STN® sequence searchable databases

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Agenda

- STN sequence searchable databases
- Comparison to NCBI and EMBL-EBI
  - Focus on patent sequence coverage

STN sequence searchable databases

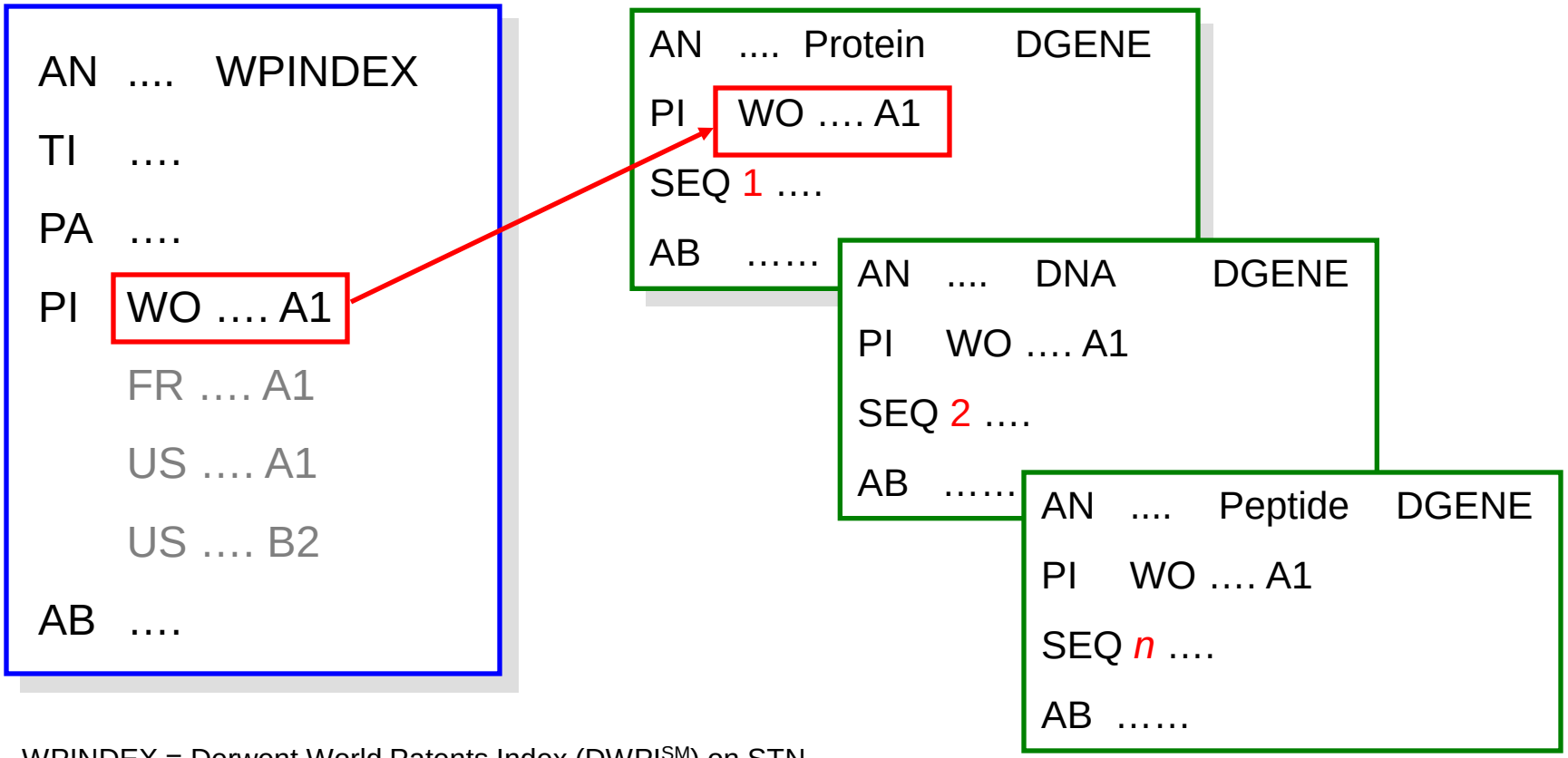
- DGENE
  - Thomson Reuters GENESEQ™
  - Value-added patent sequence data from around the globe
- USGENE®
  - The USPTO Genetic Sequence Database
  - All available sequence data from the USPTO
- PCTGEN
  - WIPO/PCT Patent Application Biosequences
  - All available e-published sequence data from WIPO
- CAS REGISTRY℠
  - Chemical Abstracts Service (CAS) REGISTRY
  - Worldwide value-added non-patent and patent sequences

Thomson Reuters GENESEQ (DGENE)

- Largest value-added patent sequence database
- Used routinely by all major patent offices*
- Sequences from the basic patents of the 48 authorities of the Derwent World Patents Index®
- Bibliography, enhanced title, abstract, indexing, and patent location provided for each sequence
- Patent Family and Legal Status display
- Updated every two weeks
- 1981 - present

* See page 10: http://www.trilateral.net/projects/biotechnology/guide2.pdf

Relationship between DWPI patent family and DGENE sequence database



WPINDEX = Derwent World Patents Index (DWPI[SM]) on STN

DGENE = GENESEQ on STN

What exactly is the “value-add” in DGENE?

