Las bibliotecas de química combinatoria:
Nuevos problemas de información, patentes y licencias

Los Lunes del Centro de Patentes

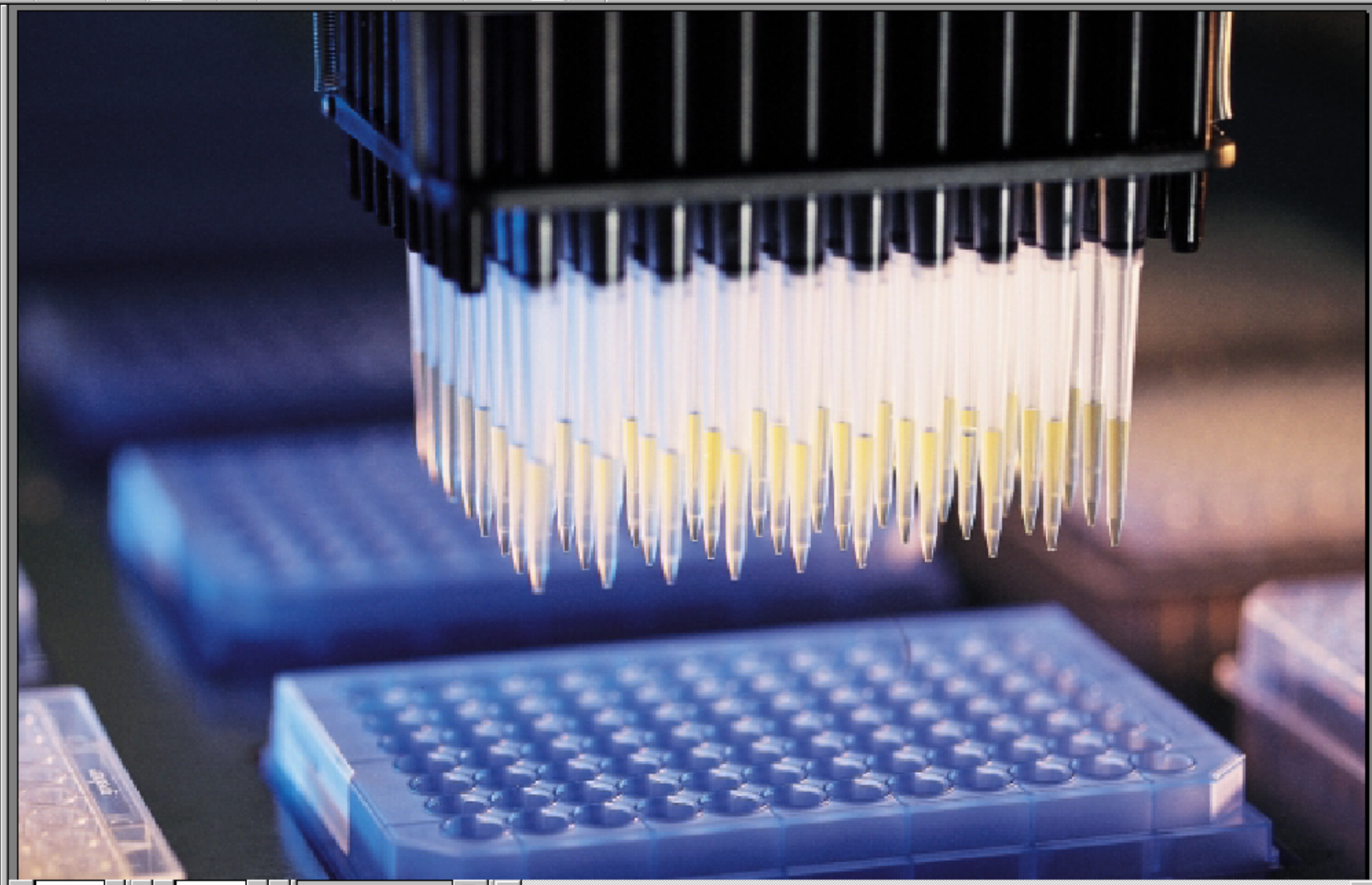
Barcelona, 28 de mayo de 2001

Pascual Segura

Combinatorial Chemistry

Is the art and science of **synthesizing** and **testing** compounds for bioactivity **en masse**, instead of one by one, the aim being to discover drugs and materials more quickly and inexpensively than was formerly possible.

