ПОДХОД К РЕПОЗИЦИОНИРОВАНИЮ ЛЕКАРСТВ, ОСНОВАННЫЙ НА СТРУКТУРЕ ЛИГАНДОВ В РАМКАХ ВЕБ-ПЛАТФОРМЫ Way2Drug

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(РНФ-DST № 16-45-02012-INT/RUS/RSF/12)

Веб платформа Way2Drug

17100
зарегистрированных пользователей

91
страна мира

630818
прогнозов

4000
видов биологической активности

12
уникальных прогностических сервиса

24/7/365
доступность из любой точки мира

Свыше **300**
опубликованных работ, выполненных с использованием нашего портала

Веб платформа Way2Drug

Мы предложили концепцию локального соответствия, согласно которой биологическая активность лекарственно-подобного органического соединения основана на молекулярном узнавании между определенными атомами лиганда и макромолекулы-мишени.

Используя эту концепцию, мы разработали систему атом-центричных дескрипторов, включая MNA (Филимонов и др., 1999), QNA (Филимонов и др., 2009), и LMNA (Рудик и др., 2014), и создали с их использованием несколько тысяч устойчивых SAR / QSAR / QSPR моделей для прогноза активности/свойств органических соединений.

Way2Drug – Drug Repositioning

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

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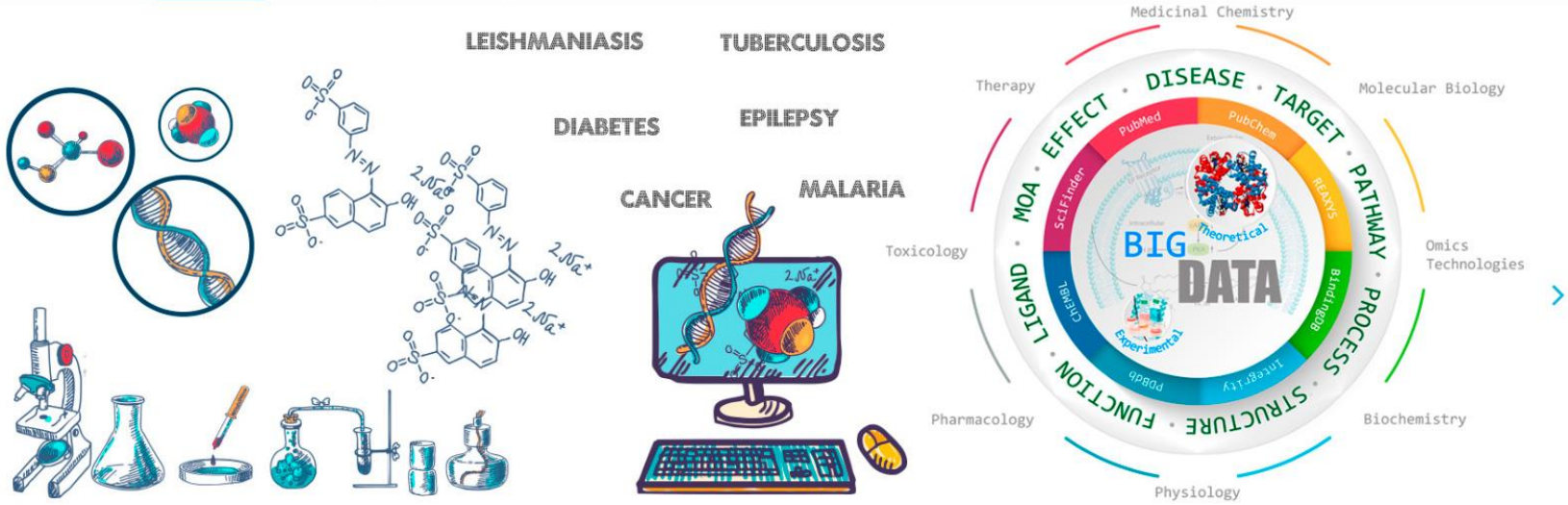

