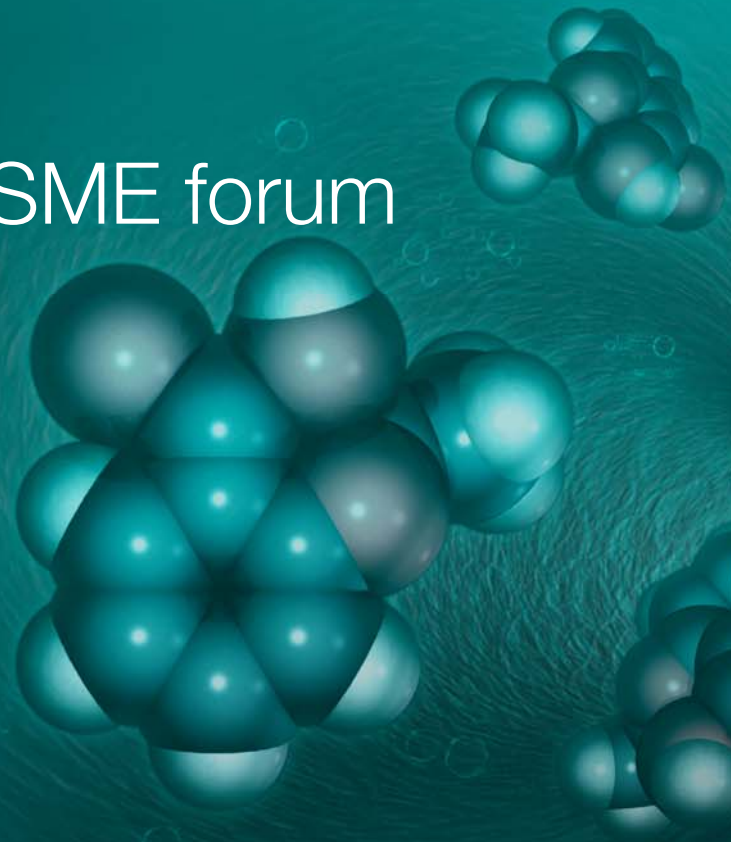
SureChEMBL – Tech Track Session

ELIXIR Innovation and SME forum

Mark Davies

Technical Lead

ChEMBL Group



EMBL-EBI

Outline

- Background
- Patent data
- Coverage and content
- Capabilities
- Future plans
- SureChEMBL interface demo
- myChEMBL example
- SureChEMBL exercises

Background

What is EMBL-EBI?

- Part of the European Molecular Biology Laboratory
- International, non-profit research institute
- Europe's hub for biological data services and research
- 500 members of staff from 53 nations.

EMBL-EBI resources & groups

Genes, genomes & variation

European Nucleotide Archive
1000 Genomes
Ensembl
Ensembl Genomes
European Genome-phenome Archive
Metagenomics portal

Gene, protein & metabolite expression

ArrayExpress
Expression Atlas
Metabolights
PRIDE

Literature & ontologies

Europe PubMed Central
Gene Ontology
Experimental Factor Ontology

Protein sequences, families & motifs

InterPro
Pfam
UniProt

Molecular structures

Protein Data Bank in Europe
Electron Microscopy Data Bank

Chemical biology

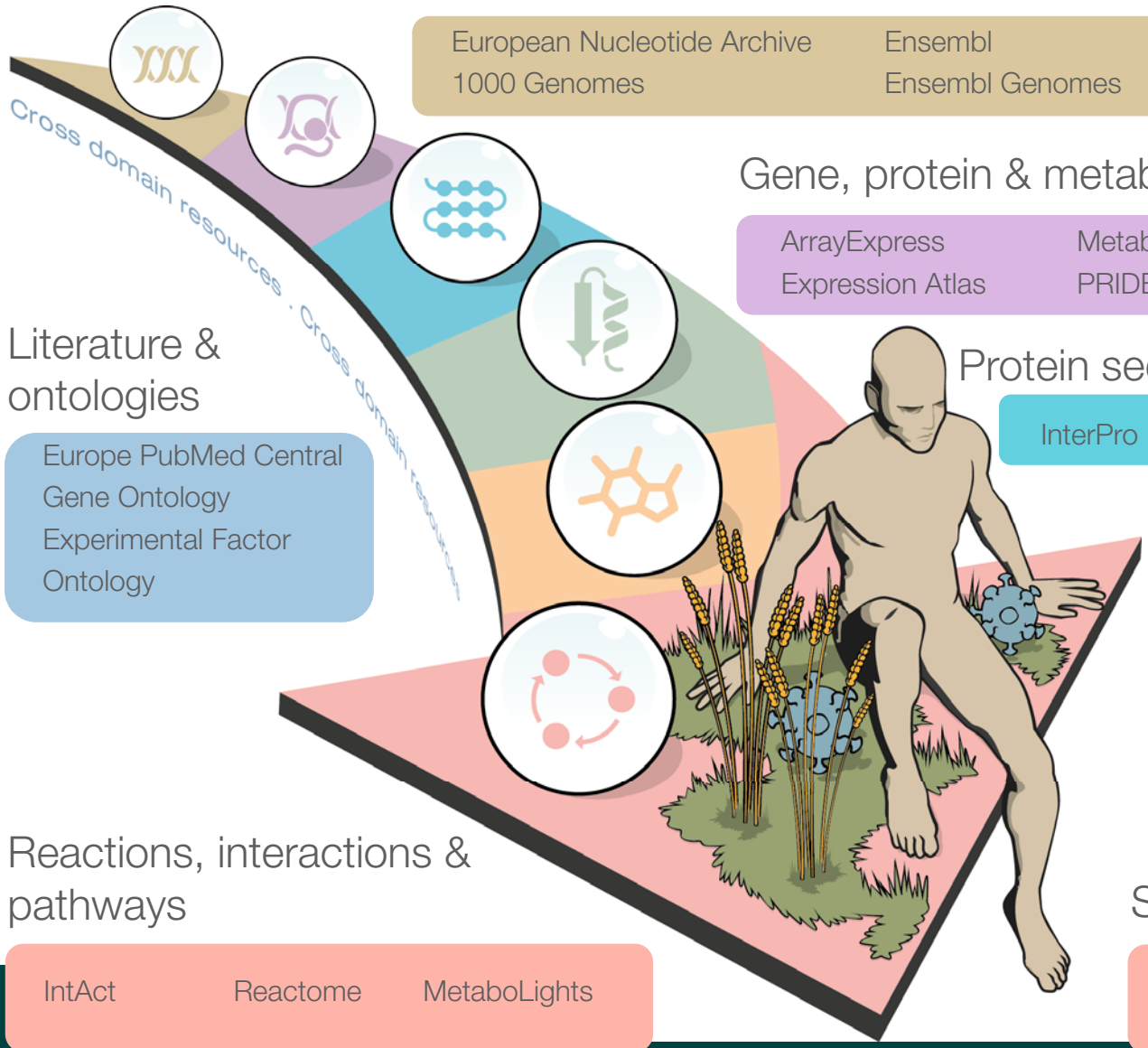
ChEMBL
ChEBI

Reactions, interactions & pathways

IntAct
Reactome
MetaboLights

Systems

BioModels
Enzyme Portal
BioSamples

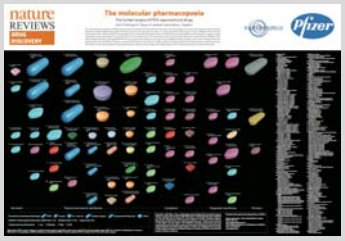


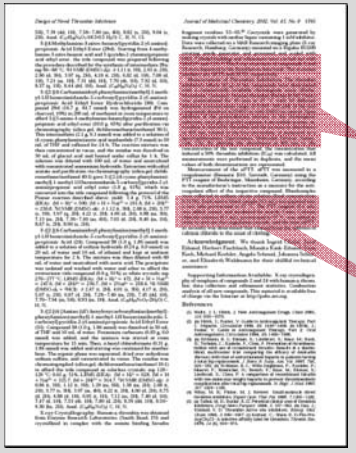
ChEMBL: Data for drug discovery

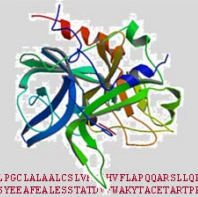
1. Scientific facts


Design of Selective Thrombin Inhibitors Based on the (R)-Phe-Pro-Arg Sequence

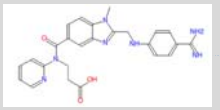
3. Insight, tools and resources for translational drug discovery







>Thrombin
MAHVRGLQLPGCLALAALCSLVHSQHVFLAPQQARSLLQRVRRANTFLEEVRKGNLE
RECVEETCSYEEAFEALESSTATDVFWAKYTACETARTPRDKLAACLEGNCAEGLGT
NYRGHVNITRSGIECQLWRSRYPHKPEINSTTHPGADLQENFCRNPDSSTTGP
TDPTVRRQECSIPVCGQDQVTVAMTPRSEGSSVNLSPPLEQCVPDRGQQYQGR
THGLPCLAWASAQAKALSKHQDFNSAVQLVENFCRNPDGDEEGVWCYVAGKPQ
CDLNYCEEAVEEETGDGLDEDSDRAIEGRTATSEYQTFFNPRTFGSGEADCGL
EKKSLEDKTERELLESYIDGRIVEGSDAEIGMSPWQVMLFRKSPQELLCGASL
WVLTAAHCLLYPPWDKNFTENDLLVRIGKHSRTRYERNIEKISMLEKIYIHPR
ENLDRDIALMKLKKPVAFSDYIHPVCLPDRETAASLLQAGYKGRVTGWGNLKE
NVGKGQPSVLQVVNLPIVERPVCKDSTRIRITDNMFCAGYKPDEGKRGDACEG
PFVMKSPFNNRWYQMGIVSWGEGCDRDGKYGFYTHVFRLKKWIQKVIDQFGE



Compound

K_i = 4.5nM

Bioactivity data

APTT = 11 min.

Assay/Target

2. Organization, integration, curation and standardization of pharmacology data

Patent data

- Historically a closed and costly data source
  - Out of reach to many academics and SMEs
- Patent literature 2-3 years ahead of published literature
- Prior art and freedom to operate
- Competitor intelligence
- Provides access to lots more data
  - High cost to extract and lots of noise

Do we include patent data in the ChEMBL database?

Patent Data

What is a patent?

- *patere* (Latin) = to lay open
- Legal and technical documents
- Agreement between Inventor and State
  - *Disclosure* of invention in exchange for *exclusive* rights
  - Usually lasts 20 years
- Requires:
  - Novelty, utility and inventive step
- Part of IP legislation, controlled by international treaties

United States Patent

Sadow

[15] **3,653,474**

[45] **Apr. 4, 1972**

[54] **ROLLING LUGGAGE**

[72] Inventor: **Bernard D. Sadow**, Chappaqua, N.Y.

[73] Assignee: **United States Luggage Corp.**, Fall River, Mass.

[22] Filed: **Feb. 16, 1970**

[21] Appl. No.: **11,383**

[52] **U.S. Cl.** .....**190/18 A**, 190/58, 280/47.17

[51] **Int. Cl.**.....**A45c 13/00**

[58] **Field of Search**.....190/18 A, 58, 59; 280/47.34, 280/47.17, 47.31

[56] **References Cited**

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1,376,529	5/1921	Grant	190/58
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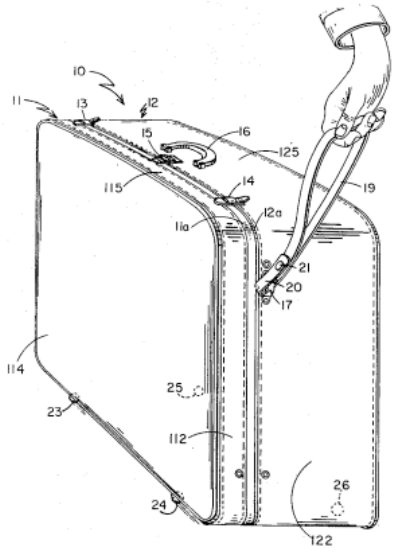
Primary Examiner—Joseph R. Leclair
Assistant Examiner—Stephen P. Garbe
Attorney—Joseph Zallen

[57] **ABSTRACT**

An article of luggage is described which has a plurality of rollers permanently mounted on its bottom wall and a flexible transport strap attached to its upper part.

3 Claims, 4 Drawing Figures



Patented April 4, 1972 3,653,474

2 Sheets-Sheet 2

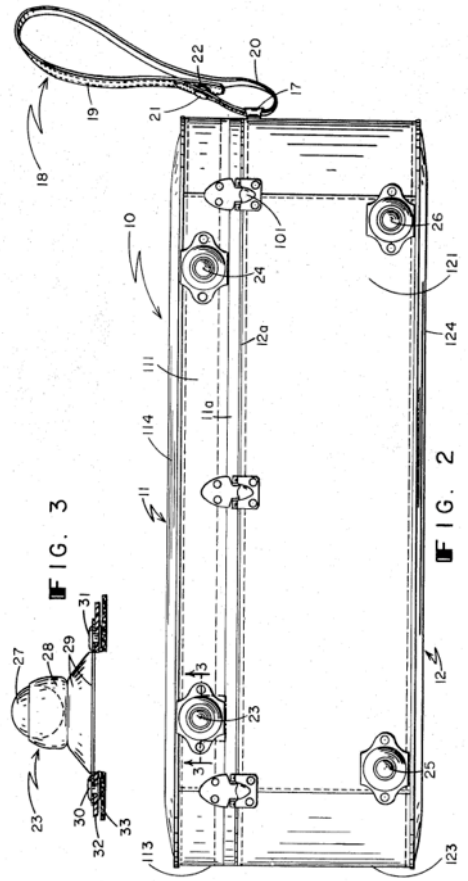


FIG. 3

FIG. 2

Front page

United States Patent [19]
Gibson

[11] **Patent Number: 5,770,599**
[45] **Date of Patent: Jun. 23, 1998**

[54] QUINAZOLINE DERIVATIVES

[75] Inventor: **Kieth Hopkinson Gibson**, Macclesfield, United Kingdom

[73] Assignee: **Zeneca Limited**, London, United Kingdom

[21] Appl. No.: **638,331**

[22] Filed: **Apr. 26, 1996**

[30] **Foreign Application Priority Data**

Apr. 27, 1995 [GB] United Kingdom 9508538

[51] **Int. Cl.**[6] **A61K 403/02**; A61K 403/04; C07D 31/535; C07D 31/54

[52] **U.S. Cl.** **514/228.2**; 514/234.5; 514/253; 514/259; 544/61; 544/119; 544/284; 544/293

[58] **Field of Search** 544/284, 293, 544/61, 119; 514/228.2, 234.5, 253, 259

[56] **References Cited**

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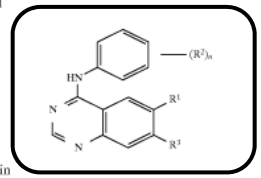
(List continued on next page.)

Primary Examiner—Matthew V. Grumbling
Attorney, Agent, or Firm—Cushman Darby & Cushman Intellectual Property Group of Pillsbury Madison & Sutro, LLP

[57] **ABSTRACT**

The invention concerns quinazoline derivatives of the formula I



I

wherein

n is 1, 2 or 3 and each R^2 is independently halogeno, trifluoromethyl or (1–4C)alkyl;

R^3 is (1–4C)alkoxy; and

R^1 is di-[(1–4C)alkyl]amino-(2–4C)alkoxy, pyrrolidin-1-yl-(2–4C)alkoxy, piperidino-(2–4C)alkoxy, morpholino-(2–4C)alkoxy, piperazin-1-yl-(2–4C) alkoxy, 4-(1–4C)alkylpiperazin-1-yl-(2–4C)alkoxy, imidazol-1-yl-(2–4C)alkoxy, di-[(1–4C)alkoxy-(2–4C) alkyl]amino-(2–4C)alkoxy, thiamorpholino-(2–4C) alkoxy, 1-oxothiamorpholino-(2–4C)alkoxy or 1,1-dioxothiamorpholino-(2–4C)alkoxy, and wherein any of the above-mentioned R^1 substituents comprising a CH_2 (methylene) group which is not attached to a N or O atom optionally bears on said CH_2 group a hydroxy substituent;

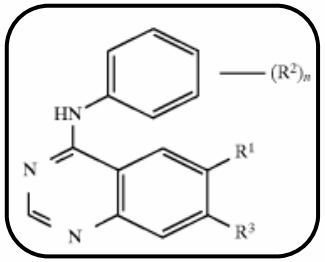
or pharmaceutically-acceptable salts thereof;

processes for their preparation, pharmaceutical compositions containing them, and the use of the receptor tyrosine kinase inhibitory properties of the compounds in the treatment of proliferative disease such as cancer.

19 Claims, No Drawings

Claims

According to the present invention there is provided a quinazoline derivative of the formula I



I

wherein

n is 1, 2 or 3 and each R^2 is independently halogeno, trifluoromethyl or (1–4C)alkyl;

R^3 is (1–4C)alkoxy; and

R^1 is di-[(1–4C)alkyl]amino-(2–4C)alkoxy, pyrrolidin-1-yl-(2–4C)alkoxy, piperidino-(2–4C)alkoxy, morpholino-(2–4C)alkoxy, piperazin-1-yl-(2–4C) alkoxy, 4-(1–4C)alkylpiperazin-1-yl-(2–4C)alkoxy, imidazol-1-yl-(2–4C)alkoxy, di-[(1–4C)alkoxy-(2–4C) alkyl]amino-(2–4C)alkoxy, thiamorpholino-(2–4C) alkoxy, 1-oxothiamorpholino-(2–4C)alkoxy or 1,1-dioxothiamorpholino-(2–4C)alkoxy,

and wherein any of the above-mentioned R^1 substituents comprising a CH_2 (methylene) group which is not attached to a N or O atom optionally bears on said CH_2 group a hydroxy substituent;

or a pharmaceutically-acceptable salt thereof.

According to a further aspect of the present invention there is provided a quinazoline derivative of the formula I wherein

n is 1, 2 or 3 and each R^2 is independently halogeno, trifluoromethyl or (1–4C)alkyl;

R^3 is (1–4C)alkoxy; and

R^1 is di-[(1–4C)alkyl]amino-(2–4C)alkoxy, pyrrolidin-1-yl-(2–4C)alkoxy, piperidino-(2–4C)alkoxy, morpholino-(2–4C)alkoxy, piperazin-1-yl-(2–4C) alkoxy, 4-(1–4C)alkylpiperazin-1-yl-(2–4C)alkoxy, imidazol-1-yl-(2–4C)alkoxy or di-[(1–4C)alkoxy-(2–4C)alkyl]amino-(2–4C)alkoxy,

and wherein any of the above-mentioned R^1 substituents comprising a CH_2 (methylene) group which is not attached

Description/Examples

EXAMPLE 5

A mixture of di-(2-methoxyethyl)amine (1.66 ml), 6-(2-bromoethoxy)-4-(3'-chloro-4'-fluoroanilino)-7-methoxyquinazoline (1.6 g) and ethanol (48 ml) was stirred and heated to reflux for 18 hours. A second portion (0.53 ml) of di-(2-methoxyethyl)amine was added and the mixture was heated to reflux for a further 18 hours. The mixture was evaporated and the residue was partitioned between ethyl acetate and a saturated aqueous sodium bicarbonate solution. The organic phase was dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography using a 97:3 mixture of methylene chloride and methanol as eluent. The material so obtained was dissolved in isopropanol, water was added and the mixture was stirred for 1 hour. The precipitate was isolated and dried. There was thus obtained 4-(3'-chloro-4'-fluoroanilino)-7-methoxy-6-{2-[di-(2-methoxyethyl)amino]ethoxy}quinazoline (0.95 g, 53%), m.p. 73°–74° C.;

NMR Spectrum: 2.6 (t, 4H), 3.05 (t, 2H), 3.25 (s, 6H), 3.45 (t, 4H), 3.95 (s, 3H), 4.2 (t, 2H), 7.2 (s, 1H), 7.4 (t, 1H), 7.8 (m, 2H), 8.1 (m, 1H), 8.5 (s, 1H), 9.5 (s, 1H);

Elemental Analysis: Found C, 56.2; H, 6.2; N, 11.3;

$C_{23}H_{28}ClFN_4O_4$ $0.7H_2O$ requires C, 56.2; H, 6.0; N, 11.4%.

