824-74-5 311824-75-6  
311824-76-7 311824-77-8 311824-78-9 311824-79-0 311824-80-3  
311824-81-4 311824-82-5 311824-83-6 311824-84-7 311824-85-8  
311824-86-9  
RL: PRP (Properties)  
(unclaimed sequence; adeno-associated virus expression **vectors**  
carrying genes for antagonists of tumor necrosis factor (TNF) for  
use in the treatment of TNF-associated disorders)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L14 74 ANSWERS HCAPLUS COPYRIGHT 2002 ACS  
TI Recombinant expression, sequence, and biol. and therapeutics uses of  
human RTD, a receptor for Apo-2 ligand/TRAIL

IT **Plasmid vectors**  
(pRK5-35663 and pRK5-35664; recombinant expression, sequence, and  
biol. and therapeutics uses of human RTD, a receptor for Apo-2  
ligand/TRAIL)

IT 202220-47-1P 216858-89-8P **220163-16-6P** 220999-15-5P  
RL: BPN (Biosynthetic preparation); BPR (Biological process); BUU  
(Biological use, unclassified); PRP (Properties); THU (Therapeutic  
use); BIOL (Biological study); PREP (Preparation); PROC (Process);  
USES (Uses)  
(amino acid sequence of two isoforms of RTD; recombinant  
expression, sequence, and biol. and therapeutics uses of human  
RTD, a receptor for Apo-2 ligand/TRAIL)

L14 74 ANSWERS HCAPLUS COPYRIGHT 2002 ACS  
TI Cloning and cDNA sequences of human tumor necrosis factor receptor  
type II-like proteins

IT **190281-49-3P**, Protein TR1 (tumor necrosis factor receptor-related  
molecule) (human clone HSABH13 reduced) **205512-95-4P**  
**205512-96-5P 205512-97-6P 205512-98-7P**  
**205512-99-8P 205537-30-0P 205537-34-4P**  
**205705-14-2P 205705-15-3P 205705-16-4P**  
**205705-17-5P**  
RL: BPN (Biosynthetic preparation); BSU (Biological study,  
unclassified); PRP (Properties); BIOL (Biological study); PREP  
(Preparation)  
(amino acid sequence; cloning and cDNA sequences of human tumor  
necrosis factor receptor type II-like proteins)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> S L8 OR L14

L15 168 L8 OR L14

(continued on next page)

=> S L15 AND PY>1999

2060689 PY>1999  
L16 131 L15 AND PY>1999

=> D IBIB ABS HITIND 130

L16 ANSWER 130 OF 131 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1991:443508 HCAPLUS [Full-text](#)  
DOCUMENT NUMBER: 115:43508  
TITLE: Cloning and expression of mammalian tumor  
necrosis  
factor receptor cDNA  
INVENTOR(S): Smith, Craig A.; Goodwin, Raymond G.; Beckmann,  
Patricia M.  
PATENT ASSIGNEE(S): Immunex Corp., USA  
SOURCE: PCT Int. Appl., 41 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 4  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9103553	A1	19910321	WO 1990-US4001	19900717
W: AU, CA, FI, KR, NO				
CA 2065346	AA	19910306	CA 1990-2065346	19900717
AU 9061781	A1	19910408	AU 1990-61781	19900717
AU 630497	B2	19921029		
ZA 9007072	A	19911030	ZA 1990-7072	19900905
DD 297664	A5	19920116	DD 1990-343823	19900905
NO 9200862	A	19920504	NO 1992-862	19920304
FI 2000000833	A	20000407	FI 2000-833	20000407 <--
PRIORITY APPLN. INFO.:			US 1989-403241	A 19890905
			US 1989-405370	A 19890911
			US 1989-421417	A 19891013
			WO 1990-US4001	A 19900717

AB The cDNA for mammalian tumor necrosis factor receptor is cloned and expressed. The receptor can be used to regulate the immune response, or can be used for detection of tumor necrosis factor or the receptor (no data). Partial cDNAs for human and mouse receptors were cloned. The human cDNA and fragments thereof encoding soluble forms of the receptor were expressed in CHO cells and yeast.

IC ICM C12N015-12  
ICS C12P021-02; A61K037-02; C12P021-08; G01N033-68

CC 3-4 (Biochemical Genetics)  
Section cross-reference(s): 15

IT **Plasmid** and Episome  
(pIXY424, soluble tumor necrosis factor receptor cDNA of human on, expression in yeast of)

IT **Plasmid** and Episome  
(psolTNFR/P6/PSVLGS, soluble tumor necrosis factor receptor cDNA of human in, expression in CHO cells of)

(continued on next page)

IT **134773-88-9**

RL: PRP (Properties)

(amino acid sequence and cloning of cDNA for)

IT 134516-50-0 134773-87-8 **134773-89-0** **134773-90-3**

**134773-91-4** **134773-92-5**

RL: PRP (Properties)

(amino acid sequence of and expression in yeast and CHO cells of cDNA for)