It has been the hottest **approach to drug discovery** of the last years. *C&EN March 8, 1999*



Chem.Folio®

LION BIOSCIENCE

LION BIOSCIENCE

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San Diego, CA 92121
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Fax: (858) 410-6501

www.lionbioscience.com

RELATED LINKS

- supplier FAQ
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About LION bioscience, Inc. (formerly Trega Biosciences)

LION has selected a subset of its vast inventory of small molecule compounds to be represented through ChemNavigator's iResearch System. Identity of each compound is determined by flow injection mass spectrometry. Compounds that were individually tested for purity are guaranteed to be at least 80% pure as determined by HPLC analysis using evaporative light scattering detection (ELSD). Compounds that were selected from combinatorial libraries have an average purity of 65% or greater. Average purity of a combinatorial library was determined by systematically analyzing 10% or more of the compounds in the library by HPLC using ELSD. Compounds can be purchased in 1.0 mg quantities and are provided in a frozen 10 mg/ml DMSO solution.

Chem.Folio Lead Generation Libraries.

Chem.Folio information-rich combinatorial libraries offer pharmaceutical, biotechnology and agricultural companies access to novel, diverse chemical structures for use in their discovery programs. Libraries are profiled to ensure compatibility with high throughput screening methods and to provide users with critical information about their templates. LION also provides high-value follow-on services, such as access to the virtual library for rapid lead optimization, validated synthesis protocols, guaranteed compound resupply, and an integrated Hit-to-Lead Program.

With over 300,000 compounds in inventory, Chem.Folio has a large selection of libraries from which to choose.

metabolism and toxicological performance.

Approaches to drug discovery

CLASSICAL: start with a compound known to be active; using structure-activity relationships select and synthesize related compds. and test them one by one.

RATIONAL DRUG DESIGN: computer modelling to mimic receptor-ligand interactions.

HIGH-THROUGHPUT SCREENING of large groups of small samples of compounds of:

- any origin (synthesized, natural, plant extracts, soil samples, fermentation broths of microorganisms...)
- **combinatorial libraries** (Combinatorial Chemistry)

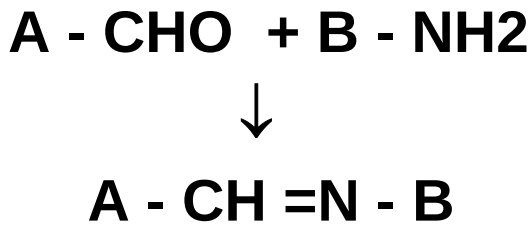
What is a combinatorial library?

A large collection of **different small compounds** which is the result of the controlled synthesis (often on a solid surface, followed or not by cleavage) by a controlled **combination** of different starting materials, reaction steps, reagents,etc.

Compounds are **separated or mixed** in the samples (plate wells), and there is a tagging or deconvolution* scheme (e.g. for re-synthesis).

*convolution =circunvolución =vuelta o rodeo

A simple two-dimensional array library



There are more than 2,000 commercial aldehydes

There are more than 500 commercial primary amines

There are more than 1,000,000 combinations for imines

A typical library preparation (in plate wells):

- select the 120 'most diverse' commercial aldehydes

- select the 80 'most diverse' amines

- synthesize a 9600-member library,
where some members are known and others are new,
every plate well has a different separate compound

A split-mix library (all with X1 in this case) **prepared by solid-phase synthesis**

n **(P)-X1**

------- **↓ (A1 / A2 /.../ A10)**

10 **(P)-X1-A1 / (P)-X1-A2 /.../ (P)-X1-A10**

↓ (B1 / B2 /.../ B10)

100 **(P)-X1-A1-B1 / (P)-X1-A1-B2 /.../ (P)-X1-A1-B1**

↓ (C1 / C2 /.../ C10)

1000 **(P)-X1-A1-B1-C1 / (P)-X1-A1-B1-C2 /.../ (P)-X1-A1-B1-C10**

↓ cleavage

1000 **X1-A1-B1-C1 / X1-A1-B1-C2 /.../ X1-A1-B1-C10**

AIM OF THE SCREENING:
To identify a lead compound as early as possible, understanding the structure/activity relationships around it

TWO DIFFERENT SITUATIONS FOR PATENTING:

- One of the compounds of the library (already known as a component of the library) will be finally marketed

- The library plays the role of a research-tool to find another product (known or new) that will be finally marketed (more often the case).

STN Terminal Emulation

File Edit Online Query Results Preferences! Web Window Help

STN Karlsruhe Inter

```
Connecting via Winsock to STN


Welcome to STN International!  Enter x:x
LOGINID:rrrkamcd
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * *   Welcome to ST                                    *

 NEWS 81  Mar 30  Search Derwent
 NEWS 80  Mar 06  INIST-CNRS now
 NEWS 79  Feb 19  TOXLINE no long

* * * * * * * * * * * * * * * * STN                                   *
FILE 'HOME' ENTERED AT 18:57:31 C

=>
```

transcript: c:\mis documentos\cas - stn\stn _cas user meeting barcelona 2001\combinatorial 3.trn | HOME | INS | Hold Off | Print Off | Online | 00:00:38