EXAMPLE 6

A mixture of 4-(3'-chloro-4'-fluoroanilino)-6-hydroxy-7-methoxyquinazoline (3 g), 2-dimethylaminoethyl chloride hydrochloride (1.5 g), potassium carbonate (7.5 g) and DMF (60 ml) was stirred and heated to 80° C. for 5 hours. The mixture was cooled to ambient temperature and poured into water. The precipitate was isolated and dried. The material so obtained was purified by column chromatography using a 9:1 mixture of methylene chloride and methanol as eluent. The material so obtained was triturated under diethyl ether and recrystallised from aqueous ethanol. There was thus obtained 4-(3'-chloro-4'-fluoroanilino)-6-(2-dimethylaminoethoxy)-7-methoxyquinazoline (1.7 g 46%), m.p. 133°–135° C.;

NMR Spectrum: 2.3 (s, 6H), 2.75 (t, 2H), 4.0 (s, 3H), 4.25 (t, 2H), 7.2 (s, 1H), 7.3 (m, 2 H), 7.4 (t, 1H), 8.1 (m, 2H), 8.5 (s, 1H), 9.5 (broad s, 1H);

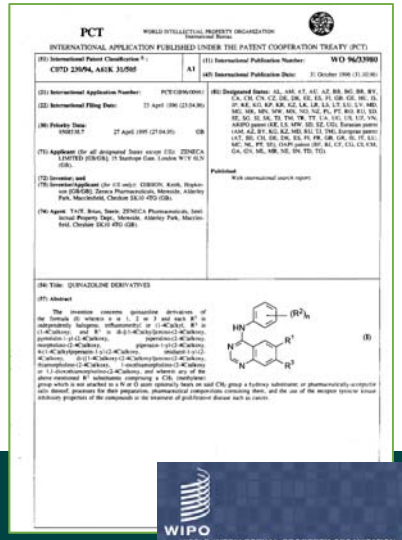
Elemental Analysis: Found C, 58.2; H, 5.2; N, 14.3;

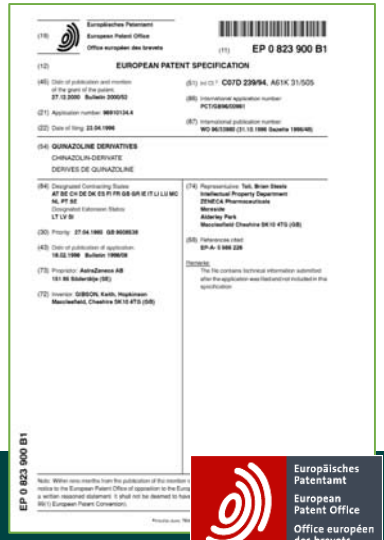
$C_{19}H_{20}ClFN_4O_2$ requires C, 58.4; H, 5.1; N, 14.3%.

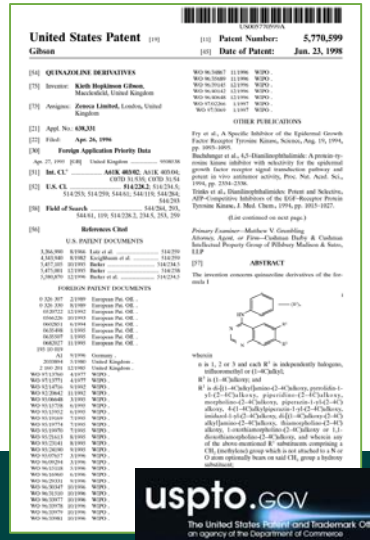
Patent authorities

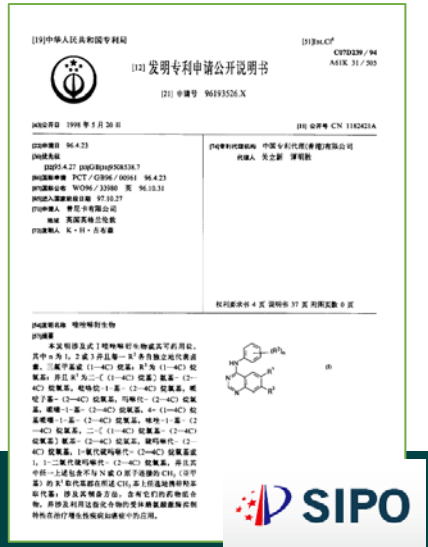
Patent families

- As defined by the EPO:
  - *A patent family is a set of either patent applications or publications taken in multiple countries to protect a single invention by a common inventor(s) and then patented in more than one country.*
  - *A first application is made in one country – the priority – and is then extended to other offices.*









Types of pharmaceutical patents

- Protein sequences
- Substances & compounds (*composition of matter*)
- Manufacturing processes
- Formulations/dosing
- Fixed-dose combinations
- Indications and uses

Patent classifications

- Classification Systems
  - International Patent Classification (IPC/IPCR)
  - Cooperative Patent Classification (CPC)
  - European CLAssification (ECLA)
  - United States Patent Classification (USPC)

Europäisches Patentamt
European Patent Office
Office européen des brevets

(19)

(11) EP 0 823 900 B1

(12) EUROPEAN PATENT SPECIFICATION

(45) Date of publication and mention of the grant of the patent:
27.12.2000 Bulletin 2000/52

(21) Application number: **96910134.4**

(22) Date of filing: **23.04.1996**

(51) Int Cl.[7]: **C07D 239/94**, A61K 31/505

(86) International application number:
PCT/GB96/00961

(87) International publication number:
WO 96/33980 (31.10.1996 Gazette 1996/48)

(54) **QUINAZOLINE DERIVATIVES**
CHINAZOLIN-DERIVATE
DERIVES DE QUINAZOLINE

(84) Designated Contracting States:
AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
Designated Extension States:
LT LV SI

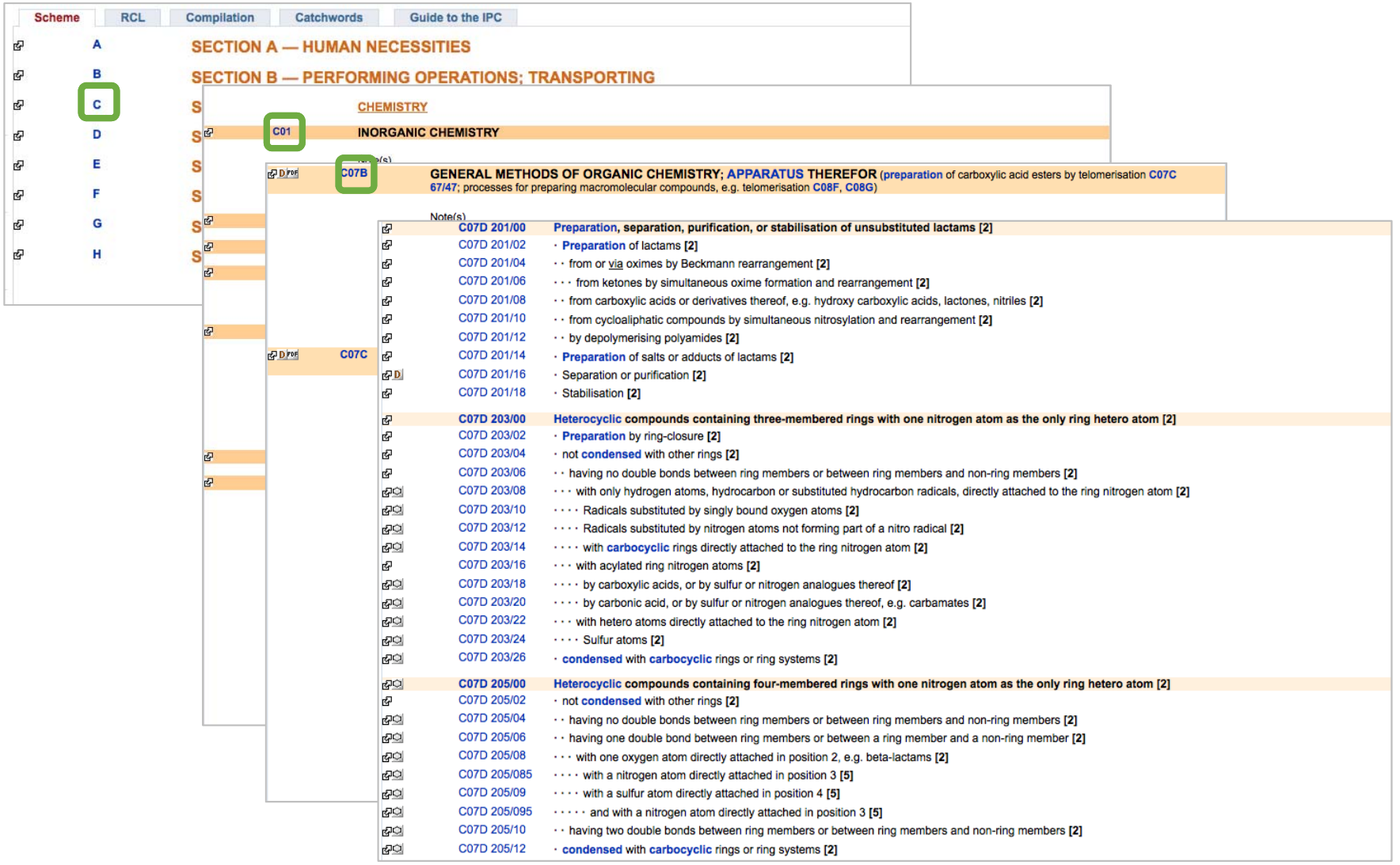
(30) Priority: **27.04.1995 GB 9508538**

(74) Representative: **Tait, Brian Steele**
Intellectual Property Department
ZENECA Pharmaceuticals
Mereside
Alderley Park
Macclesfield Cheshire SK10 4TG (GB)

C07D 239/94
- Heterocyclic Compounds

A61K 31/505
- Preparations for Medical, Dental or Toilet purposes

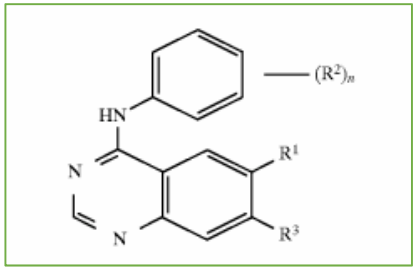
International Patent Classification



http://web2.wipo.int/ipcpub

Chemical entities in patents

- Markush structures
- Molecular formulas (e.g. C2H5)
- IUPAC nomenclature (e.g. propyl, acetylsalicylic acid)
- Trivial and trade names (e.g. aspirin)
- Images of 2D structures
- Non-structural entities (e.g. ‘pharmaceutically acceptable salt’)
- Supplementary files (e.g. molfiles, chemdraw)
- Identifiers (e.g. CAS numbers)



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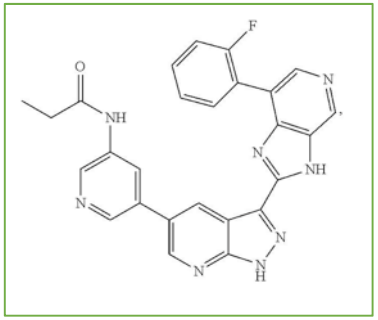


Exemplified

Why is searching chemical patents useful?

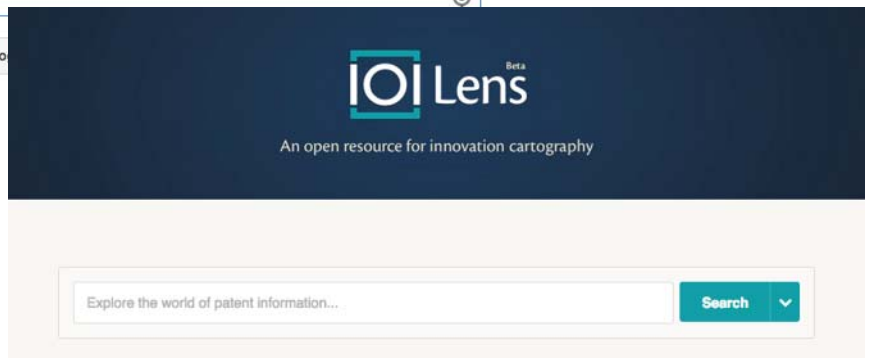
- Infringement search to avoid areas of valid patent protection (*freedom to operate*)
- Search for industrial profiles and research directions (*competitive intelligence*)
- State-of-the-art search*
  - Find claimed inhibitors of EGFR receptor published in 2014
  - Novel heterocyclic scaffolds / reaction schemes
- Search for citations and key references
- Most of the knowledge in chemical patents will never appear anywhere else

How can one search for chemical patents?

http://worldwide.espacenet.com

http://patentscope.wipo.int

https://www.google.com/patents



http://www.lens.org/lens

However…

≠

EMBL-EBI
ChEMBL

≠

Thomson Pharma ($)
CAS SciFinder ($)
Elsevier Reaxys ($)
IBM SIIPS ($)
SureChEMBL

SureChEMBL

SureChem becomes SureChEMBL

- December 2013 EMBL-EBI acquired SureChem – a leading chemistry patent mining product from Digital Science, Macmillan Group
  - SureChem not aligned with core future academic business
- Existing SureChem user base
  - Free (SureChemOpen)
  - Paying (SureChemPro + API)
- EMBL-EBI supported existing licensees during transition
- EMBL-EBI provides an ongoing, free and open resource to the entire community
- Rebranded as SureChEMBL

Rebranding process

SureChEMBL patent coverage

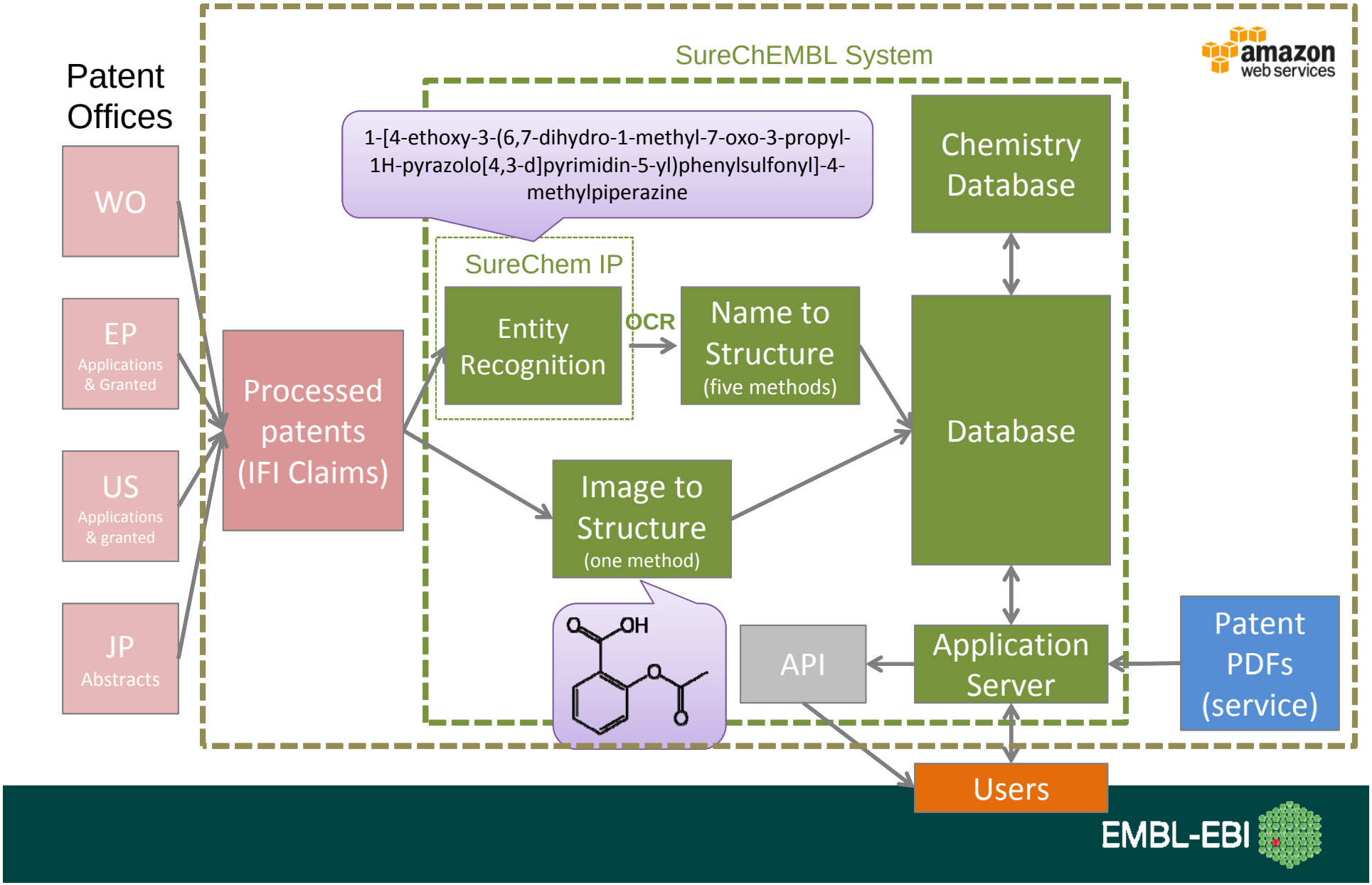
IFI CLAIMS® Patent Services
a division of Fairview Research

	Data	Description & Languages	Years
EP applications	Bib. data Full text	DocDB + Original Original (EN, DE, FR)	from 1978
EP granted	Bib. data Full text	DocDB + Original Original (EN, DE, FR)	From 1980
WO applications	Bib. data Full text	DocDB + Original Original (EN, DE, FR, ES, RU)	From 1978 From 1978
US applications	Bib. data Full text	DocDB + Original Original (EN)	From 2001 From 2001
US granted	Bib. data Full text	DocDB + Original Original (EN)	From 1920 From 1976
JP applications	Bib. Data	DocDB PAJ - English abstracts/titles	From 1973 From 1976
JP granted	Bib. data	DocDB	From 1994
90+ countries	Bib. data	DocDB	From 1920