Global research

Discovery of new safe and potent medicines based on cutting-edge knowledge of a certain pathology at the molecular, cellular, tissue and organism levels, and the most

Referential ideas

Integration of the currently available biomedical and chemical data, extraction of the useful information and generation of new knowledge in the field of chemical-biological

New services

Computational predictions based on perpetually updated information, which overcome the limits of the current knowledge and allow to expand predictive functionalities of

Collaboration

Providing framework for effective interaction of researchers working in the multidisciplinary field of drug design & discovery, to combine their complementary background,

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IBMC

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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

Туберкулез | **Лейшманиоз** | **Малярия** | **Диабет** | **Злокачественные опухоли** | **Эпилепсия**

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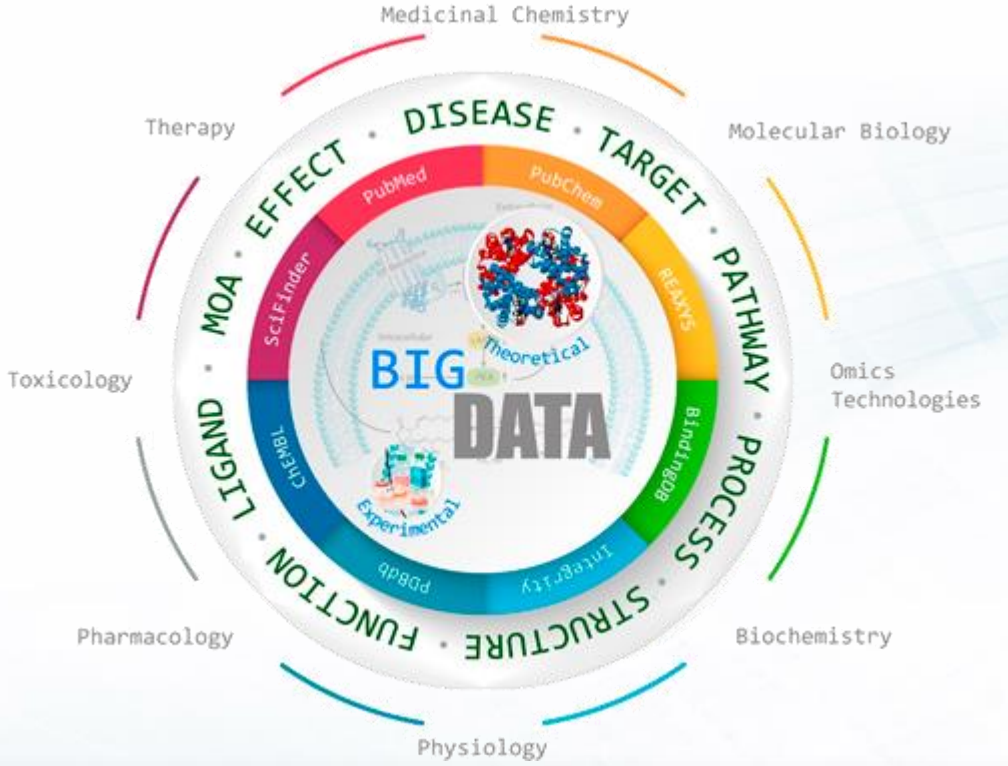

- разработка компьютерных методов поиска перспективных фармакологических мишеней и конструирования их лигандов
- интеграция разработанных методов в единую вычислительную платформу
- валидация на примерах поиска новых препаратов

Молекулярные мишени

Show 10 entries

Pharmacological Targets

Search:

Target's name	UniProt	PDB	Kegg	Pharmacotheraputic application		
				Launched	Clinical	Preclinical
1-deoxy-D-xylulose 5-phosphate reductoisomerase	Q8IKG4	PDB		Malaria	Tuberculosis	
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	Cancer	Diabetes	
4F2 cell-surface antigen heavy chain	P08195	PDB				Cancer
Target's name	**UniProt**	**PDB**	**Kegg**	**Pharmacotheraputic application**		
				Launched	**Clinical**	**Preclinical**