Inicio | Microsoft Powe... | SciFinder | Microsoft Word... | STN Express | STN Termin... | 18:54

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STN Karlsruhe Inter

```
Connecting via Winsock to STN


Welcome to STN International!  Enter x:x
LOGINID:rrrkamcd
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS 81  Mar 30  Search Derwent WPINDEX by chemical structure
 NEWS 80  Mar 06  INIST-CNRS now FIZ AutoDoc document supplier
 NEWS 79  Feb 19  TOXLINE no longer being updated

* * * * * * * * * * * * * * * * STN  Karlsruhe * * * * * * * * * * * * * * * *
FILE 'HOME' ENTERED AT 18:57:31 ON 21 APR 2001

=> file chemcats
COST IN DEUTSCHMARKS

FULL ESTIMATED COST

FILE 'CHEMCATS' ENTERED AT 18:58:50 ON 21 APR 2001
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entrar en CHEMCATS

Discover! transcript: c:\mis documentos\cas - stn\stn_cas user meeting barcelona 2001\combinatoria REGISTRY INS Hold On Print Off Online 00:16:38

Inicio Microsoft P... SciFinder Microsoft W... STN Expre... STN Ter... 19:10

STN Terminal Emulation

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STN Karlsruhe Inter

```
E3      CHEMCATS          60073 --> TREGA/CO
E4      CHEMCATS          60073     TREGA BIOSCIENCES INC/CO
E5      CHEMCATS             23     TRIPHOSPHATES/CO
E6      CHEMCATS           1816     TRIPLE/CO
E7      CHEMCATS           1780     TRIPLE CROWN AMERICA INC/CO
E8      CHEMCATS           1780     TRIPLE CROWN AMERICA PRODUCT LIST/CO
E9      CHEMCATS             10     TRIQUEST/CO
E10     CHEMCATS             10     TRIQUEST LP/CO
E11     CHEMCATS             10     TRIQUEST PRODUCT LIST/CO
E12     CHEMCATS            231     TROSTBERG/CO

=> s e3
L1         60073 TREGA/CO

=> s chemical library/st
        963745 CHEMICAL/ST
        963726 LIBRARY/ST
L2      963726 CHEMICAL LIBRARY/ST
                 ((CHEMICAL(S)LIBRARY)/ST)

=> s l1 and l2
L3         60073 L1 AND L2

=> s isoquinolinone/cns
L4           148 ISOQUINOLINONE/CNS

=> s l1 and l3
L5         60073 L1 AND L3
```

Hay casi 1M *screening compounds* con "CHEMICAL LIBRARY"en el campo ST (Supplementary Term)

Discover! transcript: c:\mis documentos\cas - stn\stn_cas user meeting barcelona 2001\combinatoria REGISTRY INS Hold On Print Off Online 00:16:38

Inicio Microsoft P... SciFinder Microsoft W... STN Expre... STN Ter... 19:11

STN Terminal Emulation

File Edit Online Query Results Preferences! Web Window Help

Structure File:

Buscar en: Queries

isoquinolinona.str

Nombre de archivo: isoquinolinona.str

Tipo de archivos: Query Files (*.str)

Abrir

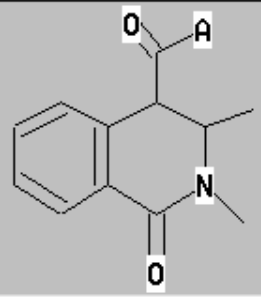
Cancelar

Ayuda

Please make sure you have switched to a file suitable for structure searching.

Modifiable Queries Use Filters

Standard



=>

entrar en REGISTRY y cargar una *query* con una fórmula general previamente dibujada

Discover! Upload structure query STNGUIDE INS Hold Off Print Off Online 00:15:33

Inicio Microsoft P... SciFinder Microsoft W... STN Expre... STN Ter... 19:09

STN Terminal Emulation

File Edit Preferences! Web Window Help

registry libraries.trn

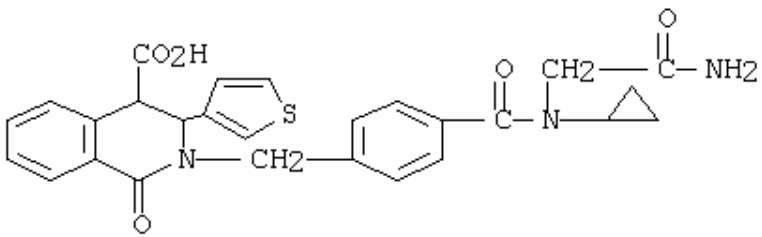
```
L1       STRUCTURE UPLOADED