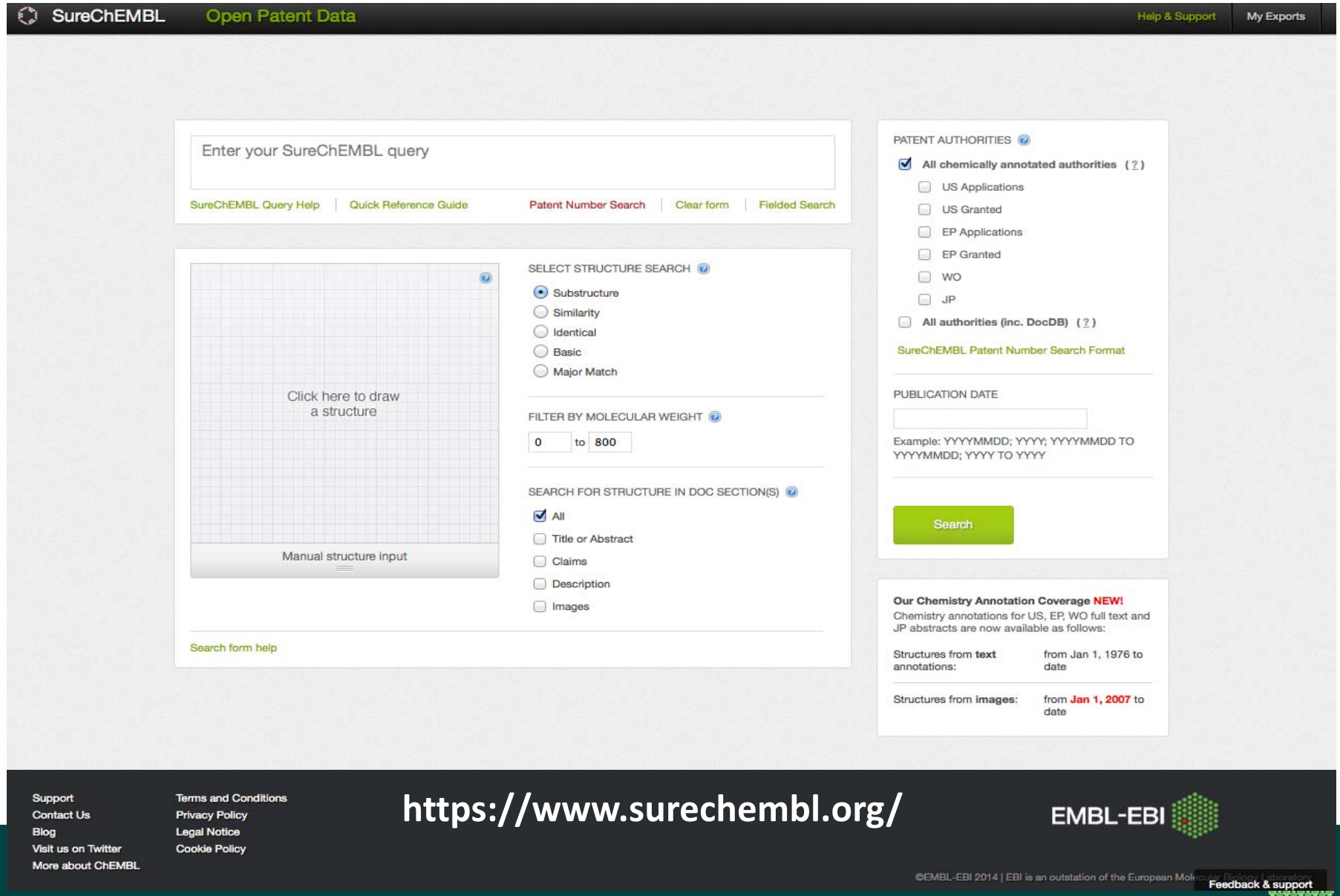
SureChEMBL chemistry data coverage

- Structures from text: 1976 onwards
  - Title, abstract, claims, description
  - IUPAC, trivial, drug names, etc.
  - SureChem Chemical Entity Recognition proprietary algorithm
  - ACD/Labs, ChemAxon, OpenEye, OPSIN, PerkinElmer name-to-structure conversion
- Structures from images: 2007 onwards
  - CLiDE image-structure conversion
- USPTO offers ‘Complex Work Units’ since 2001
  - CWU file types include MOL and CDX
  - CWUs processed as part of pipeline: 2007 onwards

SureChEMBL data pipeline



SureChEMBL user interface



SureChEMBL data content (27/10/14)

- 15,893,365 unique compounds
- 13,046,249 *annotated* patents
- ~80,000 *novel* compounds extracted from ~50,000 new patents *monthly*
- 2–7 days for a published patent to be chemically annotated and searchable in SureChEMBL
- SureChEMBL provides search access to all patents (not just chemically annotated ones)
  - ~120M patents

EMBL-EBI chemistry resources

RDF and REST API interfaces

Atlas	PDBe	ChEBI	ChEMBL	SureChEMBL	3rd Party Data
Ligand induced transcript response	Ligand structures from structurally defined protein complexes	Nomenclature of primary and secondary metabolites. Chemical Ontology	Bioactivity data from literature and depositions	Chemical structures from patent literature	ZINC, PubChem, ThomsonPharma DOTF, IUPHAR, DrugBank, KEGG, NIH NCC, eMolecules, FDA SRS, PharmGKB, Selleck, ….
750	15K	24K	1.5M	**~16M**	~55M

UniChem – InChI-based chemical resolver (full + relaxed 'lenses') >70M

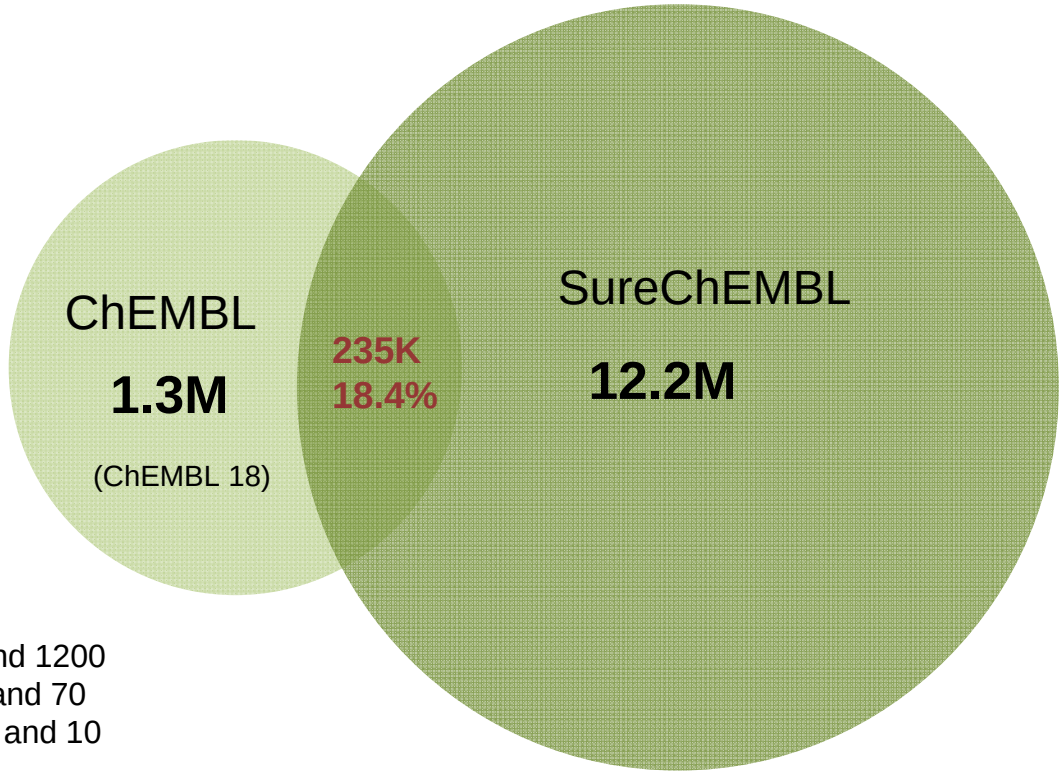
REST API Interface - https://www.ebi.ac.uk/unichem/

SureChEMBL compound data access

- UniChem ("Universal Compound Resolver")
  - Weekly updates
  - Web service lookup
    - Connectivity search
  - https://www.ebi.ac.uk/unichem/
- FTP download
  - Quarterly updates
  - All SureChEMBL compounds in SDF and CSV format
  - Raw data
  - ftp://ftp.ebi.ac.uk/pub/databases/chembl/SureChEMBL/

ChEMBL – SureChEMBL overlap

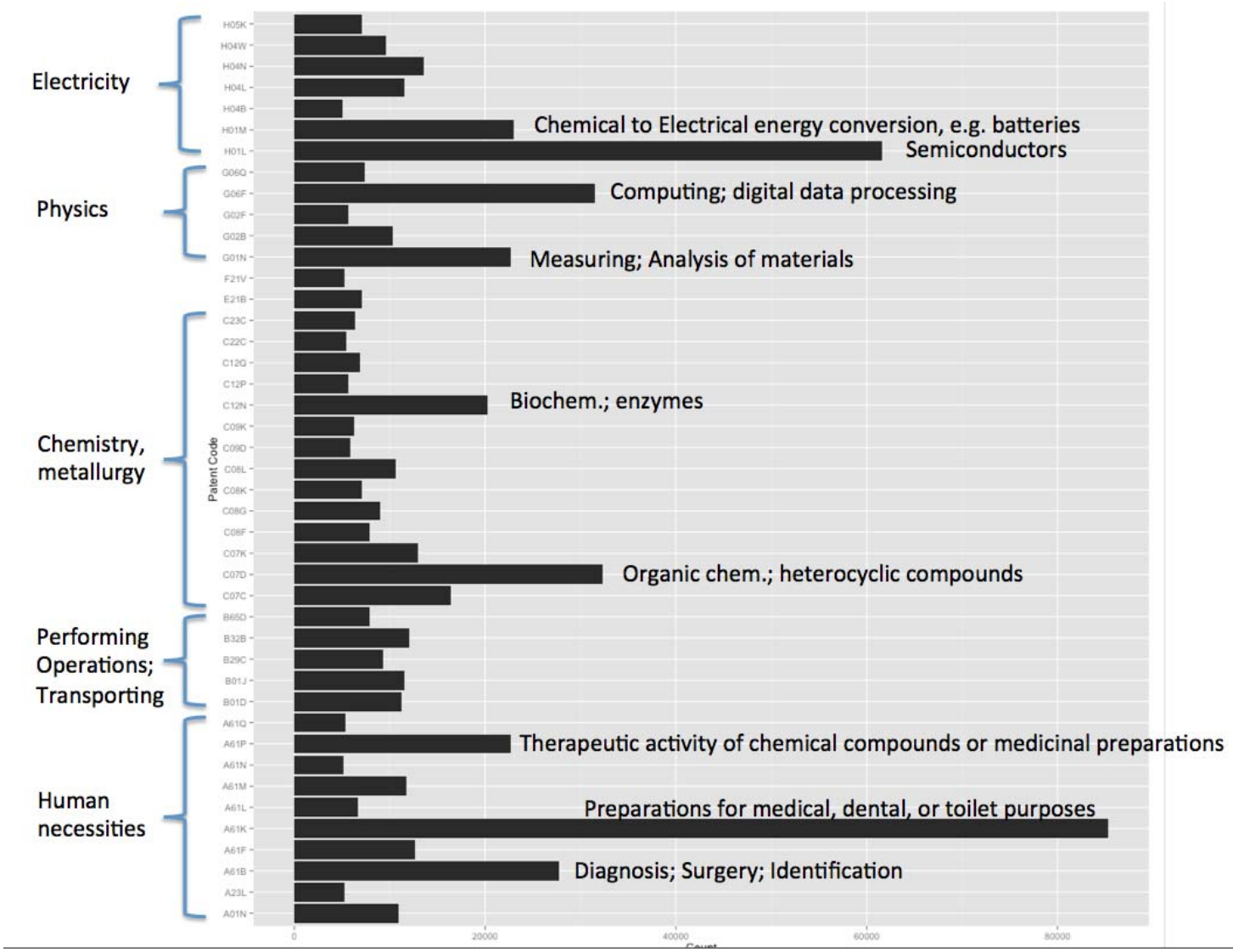
- InChI-based comparison using filtered parent compounds



Filters

- MW between 100 and 1200
- #Atoms between 6 and 70
- ALogP between -10 and 10
- #C > 0
- #Rings > 0
- #C != #Atoms
- RTB <= 20

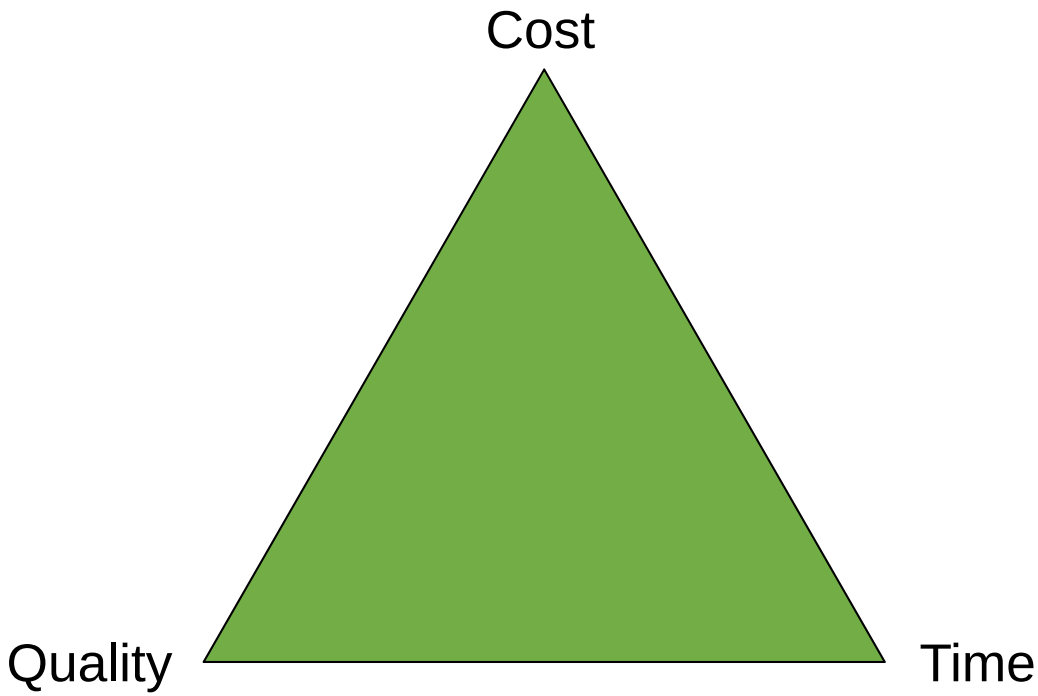
SureChEMBL IPCR classification



SureChEMBL patents from 2014 ~400K

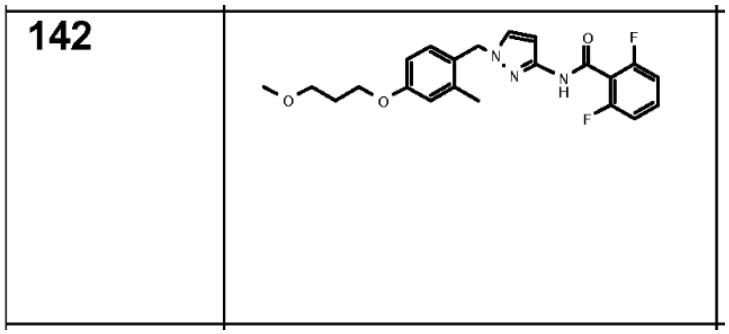
EMBL-EBI

Can we have everything?



Common sources of errors

- Small, poor quality images



- OCR errors in names (OCR done by IFI). There is an OCR correction step, but cannot fix all errors

Example 77: 2,6-Difluoro-*N*-{1-[(4-iodo-2-methylphenyl)methyl]-1*H*-pyrazol-3-yl}benzamide

-> '2,6-Difluoro-Λ/-{1 -r(4-iodo-2-methylphenyl)methvn-1 H-pyrazol-3-vDbenzamide'

- Reliability better for US patents due to inclusion of mol files

Use cases with SureChEMBL

- Chemoinformatics
  - Chemistry landscape for a particular biological target/disease
  - MDS, MCS and R-group analysis for a particular patent family claimed chemistry *see myChEMBL examples*
  - (Negative) novelty checking with UniChem
- Competitive intelligence
  - Reporting
  - Patent alerts
    - Per target/disease

Future plans

- SureChEMBL UI now available
  - https://www.surechembl.org/
- OpenPHACTS project
  - Biological entity extraction and annotation
  - Semantic integration
- Add new data sources
  - Patent authorities
  - Europe PubMedCentral (scientific literature corpus)
- Image and attachment processing prior 2007
  - Images and ‘Complex Work Units’

Enhanced entity extraction plans

- Identify new entity types e.g. proteins, diseases and cell lines
  - Working with Open PHACTS partners
  - Extend using ChEMBL dictionaries + others
  - Ontology/synonym mapping - integration
  - Target-relevance assessment
- Protein/biotherapeutic sequence extraction
  - Sequence based patent searches
- Enhanced cross-referencing
  - Tag up all commonly used identifiers (CAS, ChEBI, ChEMBL, PubChem, UniProt,…)

Bioactivity data extraction?

Compounds

Target/Assay

Bioactivity

TABLE 1-continued

Ex. No.	Compound Name	Method	Observed MS	BACE 1 FRET assay (uM	HEK cell assay (uM)
39	3-(2-amino-6-o-tolylquinolin-3-yl)-N-(1-methylpiperidin-3-yl)propanamide		403	++	++
40	3-(2-amino-6-o-tolylquinolin-3-yl)-N-((tetrahydro-2H-pyran-2-yl)methyl)propanamide		404	++++	++
3	3-(2-amino-6-(2-chlorophenyl)quinolin-3-yl)-N-(cyclohexylmethyl)propanamide		422	++++	++
41	3-(2-amino-6-(2-cyanophenyl)quinolin-3-yl)-N-(cyclohexylmethyl)propanamide		413	++++	++
42	3-(2-amino-6-(2-fluorophenyl)quinolin-3-yl)-N-(cyclohexylmethyl)propanamide		406	++++	+
43	3-(2-amino-6-(3-fluorophenyl)quinolin-3-yl)-N-(cyclohexylmethyl)propanamide		406	+++	++
44	3-(2-amino-6-(2-methoxyphenyl)quinolin-3-yl)-N-(cyclohexylmethyl)propanamide		418	++++	++
45	3-(2-amino-6-phenylquinolin-3-yl)-N-(cyclohexylmethyl)propanamide		388	+++	+
46	3-(2-amino-6-(4-methylpyridin-3-yl)quinolin-3-yl)-N-(cyclohexylmethyl)propanamide		403	++	+
47	3-(2-amino-6-o-tolylquinolin-3-yl)-N-((R)-1-cyclohexylethyl)-2-methylpropanamide		430	++++	++
48	N-(3-(2-amino-6-o-tolylquinolin-3-yl)propyl)cyclohexanecarboxamide				
49	3-(2-amino-6-(2-ethylphenyl)quinolin-3-yl)-N-(cyclohexylmethyl)propanamide				
50	2-((2-amino-6-o-tolylquinolin-3-yl)methyl)-N-(2-fluorophenyl)butanamide				
51	3-(2-amino-6-o-tolylquinolin-3-yl)-2-methyl-N-phenylpropanamide				
52	3-(2-amino-6-o-tolylquinolin-3-yl)-N-benzyl-2-methylpropanamide				
53	3-(2-amino-6-o-tolylquinolin-3-yl)-N-(2-fluoro-4-methylphenyl)propanamide				
54	3-(2-amino-6-o-tolylquinolin-3-yl)-N-((1-methyl-1H-pyrazol-3-yl)methyl)propanamide				

[0474] Compounds of the present invention that contain the aforementioned isotopes and/or other isotopes of other atoms are within the scope of this invention. Certain isotopically-labelled compounds of the present invention, for example those into which radioactive isotopes such as ^{3}H and ^{14}C are incorporated, are useful in drug and/or substrate tissue distribution assays. Tritiated, i.e., ^{3}H, and carbon-14, i.e., ^{14}C, isotopes are particularly preferred for their ease of preparation and detection. Further, substitution with heavier isotopes such as deuterium, i.e., ^{2}H, can afford certain therapeutic advantages resulting from greater metabolic stability, for example increased in vivo half-life or reduced dosage requirements and, hence, may be preferred in some circumstances. Isotopically labelled compounds of this invention can generally be prepared by substituting a readily available isotopically labelled reagent for a non-isotopically labelled reagent.

