Way2Drug Cheminformatics Platform for Drug Repurposing

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What is drug repurposing (DRP)?

"The process of finding new uses outside the scope of the original medical indication for existing drugs is also known as redirecting, repurposing, repositioning and reprofiling."

Ashburn, T.T. and Thor, K.B. Drug repositioning: identifying and developing new uses for existing drugs. *Nat. Rev. Drug Dis*cov. **200**4, 3, 673–683.

THE 6TH ANNUAL

Drug Repositioning, Repurposing and Rescue Conference

Arrowhead PUBLISHERS | CONFERENCES

Global Health Focus: Repurposing for Rare Diseases and Orphan Drug Development

June 27-28, 2017 | Chicago, IL

REGISTER

Featured Speakers

Ron Alfa, MD, Ph.D., Vice President, Discovery and Product, **Recursion Pharmaceuticals**

Bobbie Ann Austin, Ph.D., Program Officer, Drug Development Partnership Programs, NCATS, Office of the Director, **National Institutes of Health**

Xavier Paoli, CCO and VP of R&D Operations, **PharNext SA**

About the Conference

Join us in Chicago, where we will highlight the latest developments in the fields of drug repositioning, repurposing and rescue. This conference continues to serve as a global meeting place for those engaged in efforts to further drug development through new means of collaborations, including patient advocacy efforts and industry/academic /government cooperation.

A central focus at this year's event will be **the use of repurposing to find and develop new therapies for rare diseases**. Many rare diseases and disorders are serious conditions with no approved treatments. There is thus significant unmet needs for patients. The pharmaceutical industry has become engaged in a greater effort to develop drugs for these "orphan" indications. The FDA has supported this effort via various special protocols as well. There is a growing amount of evidence which suggests repurposing or repositioning research can greatly aid in the development of drugs for rare diseases. By using a more systematic approach, existing compounds are being tested for both common and neglected diseases faster and with more success.

Key Themes at This Year's Conference

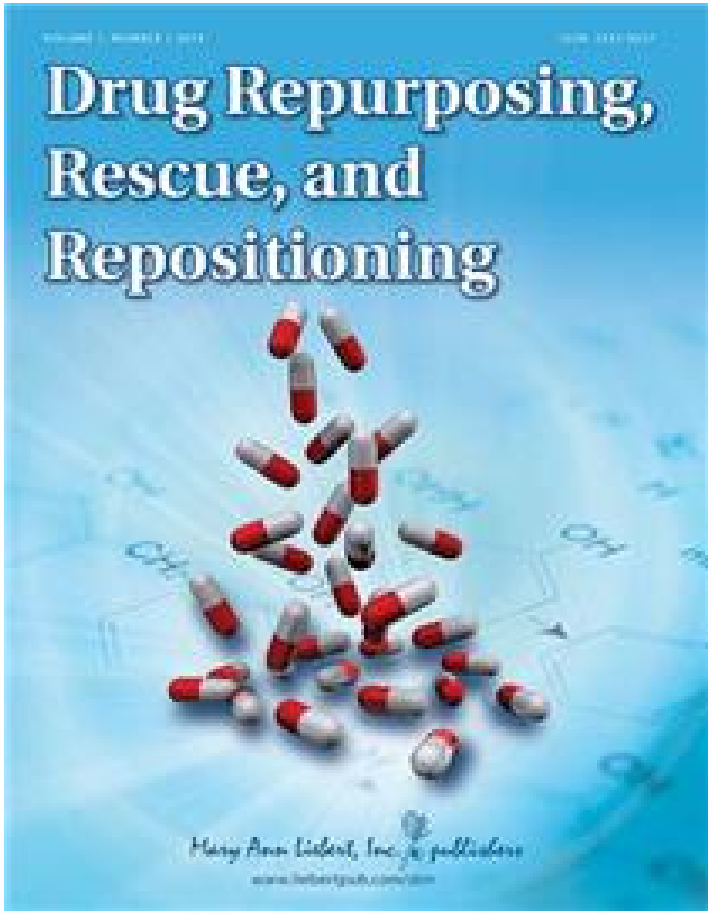
PATIENT ADVOCACY EFFORTS

Emphasis on and engagement with patient advocacy groups, who are investing in drug repositioning efforts to an unprecedented degree

NEW PARTNERSHIPS

The conference will explore how new partnerships between various groups, including government, industry and academia are teaming up to advance repurposing efforts

http://www.drugrepositioningconference.com/index/



A New Journal for the Drug Repurposing Community

Hermann A.M. Mucke, PhD

European Editor, Drug Repurposing, Rescue, and Repositioning.
H.M. Pharma Consultancy, Wien, Austria.

Dear reader:

What you are holding in your hand—or what you are looking at on your screen—is the premier issue of the first journal that is exclusively dedicated to new medical uses of known pharmaceutically active compounds: *Drug Repurposing, Rescue, and Repositioning.*

So, another peer-reviewed journal for the medical sciences. Why should this be necessary? Hundreds exist already.

INTERDISCIPLINARY BROADNESS DEMANDS HIGH-LEVEL INTEGRATION

To be sure, it is not as if there were no proper opportunities to publish quality articles addressing drug repurposing. Pertinent articles appear in life sciences journals that specialize in medicinal chemistry, systems biology, molecular modeling, has been missing until now. The product you are looking at is the first coordinated and well-supported attempt to remedy this.

OPTIMAL RESOURCE UTILIZATION IS NOT RECYCLING

Several common myths need to be dispelled before experts from so many diverse fields can collaborate with maximum efficacy. Number one is that drug repurposing, rescue, and repositioning is an inherently defensive concept, promoted by pharmaceutical companies to recoup at least part of their investments in the development of their failed late-stage drug candidates, or in drugs that had to be removed from the market for safety reasons. While such things do happen, this is only the "*rescue*" part of the story—and probably the least significant one in economic terms.

Nor is the *repositioning* of marketed drugs something as simple as what business developers call a line extension—such as expanding the approval of a cancer drug to include additional tumor types. Rather, drug repositioning implies the use in a different disease class, and while this often exploits

Drug Repurposing, Rescue, and Repositioning

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Astellas continues IT-enabled Drug Repurposing Deal Drive with Excelra hook-up

June 10th 2016, Posted By: Drug Repurposing Portal

Astellas Pharma has struck its third drug repurposing agreement of the past 6 months. The latest collaboration sees Astellas start working with Excelra, an Indian informatics company that has landed 8 similar deals on the strength of its drug repurposing database and accompanying algorithms. For Excelra, the deal with Astellas marks an advance in its attempts to establish itself as a standalone business.

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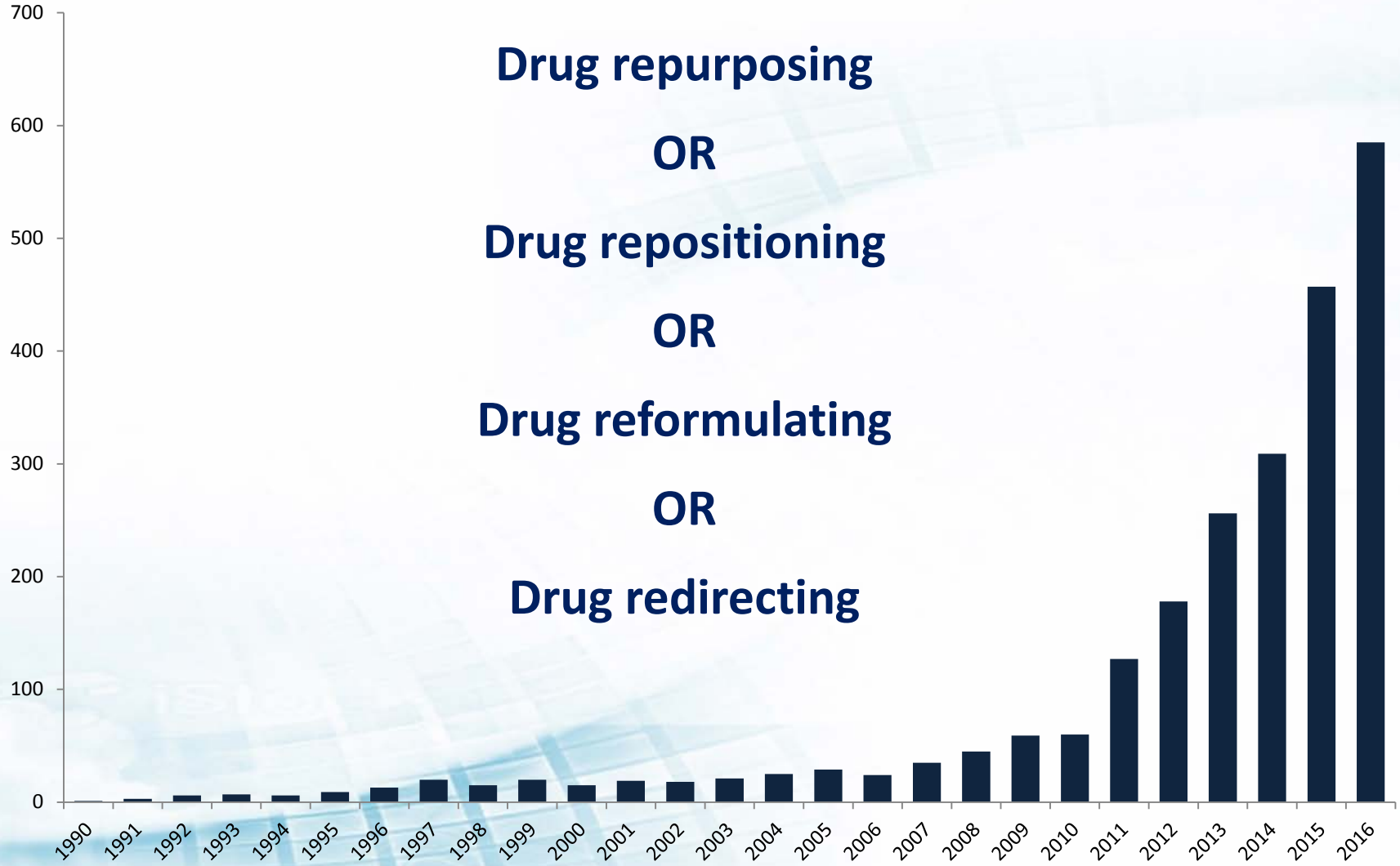
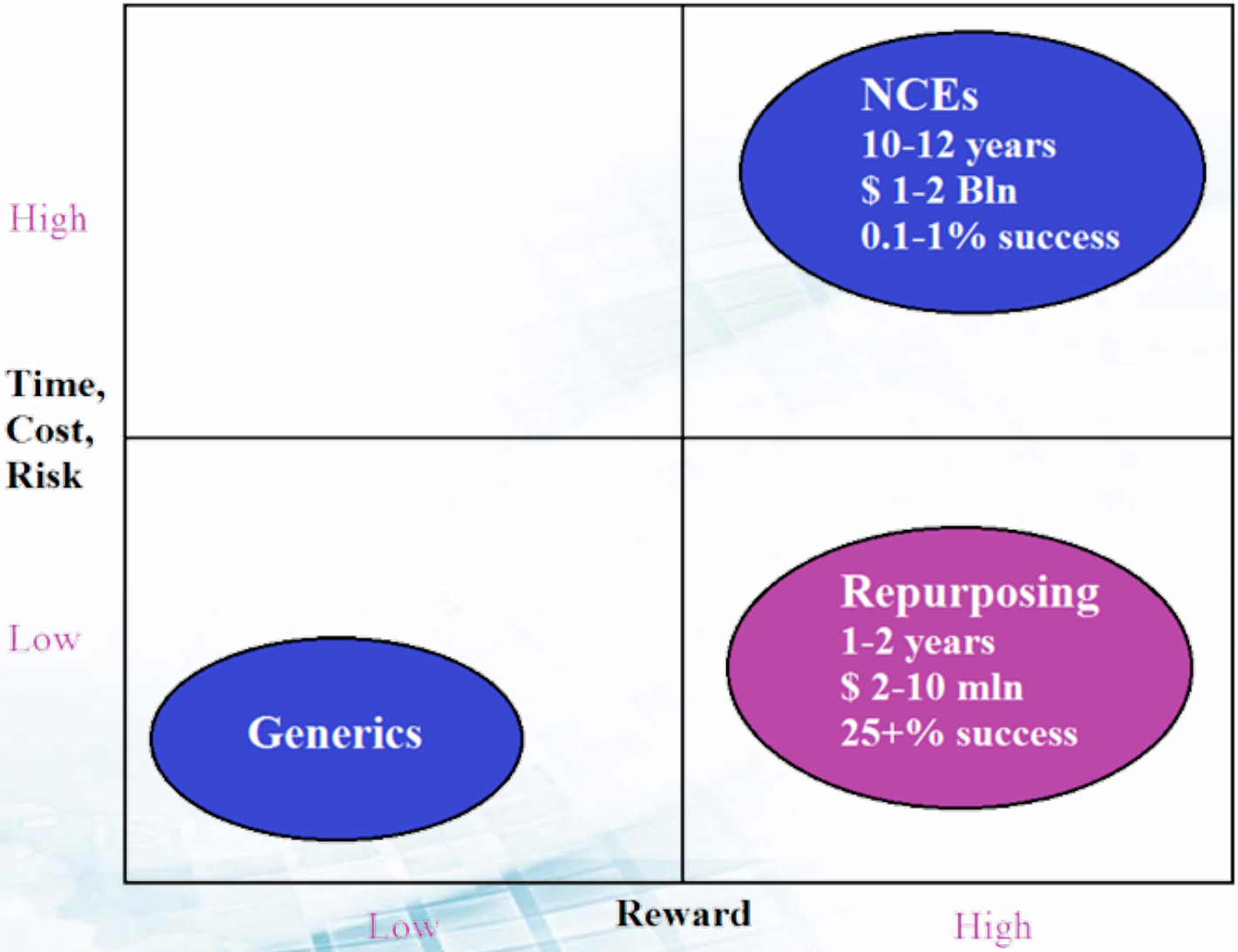
Web of Science statistics on drug repurposing (01.07.2017)