- DWPI patent title, concise sequence description, abstract, and keyword indexing *per sequence*
  - Context of *each sequence* illuminated within the invention
  - Superior text-based refinement of sequence searches
  - Efficient scanning and review of search results for relevance
- Feature tables for sequence modifications/annotations
  - Extensive detailed annotations provided by indexers
- Patent sequence location (claim, example, etc.)
  - Assigned manually by Thomson Reuters indexers
  - Flexible filtering of searches to those described in the claims
- Sequences intellectually identified or derived by indexers
  - Unique sequence hits not disclosed in formal listings

Example: derived sequence record

```
L1    ANSWER 1 OF 1  DGENE  COPYRIGHT 2013 THOMSON REUTERS on STN
AN    AEJ92622  protein       DGENE  Full-text
TI    Hydrolyzing/synthesizing carboxylic acid ester/amide from
      chiral/prochiral reactants for preparing e.g. pharmaceuticals,
      comprises  contacting reactants with a polypeptide having hydrolytic
      activity.
IN    Svendsen A; Vind J; Brask J; De Maria L
PA    (NOVO)      NOVOZYMES AS.
PI    WO 2006084470   A2   20060817                    17
AI    WO 2006-DK76          20060210
PRAI  EP 2005-388012        20050210
PSL   Claim 16
DED   19 OCT 2006  (first entry)
LA    English
OS    2006-560037 [57]
DESC  Variant fungal lipolytic hydrolase #2.
KW    hydrolysis; lipase; pharmaceutical; pesticide; enzyme; mutein.
ORGN  Thermomyces lanuginosus. Synthetic.
AB    The new invention relates to a enzymatic method of hydrolyzing or
      synthesizing carboxylic acid ester or amide from chiral or prochiral
      reactants, by providing reactants for hydrolysis or synthesis, and
      contacting the reactants with a polypeptide which has hydrolytic
      activity on ester or amide, and a sequence 50% homologous to
      Thermomyces  lanuginosus lipase. Also described is a polypeptide,
      which has hydrolase  activity on an ester or amide substrate, and has
      an amino acid sequence  that has at least 80% identity to SEQ ID No:
      5 and compared to SEQ ID No: 5 comprises a substitution corresponding
      to I90Q, N92TD, F95Y, F113Y, I202M, V203GM, L269T and 270F. . . . .
```

In this example, the indexer has intellectually derived this sequence from the wild-type lipolytic hydrolase.

Example: derived sequence record (cont.)

```
      The polypeptide is at least 80% homologous to any of SEQ ID No: 1-6
      being amino acid sequences of lipolytic enzymes  of fungus such as
      Rhizomucor miehei (SWISSPROT P19515), Rhizopus delemar, Fusarium
      oxysporum, Penicillium camemberti (SWISSPROT P25234),  Thermomyces
      lanuginosus (SWISSPROT 059952) and Thermomyces ibadanensis . . . . .
      The method is useful in the preparation of  pharmaceuticals  or
      pesticides, where the synthesis includes synthesis of 2-butyl
      propionate. This sequence is a variant fungal lipolytic hydrolase
      (lipase), V203M T231R N233R. This sequence is not shown in the
      specification, but was created by the indexer using the information
      given in claim 16.
SQL   269
SEQ     1 evsqdlfnqf nlfaqysaaa ycgknndapa gtnitctgna cpevekadat
       51 flysfedsgv gdvtgflald ntnklivlsf rgsrsienwi gnlnfdlkei
      101 ndicsgcrgh dgftsswrsv adtlrqkved avrehpdyrv vftghslgga
      151 latvagadlr gng
      201 dimprlppre fgy
      251 nipdipahlw yfg
```