=> s l1 sss full
L2          9532 SEA SSS FUL L1

=> s (chemical library)/sr
NUMERIC VALUE NOT VALID 'CHEMICAL LIBRARY'
L3            0 (CHEMICAL LIBRARY)/SR

=> d l2 ide
L2   ANSWER 1 OF 9532  REGISTRY  COPYRIGHT 2001 ACS
RN   308835-25-8  REGISTRY
CN   4-Isoquinolinecarboxylic acid, 2-[[4-[[(2-amino-2-
     oxoethyl)cyclopropylamino]carbonyl]phenyl]methyl]-1,2,3,4-tetrahydro-1-oxo-
     3-(3-thienyl)- (9CI)  (CA INDEX NAME)
FS   3D CONCORD
MF   C27 H25 N3 O5 S
SR   Chemical Library
LC   STN Files:   CHEMCATS
```

SR (Source of Registration) no es un campo que se pueda buscar ; sólo se puede visualizar



Puede limitarse la búsqueda subestructural a los *screening compounds* que se hayan registrado a partir de *combinatorial libraries* ...

Pg 2/2

Inicio Ban... Micr... ST... Micr... CO... Co... ST... ST... Micr... Micr... 18:48

STN Terminal Emulation

File Edit Online Query Results Preferences! Web Window Help

STN Karlsruhe Inter

```
=>
Uploading isoquinolinona.str

L6       STRUCTURE UPLOADED

=> s chemcats/lc
L7       586795 CHEMCATS/LC

=> s l6 sss full subset=l7
FULL SUBSET SEARCH INITIATED 19:17:07 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -    9360 TO ITERATE

100.0% PROCESSED     9360 ITERATIONS
SEARCH TIME: 00.00.03

L8          8739 SEA SUB=L7 SSS FUL L6

=> d

L8   ANSWER 1 OF 8739  REGISTRY  COPYRIGHT 2001 ACS
RN   324006-44-2  REGISTRY
CN   4-Isoquinolinecarboxylic acid, 2-[[4-[[4-(2-amino-2-oxoethyl)-1-
     piperazinyl]carbonyl]phenyl]methyl]-1,2,3,4-tetrahydro-1-oxo-3-(3-thienyl)-
      (9CI)  (CA INDEX NAME)
FS   3D CONCORD
MF   C28 H28 N4 O5 S
SR   Chemical Library
LC   STN Files:   CHEMCATS
```

Crear el conjunto de fichas de REGISTRY que tienen también ficha en CHEMCATS (LC es *RN LoCator*).

Resultan ser cerca de 600.000 compuestos

Así se crea un L8 en REGISTRY como resultado de una búsqueda subestructural limitada a los compuestos que hay en CHEMCATS (que son comerciales)

Discover! transcript: c:\mis documentos\cas - stn\stn_cas user meeting barcelona 2001\combinatori CHEMCATS INS Hold On Print Off Online 00:30:46

Inicio Microsoft P... SciFinder Microsoft W... STN Expre... STN Ter... 19:26

STN Terminal Emulation

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STN Karlsruhe Inter

```
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FILE LAST UPDATED 14 APRIL 2001 (20010414/UP)

For details on recen
(=>) prompt.  For th
HELP SPA, HELP SPBC,
For the list of curr
CTDH, HELP CTIN, HEL

This database is pro
suppliers for curren
availability, availa
WARRANTIES OF ANY KI
liable for any loss
out of the use of this database.


=> s l8
L9          8739 L8

=> s l8 and chemical library/st
            8739 L8
          963745 CHEMICAL/ST
```

entrar en CHEMCATS

Buscando en CHEMCATS por el conjunto (L8) creado en REGISTRY se crea un conjunto equivalente (L9).

Ahora se limita (L9) a los que tienen la frase CHEMICAL LIBRARY en el campo ST (Supplementary Term), o sea, a los *screening compounds* provenientes de *combinatorial libraries* (en este ejemplo resultan ser todos)

Discover! transcript: c:\mis documentos\cas - stn\stn_cas user meeting barcelona 2001\combinatori CHEMCATS INS Hold On Print Off Online 00:30:46

Inicio Microsoft P... SciFinder Microsoft W... STN Expre... STN Ter... 19:28

STN Terminal Emulation

File Edit Online Query Results Preferences! Web Window Help

STN Karlsruhe Inter

```
=> s l8 and chemical library/st
          8739 L8
        963745 CHEMICAL/ST
        963726 LIBRARY/ST
        963726 CHEMICAL LIBRARY/ST
                 ((CHEMICAL(S)LIBRARY)/ST)
L10       8739 L8 AND CHEMICAL LIBRARY/ST

=> analyze l10 1- co
ANALYZE IS APPROXIMATELY 49% COMPLETE
ANALYZE IS APPROXIMATELY 65% COMPLETE
ANALYZE IS APPROXIMATELY 81% COMPLETE
ANALYZE IS APPROXIMATELY 98% COMPLETE
L11          ANALYZE L10 1- CO :       11 TERMS