Biological Evaluation

[0475] The compounds of the invention may be modified by appending appropriate functionalities to enhance selective biological properties. Surprisingly, the compounds of the present invention exhibit improved pharmacokinetics and

[0478] Of the compounds tested, the in-vitro BACE FRET enzyme data for each of Examples 1-171, where available at the time of filing this applicacation, is provided in Table 1. Data key for the in-vitro BACE FRET assay is as follows:

[0479] "+" means the compound example has an IC_{50} value of >5.0 uM;

[0480] "++" means the compound example has an IC_{50} value in the range from 1.0 uM-5.0 uM;

[0481] "+++" means the compound example has an IC_{50} value in the range from 500 nM-1.0 uM;

[0482] "++++" means the compound example has an IC_{50} value in the range less than 500 nM.

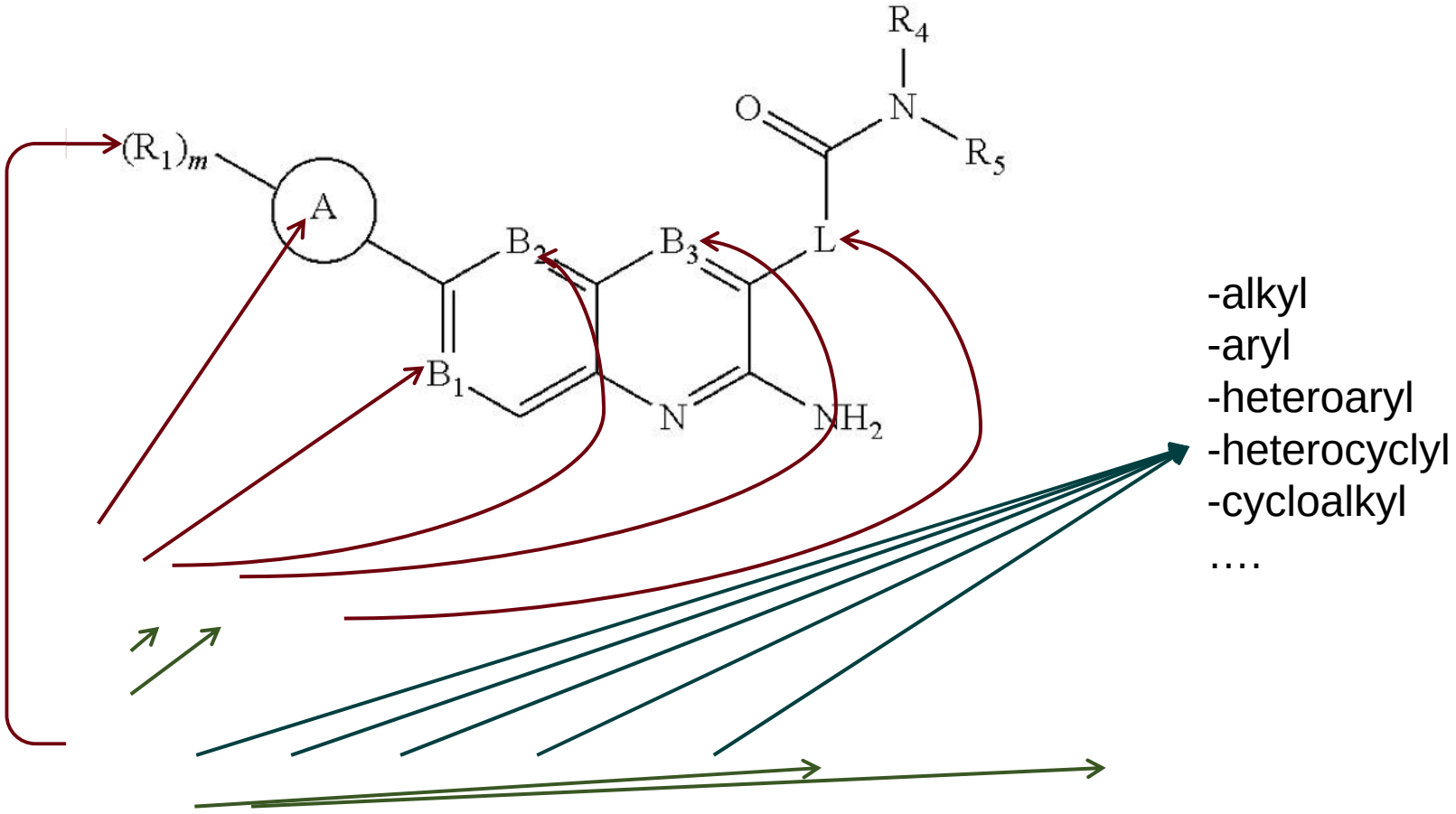
[0483] A majority of the exemplary compounds tested had IC_{50}'s for the enzyme BACE of less than 50 nM. For instance, example numbers 81, 84, 87, 90-93, 96, 98, 103, 106, 126, 128-130, 135, 136, 138, 12, 145-151, 153, 9, 156, 10, 158-164, 11 and 169-171 each exhibited an IC_{50} value of less than 50 nM in the FRET BACE enzyme assay.

[0484] In Vitro BACE Cell-Based Assay:

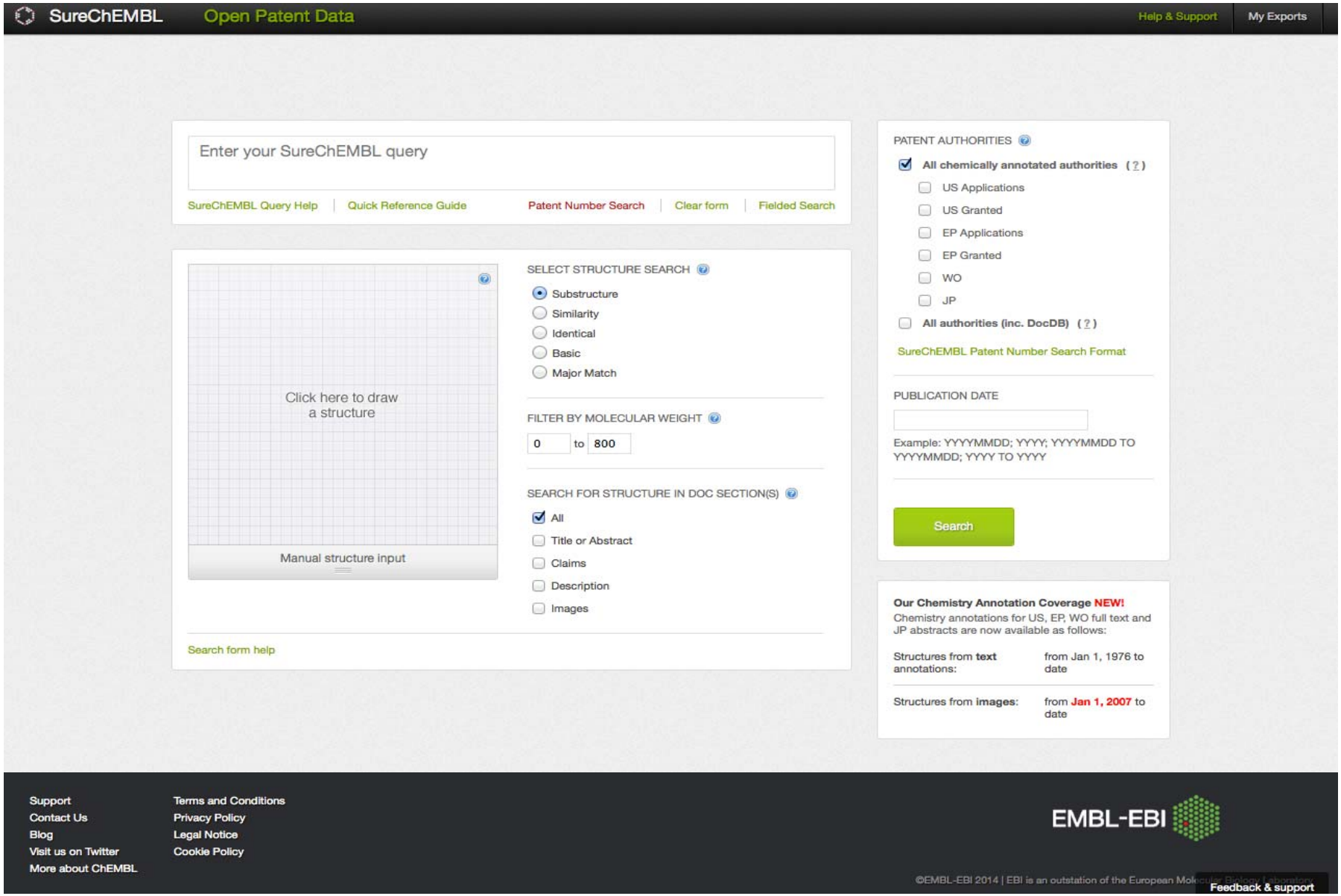
[0485] The cell-based assay measures inhibition or reduction of Aβ40 in conditioned medium of test compound treated cells expressing amyloid precursor protein.

[0486] Cells stably expressing Amyloid Precursor Protein

Markush structure extraction?



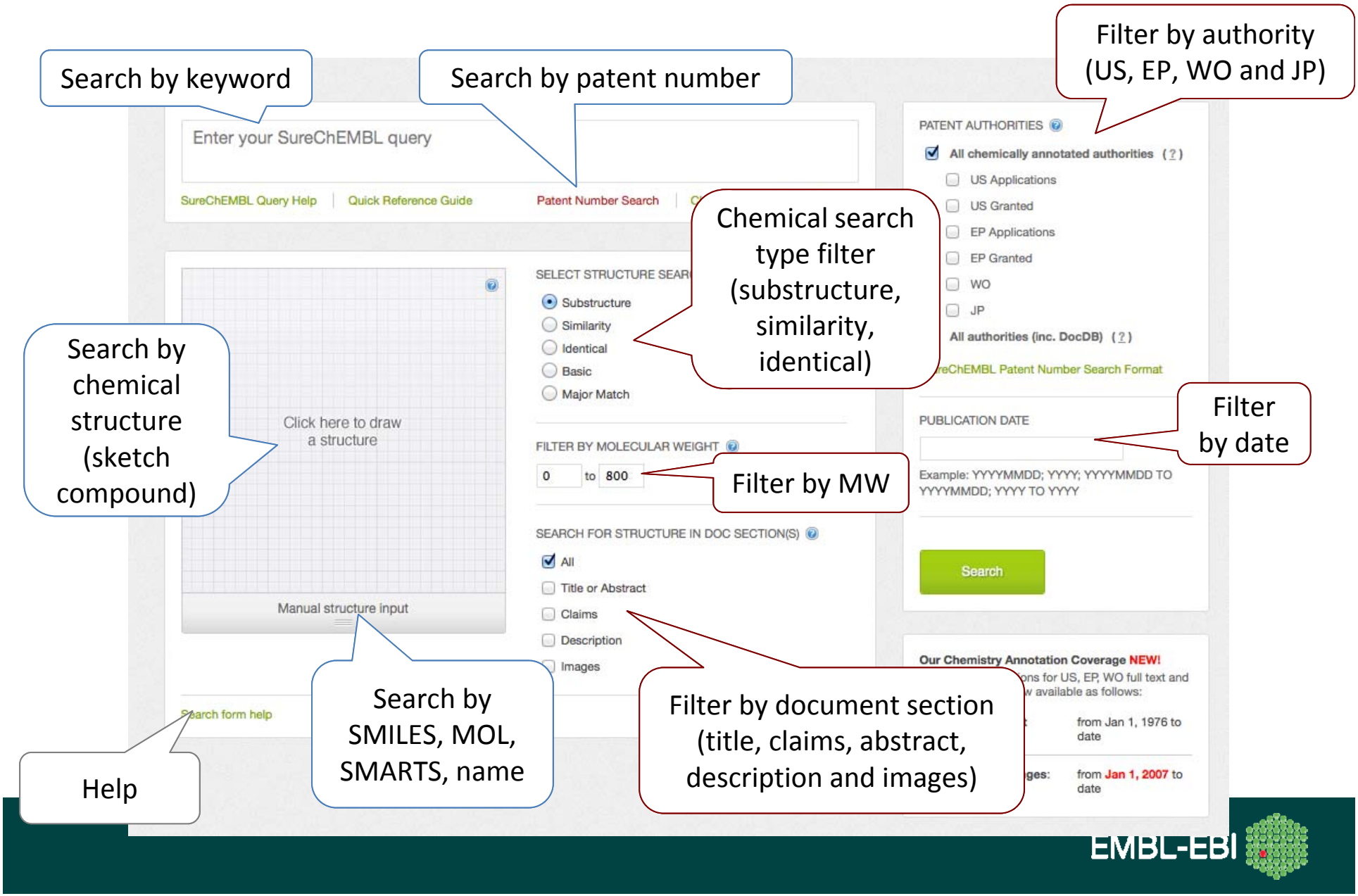
SureChEMBL Interface



https://www.surechembl.org/

EMBL-EBI

Homepage


Search by keyword
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All chemically annotated authorities (?)
US Applications
US Granted
EP Applications
EP Granted
WO
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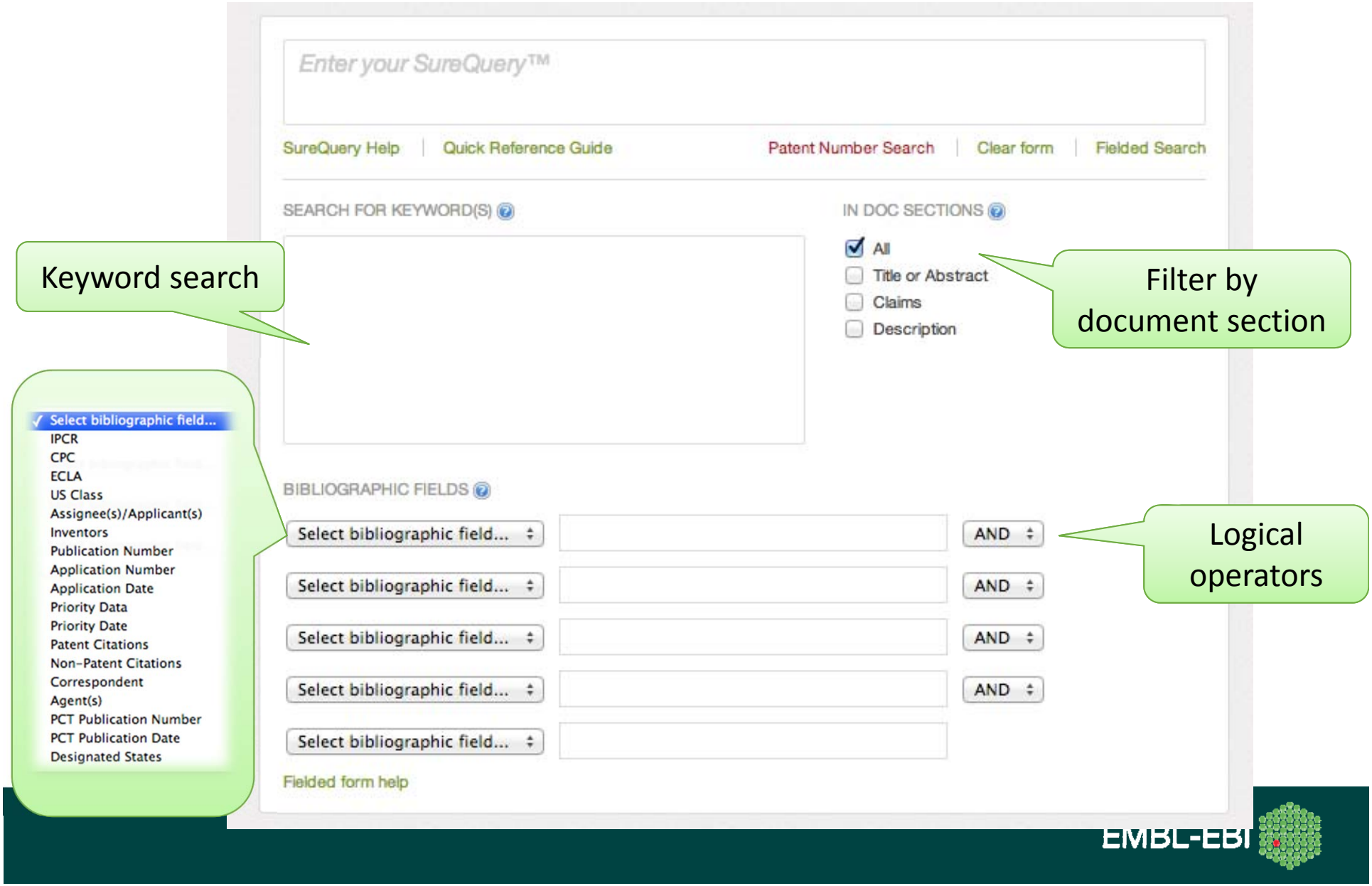
All authorities (inc. DocDB) (?)
Chemical search type filter (substructure, similarity, identical)
Substructure
Similarity
Identical
Basic
Major Match
Search by chemical structure (sketch compound)
Click here to draw a structure
Manual structure input
FILTER BY MOLECULAR WEIGHT
0
to
800
Filter by MW
PUBLICATION DATE
Filter by date
Example: YYYYMMDD; YYYY; YYYYMMDD TO YYYYMMDD; YYYY TO YYYY
SEARCH FOR STRUCTURE IN DOC SECTION(S)
All
Title or Abstract
Claims
Description
Images
Search
Search form help
Search by SMILES, MOL, SMARTS, name
Filter by document section (title, claims, abstract, description and images)
Help
Our Chemistry Annotation Coverage NEW!
from Jan 1, 1976 to date
from Jan 1, 2007 to date

Keyword-based search

- Uses Lucene Query Language
- Example searches…
  - roche **OR** novartis
  - sterili**?**e
  - kinase*****
  - pfizer C07D **“**kinase inhibitor**”**
  - **pn:**WO2011058149A1
  - (**pa:**bayer **OR** genentech **OR** merck) **AND desc:**(chemotherap***** **AND** (“phosphoinositide kinase”**~0.8 OR** Pi3K))