Showing 1 to 10 of 2,322 entries

Previous 1 2 3 4 5 ... 233 Next

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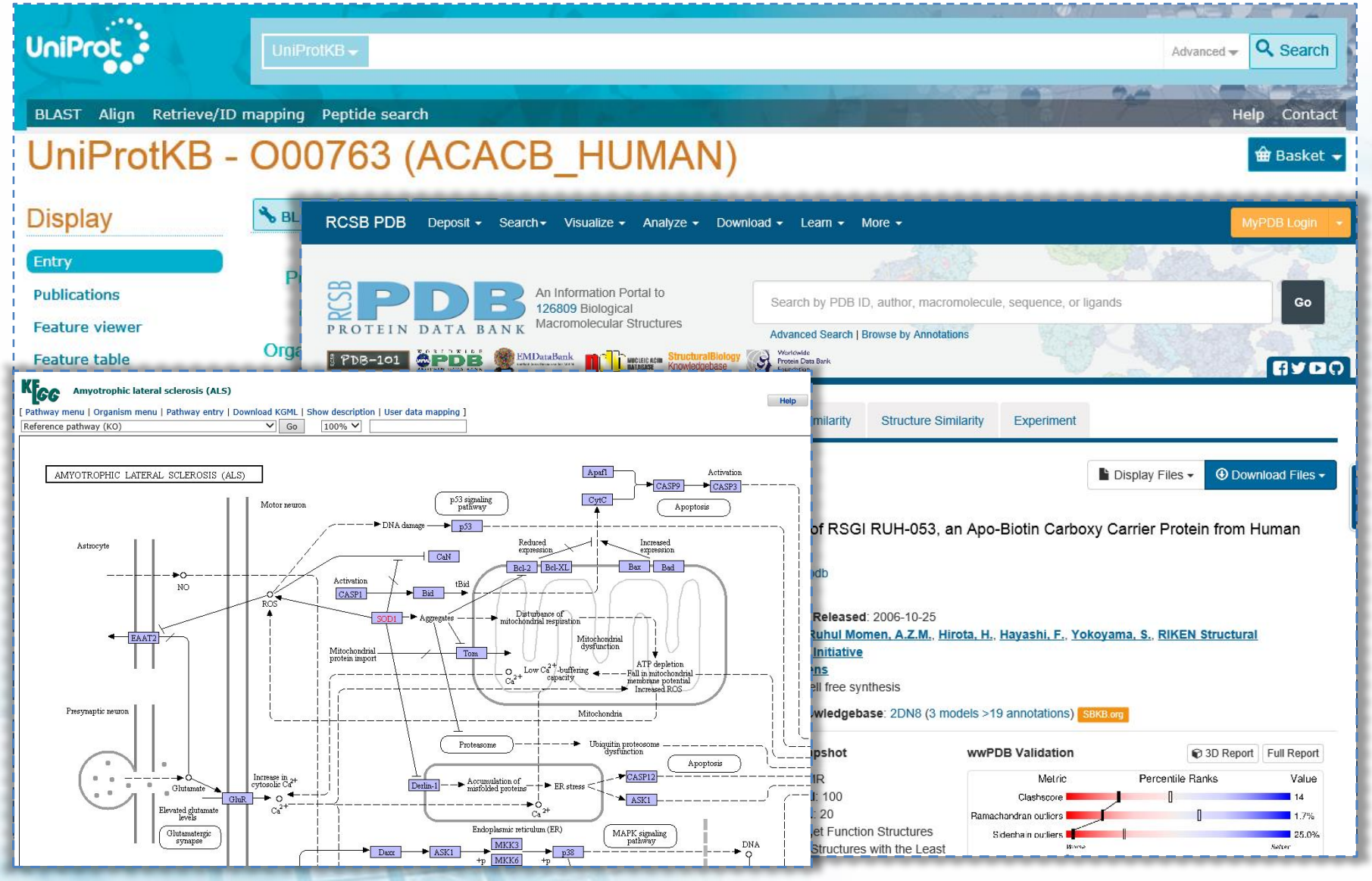
Молекулярные мишени