=> d 1- doc
L11          ANALYZE L10 1- CO :       11 TERMS

TERM #    # OCC   # DOC   % DOC CO
------ ------- ------ ------ ---------------
     1   17474   8737  99.98 CHEM.FOLIO/CO
     2    8737   8737  99.98 TREGA BIOSCIENCES, INC/CO
     3       4      2   0.02 MAYBRIDGE/CO
     4       2      2   0.02 ALTAQUIMICA/CO
     5       2      2   0.02 CHEMPUR GMBH/CO
     6       2      2   0.02 DORLAND GES.M.B.H/CO
     7       2      2   0.02 INTERCHIM S.A./CO
     8       2      2   0.02 KB CHEMTRONICA/CO
```

Para analizar los suministradores de estos *screening compounds*, se analiza el conjunto (L10) por el campo CO (Company Name and Catalog Name).

En este caso casi todos están en catálogos de CHEM.FOLIO y los suministra TREGA BIOSCIENCES (empresa titular de las patentes)

Discover! transcript: c:\mis documentos\cas - stn\stn_cas user meeting barcelona 2001\combinatori CHEMCATS INS Hold On Print Off Online 00:30:46

Inicio Microsoft P... SciFinder Microsoft W... STN Expre... STN Ter... 19:29

STN Terminal Emulation

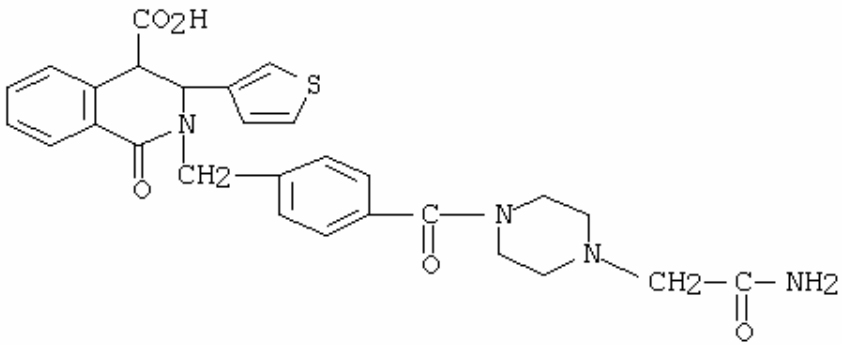
File Edit Online Query Results Preferences! Web Window Help

STN Karlsruhe Inter