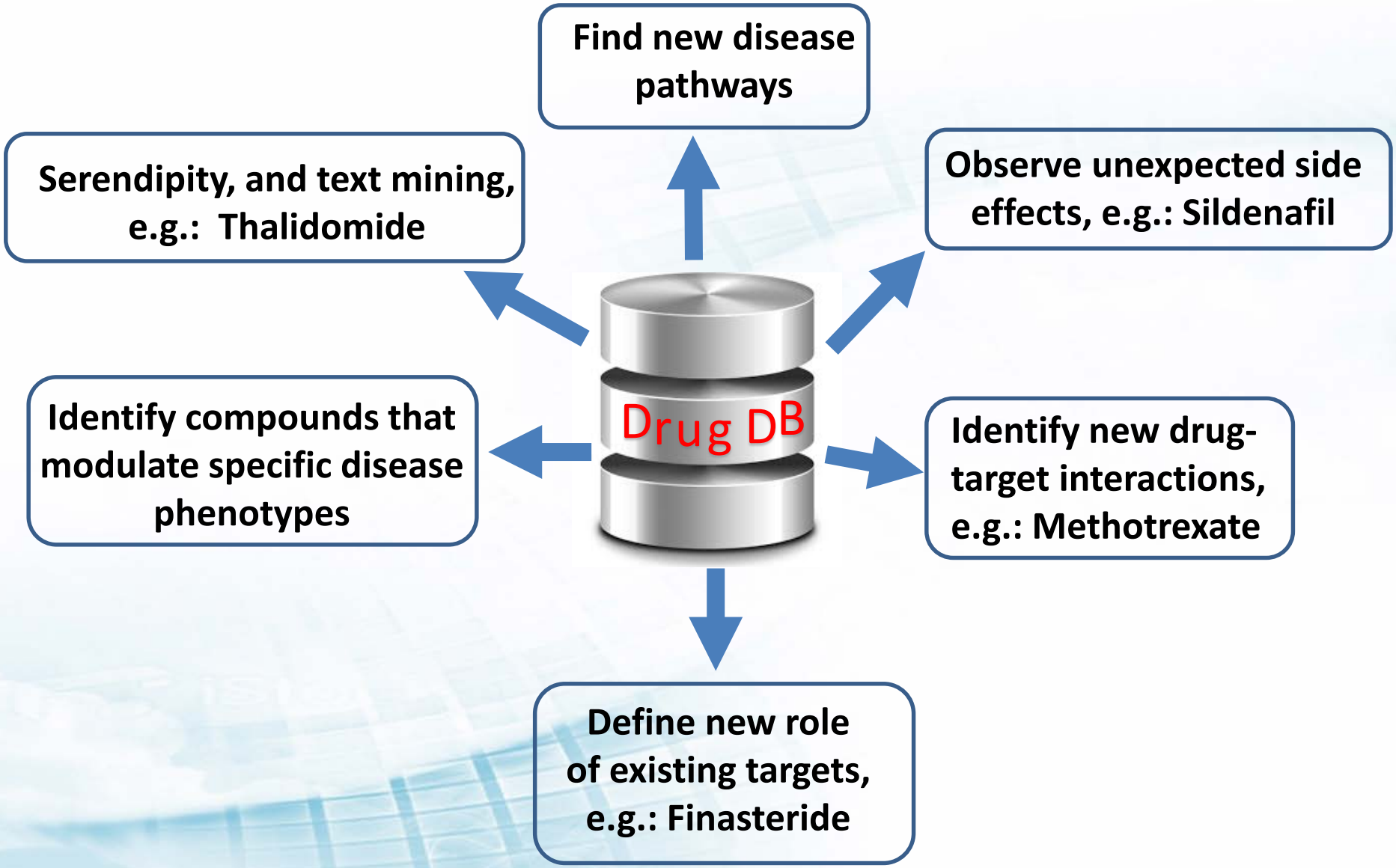


DRP: Time/Cost/Risk values



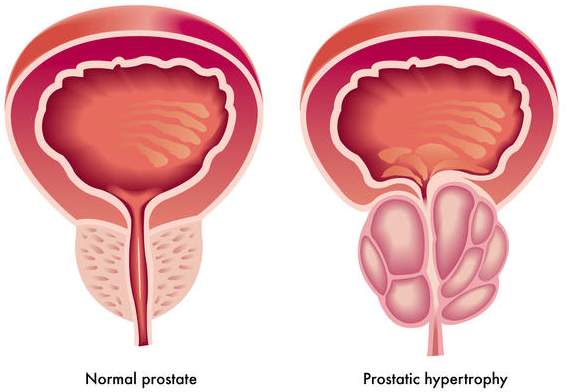
Ashburn T.T. and Thor K.B., 2004; Cavalla D., 2009.
Flower D.R., 2013; Naylor S. and Schonfeld J.M., 2014.

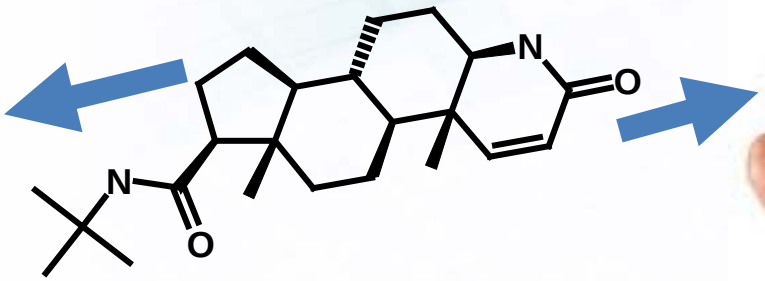
DRP: How it happens?



Define new role of existing targets: Finasteride

5-alpha-reductase inhibitor, Benign prostatic hyperplasia - 1992 (Proscar; Merck)





5-alpha-reductase inhibitor, Hair loss treatment - 1997 Propecia (with a fivefold lower dose), had worldwide sales of US $239 million in 2003

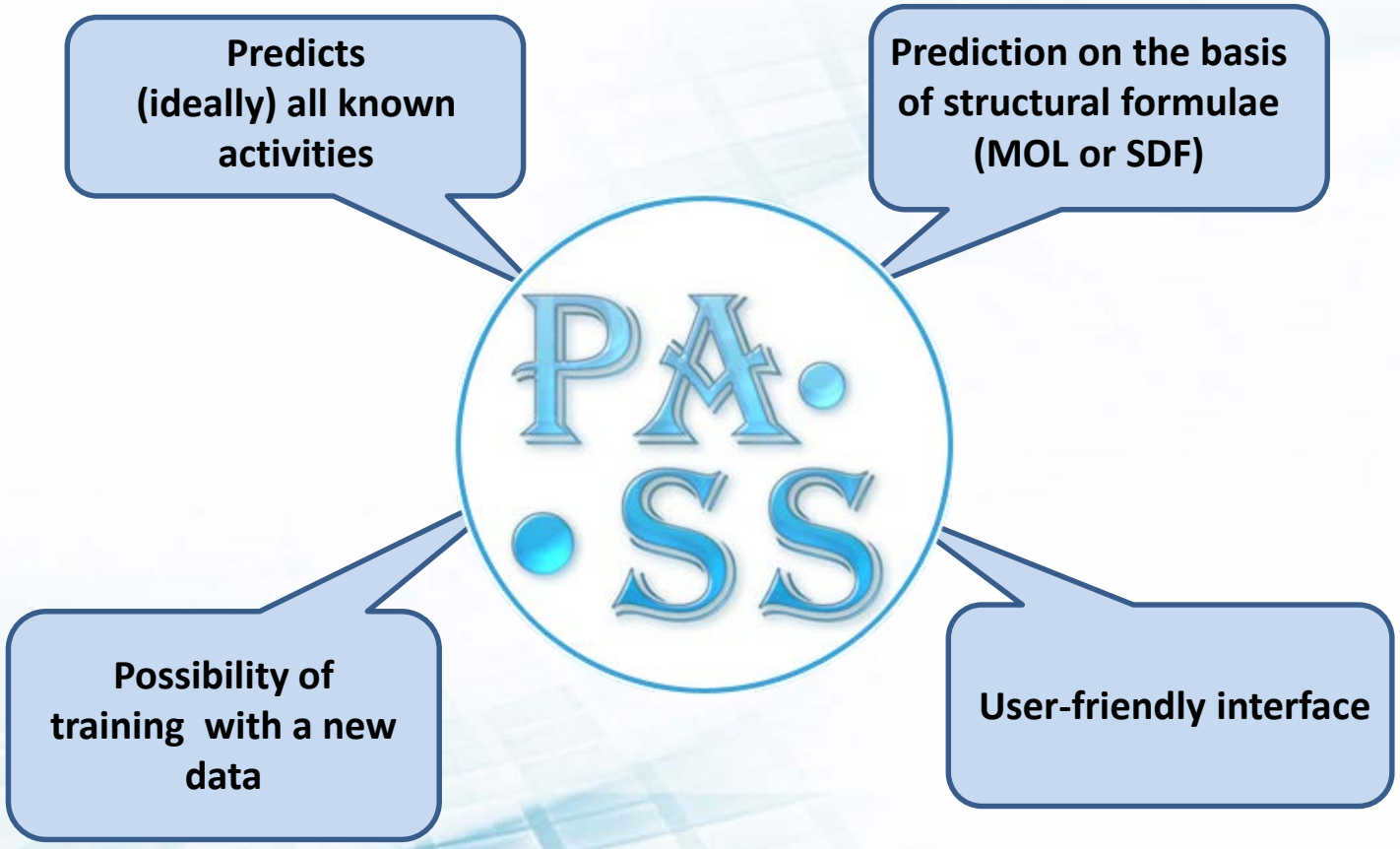
Ashburn T.T. and Thor K.B. *Nat. Rev. Drug. Discov.*, **2004**, 3: 673-683.

If you can predict the most probable targets & new effects for the existing drugs by the current chemoinformatics tools?

Yes, you can!

Both structure-based and ligand-based methods may be applied for this purpose: (Q)SAR, pharmacophore sets, inverse docking, etc.

Computer program for evaluating biological activity profiles (spectra)

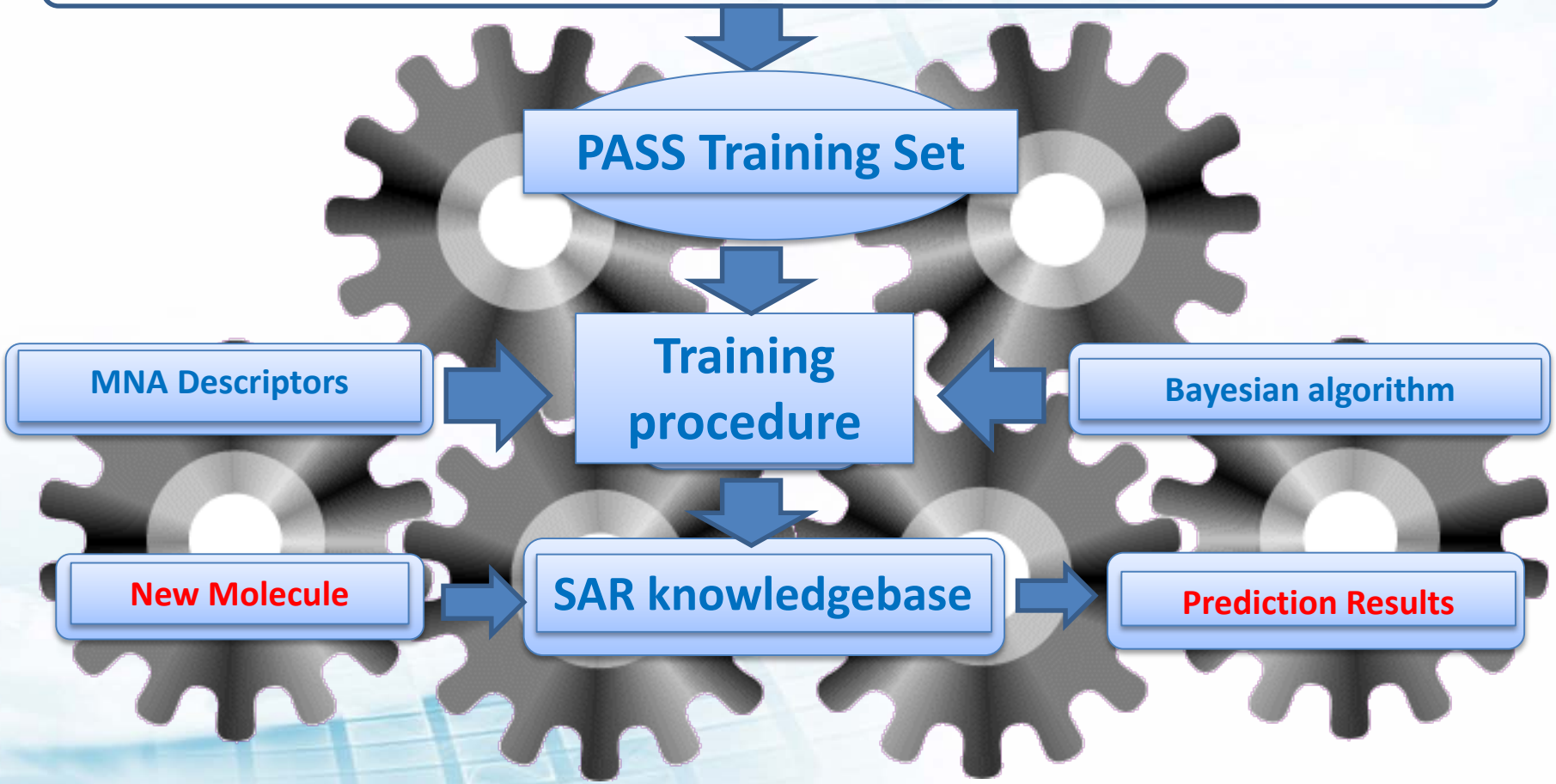


PASS: Prediction of Biological Activity Spectra for Substances

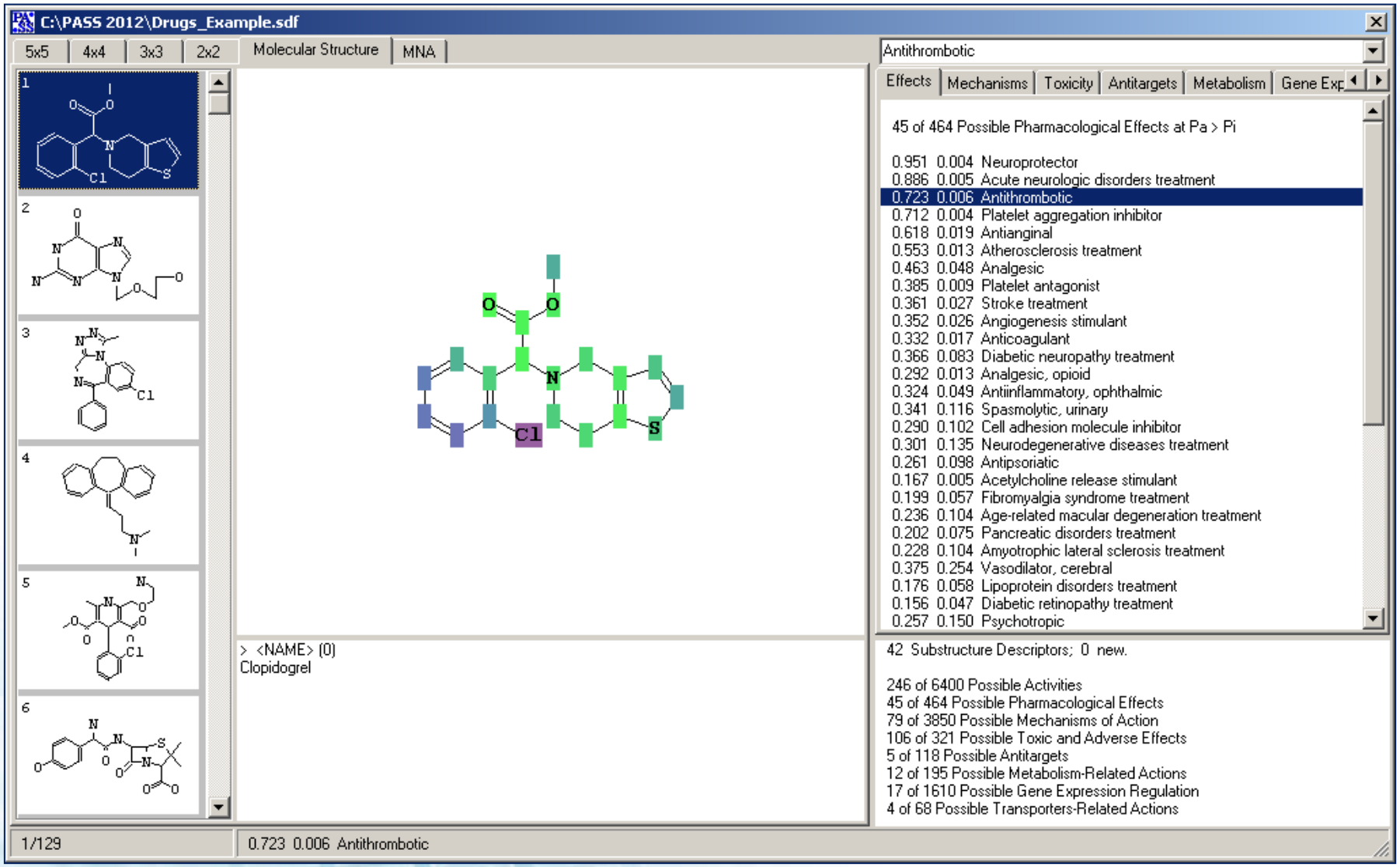
PASS: Development & updating workflow

Full text publications, databases, presentations at conferences, etc.