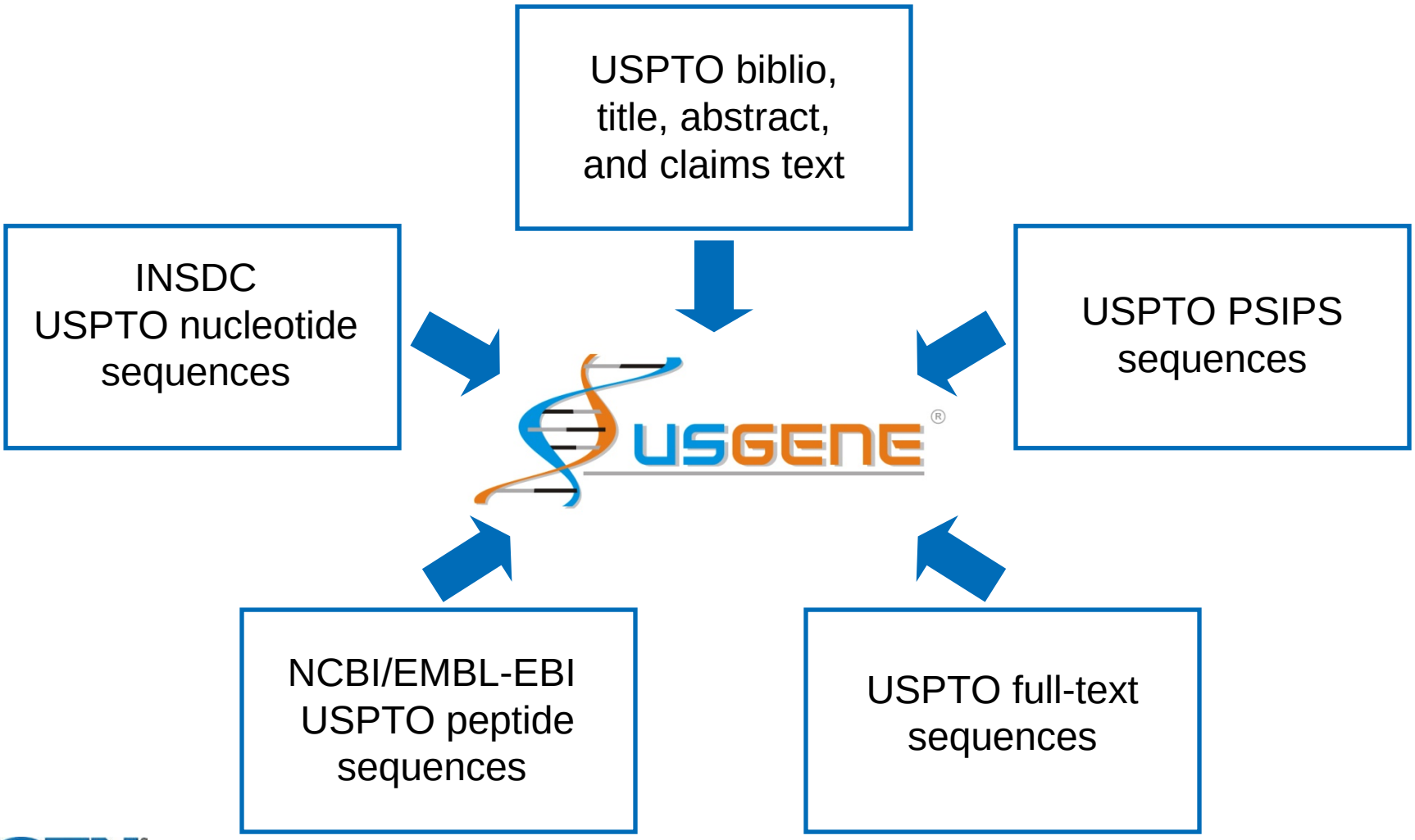
The indexer has added explanatory sentences to the abstract and annotations to the feature table.

```
FEATURE TABLE:
Key           |Location|Qualifier|
==============+========+=========+=========================
Modified-site|203      |note     |"Wild type Val replaced by
             |         |         |Met"
Modified-site|231      |note     |"Wild type Thr replaced by
             |         |         |Arg"
Modified-site|233      |note     |"Wild type Asn replaced by
             |         |         |Arg"
```