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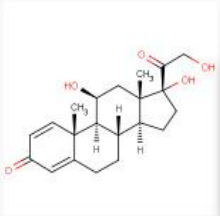
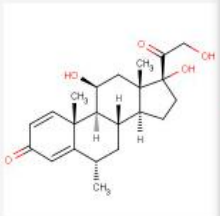
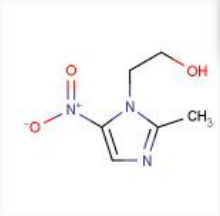
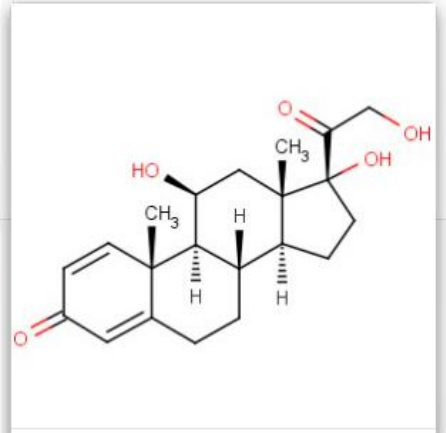
Лекарственные субстанции одобренные FDA (1035 лекарств)

Show 10 entries

FDA approved drugs

Search:

Structure	Brand Name	Generic Name	Mechanism of Action	Pharmacotheraputic application	PASSOnline prediction
	Predonine Prelone	Prednisolone	Glucocorticoid receptor agonist	Duchenne's muscular dystrophy Asthma Inflammation Lymphoma Rheumatoid arthritis Immunosuppression Ulcerative colitis Kawasaki's disease	
		Methylprednisolone	Glucocorticoid receptor agonist	Meniere's disease Asthma, allergic Leukemia, chronic	
	Rozex Zidoval	Metronidazole			



Close

PASS Online prediction for Prednisolone

Pa>0.7

Pa	Pi	Activity
0,982	0,002	CYP2C substrate
0,978	0,000	Indanol dehydrogenase inhibitor
0,975	0,001	Prostaglandin-E2 9-reductase inhibitor
0,972	0,002	CYP2C9 substrate
0,962	0,002	UDP-glucuronosyltransferase substrate
0,960	0,001	CYP3A inducer
0,959	0,000	3-Oxosteroid 1-dehydrogenase inhibitor
0,962	0,003	Antiinflammatory
0,957	0,001	CYP3A1 substrate

Злокачественные новообразования (234 препарата)

Малярия (12 препаратов)

Туберкулез (20 препаратов)

Эпилепсия (41 препарат)

Диабет (84 препарата)

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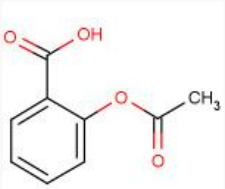
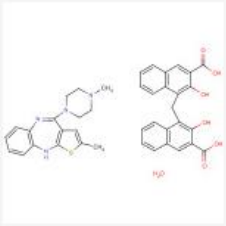
Поиск по сходству SimMNA|SimQNA

Show 10 entries

Similarity MNA & QNA

Search:

Structure	Brand Name	Generic Name	Mechanism of Action	Pharmacotheraputic application	Similarity MNA	Similarity QNA
	Asacard Aspirin Cardioaspirin Durlaza Ecotrin Nu-Seals Aspirin	Acetylsalicylic acid (BAN; USAN; JAN)	Cyclooxygenase inhibitor	Pain Stroke Polyposis coli, adenomatous Myocardial infarction Fever Hematologic Diseases Cognitive disorders Fatigue Thrombosis Ulcer, peptic Cancer, colorectal Angina pectoris, stable Cancer	1.000	1.000
	Zypadhera Zyprexa LAI Zyprexa Relprevv	Olanzapine pamoate (USAN)	Dopamine D2 antagonist Signal transduction modulator 5 Hydroxytryptamine 2A antagonist	Schizophrenia	0.417	0.692
	Metopiron Metopirone	Metyrapone (BAN; USAN; Rec INN; JAN)		Cushing's syndrome	0.231	0.549