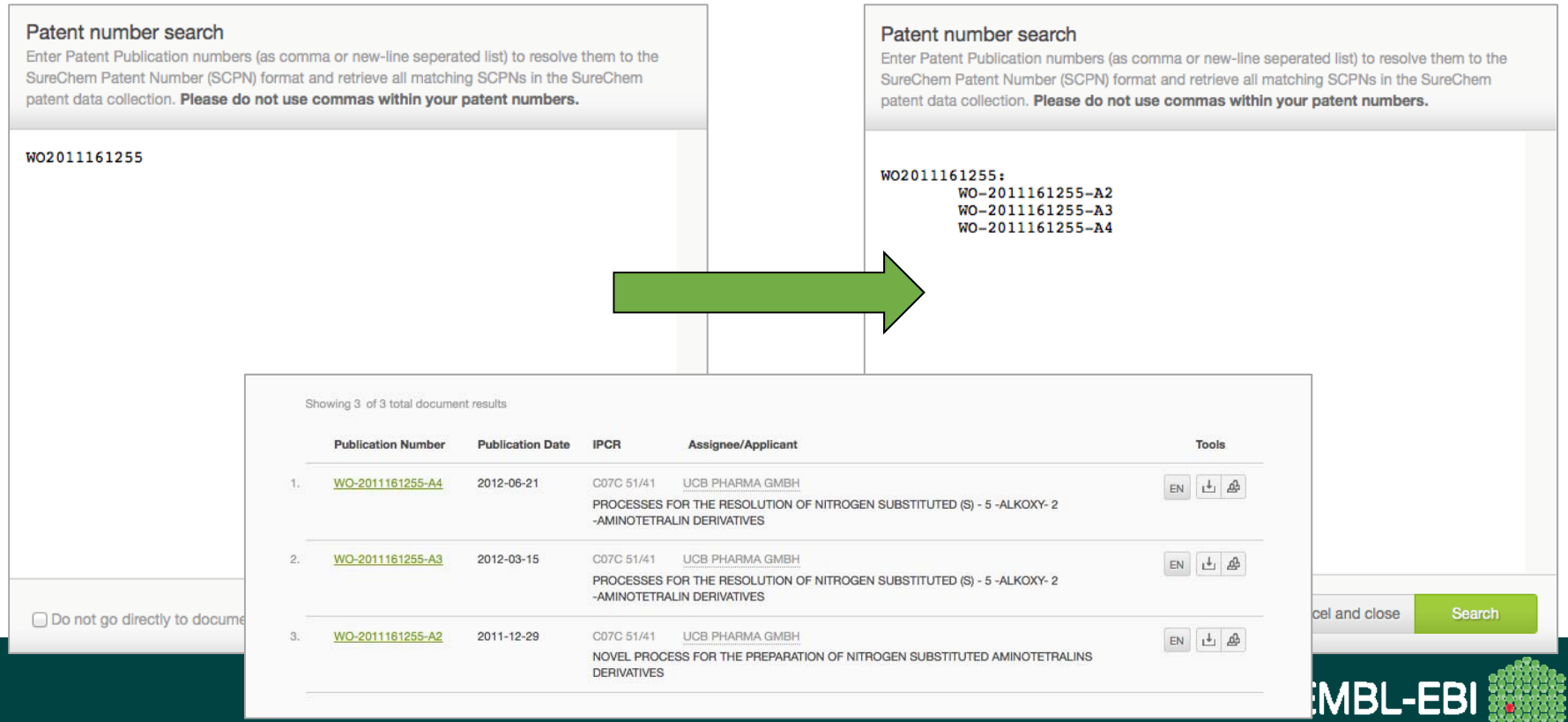
Fielded keyword search



Lucene Field	Description	Indexed Data	Sample
scpn	**SureChEMBL Patent Number (SCPN)**	EP-0555555-B1	scpn:EP-0555555-B1
pn	**publication number**	EP0555555B1	pn:ep0555555b1
pd	**publication date**	20120101	pd:20120101
an	**application number**	EP06009700A	an:EP06009700A
ad	**application date**	20061213	ad:20061213
pri	**priority(ies)**	DE19958719A 19991206	pri:“DE19958719A 19991206”
pridate	**all priority dates**	20000913	pridate:20000913
pdyear	**publication year**	2013	pdyear:2013
ds	**designated states**	DE	ds:(DE OR GB OR FR)
		GB	ds:FR
pctpn	**PCT publication number**	WO2006098969A2	pctpn:WO2006098969A2
pctpd	**PCT publication date**	20060921	pctpd:20060921
pctan	**PCT application number**	US2006008177W	pctan:US2006008177W
pctad	**PCT application date**	20060308	pctad:20060308
relan	**related application number**	Division of application No. 12/159,232	relan:US15923208
relad	**related application date**	Jun 26, 2008	relad:20080626
ic	**IPCR**	C CO8 C08K C08K0005	ic:C
cpc	**CPC**	C C07 C07D C07D0471 C07D047104	cpc:C07D
ecla	**ECLA**	C07D487/10	ecla:C07D487/10
uc	**US class**	29	uc:029
inv	**inventor(s)**	schmidt hans-werner	inv:("schmidt hans" AND thelakkat)
apl	**applicant**	Sony International (Europe) GmbH	apl:sony
asg	**assignee**	SIEMENS AKTIENGESELLSCHAFT	asg:siemens
pa apl or asg	**assignee(s) or applicant(s)**	see apl and asg above	pa:sony
cor	**correspondent**	Dr Roger Brooks	cor: “Dr Roger Brooks”
agt	**agents**	Pohlman, Sandra M	agt:”Pohlman, Sandra M”
pcit	**patent citations**	EP0748154B1	pcit:EP0748154B1
ncit	**non-patent citations**	TANG C W: ”Two-layer organic photovoltaic cell”	ncit:(tang AND ”Two-layer organic photovoltaic cell”)
ttl	**title in English, French and German**	Sonnenenergiesystem	ttl:(”solar energy” OR “énergie solaire” OR Sonnen*)
ab	**abstract in English, French and German**		
desc	**description in English, French and German**		
clm	**claims in English, French and German**		
text	**abstract or description or claims in English, French or German**		
pnlang	**publication language**	EN FR DE PT NO RU NL SV FI TR IS and more	pnlang:(NO OR FI OR SV)

SureChEMBL Patent Numbers (SCPN)

- Standardised format used to search system
- Format: CC-PATNO-KK, e.g. WO-2011161255-A2
- Batch conversion available via interface homepage link

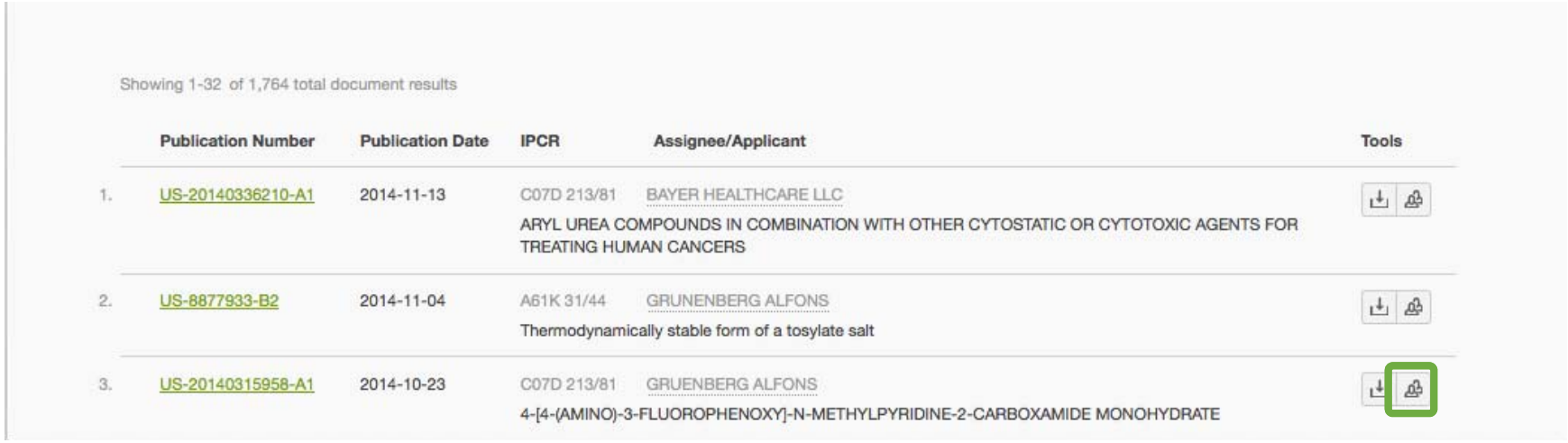


Keyword searches return documents

Showing 1-32 of 1,764 total document results

	Publication Number	Publication Date	IPCR	Assignee/Applicant	Tools
1.	US-20140336210-A1	2014-11-13	C07D 213/81	BAYER HEALTHCARE LLC ARYL UREA COMPOUNDS IN COMBINATION WITH OTHER CYTOSTATIC OR CYTOTOXIC AGENTS FOR TREATING HUMAN CANCERS	
2.	US-8877933-B2	2014-11-04	A61K 31/44	GRUNENBERG ALFONS Thermodynamically stable form of a tosylate salt	
3.	US-20140315958-A1	2014-10-23	C07D 213/81	GRUENBERG ALFONS 4-[4-(AMINO)-3-FLUOROPHENOXY]-N-METHYLPYRIDINE-2-CARBOXAMIDE MONOHYDRATE	
4.	US-20140315906-A1	2014-10-23	C07D 251/22	Lücking Ulrich 4-ARYL-N-PHENYL-1,3,5-TRIAZIN-2-AMINES CONTAINING A SULFOXIMINE GROUP	
5.	WO-2014166820-A1	2014-10-16	A61K 31/519	BAYER PHARMA AKTIENGESLLSCHAFT USE OF SUBSTITUTED 2,3-DIHYDROIMIDAZO[1,2-C]QUINAZOLINES FOR TREATING LYMPHOMAS	EN
6.	US-8859601-B2	2014-10-14	A61K 31/4196	BRÜGGEMEIER ULF Substituted benzyl and phenylsulfonyl triazolones, and use thereof	
7.	US-8859572-B2	2014-10-14	A61K 31/519	HENTEMANN MARTIN F Sulfone substituted 2,3-dihydroimidazo [1,2-C] quinazoline derivatives useful for treating hyper-proliferative disorders and diseases with angiogenesis	
8.	US-20140302010-A1	2014-10-09	C07D 235/08	KLAR ULRICH SUBSTITUTED BENZIMIDAZOLES	
9.	US-20140296231-A1	2014-10-02	C07D 487/04	EIS KNUT AMINO-SUBSTITUTED IMIDAZOPYRIDAZINES	

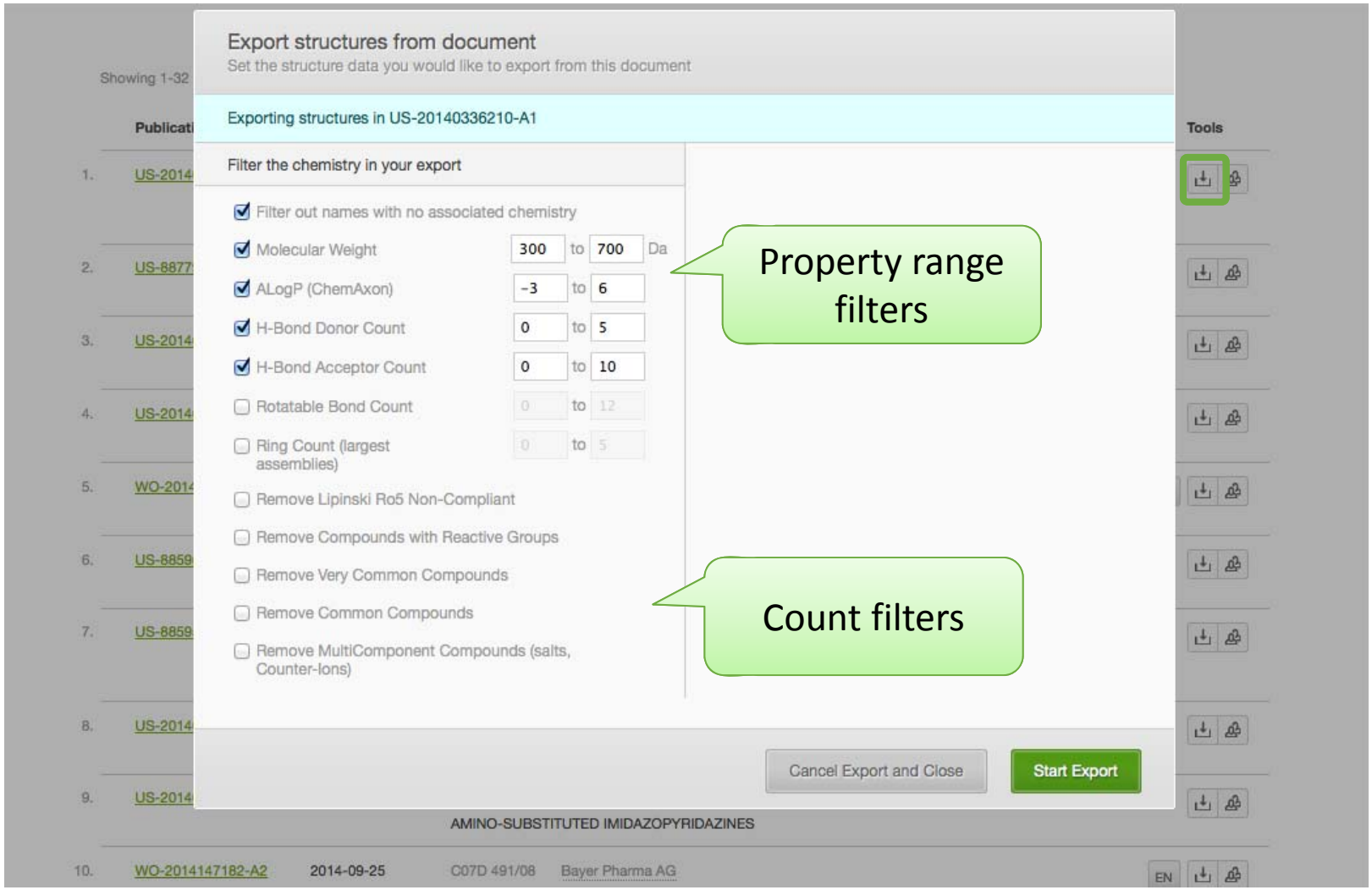
Patent family members



Showing 1-32 of 1,764 total document results

	Publication Number	Publication Date	IPCR	Assignee/Applicant	Tools
1.	US-20140336210-A1	2014-11-13	C07D 213/81	BAYER HEALTHCARE LLC	
			ARYL UREA COMPOUNDS IN COMBINATION WITH OTHER CYTOSTATIC OR CYTOTOXIC AGENTS FOR TREATING HUMAN CANCERS		
2.	US-8877933-B2	2014-11-04	A61K 31/44	GRUNENBERG ALFONS	
			Thermodynamically stable form of a tosylate salt		
3.	US-20140315958-A1	2014-10-23	C07D 213/81	GRUENBERG ALFONS	
			4-[4-(AMINO)-3-FLUOROPHENOXY]-N-METHYLPYRIDINE-2-CARBOXAMIDE MONOHYDRATE		

Export patent chemistry



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Patent view - Front page

The Front-page

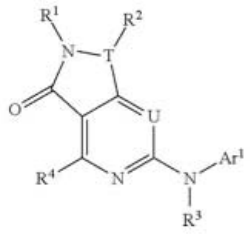
US-20140303178-A1 / 2014-10-09

EN DIHYDROPYRAZOLOPYRIMIDINONE DERIVATIVES

EN ABSTRACT

The invention relates to compounds of a general formula (I):

(I)



wherein Ar1 is an optionally-substituted aryl or heteroaromatic group; R1 is an optionally-s
alkyl group, or is an aryl, aralkyl or heteroaromatic group optionally having a substituent; R
lower alkynyl group, or is an aryl, aralkyl or heteroaromatic group optionally having a subst
hydrogen atom, a halogen atom, a hydroxyl group, a lower alkyl group or a group of —N(
The compounds of the invention have excellent Weel kinase-inhibitory effect and are theref
cancers.

PARTIES

Assignee(s)/Applicant(s)	Inventor(s)	Agent(s
MSD KK [JP]	Sagara, Takeshi [JP]	No Dat
MSD K.K. [JP]	Otsuki, Sachie [JP]	
	Sunami, Satoshi [JP]	
	Sakamoto, Toshihiro [JP]	
	Niiyama, Kenji [JP]	
	Yamamoto, Fuyuki [JP]	
	Yoshizumi, Takashi [JP]	
	Furuyama, Hidetomo [JP]	
	Goto, Yasuhiro [JP]	
	Bamba, Makoto [JP]	

Front-page | Claims | Description

Highlight additional recognised chemical terms

Export document chemistry

Export family chemistry

Download patent PDF

CLASSIFICATIONS

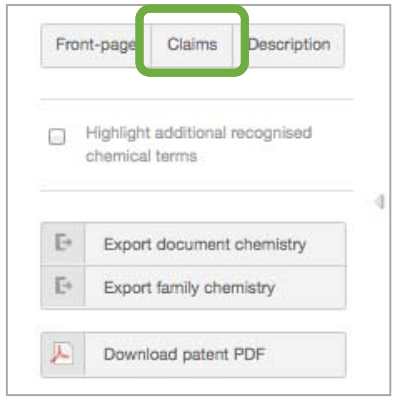
IPCR	CPC	ECLA
C07D 487/04	C07D 487/04	No Data.
IPC (1-7)	C07D 487/04	

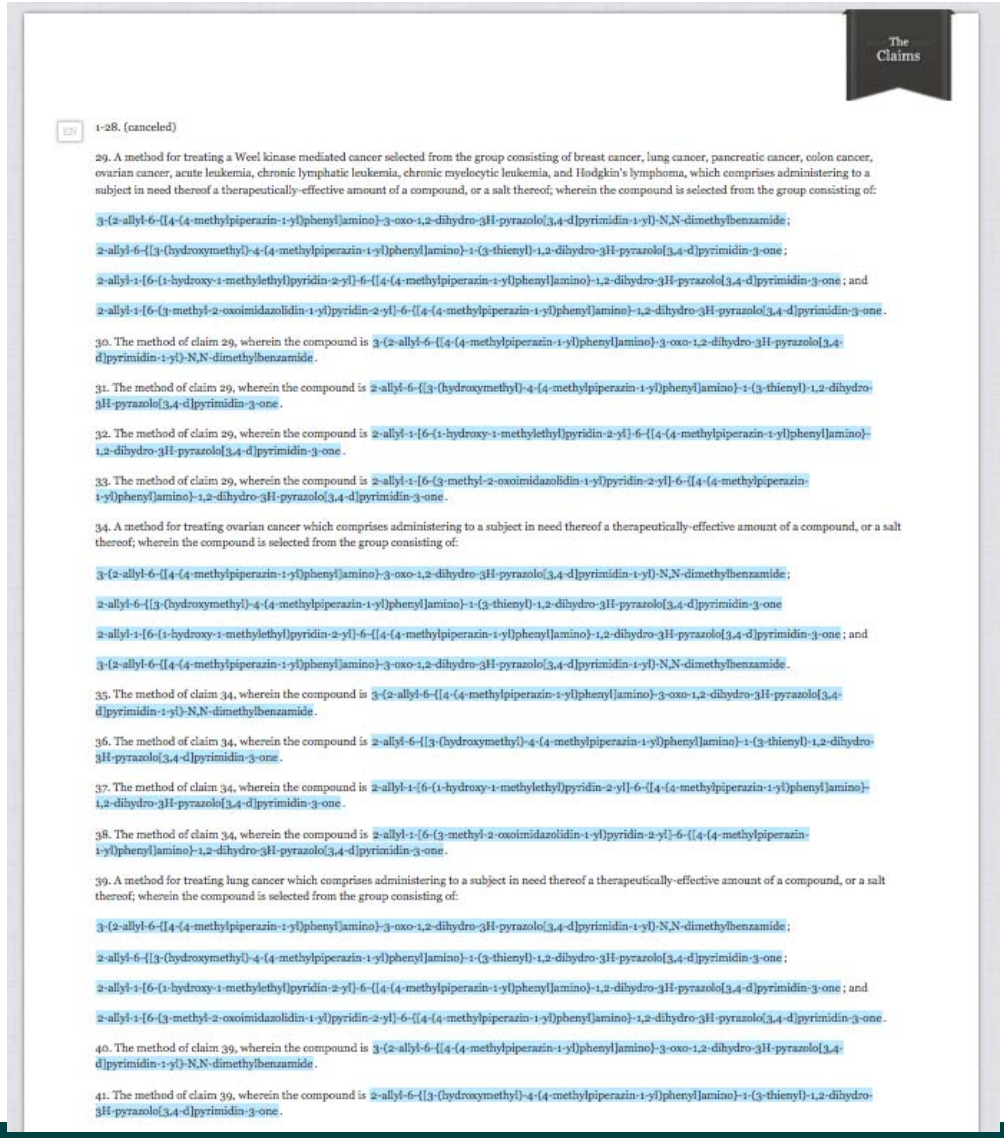
Application Number and Date	Priority Data	PCT Publication Number and Date
US-201414312982-A 20140624	US-201414312982-A 2014-06-24	No Data.
	US-201113053798-A 2011-03-22	
	US-22670708-A 2008-10-24	
	JP-2007059416-W 2007-04-25	
	JP-2006124208-A 2006-04-27	