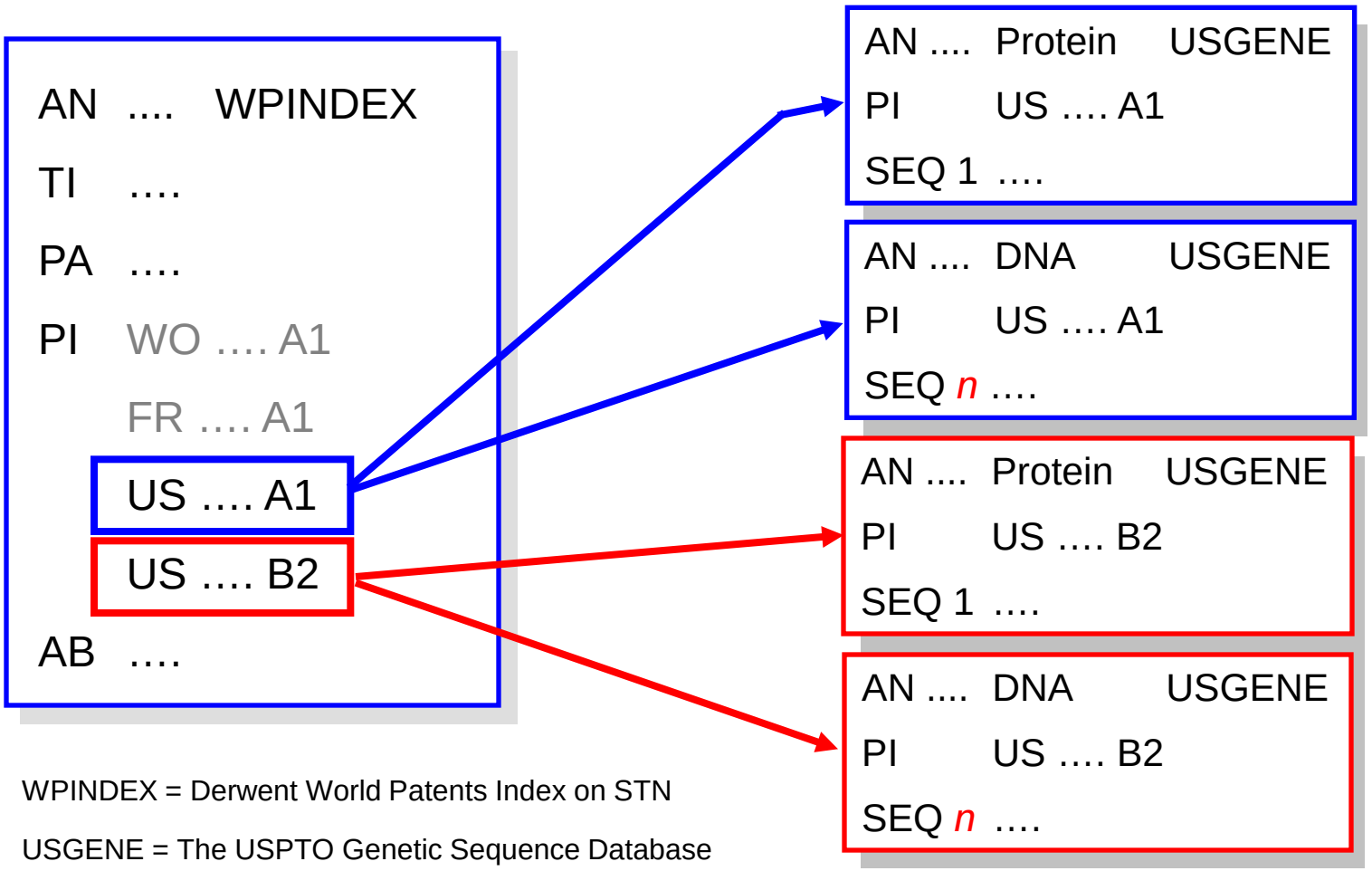
SequenceBase USGENE

- Sequences from USPTO published patent applications and granted (issued) patents
- Original publication title, abstract and claims
- Publication, application, related application and priority numbers and dates; assignees and inventors
- Organism, Sequence Length, SEQ ID NO, Molecule Type, Features, and Patent Sequence Location
- Calculated patent expiration date
- Patent Family and Legal Status display
- Updated weekly
- 1981 – present

USGENE combines sequences with bibliographic data and claims text



Relationship between DWPI patent family and USGENE sequence databases



WPINDEX = Derwent World Patents Index on STN

USGENE = The USPTO Genetic Sequence Database

Example: published application record

```
L1    ANSWER 1 OF 1  USGENE COPYRIGHT 2013 SEQUENCEBASE CORP on STN
AN    20100273154.6  DNA       USGENE  Full-text
TI    NOVEL GLYCOSYLTRANSFERASES AND POLYNUCLEOTIDES ENCODING THE SAME
      (PublishedApplication)
IN    Ochiai Misa (Osaka, JP); Fukami Harukazu ( Osaka, JP); Nakao Masahiro
      (Osaka, JP); Noguchi Akio (Osaka, JP)
PA    SUNTORY HOLDINGS LIMITED (Osaka JP)
PI    US 20100273154      A1   20101028
AI    US 2008-523068           20080118
RLI   WO 2008-JP50618          20080118
PRAI  JP 2007-10759            20070119
PSL   Claim 1; SEQ ID NO 6
DESC  Trichoderma viride DNA; Strain IAM 5141; sequence 6 of 35
DT    Patent
AB    The present invention provides novel glycosyltransferase proteins
      produced by ascomycetous filamentous
      belonging to the genus Trichoderma,
      viride), as well as genes encoding t
      proteins provided by the present inv
      an enzyme protein obtained from the
      Trichoderma viride strain IAM5141. The novel enzymes of the present
      invention allow glycosylation of flavonoid compounds to thereby
      improve their water solubility.
```

AN 20100273154.6 is SEQ ID NO: 6 from US20100273154.

Patent Sequence Location (PSL) indicates if the SEQ ID NO is referred to in the claims.

Example: published application record (cont.)

```
ECLM  US20100273154 A1: 1. A polynucleotide comprising any one of (A) to
      (K) shown below: (A) a polynucleotide which consists of all or part
      of the nucleotide sequence shown in SEQ ID NO: 6;(B) a polynucleotide
      which is hybridizable under stringent conditions with a
      polynucleotide consisting of a nucleotide sequence complementary to
      the nucleotide sequence of the polynucleotide shown in (A) and which
      encodes a protein having glycosylation activity on a flavonoid
      compound;(C) a polynucleotide which consists of a nucleotide . . . .

SSO   NUCLEIC; USPTO; APPLICATION
ORGN  Trichoderma viride
SQL   2633
SEQ
        1 tcatacaaag ctatttcgaa gaccaatatt ctacc
       51 agagccctat ggtaatgggc cgatgggttg cttat
      101 ccggggcatg cgtgtttgac atgttgaagc ttgggcagat ctgggatcgg
          . . . .
     2451 caaatagcct ttatagtccc gtgtatgctc gcaagtcttg tccgtcgtcg
     2501 ttagcctgta ttattcacat gcgtgtgtca tcgatagcct tgtgtttctc
     2551 gtgtcgcacg atttgctctt gatattgacc acattccttc ggtacaatga
     2601 gcaaatatat ataccgttgt ggtgggtaat gag

FEATURE TABLE:
Key         |Location|
============+========+======================
            |        |Strain IAM 5141
```

AN 20100273154.6 is displayed here in BRIEF format, which includes the Exemplary Claim (ECLM).