```
=> d l10 1 all

L10  ANSWER 1 OF 8739  CHEMCATS COPYRIGHT 2001 ACS
Accession No.        (AN): 2001:384784  CHEMCATS
Catalog Name         (CO): Chem.Folio
Publication Date     (PD): 20 Oct 2000
Order Number         (ON): TRG02530#05317-D
Chemical Name        (CN): 4-Isoquinolinecarboxylic acid, 2-[[4-[[4-(2-amino-2-
                           oxoethyl)-1-piperazinyl]carbonyl]phenyl]methyl]-
                           1,2,3,4-tetrahydro-1-oxo-3-(3-thienyl)-
CAS Registry No.     (RN): 324006-44-2
Supplementary Term   (ST): CHEMICAL LIBRARY
Structure                :
```

Chem. Folio en (CO) como Catalog Name



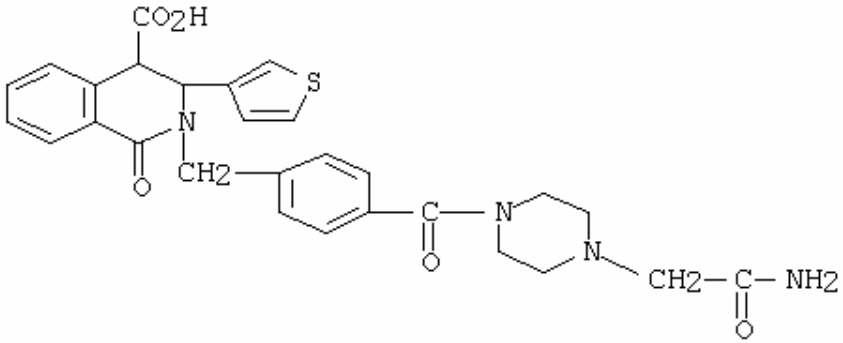
Discover! transcript: c:\mis documentos\cas - stn\stn_cas user meeting barcelona 2001\combinatori CHEMCATS INS Hold On Print Off Online 00:30:46

Inicio Microsoft P... SciFinder Microsoft W... STN Expre... STN Ter... 19:24

STN Terminal Emulation

File Edit Online Query Results Preferences! Web Window Help

STN Karlsruhe Inter



PRICES

Quantity : N/A, Price: contact supplier

COMPANY INFORMATION

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San Diego, CA, 92121
USA

Phone: (858) 410-6500
Fax: (858) 410-6501
Web: www.trega.com

Trega Biosciences como Company Name (también incluido en el campo CO)

entramos en su página web

Discover! transcript: c:\mis documentos\cas - stn\stn_cas user meeting barcelona 2001\combinatori CHEMCATS INS Hold On Print Off Online 00:36:53

Inicio Microsoft P... SciFinder Microsoft W... STN Expre... STN Ter... 19:30

Compound Libraries

LION's **Chem.Folio®** information-rich compounds offer pharmaceutical, biotechnology, agriculture and life science research companies access to novel, structurally diverse combinatorial chemistry libraries for use in their drug discovery programs.

Chem.Folio® libraries are designed to possess drug-like properties and are created using LION's proprietary technologies and medicinal chemistry principles. LION's unique technologies efficiently synthesize and generate highly pure compounds, while allowing rapid follow-up synthesis for lead development.

The distinguishing factor of **Chem.Folio®** is the information component consisting of solubility, purity, cytotoxicity and ultimately, ADME characteristics.

Chem.Folio® libraries are sold on both an exclusive and non-exclusive basis, with licensing terms flexible enough to meet the needs of both large and small pharmaceutical and biotechnology customers.

In addition to traditional sales channels, **Chem.Folio®** compounds are distributed via the Internet through LION's strategic partnership with ChemNavigator.com, Inc.

brochure download

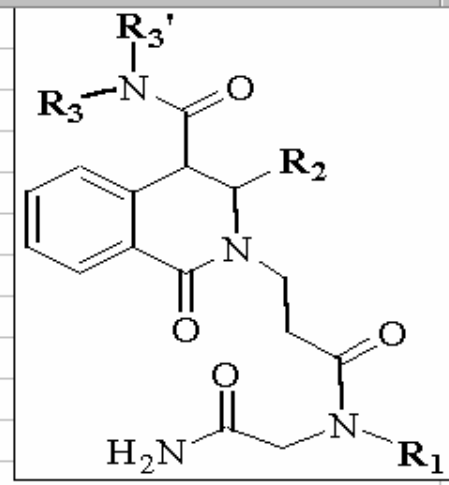
PDF Chem.Folio®-brochure [1.12 MB]

Patented Libraries

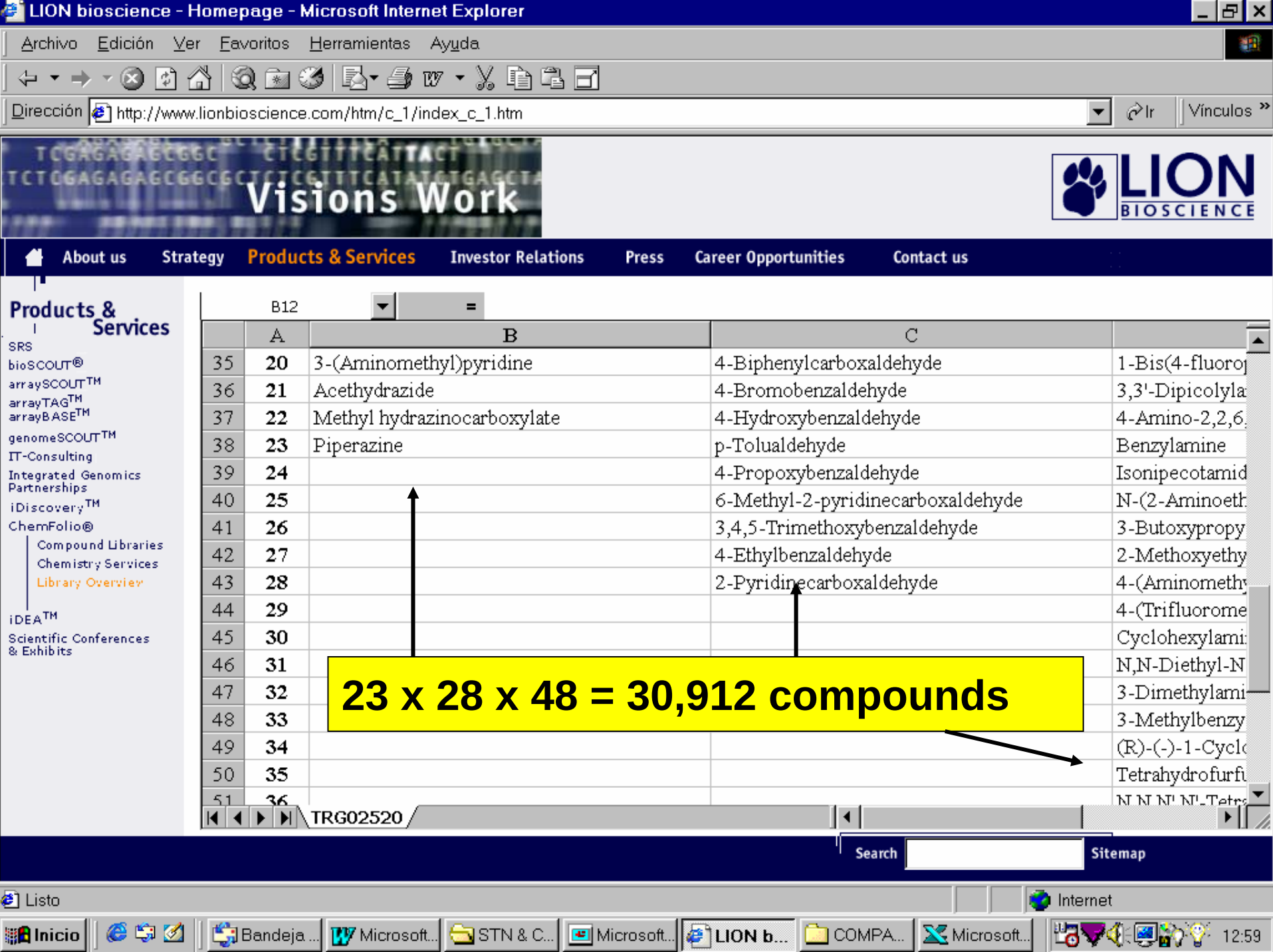
LION bioscience offers over 400,000 compounds subdivided into nearly 40 different libraries, each with interesting and unique scaffolds. Below is a listing of all libraries currently available for sale. Selected libraries have scaffold and substructure information available by clicking on the links. Please note, however, that not all combinations were actually synthesized. To obtain more information on our entire inventory of diverse, drug-like compounds, please go to our contact form.

Library	**Name** (click for scaffolds and R groups)
EXCEL TRG02520 [0.02 MB]	Dihydroisoquinolones/Peptoids