Reliable data on structure and activity of drug-like molecules



Example of prediction for Clopidogrel

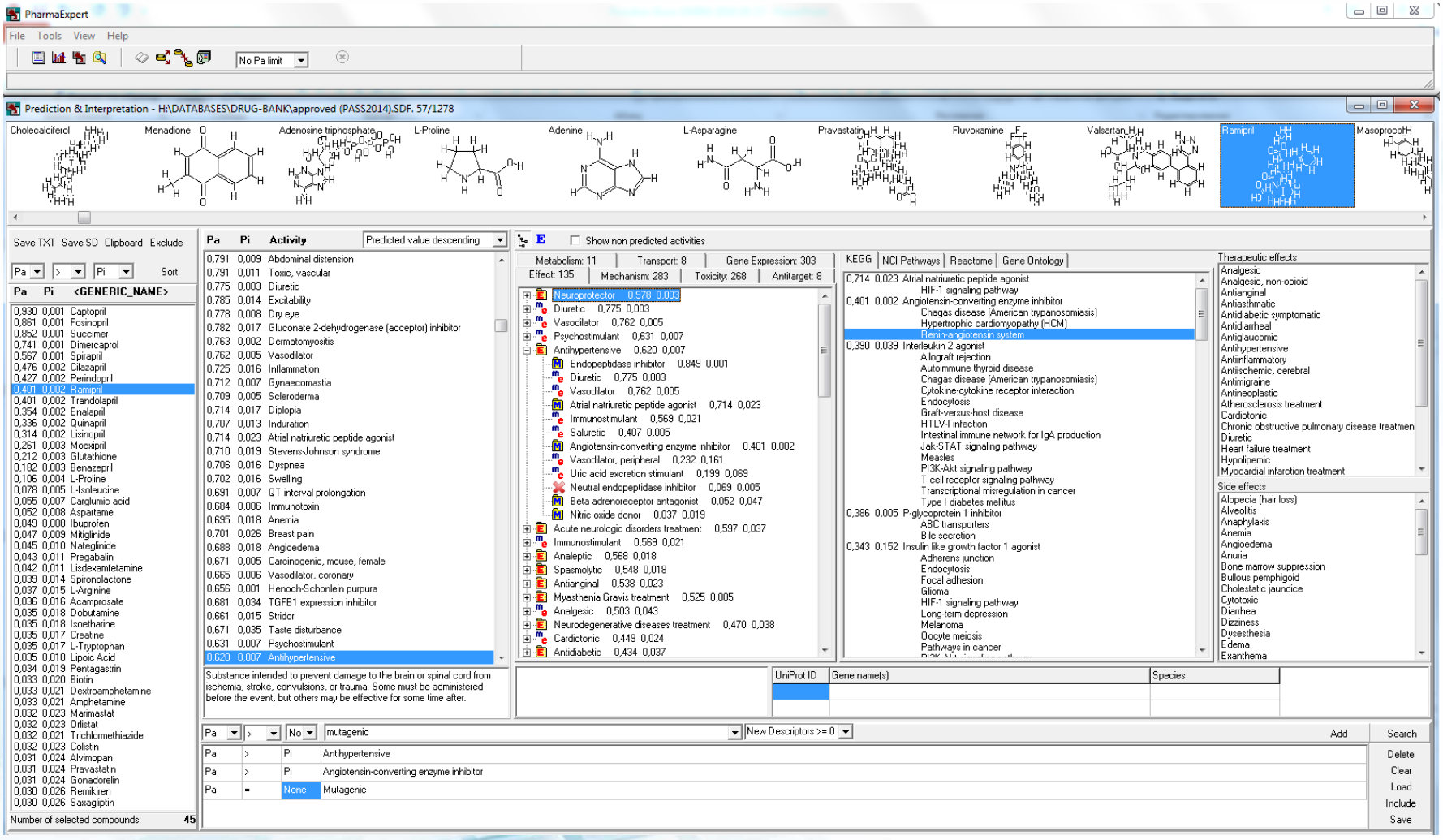


Clopidogrel: predicted vs. known activities

Abdominal pain
Acute neurologic disorders treatment
Agranulocytosis
Allergic reaction
Anaphylaxis
Anemia
Angioedema
Angiogenesis inhibitor
Antianginal
Antiarthritic
Anticoagulant
Antineoplastic
Antipsoriatic
Antithrombotic
Anxiety
Arthralgia
Atherosclerosis treatment
Back pain
Behavioral disturbance
Blindness
Bronchoconstrictor
Cardiotoxic
Cataract
CCL4 expression enhancer
CCL5 expression enhancer
Chest pain
Colic
Colitis
Conjunctivitis
Consciousness alteration
Constipation
Cough
CYP2 substrate
CYP2C substrate
CYP2C19 inhibitor
CYP2C19 substrate
CYP2C9 inhibitor
CYP3A substrate
CYP3A4 substrate
Cytochrome P450 inhibitor
Dermatitis
Dermatologic
Dizziness
Drug eruption
Dyspepsia
Emetic
Eosinophilia
Erythema
Erythema multiforme
Exanthema
Flatulence
GP IIb/IIIa receptor antagonist
Hallucinogen
Headache
Heart failure
Hematotoxic
Hemorrhage
Henoch-Schonlein purpura
Hepatic failure
Hepatitis
Hepatotoxic
Hypertensive
Hyperthermic
Hypotension
Infection
Insomnia
Lassitude
Leukopenia
Lichen planus
Lichenoid eruption
Malaise
Menstruation disturbance
Myalgia
Nausea
Necrosis
Nephrotoxic
Neuroprotect
Neutropenia
Ocular toxicity
Pain
Pancreatitis
Pancytopenia
Platelet aggregation inhibitor
Platelet antagonist
Pruritus
Pulmonary embolism
Purinergic P2 antagonist
Purinergic P2T antagonist
Purinergic P2Y antagonist
Purinergic P2Y12 antagonist
Purinergic receptor antagonist
Purpura
Renal colic
Reproductive dysfunction
Rhinitis
Sensory disturbance
Serum sickness
Shock
Sinusitis
Sleep disturbance
Stomatitis
Syncope
THBS1 expression enhancer
Thrombocytopenia
Toxic
Toxic epidermal necrolysis
Toxic, gastrointestinal
TP53 expression enhancer
Urticaria
Vasculitis
Vertigo
Vision disturbance

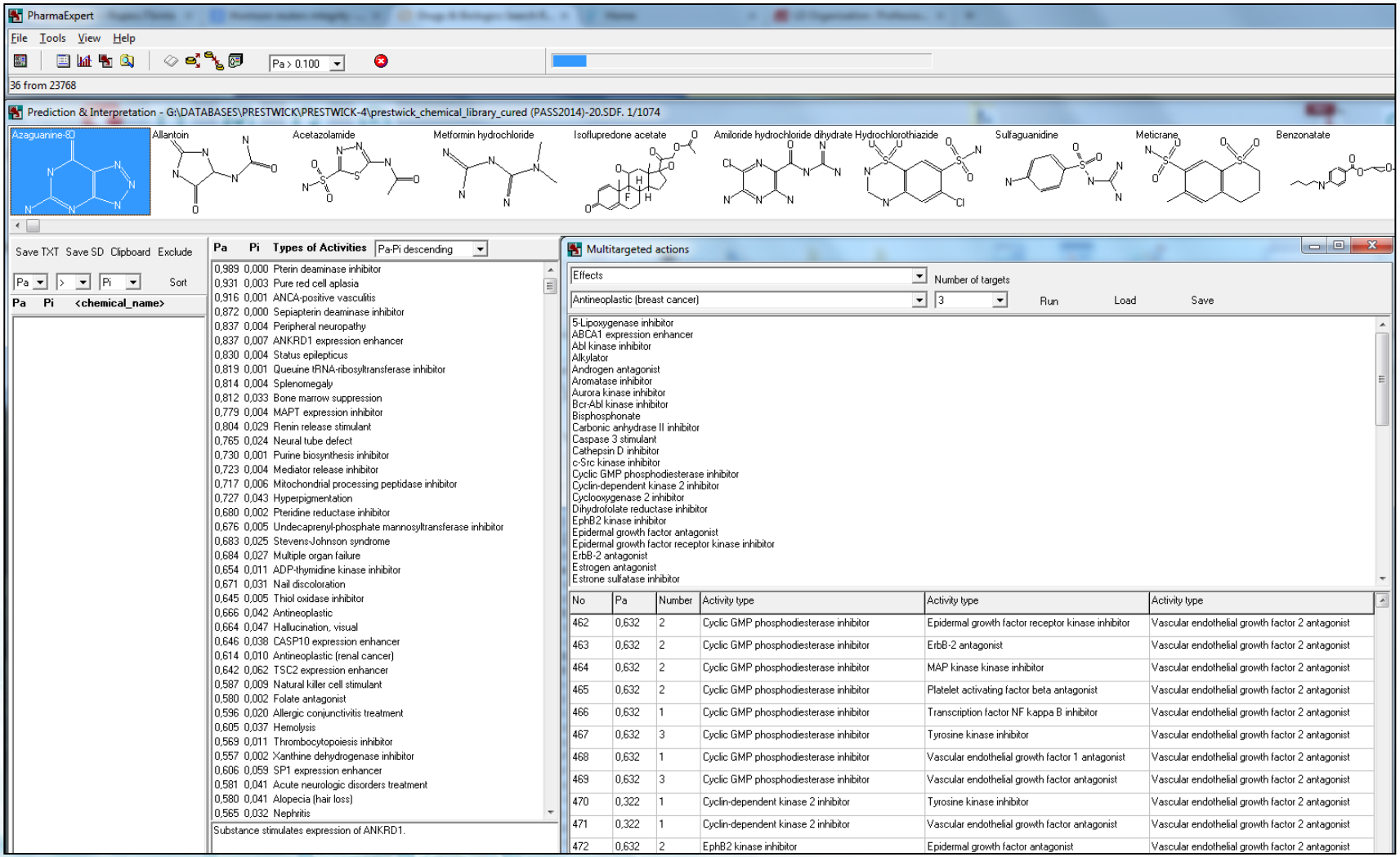
Blue – predictions coincided with the experiment.
Black – unpredictable activities.
Red – unpredicted activities.

PharmaExpert: Interpretation of the predictions

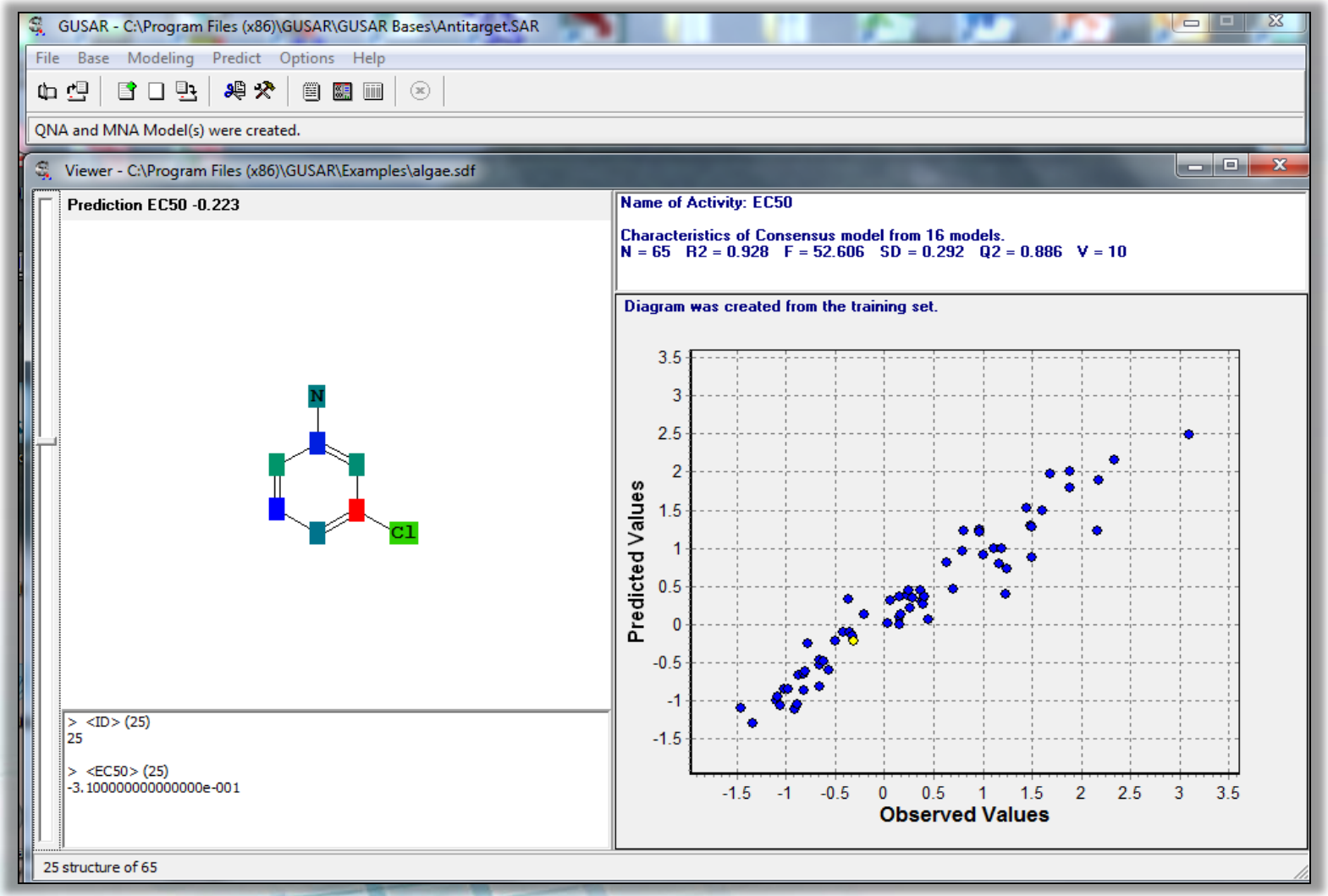


Poroikov V. et al. PharmaExpert: diseases, targets and ligands – three in one. In: *QSAR and Molecular Modelling in Rational Design of Bioactive Molecules*. Ankara (Turkey), CADD & D Society, **2005**, p.514-515.

PharmaExpert: Search for multitargeted antineoplastic agents

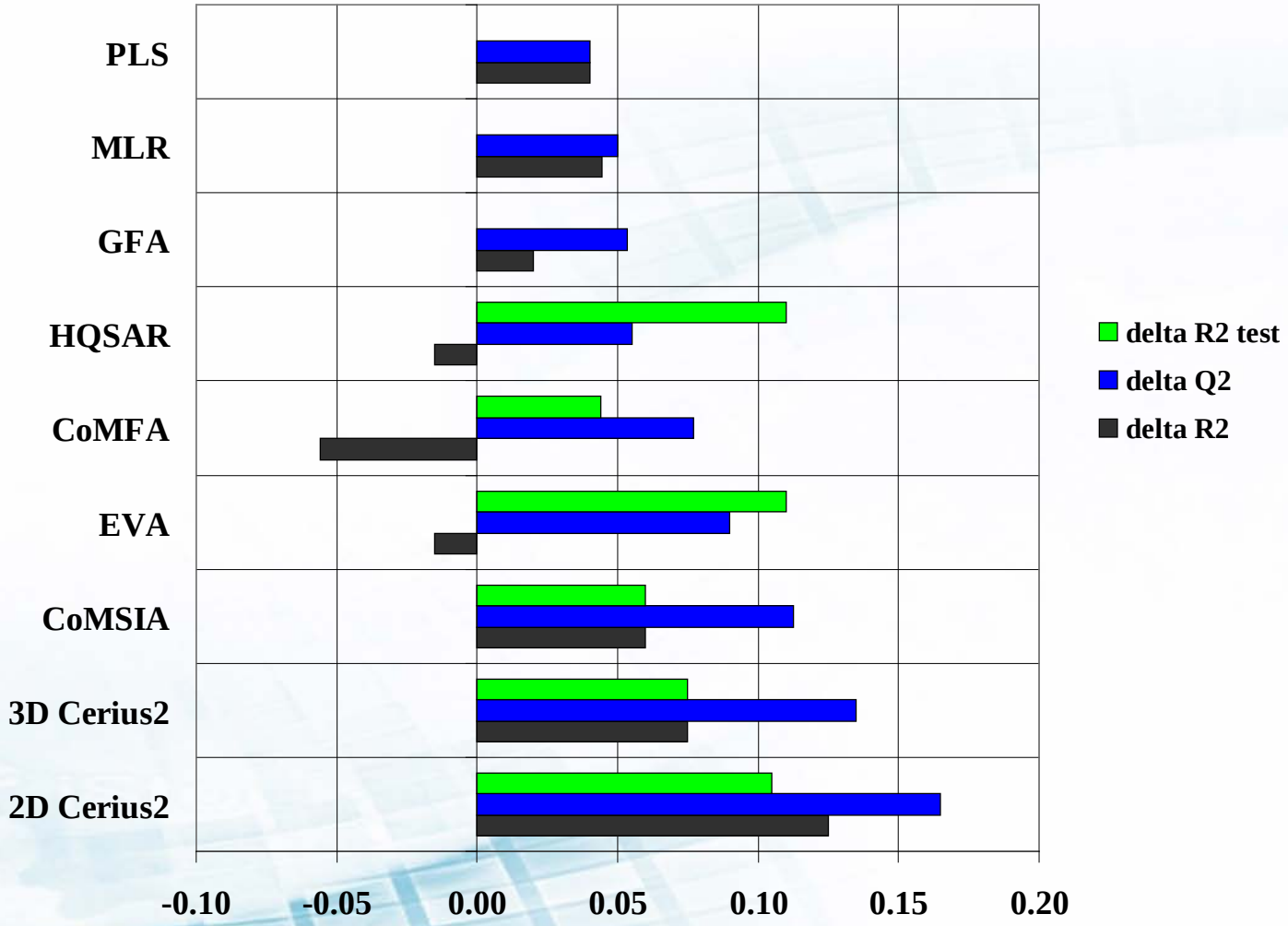


GUSAR: General Unrestricted Structure-Activity Relationships



Filimonov D.A. et al. *SAR and QSAR Environ. Res.*, 2009, **20**: 679-709.