Patent Family Members

US-20140303178-A1 US-20110189130-A1 US-8791125-B2 US-7935708-B2 US-20100063024-A1 EP-2016080-A4 EP-2016080-A1 EP-2017278-A1 EP-2016080-B1 EP-2017278-A4 WO-2007126128-A1 WO-2007126122-A1 JP-5167291-B2 JP-2010132689-A JP-4513919-B2 AR-060635-A1 AT-475662-T AU-2007244185-A1 AU-2007244185-B2 BR-PI0710081-A2 CA-2650119-A1 CN-101432284-A CN-101432284-B CR-10359-A DE-602007008085-D1 DK-2016080-T3 DO-P2007000084-A EC-SP088812-A ES-2348751-T3 GT-2008000211-A HK-1132498-A1 HN-2008001532-A HR-20100563-T1 HR-P20100563-T1 IL-194367-D0 KR-101409161-B1 KR-20080017491-A MA-30428-B1 MX-2008013063-A MY-145408-A NO-20084968-A NZ-571196-A PE-06952008-A1 PT-2016080-E RU-2008146759-A RU-2437885-C2 SI-2016080-T1 SV-2009003060-A TW-200811176-A TW-I409262-B UA-96152-C2 ZA-200807748-A

Patent view - Claims





The Claims

1-28. (canceled)

29. A method for treating a Weel kinase mediated cancer selected from the group consisting of breast cancer, lung cancer, pancreatic cancer, colon cancer, ovarian cancer, acute leukemia, chronic lymphatic leukemia, chronic myelocytic leukemia, and Hodgkin's lymphoma, which comprises administering to a subject in need thereof a therapeutically-effective amount of a compound, or a salt thereof, wherein the compound is selected from the group consisting of:

3-(2-allyl-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-3-oxo-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-1-yl)-N,N-dimethylbenzamide;

2-allyl-6-{[3-(hydroxymethyl)-4-(4-methylpiperazin-1-yl)phenyl]amino}-1-(3-thienyl)-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one;

2-allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one; and

2-allyl-1-[6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one.

30. The method of claim 29, wherein the compound is 3-(2-allyl-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-3-oxo-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-1-yl)-N,N-dimethylbenzamide.

31. The method of claim 29, wherein the compound is 2-allyl-6-{[3-(hydroxymethyl)-4-(4-methylpiperazin-1-yl)phenyl]amino}-1-(3-thienyl)-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one.

32. The method of claim 29, wherein the compound is 2-allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one.

33. The method of claim 29, wherein the compound is 2-allyl-1-[6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one.

34. A method for treating ovarian cancer which comprises administering to a subject in need thereof a therapeutically-effective amount of a compound, or a salt thereof, wherein the compound is selected from the group consisting of:

3-(2-allyl-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-3-oxo-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-1-yl)-N,N-dimethylbenzamide;

2-allyl-6-{[3-(hydroxymethyl)-4-(4-methylpiperazin-1-yl)phenyl]amino}-1-(3-thienyl)-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one

2-allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one; and

3-(2-allyl-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-3-oxo-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-1-yl)-N,N-dimethylbenzamide.

35. The method of claim 34, wherein the compound is 3-(2-allyl-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-3-oxo-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-1-yl)-N,N-dimethylbenzamide.

36. The method of claim 34, wherein the compound is 2-allyl-6-{[3-(hydroxymethyl)-4-(4-methylpiperazin-1-yl)phenyl]amino}-1-(3-thienyl)-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one.

37. The method of claim 34, wherein the compound is 2-allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one.

38. The method of claim 34, wherein the compound is 2-allyl-1-[6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one.

39. A method for treating lung cancer which comprises administering to a subject in need thereof a therapeutically-effective amount of a compound, or a salt thereof, wherein the compound is selected from the group consisting of:

3-(2-allyl-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-3-oxo-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-1-yl)-N,N-dimethylbenzamide;

2-allyl-6-{[3-(hydroxymethyl)-4-(4-methylpiperazin-1-yl)phenyl]amino}-1-(3-thienyl)-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one;

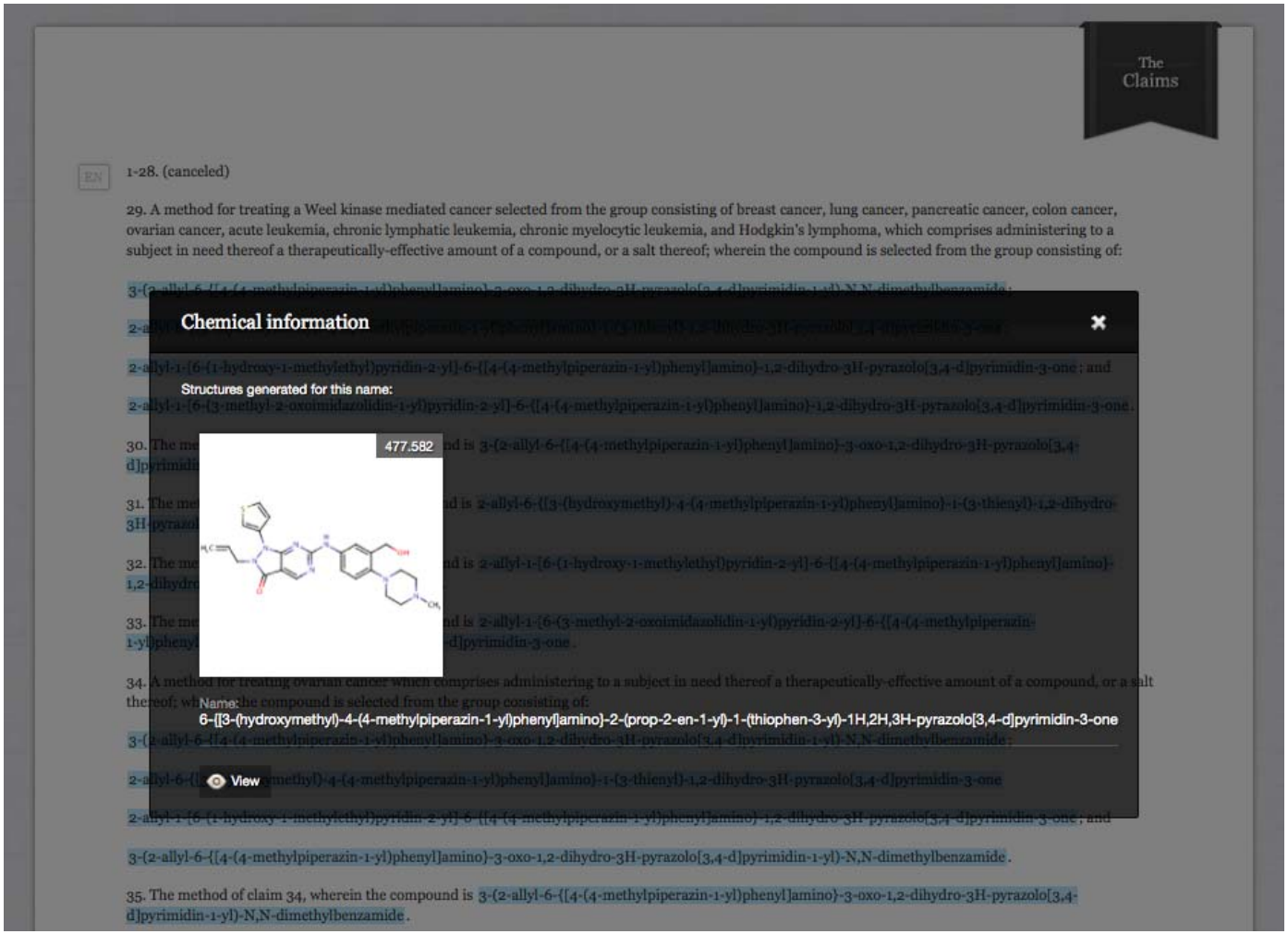
2-allyl-1-[6-(1-hydroxy-1-methylethyl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one; and

2-allyl-1-[6-(3-methyl-2-oxoimidazolidin-1-yl)pyridin-2-yl]-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one.

40. The method of claim 39, wherein the compound is 3-(2-allyl-6-{[4-(4-methylpiperazin-1-yl)phenyl]amino}-3-oxo-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-1-yl)-N,N-dimethylbenzamide.

41. The method of claim 39, wherein the compound is 2-allyl-6-{[3-(hydroxymethyl)-4-(4-methylpiperazin-1-yl)phenyl]amino}-1-(3-thienyl)-1,2-dihydro-3H-pyrazolo[3,4-d]pyrimidin-3-one.

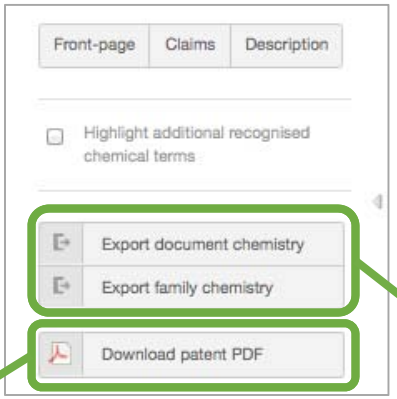
Chemical entities in patent



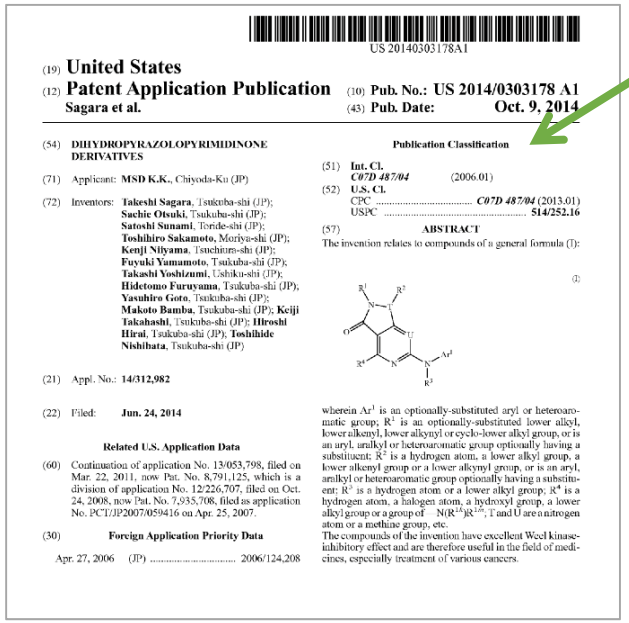
Click on blue highlighted text to see chemical info box

Patent view - Tools

Access to source document PDF



Export chemistry for document or family



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Sagara et al.

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(43) **Pub. Date: Oct. 9, 2014**

(54) **DIHYDROPYRAZOLOPYRIMIDINONE DERIVATIVES**

(71) Applicant: **MSD K.K.**, Chiyoda-Ku (JP)

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(21) Appl. No.: **14/312,982**

(22) Filed: **Jun. 24, 2014**

Related U.S. Application Data

(60) Continuation of application No. 13/053,798, filed on Mar. 22, 2011, now Pat. No. 8,791,125, which is a division of application No. 12/226,707, filed on Oct. 24, 2008, now Pat. No. 7,935,708, filed as application No. PCT/JP2007/059416 on Apr. 25, 2007.

(30) **Foreign Application Priority Data**

Apr. 27, 2006 (JP) 2006/124,208

Publication Classification

(51) **Int. Cl.**
C07D 487/04 (2006.01)

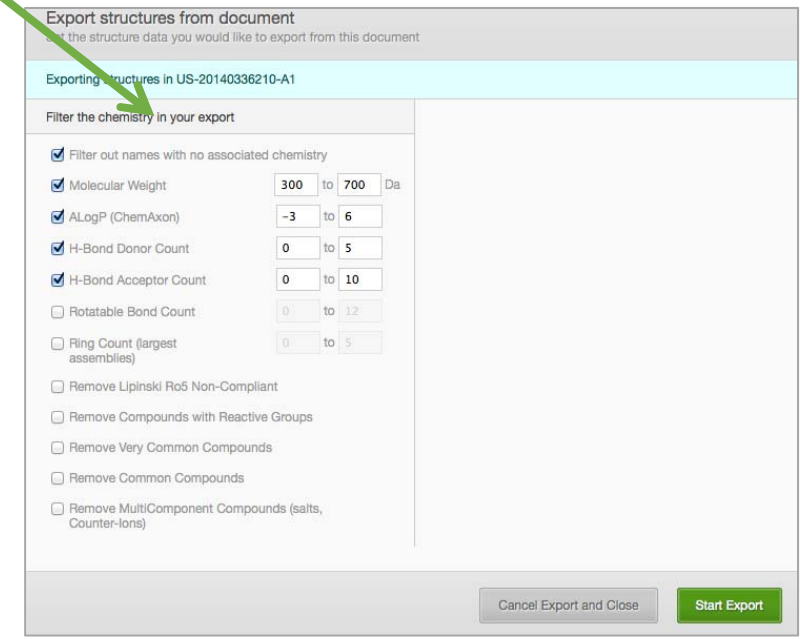
(52) **U.S. Cl.**
CPC ***C07D 487/04*** (2013.01)
USPC **514/252.16**

(57) **ABSTRACT**

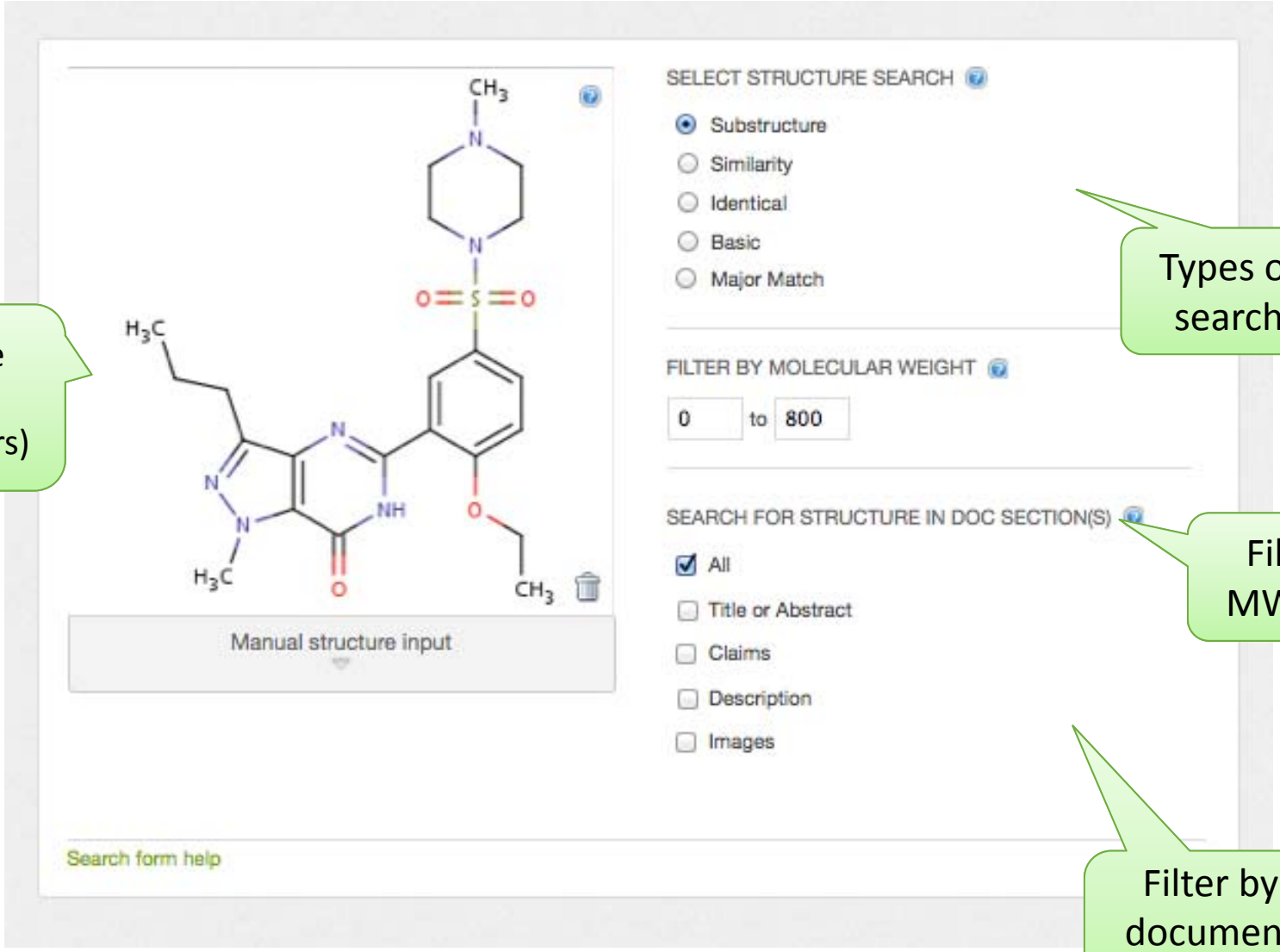
The invention relates to compounds of a general formula (I):

wherein Ar^1 is an optionally-substituted aryl or heteroaromatic group; R^1 is an optionally-substituted lower alkyl, lower alkenyl, lower alkynyl or cyclo-lower alkyl group, or is an aryl, arylkyl or heteroaromatic group optionally having a substituent; R^2 is a hydrogen atom, a lower alkyl group, a lower alkenyl group or a lower alkynyl group, or is an aryl, arylkyl or heteroaromatic group optionally having a substituent; R^3 is a hydrogen atom or a lower alkyl group; R^4 is a hydrogen atom, a halogen atom, a hydroxyl group, a lower alkyl group or a group of $-N(R^{2A})R^{2B}$; T and U are a nitrogen atom or a methine group, etc.