EXCEL TRG02530 [0.03 MB]	Dihydroisoquinolones/Peptoids
EXCEL TRG03900 [0.02 MB]	Oxadiazole Sulfonamides
EXCEL TRG04000 [0.03 MB]	Oxadiazole Carboxamides/Ureas
EXCEL TRG04201 [0.03 MB]	Aminodihydroisoquinolones
EXCEL TRG04500 [0.02 MB]	Benzimidazoles

B12 =

	A	B	C
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			
13			**TRG02520 Dihydroisoquinolones/Peptoids**
14			
15		**R1 Amine**	**R2 Aldehyde**	**R3 Amine**
16	1	N,N-Dimethylethylenediamine	Benzaldehyde	N-(2-Aminoeth

TRG02520


LION bioscience - Homepage - Microsoft Internet Explorer
Archivo Edición Ver Favoritos Herramientas Ayuda
Dirección http://www.lionbioscience.com/htm/c_1/index_c_1.htm
Ir Vínculos
Visions Work
LION BIOSCIENCE
About us Strategy Products & Services Investor Relations Press Career Opportunities Contact us
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SRS
bioSCOUT®
arraySCOUT™
arrayTAG™
arrayBASE™
genomeSCOUT™
IT-Consulting
Integrated Genomics Partnerships
iDiscovery™
ChemFolio®
Compound Libraries
Chemistry Services
Library Overview
iDEA™
Scientific Conferences & Exhibits
B12
=
A B C
35 20 3-(Aminomethyl)pyridine 4-Biphenylcarboxaldehyde 1-Bis(4-fluoro
36 21 Acethydrazide 4-Bromobenzaldehyde 3,3'-Dipicolyla
37 22 Methyl hydrazinocarboxylate 4-Hydroxybenzaldehyde 4-Amino-2,2,6
38 23 Piperazine p-Tolualdehyde Benzylamine
39 24 4-Propoxybenzaldehyde Isonipecotamid
40 25 6-Methyl-2-pyridinecarboxaldehyde N-(2-Aminoeth
41 26 3,4,5-Trimethoxybenzaldehyde 3-Butoxypropy
42 27 4-Ethylbenzaldehyde 2-Methoxyethy
43 28 2-Pyridinecarboxaldehyde 4-(Aminomethy
44 29 4-(Trifluorome
45 30 Cyclohexylami
46 31 N,N-Diethyl-N
47 32 3-Dimethylami
48 33 3-Methylbenzy
49 34 (R)-(-)-1-Cyclo
50 35 Tetrahydrofurfu
TRG02520
23 x 28 x 48 = 30,912 compounds
Search Sitemap
Listo
Internet
Inicio Bandeja ... Microsoft... STN & C... Microsoft... LION b... COMPA... Microsoft... 12:59

Summary

REGISTRY

L1 STRUCTURE UPLOADED

=>s chemcats / LC

L2 606360 CHEMCATS / LC

=>s L1 sss full subset=L2

(SR =Chemical Library, only as display field)

CHEMCATS

=>s chemical library / ST

L3 963745 CHEMICAL LIBRARY / ST

CAplus

=>s combinatorial library / IT

L4 3435 COMBINATORIAL LIBRARY / IT

=>s combinatorial chemistry / IT

L5 1367 COMBINATORIAL CHEMISTRY / IT

L6 4325 L4 or L5

L7 999 L6 and patent / DT

Combinatorial Chemistry:
una química moderna (sólo desde principio de los años 90), que tiene su jerga especial (1M de *combinatorial screening compounds*) y crea interesantes problemas de patentes (ya hay unas más de 1.000) y de licencias.

Licencing problems with combinatorial libraries

Contracts may include:

- sale or 'lease' or a physical collection of compounds;

- patents and other IP rights to discoveries made using the library;

- know-how transfer;

- exclusivities (see next)

Licencing problems with combinatorial libraries

Exclusivities may include licensor's agreement…

- not to collaborate with third parties with respect to the same targets;

- not to distribute selected compounds or libraries;

- not to use information obtained during the agreement; etc.

Licencing problems with combinatorial libraries

The 'many partners' problem

The owner would like to license the same libraries to as many third parties as possible.

However, the third parties are likely to require exclusive rights to any lead compounds identified.

Licencing problems with combinatorial libraries

The 'Swiss cheese effect'