Example: issued patent record

```
L1    ANSWER 1 OF 1   USGENE COPYRIGHT 2013 SEQUENCEBASE CORP on STN
AN    8278088.6  DNA        USGENE  Full-text
TI    Polynucleotide encoding a polypeptide having glycosylation activity
      on a flavonoid (Patent)
IN    Ochiai Misa (Osaka, JP); Fukami Harukazu (Osaka, JP); Nakao Masahiro
      (Osaka, JP); Noguchi Akio (Osaka, JP)
PA    Suntory Holdings Limited (Osaka JP)
PI    US 8278088           B2   20121002
      US 20100273154       A1   20101028
      WO 2008088046        A    20080724
AI    US 2008-523068            20080118
RLI   WO 2008-JP50618           20080118
PRAI  JP 2007-10759             20070119
XPD   20280118 (calculated)
PSL   Claim 1; SEQ ID NO 6
DESC  Trichoderma viride DNA; Strain IAM 5141; sequence 6 of 33
DT    Patent
AB    The present invention provides novel glycosyltransferase proteins
      produced by ascomycetous filamentous
      belonging to the genus Trichoderma,
      viride), as well as genes encoding t
      proteins provided by the present inv
      an enzyme protein obtained from the
      Trichoderma viride strain IAM5141. The novel enzymes of the present
      invention allow glycosylation of flavonoid compounds to thereby
      improve their water solubility.
```

AN 8278088.6 is SEQ ID NO: 6 from US8278088.

Patent Sequence Location (PSL) indicates if the SEQ ID NO is referred to in the claims.

Example: issued patent record (cont.)

```
ECLM  US8278088 B2: 1. An isolated polynucleotide comprising a
      polynucleotide selected from the group consisting of: (A) a
      polynucleotide consisting of the nucleotide sequence of SEQ ID NO:6;
      (B) a polynucleotide consisting of the nucleotide sequence of SEQ ID
      NO:6, except 1 to 9 nucleotides are substituted, deleted, inserted,
      and/or added, wherein the polynucleotide encodes a protein having
      flavonoid glycosylation activity;(C) a polynucleotide . . . .

SSO   NUCLEIC; USPTO; GRANTED
ORGN  Trichoderma viride
SQL   2633
SEQ
        1 tcatacaaag ctatttcgaa gaccaatatt ctac
       51 agagccctat ggtaatgggc cgatgggttg ctta
      101 ccggggcatg cgtgtttgac atgttgaagc ttgg
          . . . .
     2451 caaatagcct ttatagtccc gtgtatgctc gcaagtcttg tccgtcgtcg
     2501 ttagcctgta ttattcacat gcgtgtgtca tcgatagcct tgtgtttctc
     2551 gtgtcgcacg atttgctctt gatattgacc acattccttc ggtacaatga
     2601 gcaaatatat ataccgttgt ggtgggtaat gag

FEATURE TABLE:
Key        |Location|
===========+========+==============================================
USGENE     |1..2633 |http://www.sequencebase.com/usgene.php?d=8278088.6
other_info|1..2633 |Strain IAM 5141
```

AN 8278088.6 is displayed here in BRIEF format, which includes the Exemplary Claim (ECLM).

WIPO/FIZ Karlsruhe PCTGEN

- Produced from sequence listings published electronically by WIPO
- Image and text based sequence listings are processed by FIZ Karlsruhe editorial
- Publication number and date, patent applicant name(s) and the original publication title are provided for each sequence
- Sequence length, SEQ ID NO, organism, and molecule type are included for each sequence
- Updated weekly – within 24 hours of publication
- August 2001 – present

Example: sequence record from PCTGEN

```
L1    ANSWER 1 OF 1  PCTGEN COPYRIGHT 2013 WIPO on STN
AN    2012131673.6 RNA       PCTGEN  Full-text
TI    CCAT-1 SILENCING NUCLEIC ACID AGENTS FOR TREATING CANCER [File
      created by using OCR software]
PA    Hadasit Medical Research Services a
      MOR Research Applications LTD.
PI    WO 2012131673     20121004
RLI   US 2011-469849P 20110331
ED    20121005
DT    Patent
ORGN  Artificial
SQL   25
SEQ
        1 cacauaguag cuaaugccua cucnn



FEATURE TABLE:
Key          |Location  |
=============+==========+=======================
             |          |synthetic Polynucleotide
misc_feature|(24)..(25)|Deoxycytidine
```

AN 2012131673.6 is SEQ ID NO: 6 from WO2012131673 .

Sequences are typically added to PCTGEN within 24 hours of publication by WIPO.