The compounds of the invention have excellent Wee1 kinase-inhibitory effect and are therefore useful in the field of medicines, especially treatment of various cancers.



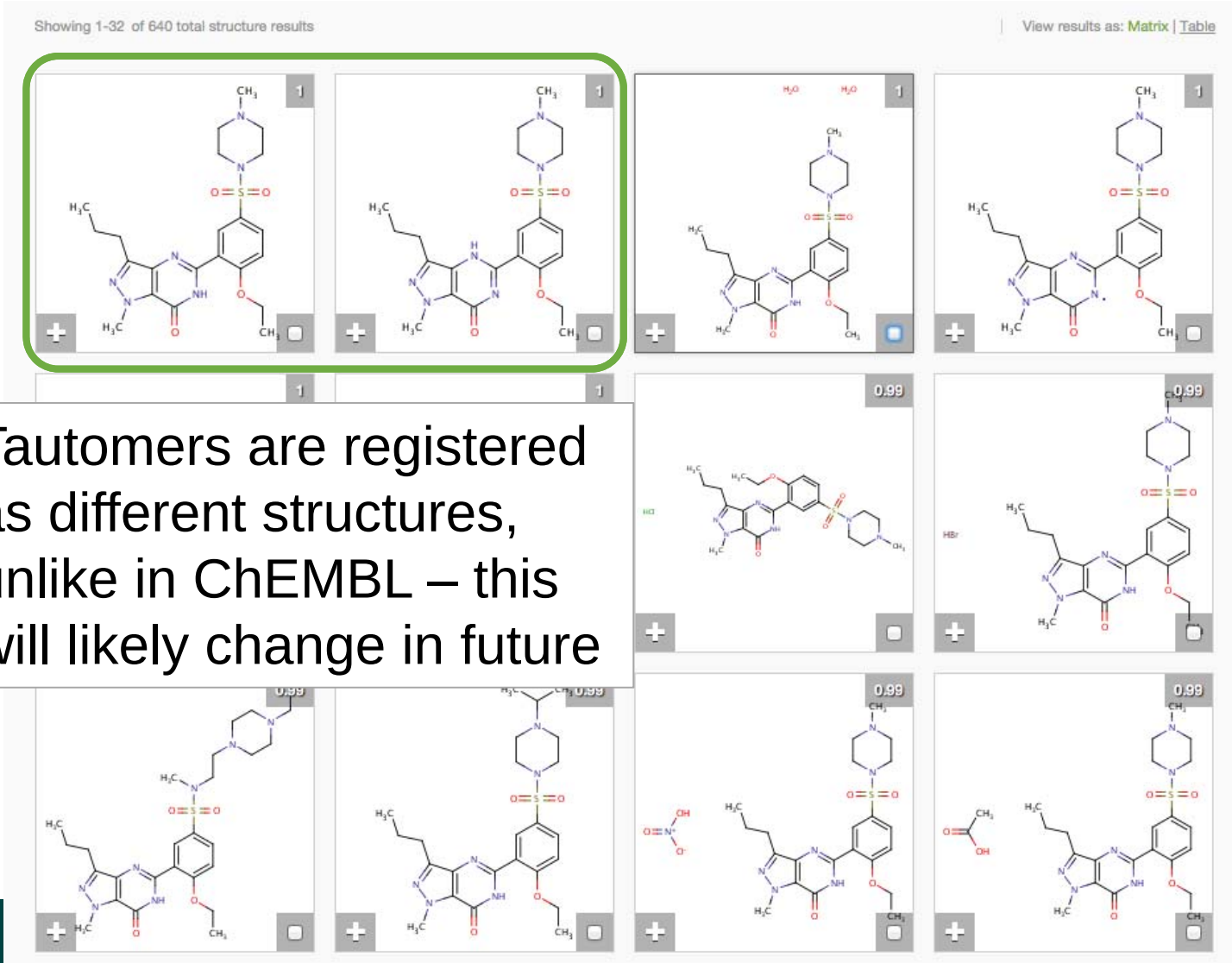
Chemistry-based searching



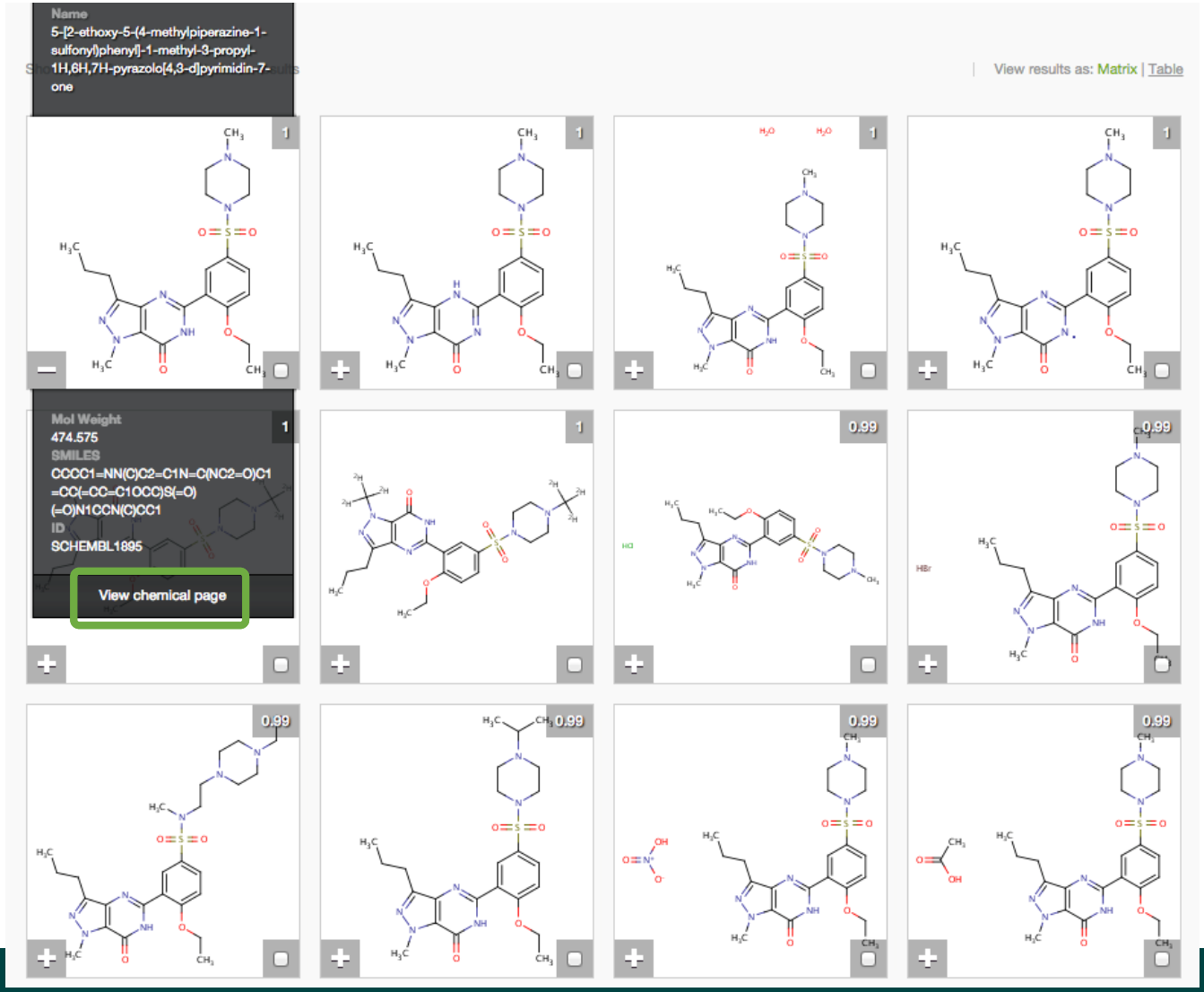
Structure search type differences

Search Type	Search Feature							
	Similarity	Tests if the target contains query	Tests if the query contains target	Full fragment coverage	Exact topology matching	Exact stereo matching	Exact atom features matching	Exact bond matching
SUBSTRUCTURE	n/a	✓	✗	✗	✗	✗	✗	✗
MAJOR MATCH	n/a	n/a	✓	✗	✓	✗	✗	✗
BASIC	n/a	✓	✓	✓	✓	✗	✗	✗
IDENTICAL	n/a	✓	✓	✓	✓	✓	✓	✓
SIMILARITY	✓	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Chemistry searches return structures



Review chemistry hits



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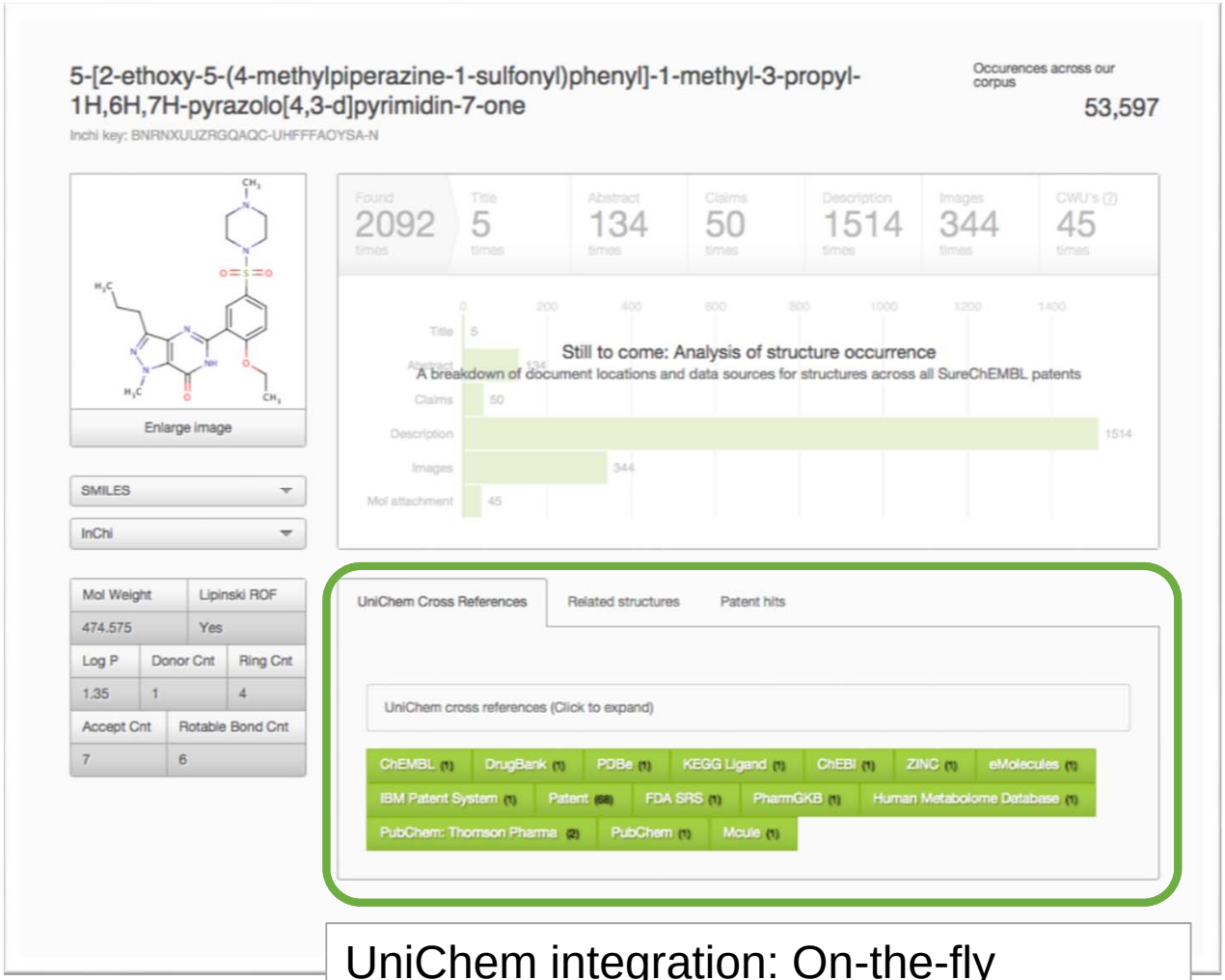
Compound report page



UniChem integration: On-the-fly integration with 71M structures and from 25 data sources

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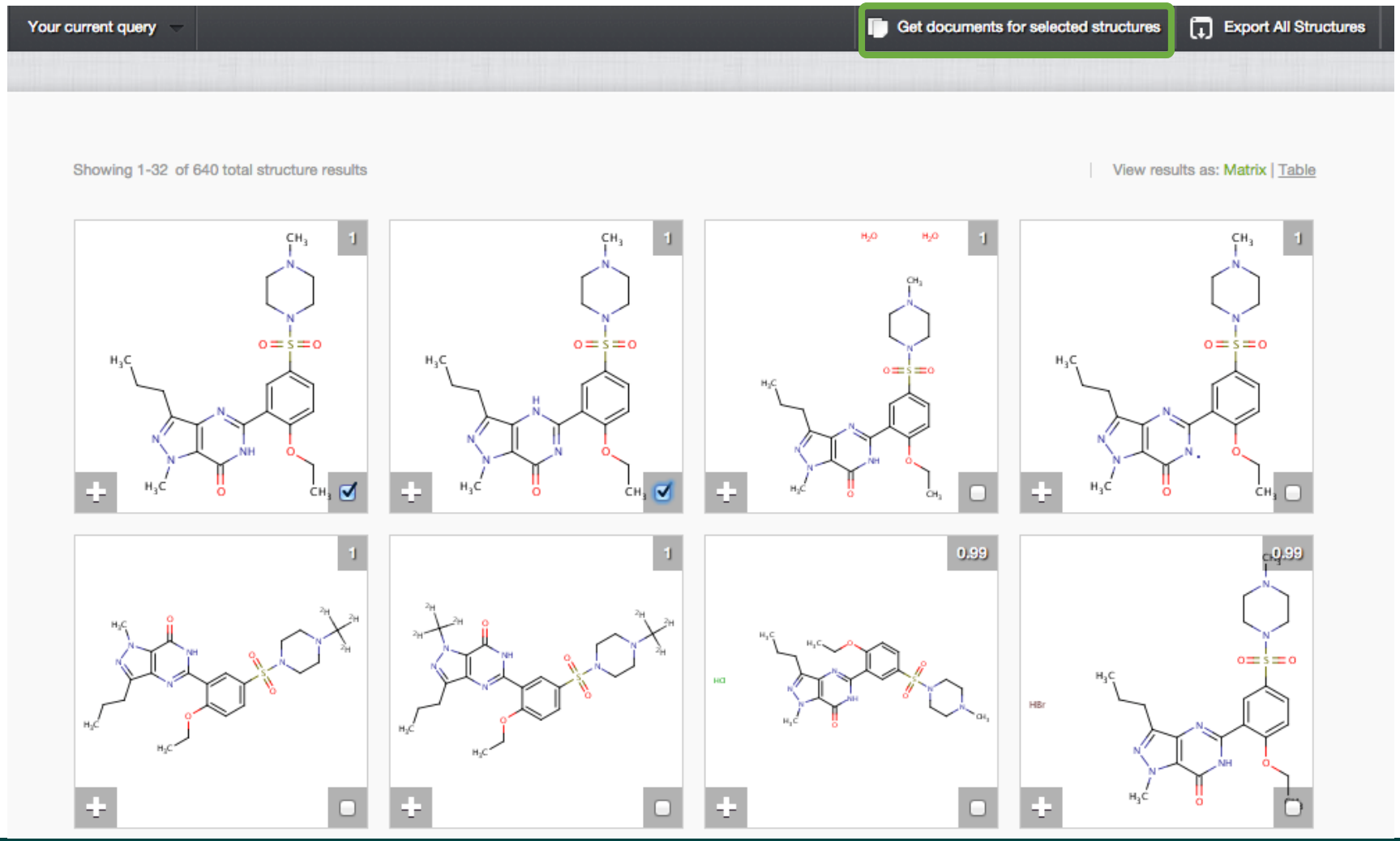
Review patent documents for chemistry



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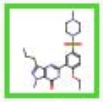
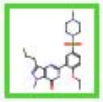
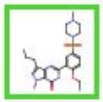
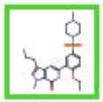
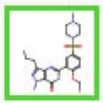
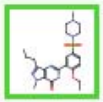
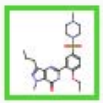
Review patent documents for chemistry

Showing 1-32 of 12,704 total documents for structures results

	Publication Number	Publication Date	IPCR	Assignee/Applicant	Structure hits	Tools
1.	EP-2780018-A1	2014-09-24	A61K 31/568	Bhasin, Shalender COMBINATION OF TESTOSTERONE AND ORNITHINE DECARBOXYLASE (ODC) INHIBITORS	EN 	
2.	EP-2779997-A1	2014-09-24	A61K 9/107	Mylan Inc. LIQUID-FILLED HARD GEL CAPSULE PHARMACEUTICAL FORMULATIONS	EN 	
3.	EP-2781217-A1	2014-09-24	A61K 31/575	ETH Zurich ROR gamma modulators	EN 	
4.	EP-2781513-A1	2014-09-24	C07D 307/79	Takeda Pharmaceutical Company Limited Benzofuran derivatives	EN 	
5.	EP-2780467-A2	2014-09-24	C12Q 1/68	The General Hospital Corporation ASSAYS AND METHODS FOR SELECTING A TREATMENT REGIMEN FOR A SUBJECT WITH DEPRESSION AND METHODS FOR TREATMENT	EN 	
6.	EP-2398483-B1	2014-09-24	A61K 38/00	Merck Sharp & Dohme Corp. OXYNTOMODULIN ANALOGS	EN 	
7.	EP-2352374-B1	2014-09-24	C07D 235/26	Merck Sharp & Dohme Corp. NOVEL CYCLIC BENZIMIDAZOLE DERIVATIVES USEFUL ANTI-DIABETIC AGENTS	EN 	