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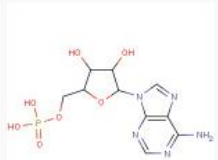
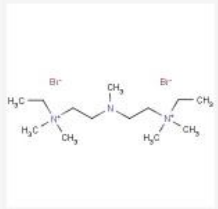
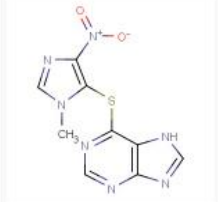
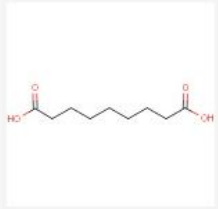
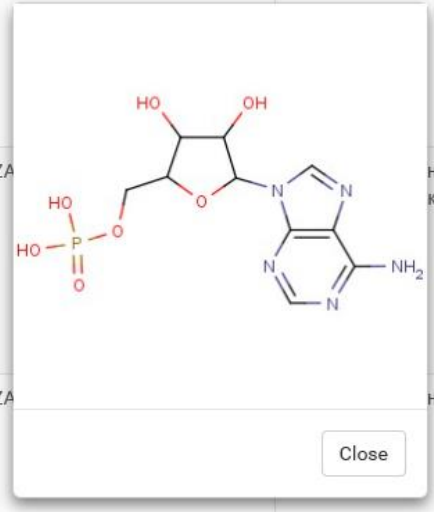
Субстанции лекарственных препаратов, зарегистрированных в РФ

Show 10 entries

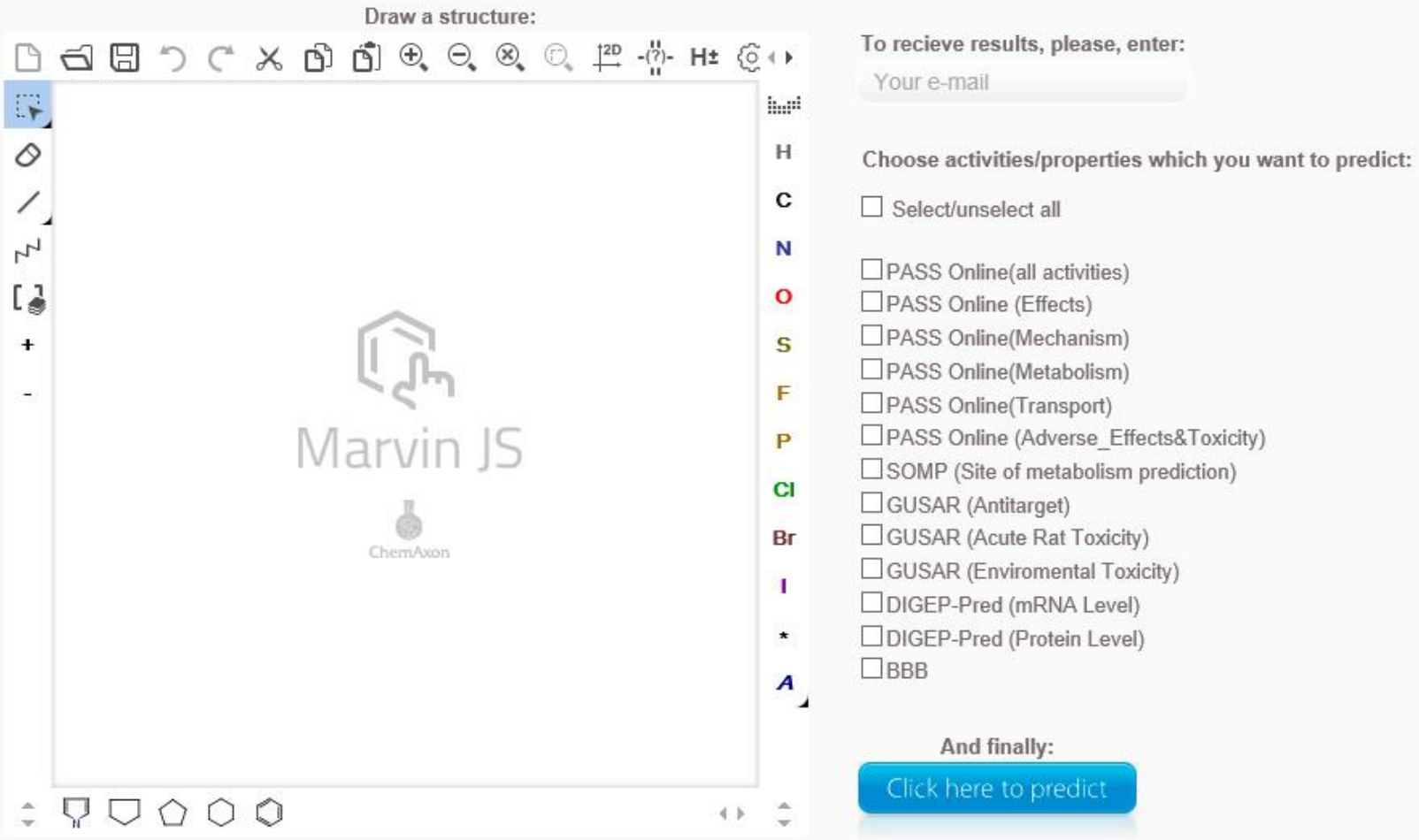
Pharmaceutical Substances Registered in Russia