CAS REGISTRY

- Sequences from >3000 life science journals and the basic patents of the 62 authorities of CAplus[SM]
- Patent number, location, and standardized nomenclature provided for each sequence
- Updated daily
- 1907 - present

Example: patent sequence record

```
L1    ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2013 ACS on STN
ED    Entered STN:  16 Jan 2007
RN    917531-59-0  REGISTRY
CN    20: PN: WO2006137596 SEQI
FS    PROTEIN SEQUENCE
SQL   128

PATENT ANNOTATIONS (PNTE):
Sequence |Patent
Source   |Reference
=========+============
Not Given|WO2006137596
         |unclaimed
         |SEQID 21

SEQ       1 KCDLALDPDL ARIMAHSR
         51 HAARLNGFHD AGQQQREAYE DSDINSQLTE LWATLAPLYR ELHAYVRRHL
        101 VQRYGPERVR PDGPMPAHLL GNMWSRAN
MF    Unspecified
CI    MAN
SR    CA
LC    STN Files:   CA, CAPLUS
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  PRP (Properties)
```

WIPO and other patent sequences typically enter REGISTRY within 27 days of publication – in this example only 20 days.

Since October 1999, CAS REGISTRY patent sequence records include the publication number, SEQ ID number, and an intellectually assigned claimed/unclaimed notation.

Text describing a patent sequence is typically provided in the CAplus indexing (next slide).

Example: corresponding CAplus record

```
L1   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2010 ACS on STN
AN   2006:1357195  CAPLUS
DN   146:95066
TI   Screening for effectors of insect dipeptidyl carboxypeptidase A as
     insecticides
IN   Shimokawatoko, Yasutaka; Craen, Marc Van De; Nooren, Irene; Turconi,
     Sandra; Naudet, Yann; Nys, Guy; Debaveye, Jurgen
PA   Sumitomo Chemical Company, Limited, Japan
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     --------------      ----   --------    --------------------    --------
PI   WO 2006137596        A2    20061228    WO 2006-JP313039        20060623
     JP 2007000060        A     20070111    JP 2005-183031          20050623
PRAI JP 2005-183031       A     20050623
AB   Methods of screening for effector of the dipeptidyl carboxypeptidase A
     (I) of insects for use as insecticides is described.  . . . .
IC   ICM  A01N
CC   5-4 (Agrochemical Bioregula
     Section cross-reference(s)
     . . . .
IT   917531-51-2   917531-53-4   917531-55-6   917531-57-8 917531-59-0
     RL: PRP (Properties)
        (unclaimed protein sequence; screening for effectors of insect
        dipeptidyl carboxypeptidase A as insecticides)
```

CAS provides value-added abstracting and indexing for the CAplus basic publication.

The sequence is linked to the CAplus patent family record by its CAS Registry Number®.

Agenda

- STN sequence searchable databases
- Comparison to NCBI and EMBL-EBI
  - Focus on patent sequence coverage

There are three main web resources that provide searchable patent sequence data

- National Center for Biotechnology Information (NCBI) of the U.S. National Library of Medicine
  - www.ncbi.nlm.nih.gov
- European Molecular Biology Laboratory – European Bioinformatics Institute (EMBL-EBI)
  - www.ebi.ac.uk
- DNA DataBank of Japan (DDBJ)
  - www.ddbj.nig.ac.jp

Note: The USPTO, EPO and JPO/KIPO rely on the NCBI, EMBL-EBI and DDBJ, respectively, to provide an interface for searching patent sequence data.

Why does STN have more patent sequences than NCBI, EBI and DDBJ?

1. NCBI/EBI/DDBJ have a significantly incomplete collection of WIPO/PCT sequence data
2. NCBI/EBI/DDBJ do not provide any USPTO published patent application sequence data
3. NCBI/EBI/DDBJ have an incomplete collection of USPTO granted patent sequence data
4. DGENE and REGISTRY cover many more patent authorities than NCBI/EBI/DDBJ
5. DGENE, USGENE, PCTGEN and REGISTRY are typically more timely than NCBI/EBI/DDBJ