GUSAR: Superiority in performance in comparison with some other (Q)SAR methods



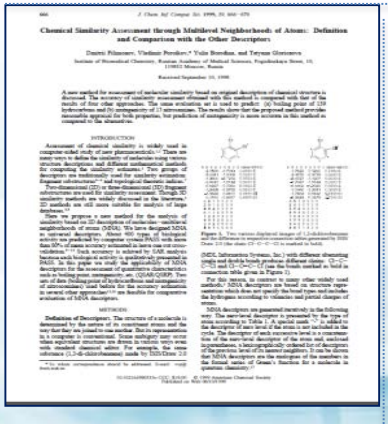
Filimonov D.A. et al. *SAR and QSAR Environ. Res.*, 2009, **20**: 679-709.

PASS: Methods and some applications

Filimonov D.A., Lagunin A.A., Gloriozova T.A., Rudik A.V., Druzhilovskiy D.S., Pogodin P.V., Poroikov V.V. (2014). Prediction of the biological activity spectra of organic compounds using the PASS online web resource. *Chemistry of Heterocyclic Compounds*, 50: 444-457.

Filimonov D.A., Poroikov V.V. (2008). Probabilistic Approach in Virtual Screening. In: *Chemoinformatics Approaches to Virtual Screening*. Alexander Varnek and Alexander Tropsha, Eds. RSC Publishing, 182-216.

Filimonov D.A., Poroikov V.V. (2006). Prediction of biological activity spectra for organic compounds. *Russian Journal of General Chemistry*, 50: 66-75.


Chemical Similarity Assessment through Multilevel Neighborhoods of Atoms: Definition and Comparison with the Other Descriptors

Descriptors (1999)


Robustness of Biological Activity Spectra Predicting by Computer Program PASS for Noncongeneric Set of Chemical Compounds

Robustness (2000)


BIOINFORMATICS APPLICATIONS NOTE

PASS: prediction of activity spectra for biologically active substances

PASS Online (2000)

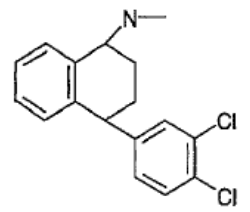

Discriminating between Drugs and Nondrugs by Prediction of Activity Spectra for Substances (PASS)

Drug-likeness (2001)

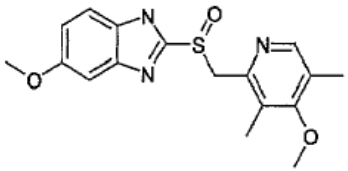

PASS Biological Activity Spectrum Prediction: in the Enhanced Open NCI Database Browser

NCI Browser (2003)

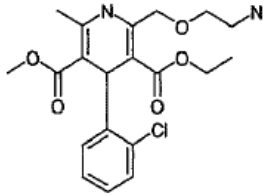
Our experience in DRP: Prediction for Top200 drugs



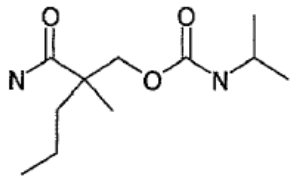
Sertraline
Adrenergic transmitter uptake inhibitor (0.770)
Antiparkinsonian (0.609)
Leukopoiesis inhibitor (0.582)
Cocain dependency treatment (0.560)
Acute neurologic disorders treatment (0.541)



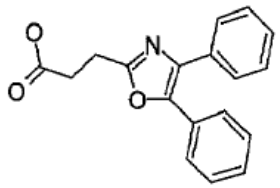
Omeprazole
TNF-alpha release inhibitor (0.658)
Atherosclerosis treatment (0.541)



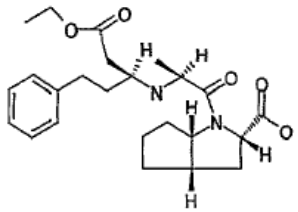
Amlodipine
Antineoplastic enhancer (0.608)
Multiple sclerosis treatment (0.508)



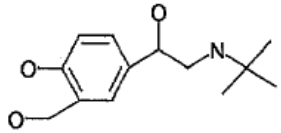
Carisoprodol
Angiogenesis inhibitor (0.569)
Multiple sclerosis treatment (0.549)



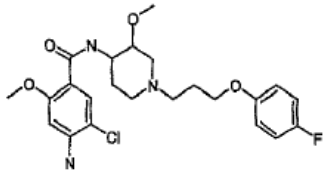
Oxaprozin
Bone formation stimulant (0.785)
Interleukin 1 antagonist (0.640)



Ramipril
Multiple sclerosis treatment (0.589)
Cognition disorders treatment (0.562)
Antiarthritic (0.454)



Albuterol
Antiobesity (0.784)



Cisapride
Irritable Bowel syndrome therapy(0.720)
Rhinitis treatment (0.524)

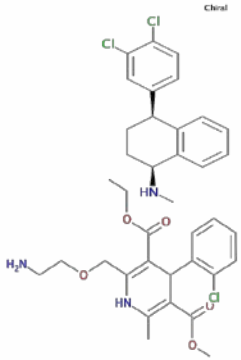
FIGURE 3 Examples of biological activities predicted de novo for some pharmaceuticals from the Top 200 list, which may become a reason for a new application. Pa values are given in brackets.

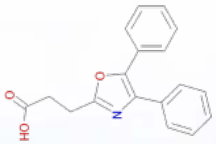
Poroikov V.V. et al. *SAR & QSAR Environ. Res.*, **2001**, 12: 327-344.

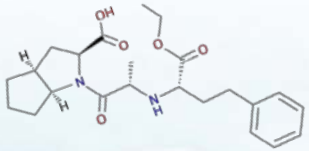
Four new indications confirmed by further studies

In 2001 we published predictions of new effects for 8 medicines from the list of Top200 Drugs [1].

Which predictions are confirmed? (informational search, September 2014)







			Ref.
Sertraline	**Cocain dependency treatment**	+	[2]
Amlodipine	**Antineoplastic enhancer (moderate BCRP/ABCG2 inhibitor)**	+	[3]
Oxaprozin	**Interleukin 1 antagonist (Inhibitor of production of Interleukin 1β)**	+	[4]
Ramipril	**Antiarthritic**	+	[5]

1. Poroikov V. et al. *SAR and QSAR Environ. Res.*, **200**1, 12: 327-344.
2. Mancino M.J. et al. *J. Clin. Psychopharmacol*., **2014**, 34: 234–239.
3. Takara K. et al. *Mol. Med. Rep*., **2012**, 5: 603-609.
4. Rainsford K.D. et al. *Inflammopharmacology*, **2002**, 10: 85–239.
5. Shi Q. et al. *Arthritis Res. Ther*., **2012**, 14: R223.

Nootropic effect in some antihypertensive drugs?

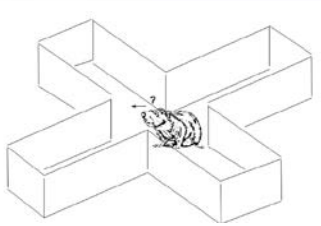
1

PASS

2

Name	Pa (Nootropic effect), %
Captopril	44,6
Enalapril	65,5
Lisinopril	61,8
Perindopril	60,9
Quinapril	65,1
Ramipril	63,3
Monopril	30,9
Piracetam	81,7
Amlodipin	-
Hydrochlorothiazide	-

3



4

Perindopril in dose of 1 mg/kg, and quinapril and monopril in doses of 10 mg/kg improved the patrolling behavior in the maze, like piracetam and meclofenoxate (in doses of 300 and 120 mg/kg, respectively).

5

BMJ Open 2013;**3**:e002881 doi:10.1136/bmjopen-2013-002881

Geriatric medicine

Effects of centrally acting ACE inhibitors on the rate of cognitive decline in dementia

Yang Gao[1,2], Rónán O'Caoimh[1], Liam Healy[1], David M Kerins[3,4], Joseph Eustace[5], Gordon Guyatt[6], David Sammon[2], D William Molloy[1,7]

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Published 22 July 2013

Kryzhanovskii S.A. et al. *Pharmaceutical Chemistry Journal,* 2012, 45: 605-611.

PASS Online: The first publication & Some comments

BIOINFORMATICS APPLICATIONS NOTE
Vol. 16 no. 8 2000
Pages 747–748

PASS: prediction of activity spectra for biologically active substances

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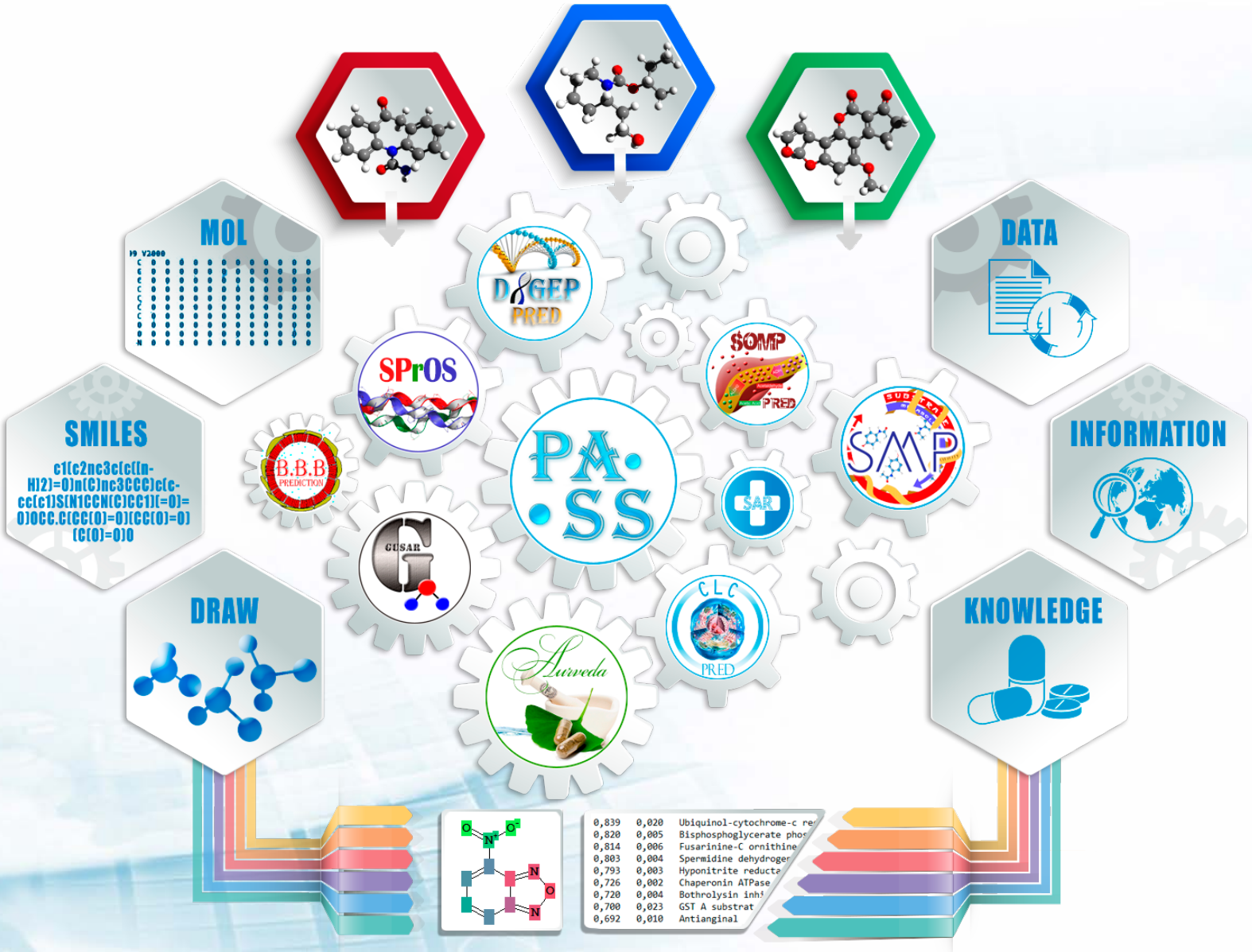
Received on November 26, 1999; revised on December 11, 1999; accepted on March 21, 2000

"One of the earliest and most widely used examples of data-mining target elucidation is the continuously curated and expanded Prediction of Activity Spectra for Substances (PASS) software, which was assimilated from the bioactivites of more than 270,000 compound-ligand pairs."