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 . . .



PASS Total:
выбор прогнозируемых характеристик



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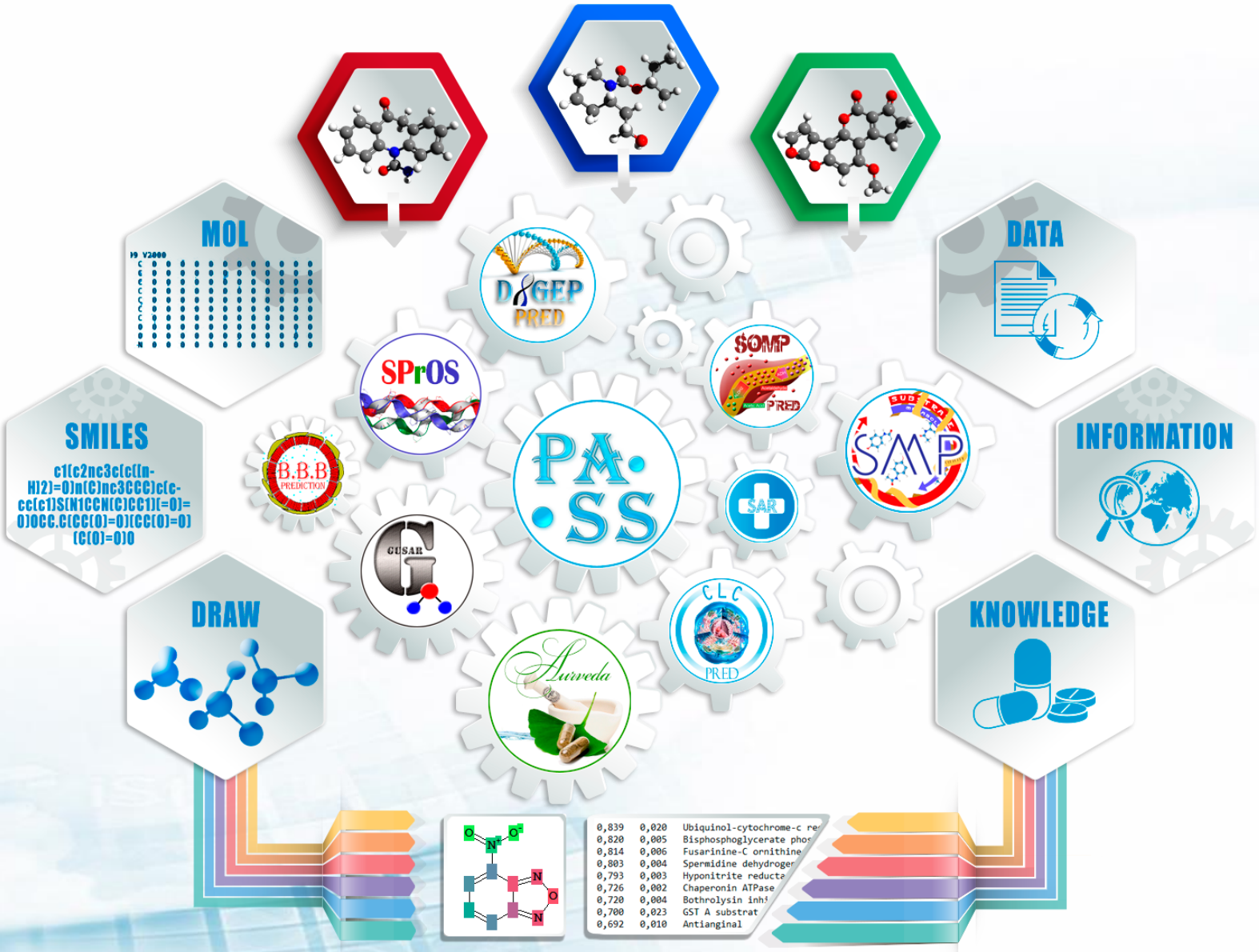
PASS Total: основные «инструменты»