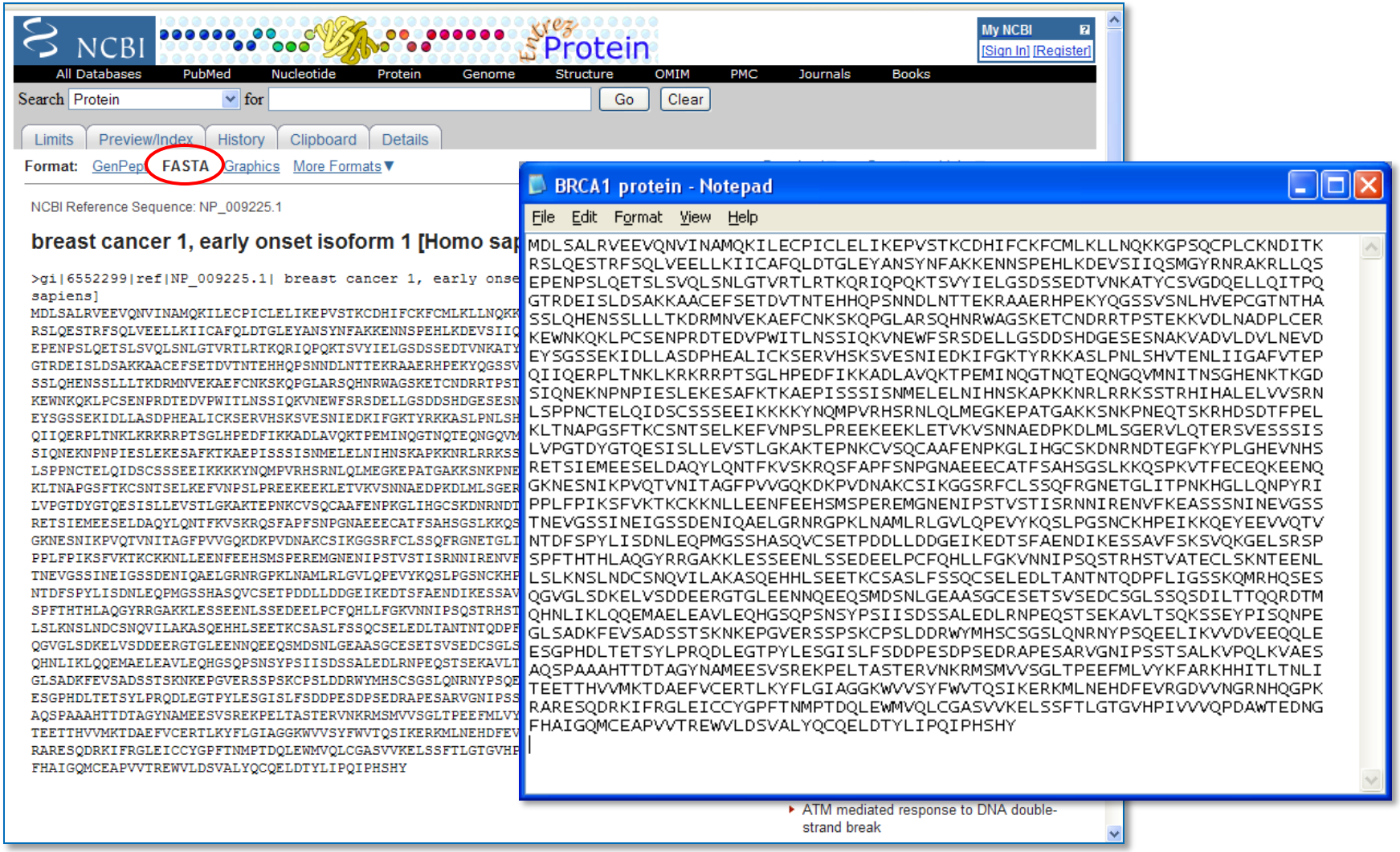
A simple BLAST® example shows the importance of using STN databases

Search Question:

Find all patent references to Breast Cancer 1, early onset isoform 1 [Homo sapiens] protein, or other very similar proteins (i.e. >80% match).

(Search conducted on 28th October 2011.)

Breast Cancer 1, early onset isoform 1 [Homo sapiens] protein (NCBI: NP_009225)