Mervin L.H., … , Bender A. J. Cheminform., ***2015****, 7: 51.*

Way2Drug web platform



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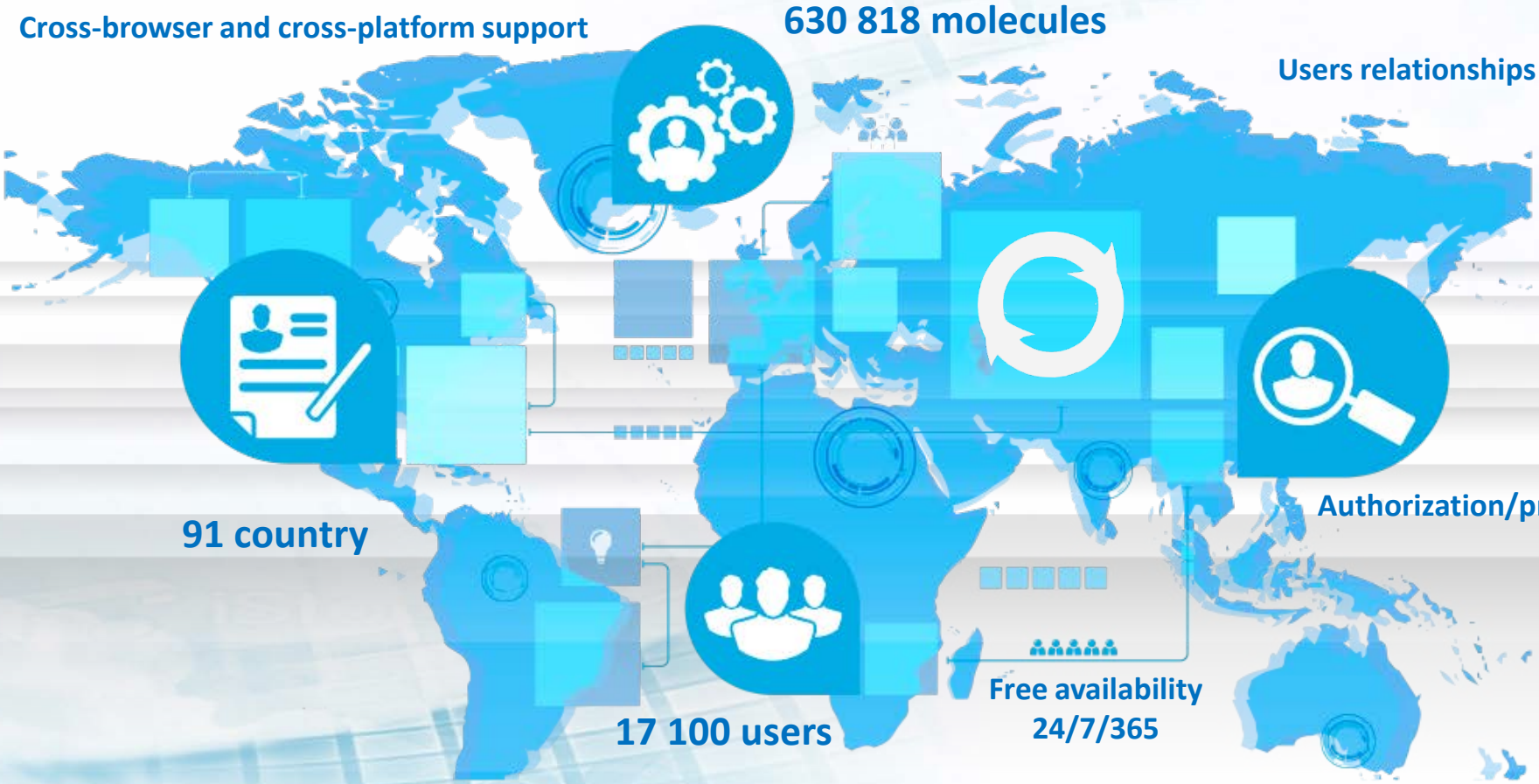
Kazakhstan Brazil Other



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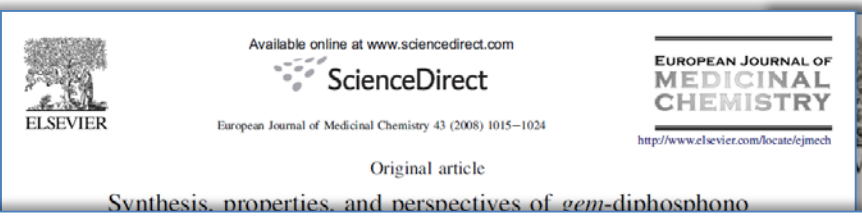
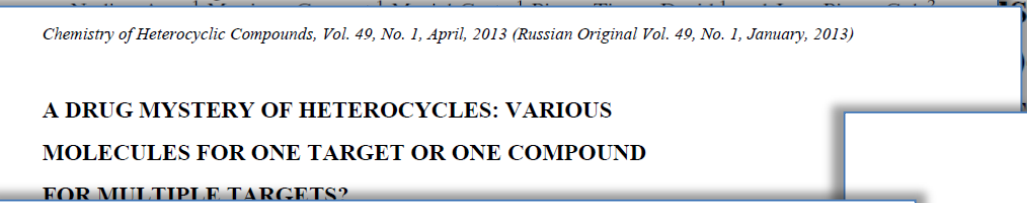

Available online at www.sciencedirect.com
ScienceDirect
European Journal of Medicinal Chemistry 43 (2008) 1015–1024
EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY
http://www.elsevier.com/locate/ejmech
Original article
Synthesis, properties, and perspectives of *gem*-diphosphono

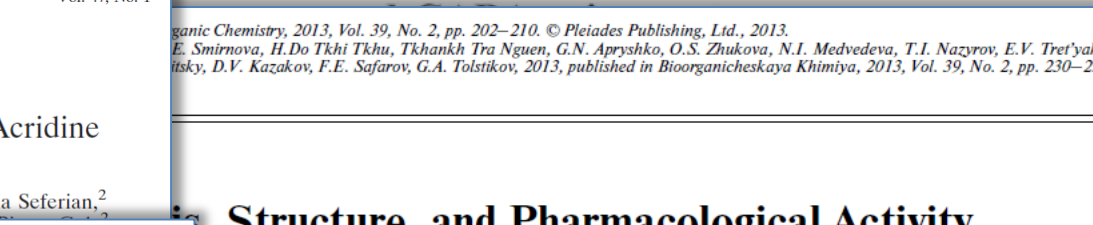

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Jan. 2003, p. 174–180 Vol. 47, No. 1
0066-4804/03/$08.00+0 DOI: 10.1128/AAC.47.1.174–180.2003
Copyright © 2003, American Society for Microbiology. All Rights Reserved.
In Vitro Activities of 7-Substituted 9-Chloro and 9-Amino-2-Methoxyacridines and Their Bis- and Tetra-Acridine Complexes against *Leishmania infantum*
Carole Di Giorgio,[1]* Florence Delmas,[1] Nathalie Filloux,[2] Maxime Robin,[2] Laetitia Seferian,[2]

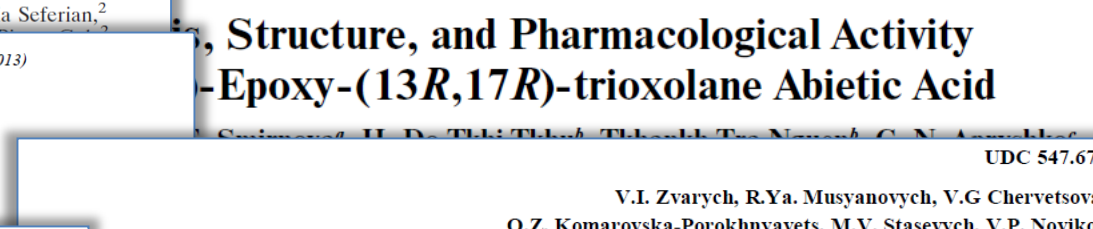

Chemistry of Heterocyclic Compounds, Vol. 49, No. 1, April, 2013 (Russian Original Vol. 49, No. 1, January, 2013)
A DRUG MYSTERY OF HETEROCYCLES: VARIOUS MOLECULES FOR ONE TARGET OR ONE COMPOUND FOR MULTIPLE TARGETS?

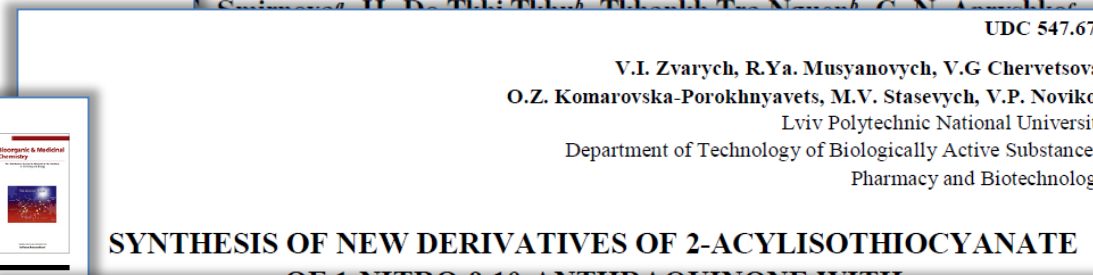

Bioorganic & Medicinal Chemistry 20 (2012) 2930–2939
Contents lists available at SciVerse ScienceDirect
Bioorganic & Medicinal Chemistry
journal homepage: www.elsevier.com/locate/bmc
Identification of novel isocytosine derivatives as xanthine oxidase inhibitors from a set of virtual screening hits

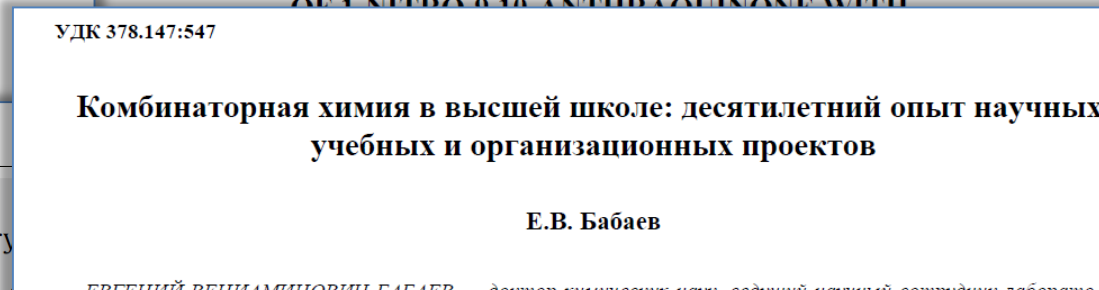

European Journal of Medicinal Chemistry 45 (2010) 2606–2612
Contents lists available at ScienceDirect
European Journal of Medicinal Chemistry


Available online at www.sciencedirect.com
SCIENCE DIRECT
Bioorganic & Medicinal Chemistry Letters
Bioorganic & Medicinal Chemistry Letters 15 (2005) 2145–2148
nazolines revisited: search for novel anxiolytic

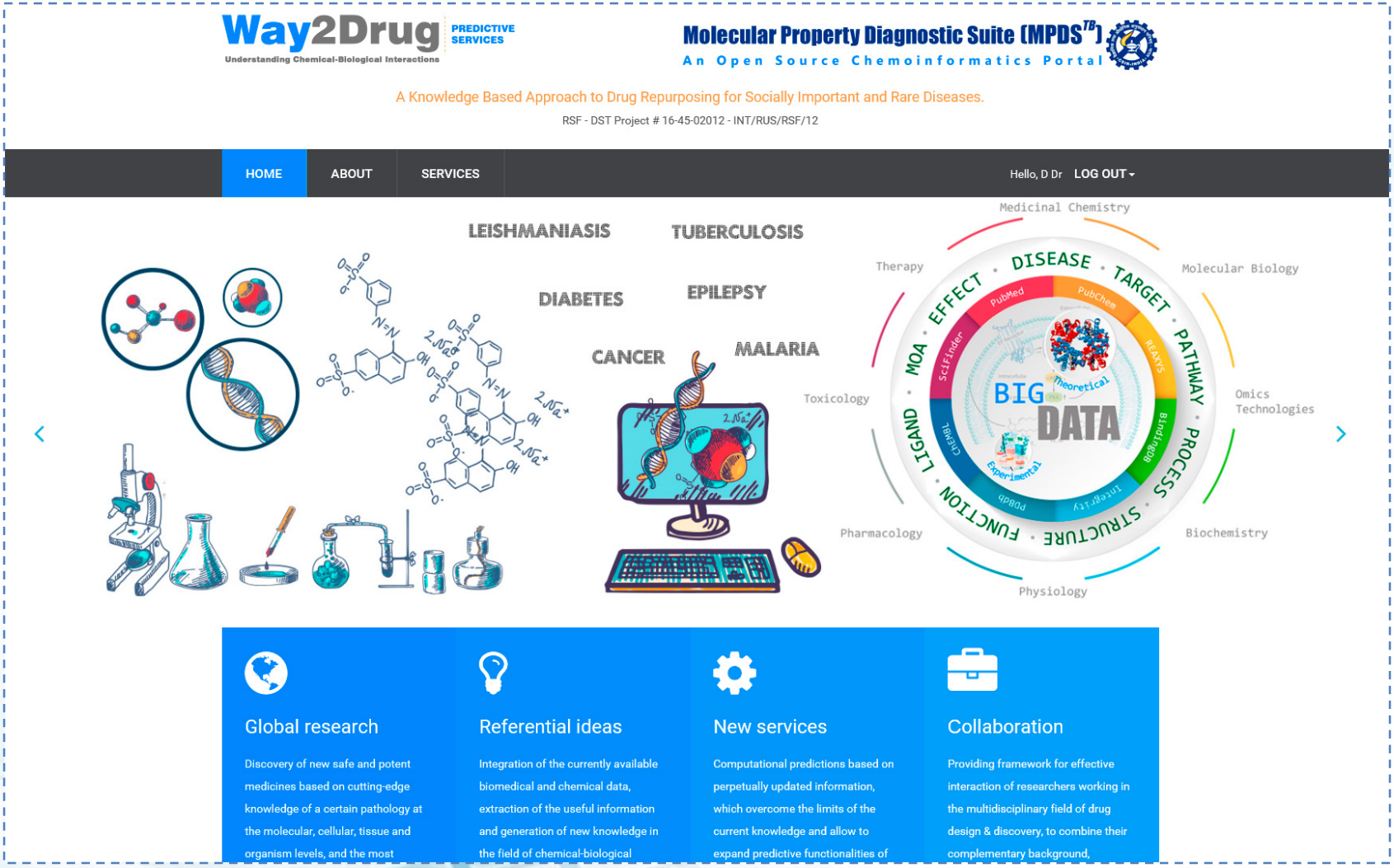

ganic Chemistry, 2013, Vol. 39, No. 2, pp. 202–210. © Pleiades Publishing, Ltd., 2013.
E. Smirnova, H.Do Tkhi Tkhu, Tkhankh Tra Nguen, G.N. Apryshko, O.S. Zhukova, N.I. Medvedeva, T.I. Nazyrov, E.V. Tret'yak
itsky, D.V. Kazakov, F.E. Safarov, G.A. Tolstikov, 2013, published in Bioorganicheskaya Khimiya, 2013, Vol. 39, No. 2, pp. 230–2


, Structure, and Pharmacological Activity
-Epoxy-(13*R*,17*R*)-trioxolane Abietic Acid


UDC 547.67
V.I. Zvarych, R.Ya. Musyanovych, V.G Chervetsov
O.Z. Komarovska-Porokhnyavets, M.V. Stasevych, V.P. Novik
Lviv Polytechnic National Universi
Department of Technology of Biologically Active Substance
Pharmacy and Biotechnolog
SYNTHESIS OF NEW DERIVATIVES OF 2-ACYLISOTHIOCYANATE


УДК 378.147:547
Комбинаторная химия в высшей школе: десятилетний опыт научных учебных и организационных проектов
Е.В. Бабаев

Way2Drug Drug Repurposing Platform



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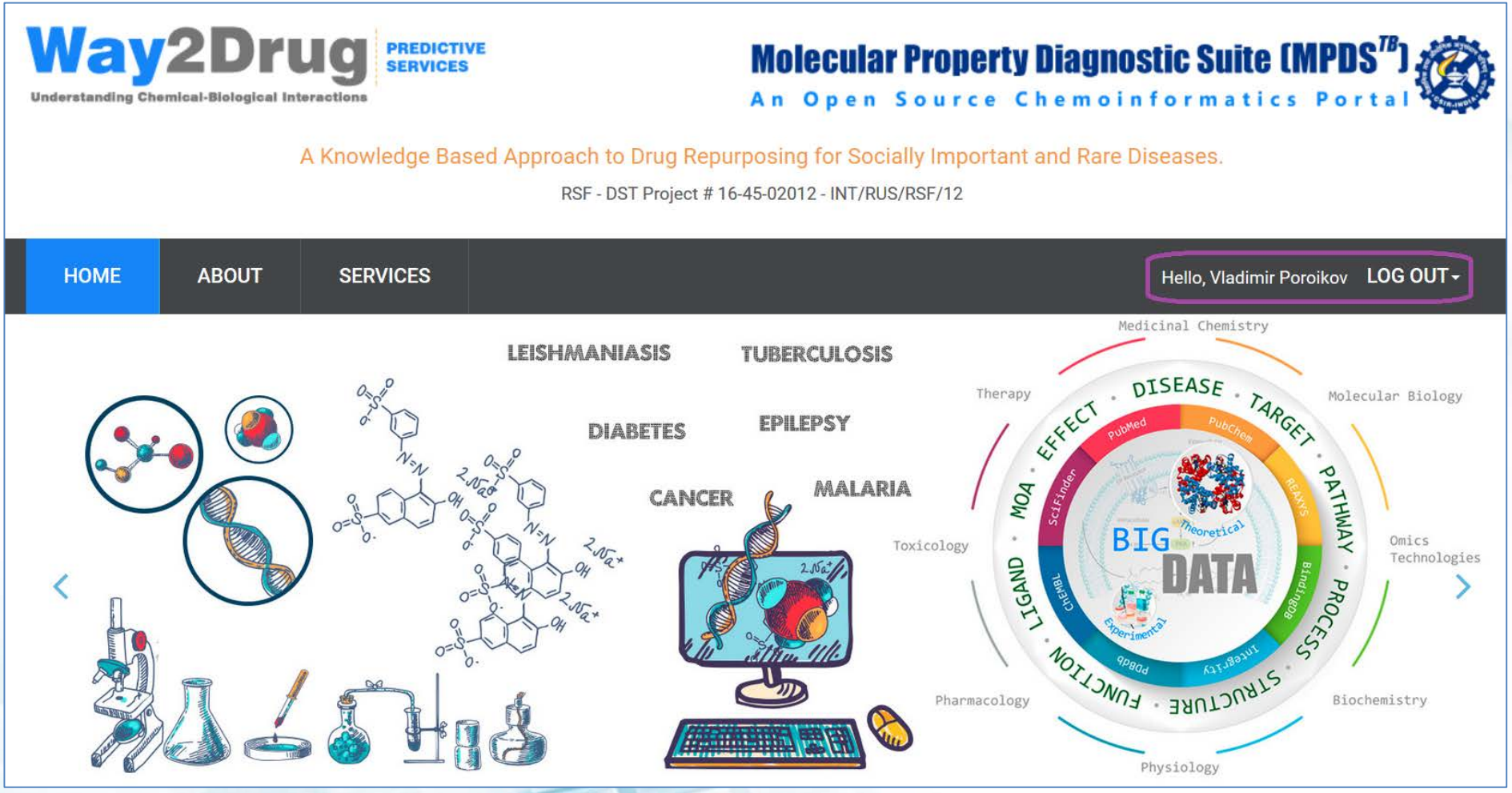
Supported by the RSF-DST grant (project No. 16-45-02012 - INT/RUS/RSF/12)

Way2Drug DRP: Login



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IBMC

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Understanding Chemical-Biological Interactions
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Way2Drug DRP: Pharmacotherapeutic Areas

Orphan diseases

A disease is considered rare* when no more than **1 out of 2000** people suffer from it

Estimates indicate **>300 million** people living with a rare disease worldwide

Tests for **3500** rare diseases are now available...