PASS Selector

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

PAS

×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

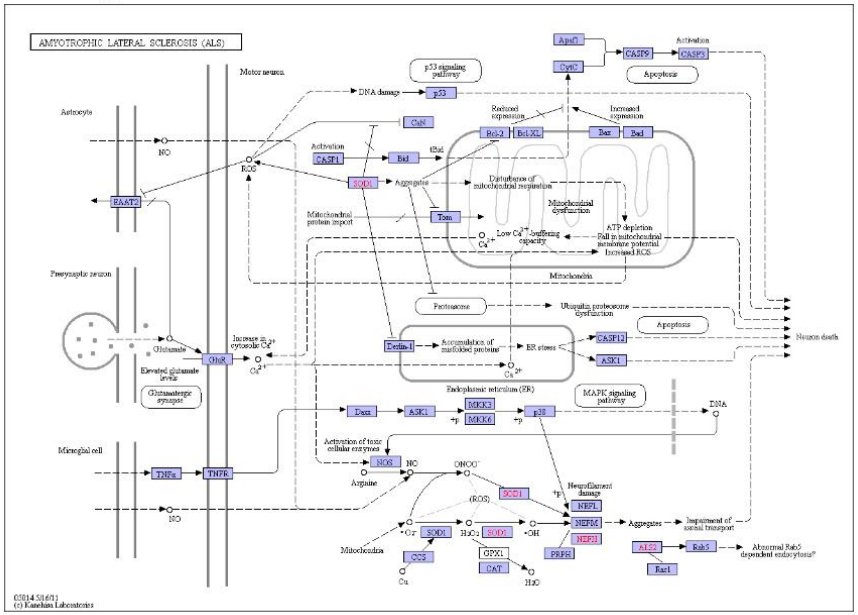
Peroxisome

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