Example: The best answer from DGENE

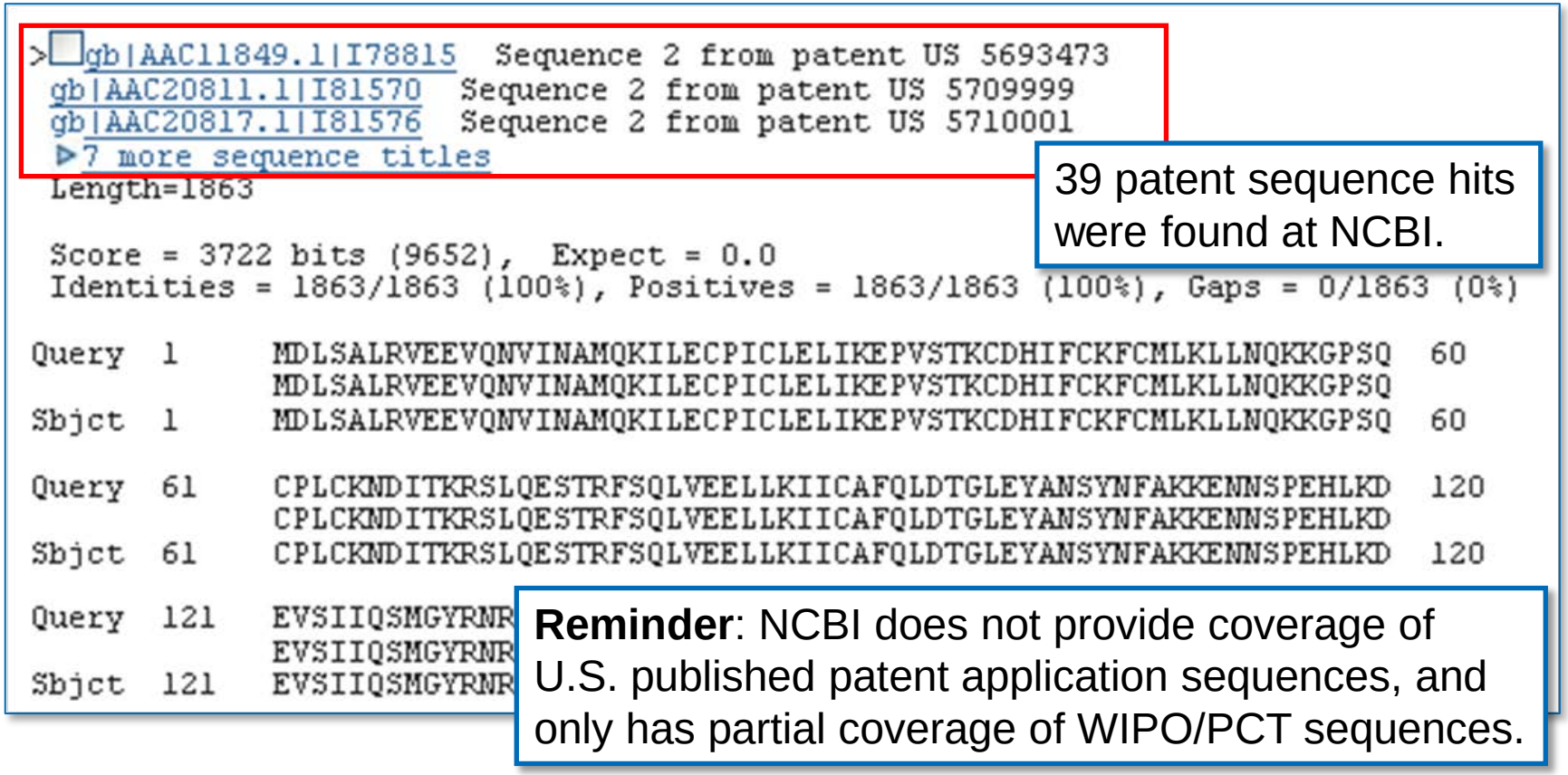
```
=> D L2 BIB SCORE ALIGN 1

L2    ANSWER 1 OF 140  DGENE  COPYRIGHT 2011 THOM
AN    AZI42431  protein       DGENE  Full-text
TI    Determining whether tumor sample from breast cancer patient has
      breast cancer-associated gene (BRCA) deficiency, somatic BRCA
      deficiency and germline BRCA deficiency, useful for treating cancer
      e.g. breast and ovarian cancer.
IN    Timms K; Potter J; Lanchbury J
PA    (MYRI)      MYRIAD GENETICS INC.
PI    WO 2011057125   A2   20110512
AI    WO 2010-US55708      20101105
PRAI  US 2009-258504P      20091105
PSL   Disclosure; SEQ ID NO 2
DT    Patent
LA    English
OS    2011-F19431 [34]
CR    N-PSDB: AZI42430
      PC-NCBI: gi6552299
      PC-SWISSPROT: P38398
      PC-BIND: 151619; 12718; 12717; 149281
DESC  Human breast cancer 1 susceptibility protein, SEQ ID:2.
SCORE 3722      100% of query self score 3722
BLASTALIGN
   Query  = 1863 letters
   Length = 1863
   Score  = 3722 bits (9652), Expect = 0.0
   Identities = 1863/1863 (100%), Positives = 1863/1863 (100%)
   . . . .
```

140 patent sequence hits were found in DGENE.

DGENE records feature extensive Thomson Reuters value-added content.

Example: The best patent answer from NCBI



39 patent sequence hits were found at NCBI.

Reminder: NCBI does not provide coverage of U.S. published patent application sequences, and only has partial coverage of WIPO/PCT sequences.

Summary of results: Breast Cancer 1, early onset isoform 1 [Homo sapiens] protein

	Sequences > 80%	Patent Families
DGENE	140	40
USGENE	138	33 (5)*
PCTGEN	13	9
REGISTRY	65	33 (1)*
NCBI	39	13
Total Unique	-	**46**

* Indicated in **(red)** are the number of additional families retrieved which contribute to the **Total Unique**.

Comparing databases…

- DGENE
  - The most comprehensive global patent sequence database
  - Implemented in-house at major patent offices*
- USGENE
  - Sequences from equivalent USPTO applications and patents
  - Incorporates all U.S. patent sequence data available at NCBI
- PCTGEN
  - Sequences from equivalent WIPO/PCT publications
  - The complete collection of e-published sequences from WIPO
- REGISTRY
  - Complementary value-added indexing to DGENE
  - Unique non-patent literature coverage

* See page 10: www.trilateral.net/projects/biotechnology/guide2.pdf

Database timeliness is an important factor in understanding comprehensiveness

	Update Frequency	Typical patent Timeliness
DGENE	Biweekly	65 days
USGENE	Weekly	3 days
PCTGEN	Weekly	24 hours
REGISTRY	Daily	27 days
NCBI	Daily	1-6 months

Summary

- STN sequence searchable databases
  - DGENE, USGENE, PCTGEN and REGISTRY
- Comparison to NCBI and EMBL-EBI
  - Focus on patent sequence coverage

Resources for sequence searching on STN

- Recorded e-Seminars (audio/video)
  http://www.stn-international.com/recorded_events.html
  - Sequence Basics (all databases)
  - Multifile patent sequence searching (all databases)

- DGENE Workshop Manual
  http://www.stn-international.com/dgene_wm.html

- USGENE Workshop Manual
  http://www.stn-international.com/usgene_wm.html

For more information …

CAS
E-mail: help@cas.org
Support and Training:
www.cas.org

FIZ Karlsruhe
helpdesk@fiz-karlsruhe.de
Support and Training:
www.stn-international.de

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