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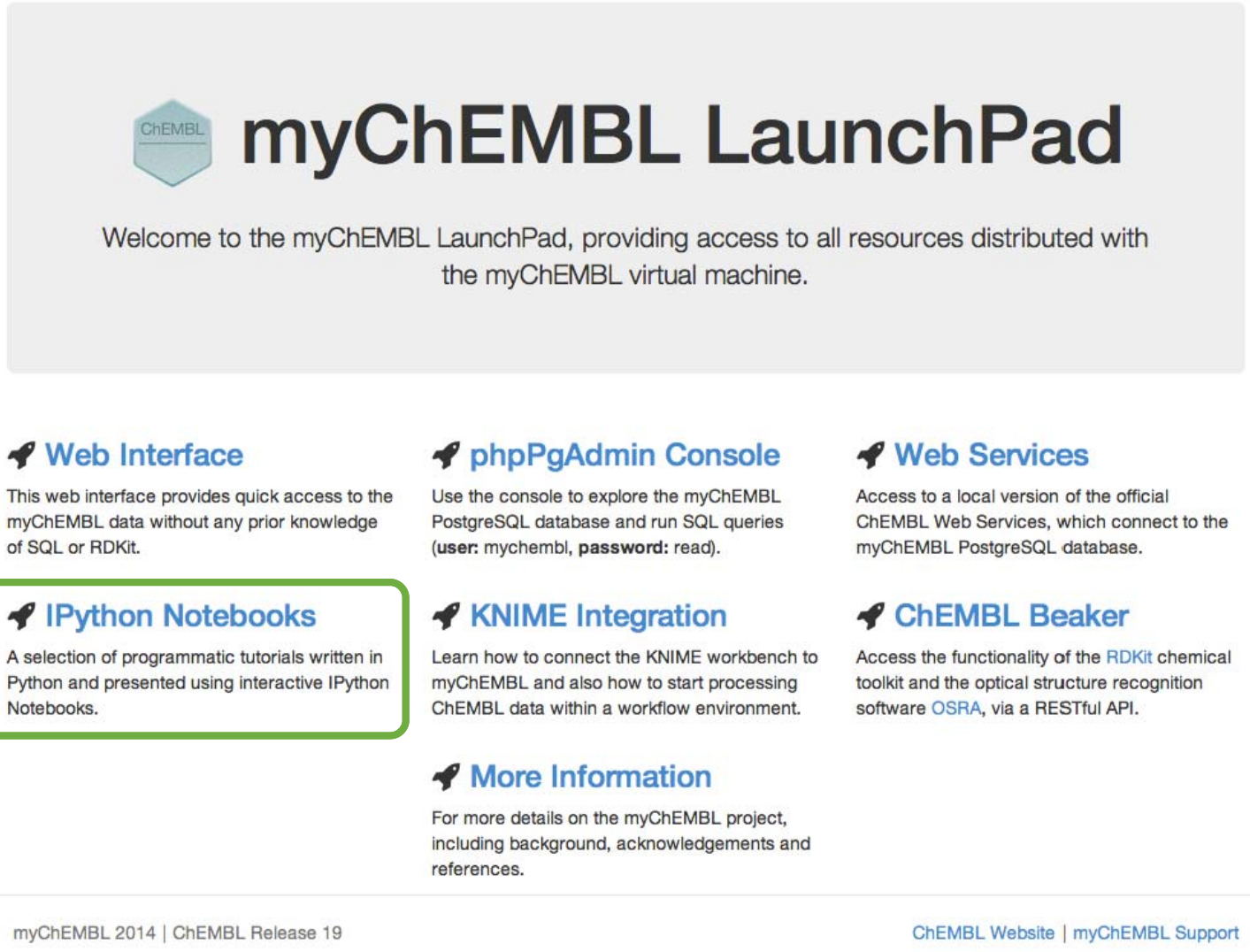
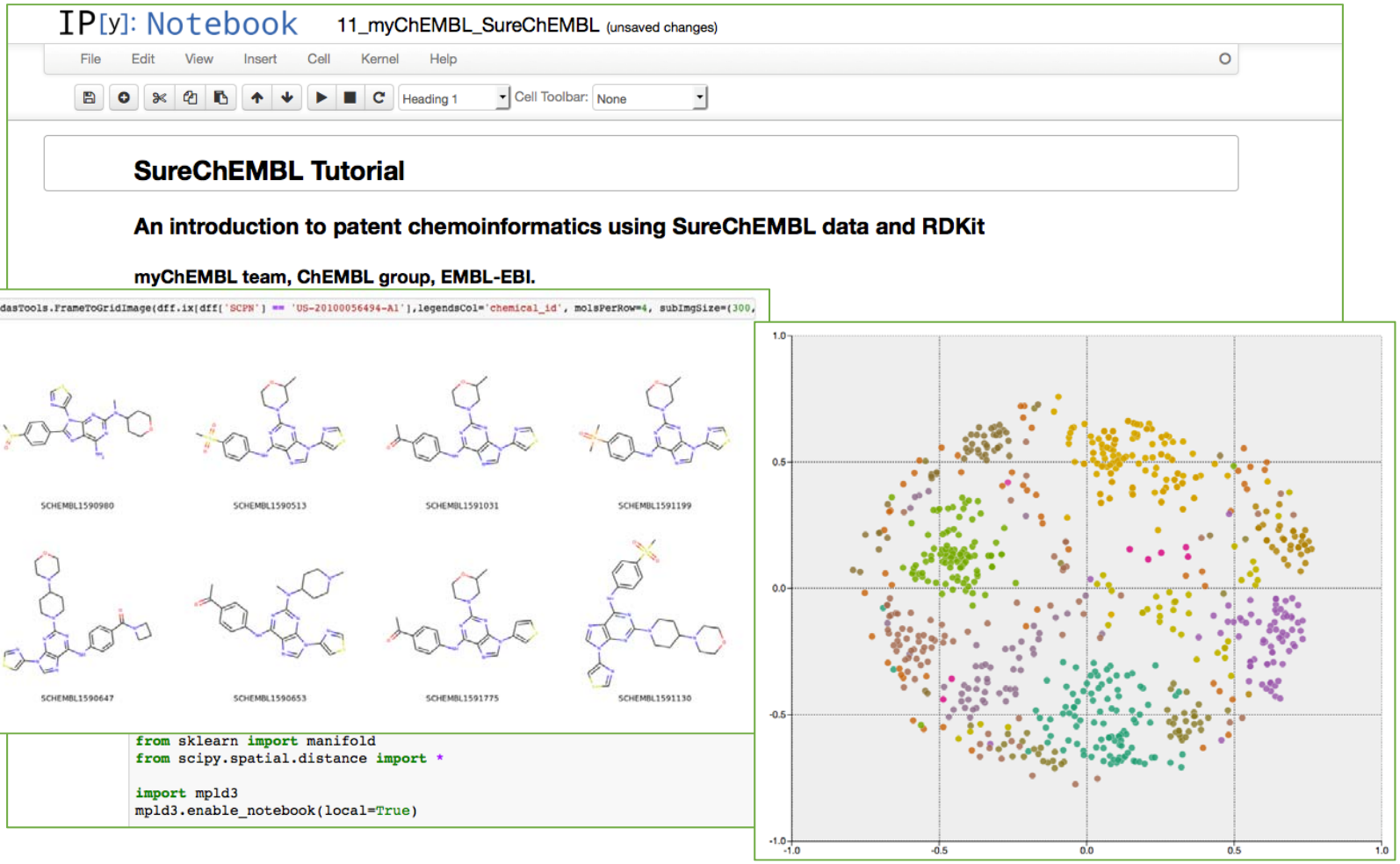
Example SureChEMBL Workflow

myChEMBL Example

myChEMBL LaunchPad



SureChEMBL and myChEMBL



More: http://chembl.blogspot.co.uk/2014/10/mychembl-19-released.html

Download: ftp://ftp.ebi.ac.uk/pub/databases/chembl/VM/myChEMBL/current/

SureChEMBL and myChEMBL

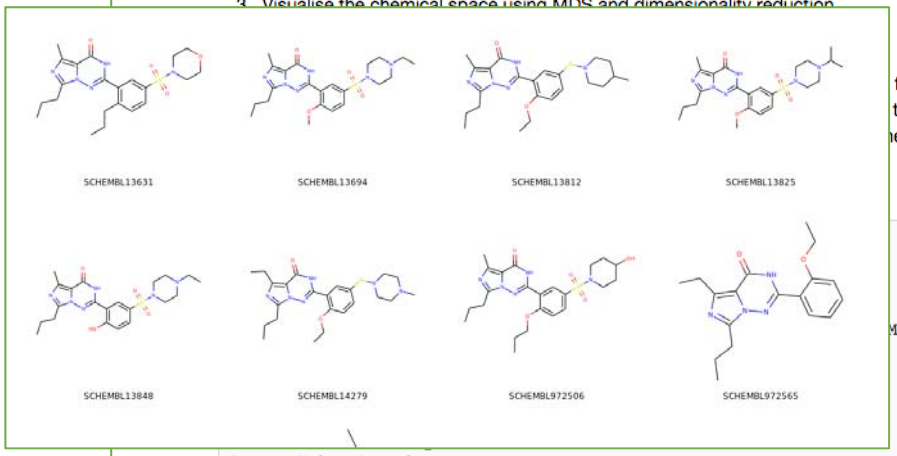
SureChEMBL iPython Notebook Tutorial

An introduction to patent chemoinformatics using SureChEMBL data and the RDKit toolkit

George Papadatos, ChEMBL group, EMBL-EBI

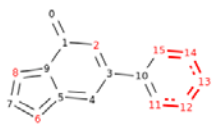
In this tutorial:

1. Read a file that contains all chemistry extracted from the Levitra US patent (US6566360) along with *all* the other members of the same patent family.
2. Filter by different text-mining and chemoinformatics properties to remove noise and enrich the genuinely novel structures claimed in the patent documents.
3. Visualise the chemical space using MDS and dimensionality reduction




```
from rdkit.Chem import MCS
```

```
In [147]: Draw.MolToImage(core,includeAtomNumbers=True,highlightAtoms=pind)
Out[147]:
```



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,0.,0.)  # draw dummy atoms
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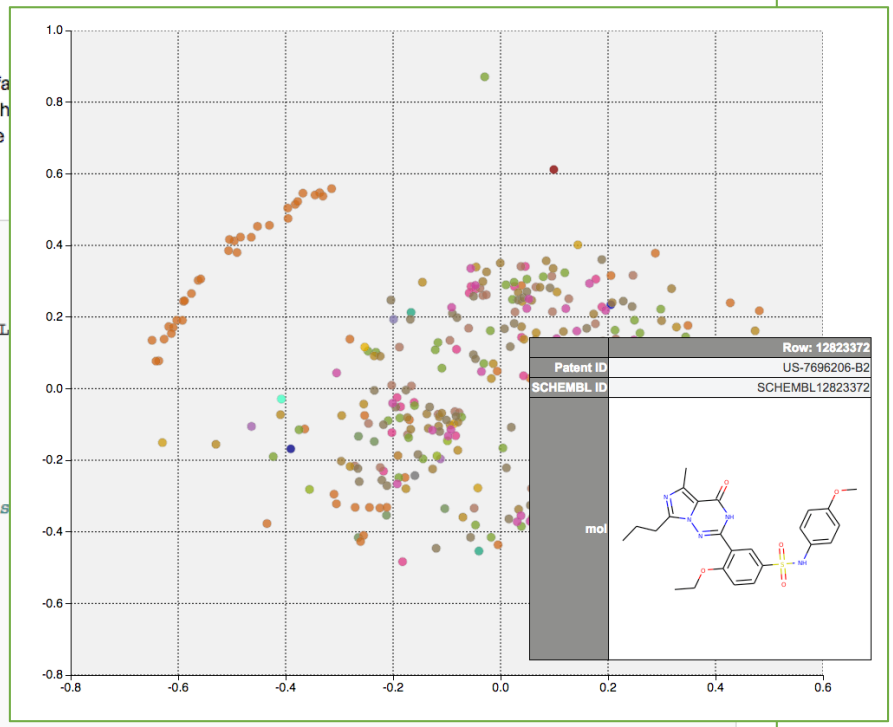


http://nbviewer.ipython.org/github/rdkit/UGM_2014/blob/master/Notebooks/Vardenafil.ipynb

Exercises

Exercises

1. What are the IPCR codes for Heterocyclic Compounds and Peptides?

1. How many patents are classified as containing
   - Heterocyclic compounds
   - Peptides
   - Heterocyclic compounds AND Peptides in 2013

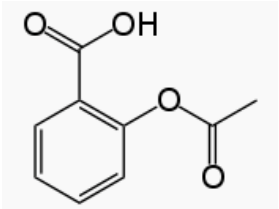
2. How many family members does the patent WO-2011058149-A1 have?

Exercises

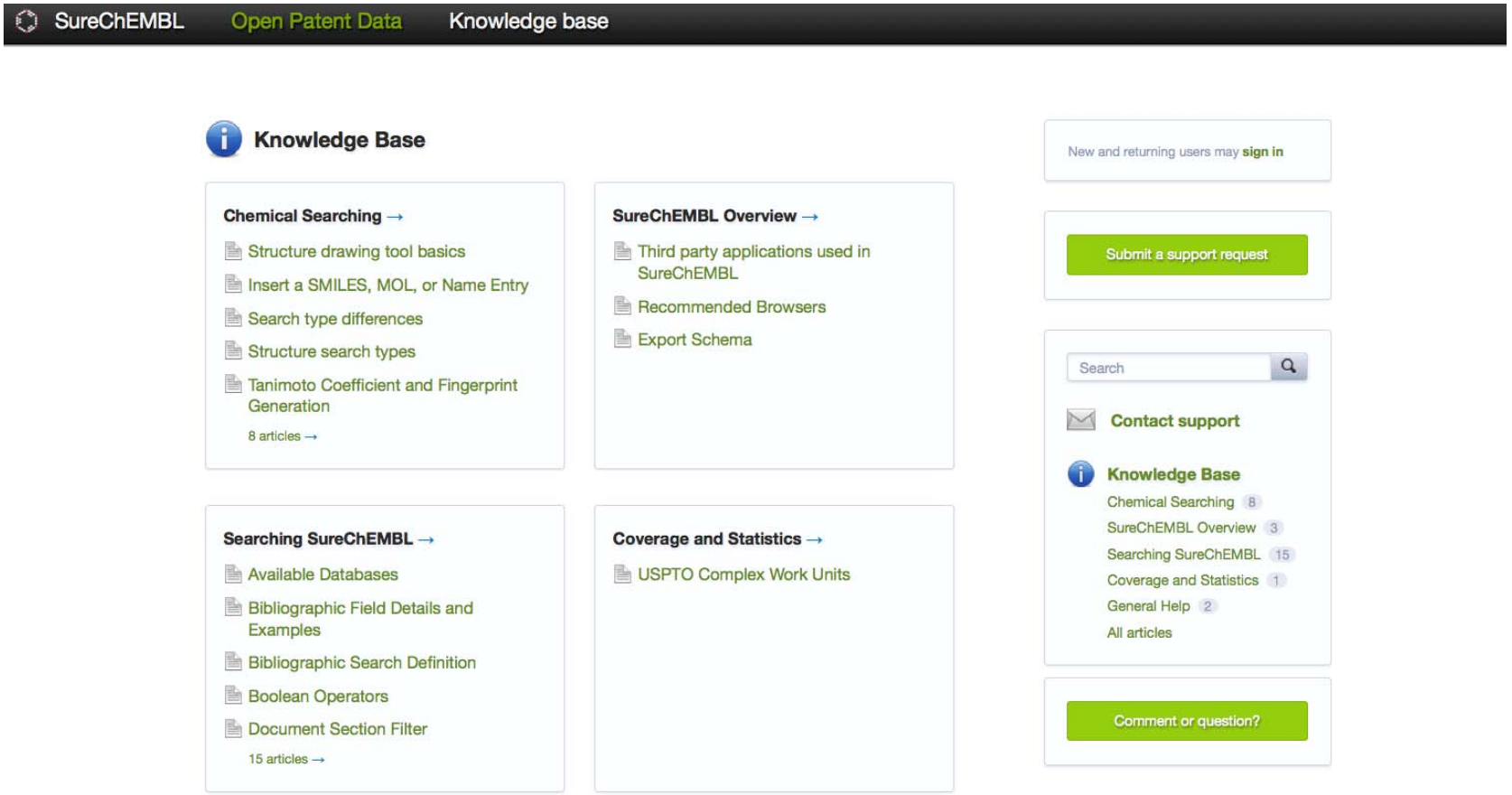
4. How many compounds have a structure similar (>90% Tanimoto) to the approved drug gefitinib?

4. How many patents contain the structure of gefitinib? And what is the priority number of the earliest patent?

5. Extract the chemistry from a recent patent family which makes reference to inflammation and also contains the following structure:



SureChEMBL knowledge base



https://surechembl.uservoice.com/

SureChEMBL support

surechembl-help@ebi.ac.uk

Acknowledgements

- ChEMBL team
  - John Overington
  - Jon Chambers
  - George Papadatos
  - Mark Davies
  - Nathan Dedman
  - Anna Gaulton
- Digital Science
  - Nicko Goncharoff
  - James Siddle
  - Richard Koks
- Open PHACTS consortium
  - http://www.openphacts.org/partners/consortium

Funding:

Innovative Medicines Initiative Joint Undertaking, grant agreement no. 115191 (Open PHACTS)

Wellcome Trust Strategic Award for Chemogenomics, WT086151/Z/08/Z

European Molecular Biology Laboratory

European Commission FP7 Capacities Specific Programme, grant agreement no. 284209 (BioMedBridges)

Software:

Answers

1. Go to http://web2.wipo.int/ipcpub website and search for terms (note searching is a bit tricky):
   - Heterocyclic compounds = C07D
   - Peptides = C07K

2. Go to SureChEMBL (https://www.surechembl.org) site and carry out the following searches:
   - ic:C07D *(returned 848,603 hits 21/11/14)*
   - ic:C07K *(returned 496,289 hits 21/11/14)*
   - ic:(C07K AND C07D) AND pdyear:2013 *(returned 424 hits 21/11/14)*

Answers

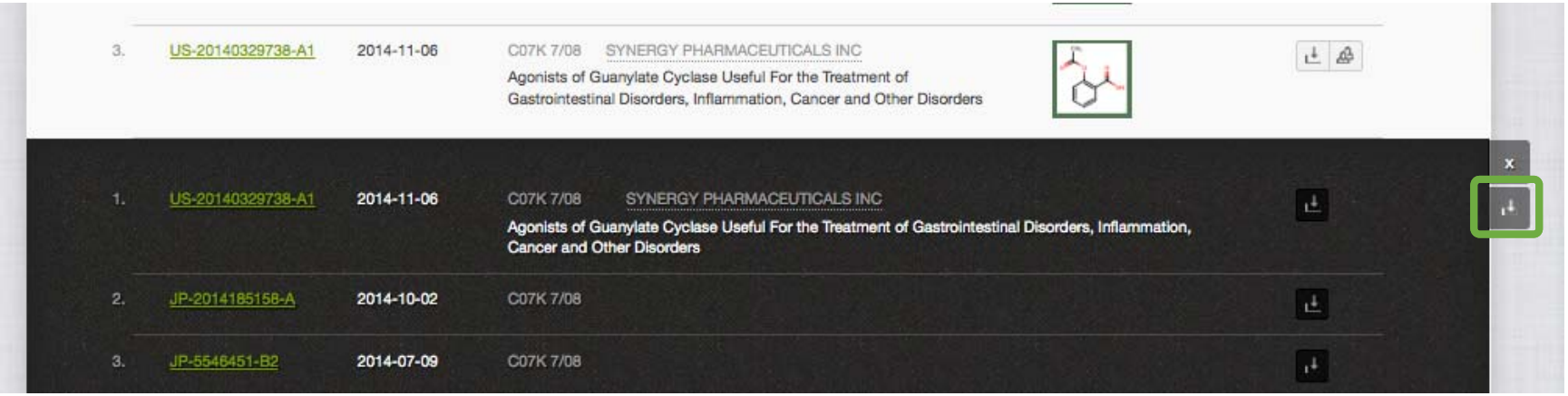
3. Carry out patent number search for WO-2011058149-A1 and click on family icon on results table
   - 12 family members

4. Type the term ‘gefitinib’ into Manual structure input, check the Similarity search radio button and set the Tanimoto coefficient to 90%
   - 50 structures are returned

5. Identical search for gefitinib, click on compound to retrieve patents, go to last page (*sorry no sort function at present*)
   - WO-1996033980-A1
   - GB-9508538-A 1995-04-27

Answers

6. Conduct a keyword search for ttl:inflammation and draw the structure of aspirin. Choose an appropriate search method and press search button. Select 1 or more compounds and view patent results. To download chemistry press the “Export chemistry for this family” button:



(Make sure export settings are updated as aspirin molweight is 180)