...but only about **400 rare diseases** have therapies

80% of rare diseases have a genetic component

50% of those affected by rare diseases are children

Reported rates of medication adherence range from **58-65%**

There are **6,000 to 7,000** rare diseases

DIABETES

DIABETES IS ON THE RISE

422 MILLION adults have diabetes

3.7 MILLION deaths due to diabetes and high blood glucose

1.5 MILLION deaths caused by diabetes

Epilepsy

Epilepsy is a condition that affects the brain and causes repeated seizures

65 MILLION people worldwide currently live with epilepsy.

200,000 people, per year are diagnosed with epilepsy

TUBERCULOSIS (TB) FACTS

TB is a serious disease. It can infect many body parts, but is most common in the lungs.

1,500,000 died from the disease*

9,000,000 people fell ill with TB

TB is a **leading cause of death** in patients with **HIV.**

MALARIA FACTS

Malaria is a serious disease that is **PREVENTABLE** and **TREATABLE.**

97 countries and territories had ongoing malaria transmission in 2015.[1]

every **2** minutes a child dies from malaria in Sub-Saharan Africa.[4]

Cancer Facts

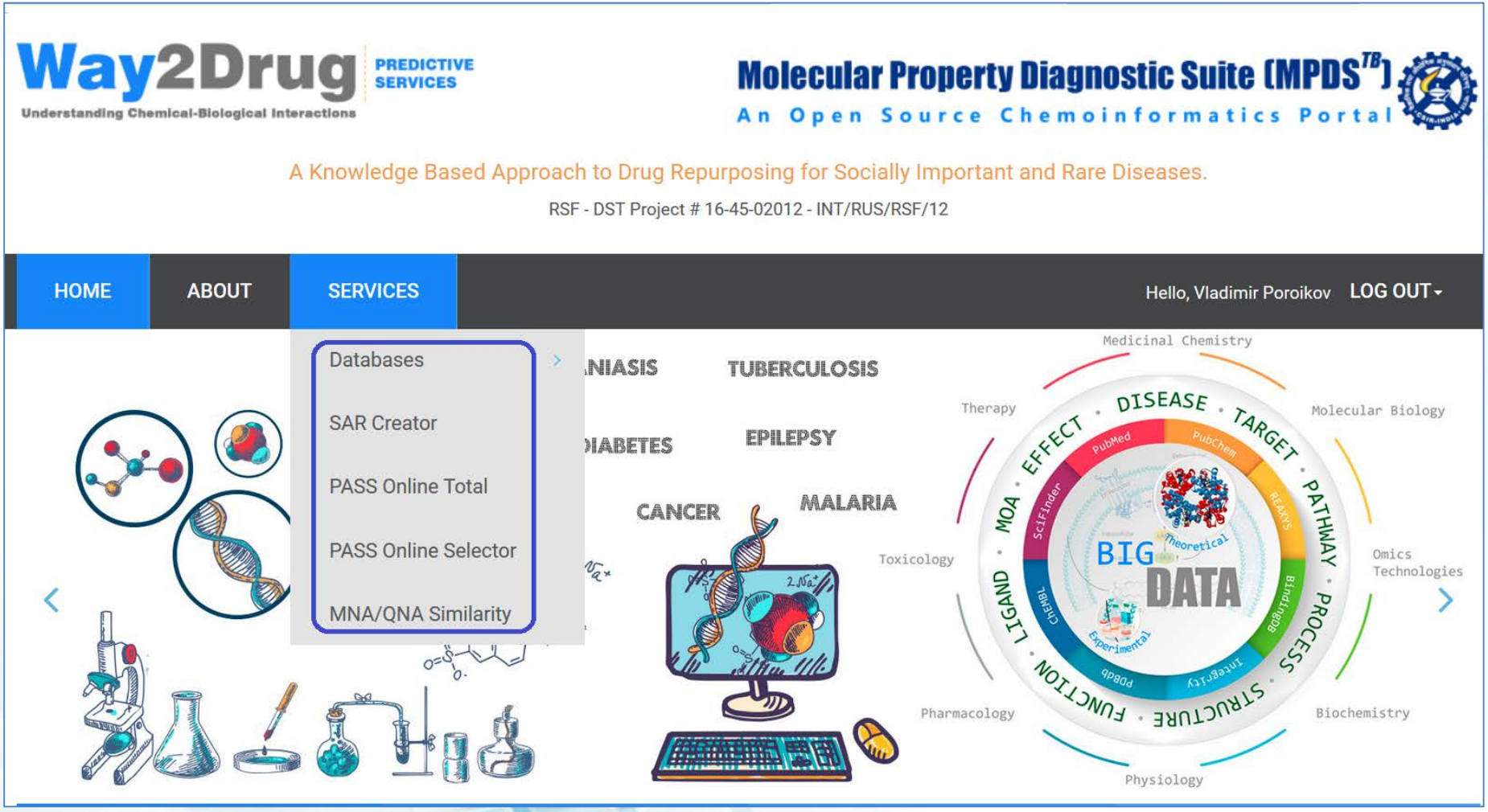
approximately 14 million new cases

The disease accounts for 7.4 million deaths worldwide.

It's the leading cause of death worldwide, causing around 13% of all deaths worldwide

Tuberculosis | **Leishmaniasis** | **Malaria** | **Diabetes** | **Cancer** | **Epilepsy**

Way2Drug DRP: Services



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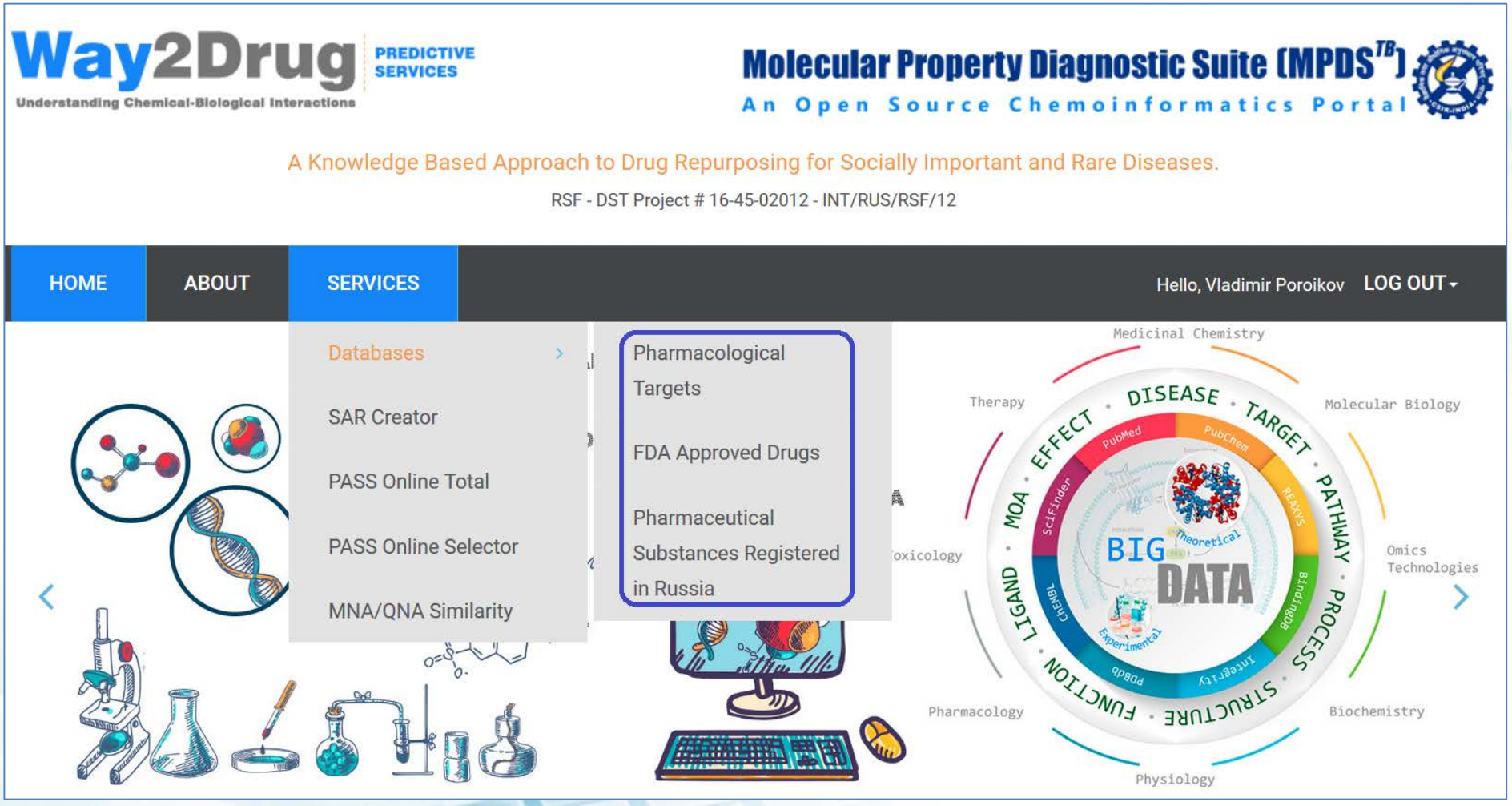
Way2Drug DRP: Databases



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Way2Drug DRP: Molecular targets

Pharmacological Targets

Show 10 entries

Search:

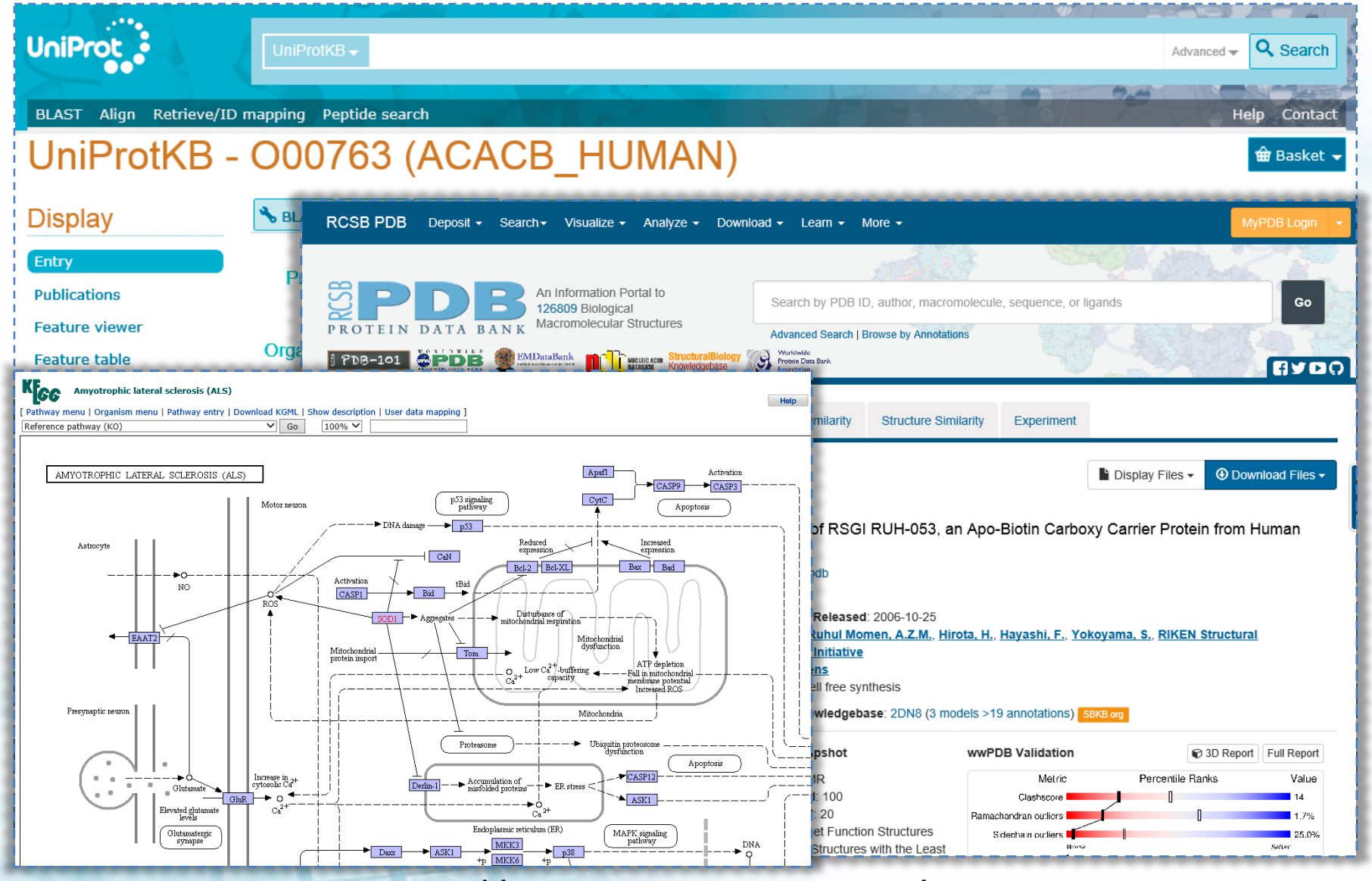
Target's name	UniProt	PDB	Kegg	Pharmacotheraputic application		
				PreClinical	Clinical	Launched
1-deoxy-D-xylulose 5-phosphate reductoisomerase	Q8IKG4	PDB			Tuberculosis	Malaria
1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase gamma-1	P19174	PDB	KEGG		Cancer	
11beta-Hydroxysteroid Dehydrogenase (nonspecified subtype)	P24385	PDB	KEGG			Diabetes Cancer
14-3-3 protein epsilon	P62258	PDB	KEGG	Cancer		
15-hydroxyprostaglandin dehydrogenase (NAD+) (isoform 1)	P15428	PDB			Cancer	
17beta-Hydroxysteroid dehydrogenase (nonspecified subtype)	P24864	PDB	KEGG		Cancer Diabetes	
2-amino-3-carboxymuconate-6-semialdehyde	Q8TDX5	PDB			Diabetes	
3-oxoacyl-(acyl-carrier protein) reductase	Q8I2S7	PDB			Cancer Leishmaniasis Malaria	
3-phosphoinositide-dependent protein kinase 1 (isoform 1)	O15530	PDB	KEGG		Diabetes	Cancer
4F2 cell-surface antigen heavy chain	P08195	PDB		Cancer		
Target's name	**UniProt**	**PDB**	**Kegg**	**Pharmacotheraputic application**		
				PreClinical	**Clinical**	**Launched**