Granting the licensee exclusive rights to some individual compounds (tipically with some 'generic' space around) leaves a 'hole' devoid of usable compounds.

Holes may accumulate to the point where the library fails to represent the diversity originally intendend. The resulting 'Swiss cheese' library may become useless.

Licencing problems with combinatorial libraries

The 'converging partners' problem

Different partners may become interested in the same (or similar) compounds, even looking for different mechanisms or targets.

Even when different partners are given non-overlapping libraries, licensor may be forced to make 'follow-up' libraries based on data collected from the first library.

Patents in Combinatorial Chemistry

There is not any single invention which covers the whole field, similar to:

- Köhler & Milsteins' work on monoclonal antibodies,
- Cohen & Boyer's work on gene splicing,
- Mullis's work on PCR; etc.

Rather Combinatorial Chemistry comes from the evolution of several technologies: chemistry, precision engineering, robotics, data handling, etc.

Types of combinatorial inventions*

- Lead compounds.
- Chemical scaffolds (*andamios*) and structures for diversifications; methods of synthesizing scaffolds and structures; methods of optimizing.
- Specialized chemistry directed to combinatorials.
- Machines; Automation.
- Manipulations.
- Combinatorial methodology.
- **Combinatorial libraries.**

(*) J.W. Caldwell, *Biotech. Bioeng. (Combin. Chem.)* 1998, 61, p 69-75

Claiming and arrayed combinatorial library *per se*

"Claim 1. An array of 10,240 different compounds, each comprising the reaction product of an oxazolone, aldehyde and amine, with the oxazolone being one of the eight oxazolones of Table 1, the aldehyde being one of the thirty-two aldehydes of Table 2 and the amine being one of the forty amines of Table 3.

US 5,962,736 (Arqule, Inc.)

Claiming the individual compounds in the library

"Claim 1: A single isoquinoline compound of the formula (I):.."

US 5,874,443 (Trega Biosciences)

- All compounds must be chemically unknown for the general formula claim to have **novelty.**

- This claim may be considered **non-patentable** if most of the claimed compounds do not have **industrial application (utility)** *per se.*

Claiming the library *per se*, defined as a general formula

"Claim 10: An isoquinoline library of an approximately equimolar mixture of two or more compounds of the formula (I)..."

US 5,874,443 (Trega Biosciences)

- It has **novelty** if none of the claimed combinations have been disclosed.

- It may be considered with **industrial application (utility),** because the library itself is commercialized as a tool for research (some successful examples should be included).

Patenting libraries as mixtures

In order to have novelty, one should be careful to claim a combinatorial library as a mixture of:

- compounds that includes **one or more novel** compounds, or

- **known** compounds that are **not** likely to have been **described in association previously.**

Tema para discusión:

- ¿Tiene novedad una reivindicación de producto químico específico (p.ej. para ser usado como principio activo farmacéutico) si el producto únicamente ha sido mencionado en un catálogo comercial de una quimioteca?

- ¿Influye el hecho de que se haya recogido o no en las bases de datos REGISTRY y CHEMCATS de CAS?