Showing 1 to 10 of 2,322 entries

Previous 1 2 3 4 5 … 233 Next

http://www.way2drug.com/dr

Molecular targets: Links to the external resources



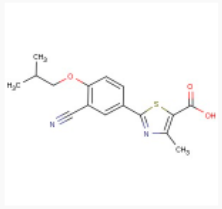
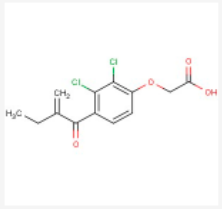
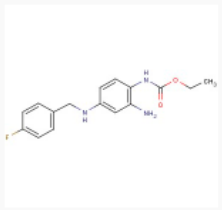
http://www.way2drug.com/dr

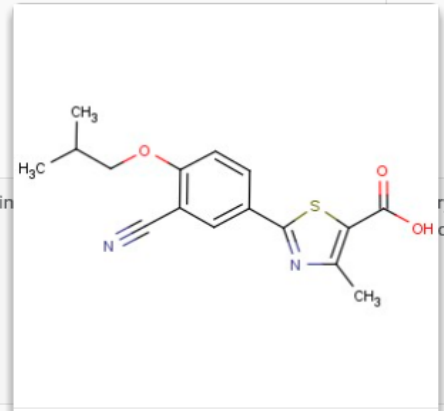
Way2Drug DRP: FDA Approved Drug Substances

Show 10 entries

FDA approved drugs

Search:

Structure	Brand Name	Generic Name	Mechanism of Action	Pharmacotheraputic application
	Adenuric Febric Feburic Uloric	Febuxostat (USAN; Rec INN)	Xanthine Oxidase Inhibitors	Gout Hyperuricemia Cancer therapy associated disorders Angina pectoris, stable Hematologic-blood cancer
	Edecrin Hydromedin	rynic acid (Rec INN; JAN) crynic acid (BAN; USAN)	Wnt Signaling Inhibitors	Hypertension
	Potiga Trobalt	abine (USAN) Retigabine (Prop USAN)	Voltage-Gated K(V) 7.2/7.3 (KCNQ2/3) Channel Activators Voltage-Gated K(V) 7.2 (KCNQ2) Channel Activators Voltage-Gated K(V) 7.3 (KCNQ3) Channel Activators P-Glycoprotein (MDR-1; ABCB1) Inhibitors GABA Aminotransferase Inhibitors	Epilepsy Lennox-Gastaut syndrome Neuralgia, postherpetic (PHN) Amyotrophic lateral sclerosis Epilepsy, partial seizures



Close

Neoplastic disorders (234 drugs) | **Malaria (12 drugs)** | **Tuberculosis (20 drugs)** | **Epilepsy (41 drugs)** | **Diabetes (84 drugs)**

http://www.way2drug.com/dr

Way2Drug DRP: Search for Clopidogrel

Way2Drug PREDICTIVE SERVICES
Understanding Chemical-Biological Interactions

Molecular Property Diagnostic Suite (MPDS^{TB})
An Open Source Chemoinformatics Portal

A Knowledge Based Approach to Drug Repurposing for Socially Important and Rare Diseases

RSF - DST Project # 16-45-02012 - INT/RUS/RSF/12

HOME | ABOUT | SERVICES | Hello, Vladimir Poroikov | LOG OUT

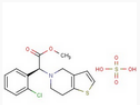
FDA approved drugs

Database contains information on about 1,000 medications, including the name of the drug, synonyms, the structural formula of the drug substance, pharmacotherapeutic fields and mechanisms of action.

One may browse the records in the database or search for a particular drug using drug name as a query.

Show 10 entries

Search: Clopido

Structure	Brand Name	Generic Name	Mechanism of Action	Pharmacotheraputic application	PASSOnline prediction
	Iscover Plavix	Clopidogrel bisulfate (USAN) Clopidogrel hydrogensulfate	Purinergic P2T antagonist Signal transduction modulator	Arrhythmia Stroke Disorders of hemostasis Fibrillation, atrial	PA SS

http://www.way2drug.com/dr

IBMC

Way2Drug PREDICTIVE SERVICES
Understanding Chemical-Biological Interactions
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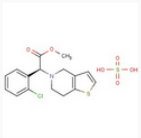
Way2Drug DRP: PASS Prediction for Clopidogrel Bisulfate

HOME | ABOUT | SERVICES | Hello, Vladimir Poroikov | LOG OUT

One may browse the records in the database or search for a particular drug using drug name as a query.

Show 10 entries Search: Clopido

Structure	Brand Name	Generic Name	Mechanism of Action	Pharmacotheraputic application	PASSOnline prediction
	Iscover Plavix	Clopidogrel bisulfate (USAN) Clopidogrel hydrogensulfate	Purinergic P2T antagonist	Arrhythmia Stroke Components: 2 Atherosclerosis Thrombosis Systemic lupus erythematosus Angina pectoris, stable Acute coronary syndrome	PASS
Structure	Brand Name	Generic Name	Mechanism of Action	Pharmacotheraputic application	PASSOnline prediction

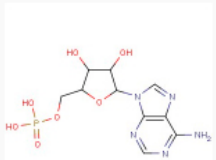
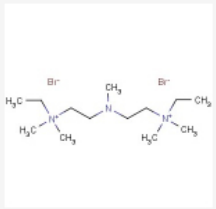
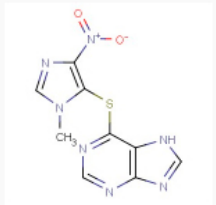
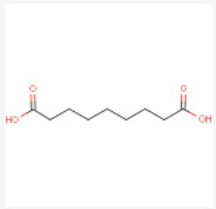
http://www.way2drug.com/dr

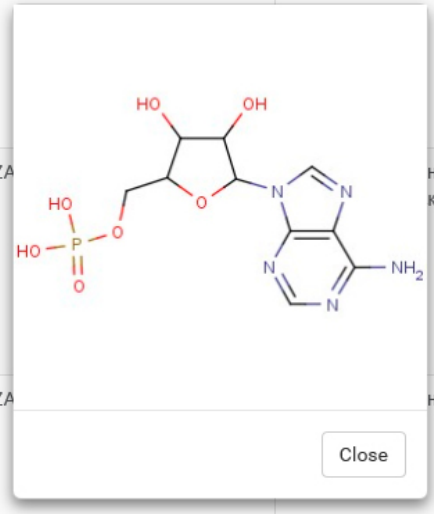
Way2Drug DRP: Drug Substances Registered in Russia

Show 10 entries

Pharmaceutical Substances Registered in Russia

Search:

Structure	Trade name	Substance name	Comments
	Фосфаден	ADENOSINE PHOSPHATE	Торговое название: Фосфаден Международное название: Аденозина фосфат Страна: Россия . дата актуализации - 17.05.1999 (РЛС)
	Пентамин	AZA	ние: Пентамин Международное название: Азаметония бромид Страна: Россия . В колько препаратов, несколько дат регистрации.
	Азатиоприн	AZA	ние: Азатиоприн Международное название: Азатиоприн Страна: Россия
	СКИНОРЕН	AZELAIC ACID	мазь . Торговое название Скинорен (Skinoren) Страна-производитель Германия Фирма-производитель Schering AG - 10.11.1998 . . .



http://www.way2drug.com/dr

New opportunities for drug repurposing?

МИНИСТЕРСТВО ПРОМЫШЛЕННОСТИ И ТОРГОВЛИ РОССИЙСКОЙ ФЕДЕРАЦИИ
(Минпромторг России)

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РОССИЙСКОЙ ФЕДЕРАЦИИ
(Минздрав России)

МИНИСТЕРСТВО ЮСТИЦИИ РОССИЙСКОЙ ФЕДЕРАЦИИ
ЗАРЕГИСТРИРОВАНО
Регистрационный № 42464
от "08" июня 2016

ПРИКАЗ

19 мая 2016 г. № 160/308н

Москва

Об утверждении перечня биомишеней для разработки схожих по фармакотерапевтическому действию и улучшенных аналогов инновационных лекарственных препаратов

В соответствии с пунктом 3 Правил предоставления субсидий из федерального бюджета российским организациям на возмещение части затрат на реализацию проектов по разработке схожих по фармакотерапевтическому действию и улучшенных аналогов инновационных лекарственных препаратов, утвержденных постановлением Правительства Российской Федерации от 30 декабря 2015 г. № 1503 (Собрание законодательства Российской Федерации 11.01.2016, № 2 ст. 377), п р и к а з ы в а е м :

Утвердить прилагаемый перечень биомишеней для разработки схожих по фармакотерапевтическому действию и улучшенных аналогов инновационных лекарственных препаратов.

Врио Министра промышленности и торговли Российской Федерации — Г.С. Никитин

Министр здравоохранения Российской Федерации — В.И. Скворцова

Partial statistics of PASS predictions

Pa>50%	Pa>70%	Types of Activity
227	73	Proteasome ATPase inhibitor
89	31	Meprin B inhibitor
63	52	Androgen antagonist
55	37	Estrogen antagonist
45	23	Phenylalanine 4-hydroxylase inhibitor
40	22	Progesterone agonist
32	10	Fibroblast growth factor 1 agonist
30	5	Fibroblast growth factor 4 antagonist
26	10	Potassium channel (Voltage-sensitive) blocker
24	17	Interleukin 6 antagonist
20	8	5 Hydroxytryptamine 2A antagonist
18	10	Dopamine D2 antagonist
18	11	Interleukin 5 antagonist
14	4	Meprin A inhibitor
13	5	Tumour necrosis factor alpha release inhibitor
11	1	AMP-activated protein kinase, alpha-1 subunit inhibitor
10	6	Opioid kappa receptor agonist
10	9	Dopamine D2 agonist
9	2	Histone deacetylase SIRT1 inhibitor
		. . .

Partial statistics of PASS predictions

Pa>50%	Pa>70%	Types of Activity
227	73	Proteasome ATPase inhibitor
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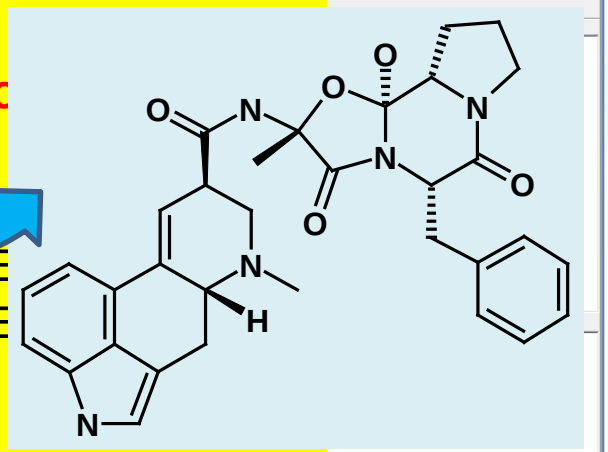
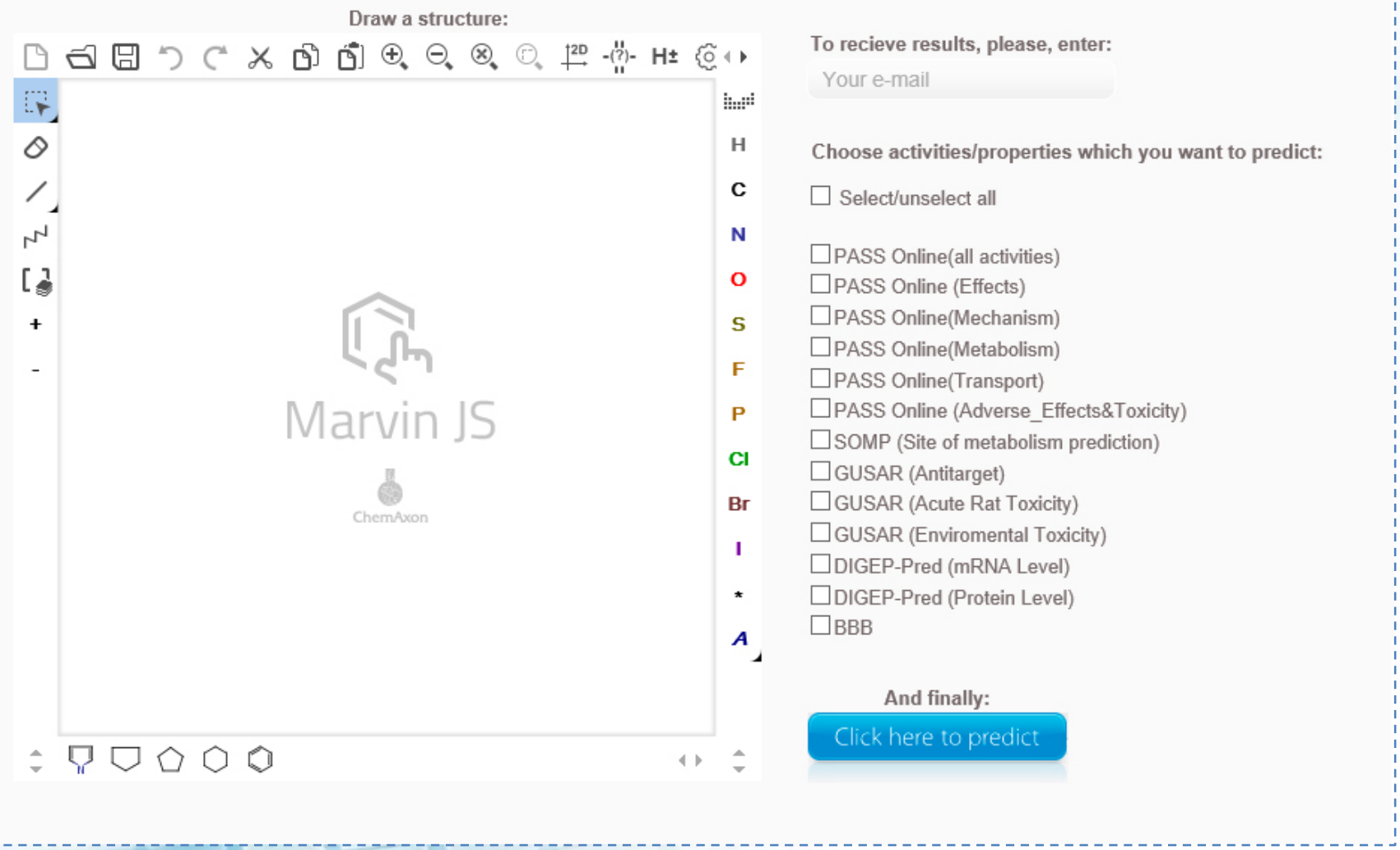
30	5	Fibroblast growth factor 4 antagonist
26	10	Potassium channel (Voltage-sensitive) blocker
24	17	Interleukin 6 antagonist
20	**8**	**5 Hydroxytryptamine 2A antagonist**
18	10	Dopamine D2 antagonist
18	11	Interleukin 5 antagonist
14	4	Meprin A inhibitor
13	5	Tumour necrosis factor alpha release inhibitor
11	1	AMP-activated protein kinase, alpha-1 subunit inhibitor
10	6	Opioid kappa receptor agonist
10	9	Dopamine D2 agonist
9	2	Histone deacetylase SIRT1 inhibitor
		. . .

PharmaExpert Search: 5 HT 2A antagonists

Pa	Pi	<substance_name>
0,892	0,003	ZIPRASIDONE
0,882	**0,003**	**Ergotamine**
0,876	0,003	MIANSERIN
0,827	**0,003**	**Dihydroergo**
0,791	0,004	Sertindole
0,765	0,004	Paliperido
0,740	0,004	RISPERIDONE
0,711	0,004	MIRTAZAPINE
0,669	**0,004**	**DROPERIDOL**
0,659	0,004	OLANZAPINE
0,632	**0,004**	**DIHYDROERGOCRISTINE**
0,607	**0,004**	**AMITRIPTYLINE**

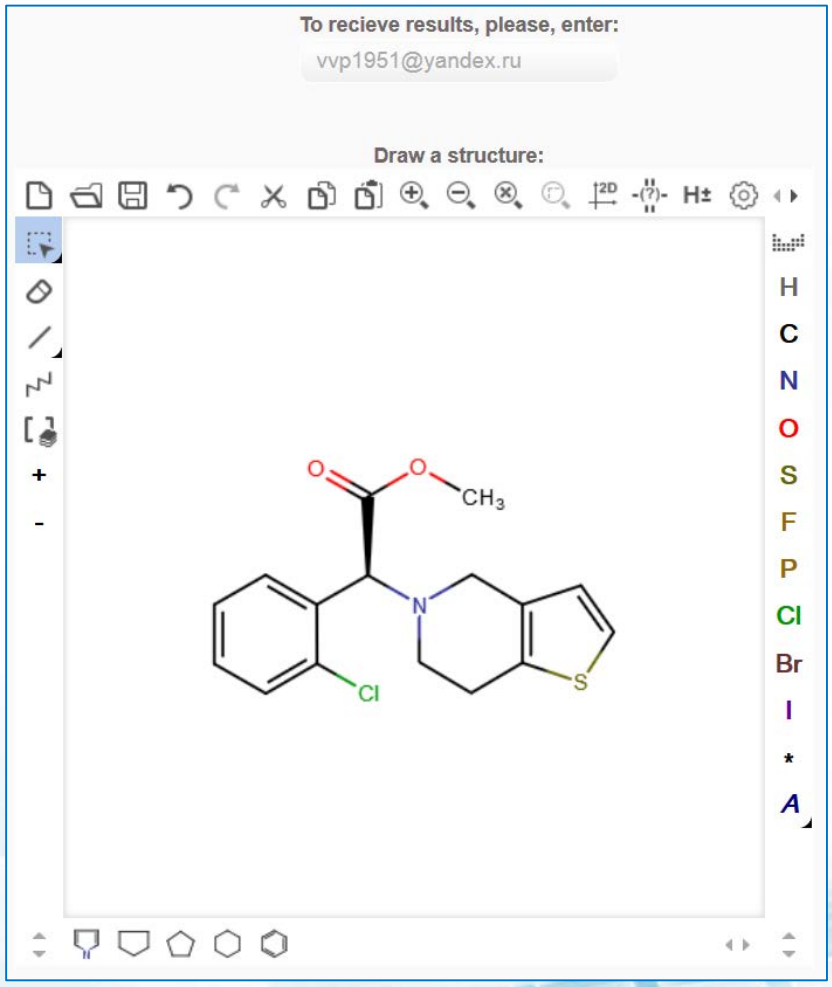


Way2Drug DRP: Selection of the desirable properties



http://www.way2drug.com/dr

Way2Drug DRP: Total predictions for Clopidogrel



Choose activities/properties which you want to predict:

- [x] Select/unselect all
- [x] PASS Online(all activities)
- [x] PASS Online (Effects)
- [x] PASS Online(Mechanism)
- [x] PASS Online(Metabolism)
- [x] PASS Online(Transport)
- [x] PASS Online (Adverse_Effects&Toxicity)
- [x] SOMP (Site of metabolism prediction)
- [x] GUSAR (Antitarget)
- [x] GUSAR (Acute Rat Toxicity)
- [x] GUSAR (Enviromental Toxicity)
- [x] DIGEP-Pred (mRNA Level)
- [x] DIGEP-Pred (Protein Level)
- [x] BBB

And finally:

Click here to predict

http://www.way2drug.com/dr

Way2Drug DRP: Prediction results for Clopidogrel

WAY2DRUG results

pass@ibmc.msk.ru pass@ibmc.msk.ru
Вам: vvp1951@yandex.ru

5 июл в 7:07

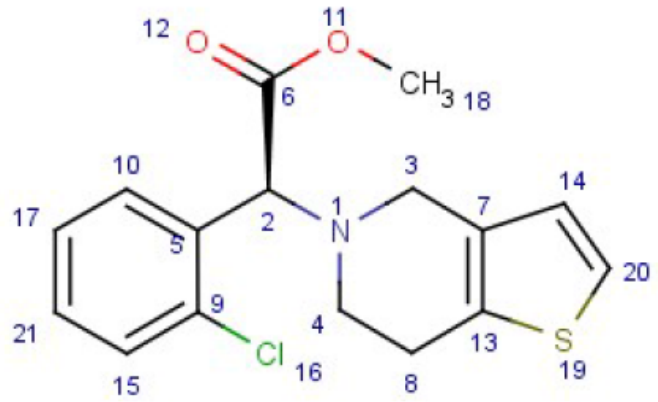
Язык письма — английский. Перевести на русский? Перевести

PASS_Online-All_Activities.pdf PDF | PASS_Online-Effects.pdf PDF | PASS_Online-Mechanism.pdf PDF | PASS_Online-Metabolism.pdf | PASS_Online-Transport.pdf | PASS_Online-Adverse_Effects

14

This is a file(s) with results from http://way2d

PASS_Online-Mechanism Web Server prediction results

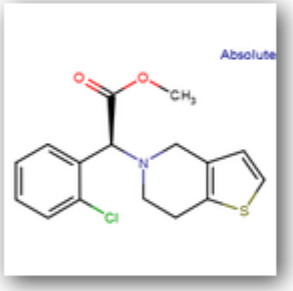


Pa	Pi	Activity
0,784	0,008	Muramoyltetrapeptide carboxypeptidase inhibitor
0,768	0,015	Anaphylatoxin receptor antagonist
0,712	0,004	Platelet aggregation inhibitor

Way2Drug DRP: Similarity search

HOME | ABOUT | SERVICES

Similarity



Cut-off value

0.4

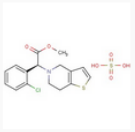
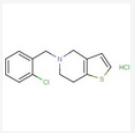
Find structures

Way2Drug DRP: Similarity search

HOME | ABOUT | SERVICES

Similarity

Show 10 entries Search:

Structure	Brand Name	Generic Name	Mechanism of Action	Pharmacotheraputic application	Similarity MNA	Similarity QNA
	Iscover Plavix	Clopidogrel bisulfate (USAN) Clopidogrel hydrogensulfate	Purinergic P2T antagonist Signal transduction modulator	Arrhythmia Stroke Disorders of hemostasis Fibrillation, atrial Peripheral arterial disease (PAD) Angina pectoris, unstable Myocardial infarction Thrombotic Disorders Atherosclerosis Thrombosis Systemic lupus erythematosus	1.000	1.000
	Aplaket Ipaton Panaldine Ticlid Ticlodix Ticlodone Tiklid Tiklyd	Ticlopidine hydrochloride (DCF; Rec INNM; BAN; USAN)	Purinergic P2T antagonist Signal transduction modulator	Stroke Coronary artery disease Thrombosis	0.609	0.518
Structure	Brand Name	Generic Name	Mechanism of Action	Pharmacotheraputic application	Similarity MNA	Similarity QNA

Way2Drug DRP: PASS Selector

PAS

Antidiabetic
Antidiabetic (type 1)
Antidiabetic (type 2)
Antidiabetic symptomatic
Antituberculosic
Kegg link
all activity

×CLOSE

◉Pa>Pi ○Pa>0,3 ○Pa>0,7

0,847	0,005	Superoxide dismutase inhibitor
0,783	0,004	Transketolase inhibitor
0,646	0,008	Erythropoiesis stimulant
0,575	0,014	APOA1 expression enhancer
0,576	0,033	Calcium channel (voltage-sensitive) activator
0,519	0,014	Caspase 8 stimulant
0,496	0,006	TRPA1 agonist
0,486	0,007	Monophenol monooxygenase inhibitor
0,453	0,036	Caspase 3 stimulant
0,412	0,006	Alcohol dehydrogenase inhibitor
0,361	0,019	Dihydroorotase inhibitor
0,337	0,007	Glutamine-tRNA ligase inhibitor
0,395	0,066	Fibroblast growth factor agonist
0,368	0,047	CF transmembrane conductance regulator

Homo sapiens(P00441)

Click to Unirpot

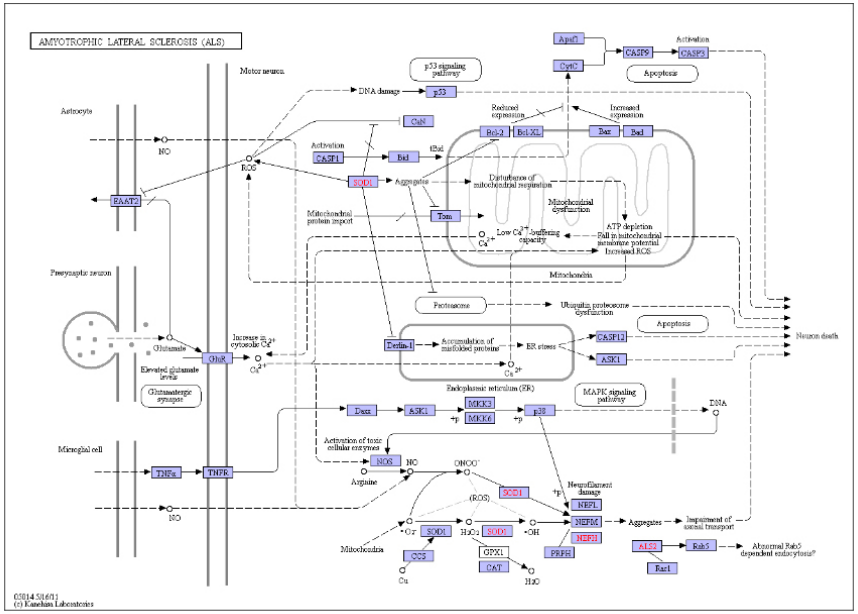
Peroxisome

Amyotrophic lateral sclerosis (ALS)

Huntington's disease

Prion diseases

Click to view kegg db



Mus musculus

Rattus norvegicus

Homo sapiens

Antidiabetic
Antidiabetic (type I)
Antidiabetic (type II)
Antidiabetic symptomatic
Antituberculosic

http://www.way2drug.com/dr

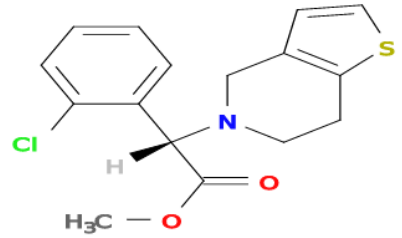
Molecule Properties Prediction from Molecular Property Diagnostic Suite

Clopidogrel

MPDS Unique ID Card

Molecular Property Diagnostic Suite

MPDS ID: 25-12-047870



Molecular Formula:
$C_{16}H_{16}ClNO_2S$

IUPAC Name:
1-[2-(5-bromo-8-hydroxyquinolin-2-yl)ethyl]pyrrolidin-1-ium

Remarks:

Remarks here...

Name/Synonyms:

Name/Synonyms here...

Molecular Properties:

Mol. Wt.	321.06	LogP	0.94
HBD	0	LogS	-4.27
HBA	3	pKa	pKa1: ; pKa2: ; pKa3: 4.77; pKa4: -7.74
Molar refractivity	43.95	Polar surface area	57.78
Heavy atoms count	21	Rings count	3.00
Rotatable bonds	6.00	Polarizability	1.78

Molecular Descriptors

Descriptor	Mol.Wt.	AlogP	XlogP	Mol. Refractivity	Pol. Surf. Area	H-Bond Donors	H-Bond Acceptors
mol1	321.059	1.542	2.732	90.777	54.84	0	3

	No. of Atoms	Rot. Bond Count	Acid Group Count	No. of Rigid Bonds	No. of Rings	Struct. Alerts	No. of Aromatic Rings
	37	4	0	19	3	1	2

Biopharmaceutics Classification System (BCS Classification)

Molecule/Descriptor	logS	XlogP	BCS Class	Solubility	Permeability
mol1	-3.675	2.732	I	High	High

BCS class	Solubility	Permeability
I	High	High
II	Low	High
III	High	Low
IV	Low	Low

Drug-likeness Prediction (DruLiTo)

Filters	Lipinski Rule	Ghose Filter	CMC Filter	Veber Filter	MDDR Like Rule	BBB-Likeness	Unweigthed QED	Weighted QED
mol1	+	+	+	+	-	+	+	+

Toxicophoric Groups

```
##############################################
#       Summary of Toxicity Filter results:     #
#       Date: Wed Jul 05 10:20:39 IST 2017      #
##############################################

Molecule 1
Structural Alert found: >_2_ester_groups (C(=O)O[C,H1].C(=O)O[C,H1].C(=O)O[C,H1])
Occurrence count: 1
```

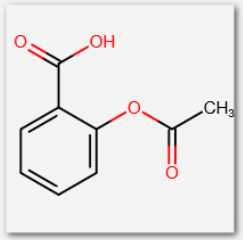
MPDS website Hosted at Centre for Molecular Modeling, CSIR-IICT, Hyderabad, India
http://mpds.osdd.net/

Way2Drug DRP: SAR Creator

SAR Creator

ADD STRUCTURE | VIEW STRUCTURES | VIEW/CREATE SDF FILES | I NEED HELP

Structure



SMILES

CC(=O)Oc1ccccc1C(=O)O

CHEMBL ID

CHEMBL25

INCHI Key

BSYNRYMUTXBXSQ-UHFFFAOYSA-N

Structure | Compound's name | Activity | Group | Save

http://www.way2drug.com/dr

Summary

- Drug repurposing is a promising way for finding new medicines.
- Chemoinformatics methods help to identify the most prospective directions of research.
- Based on the long-term projects in chemoinformatics, we are developing Way2Drug Drug Repurposing Platform.
- Further development of the DRP Platform requires integration, curation of the information, improvement of functionality, etc.
- Active cooperation between the researchers working in the field of computer-aided drug discovery will be beneficial for all parties.

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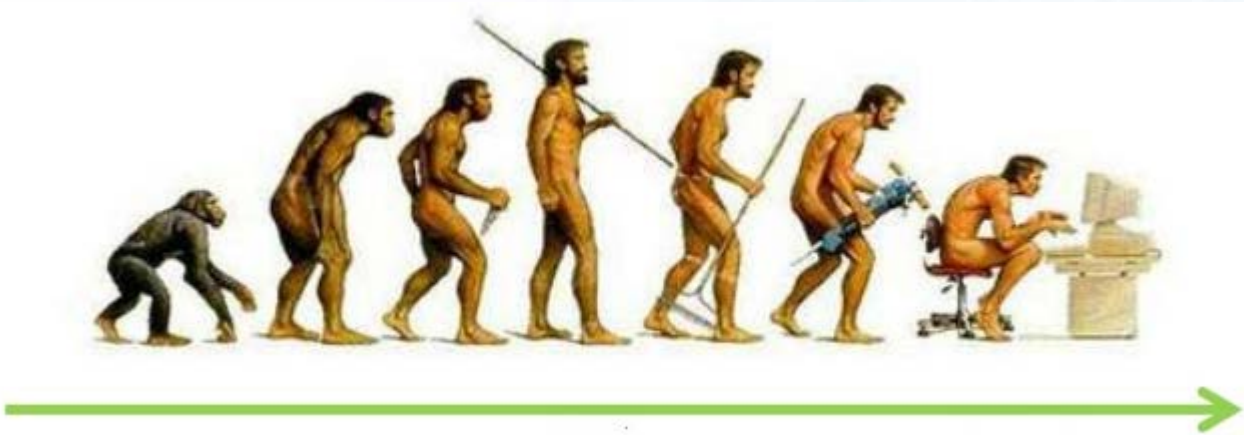
Thank you for your kind attention!



We are open for collaboration.

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vvp1951@yandex.ru