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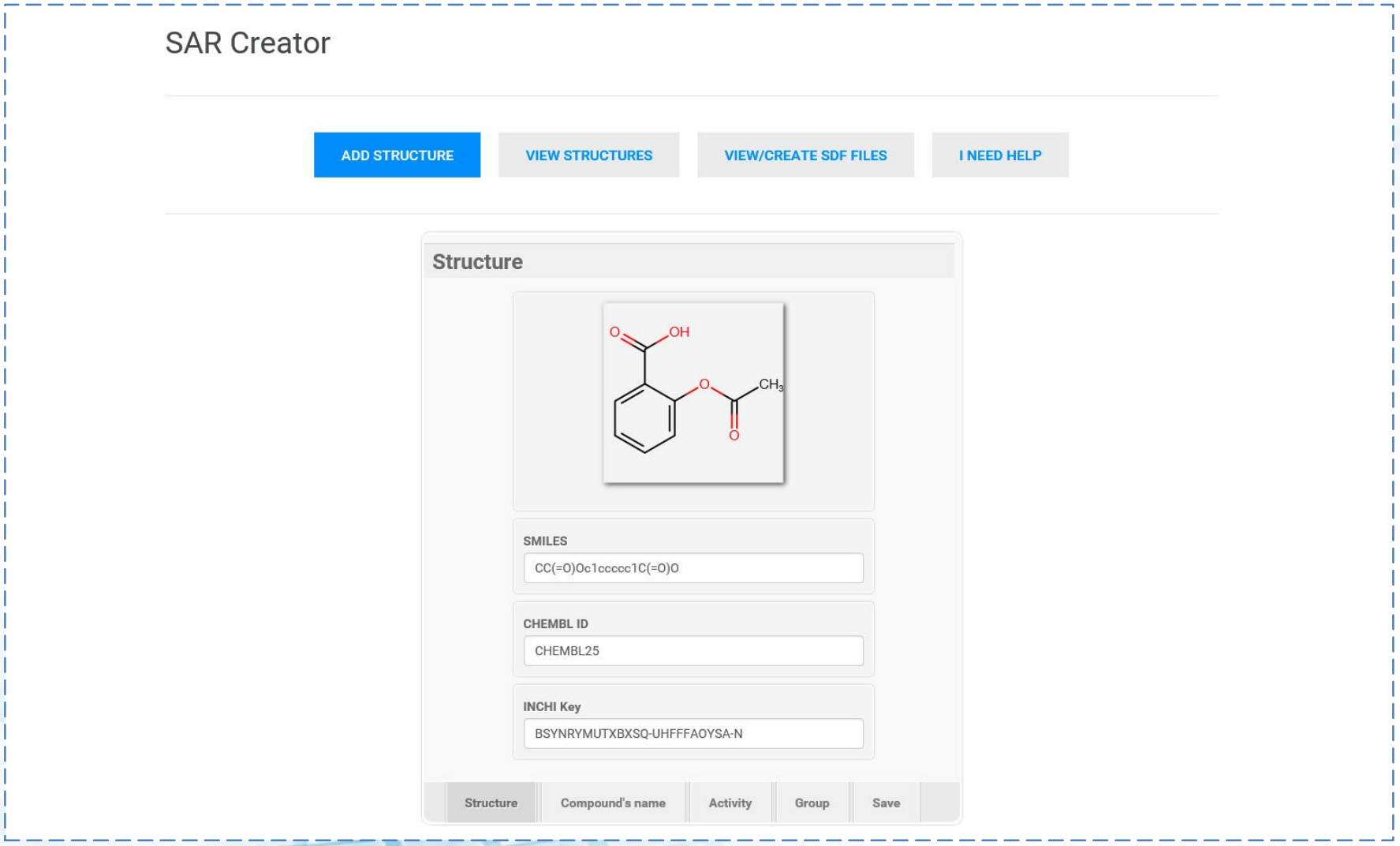
SAR Creator


SAR Creator
ADD STRUCTURE
VIEW STRUCTURES
VIEW/CREATE SDF FILES
I NEED HELP
Structure
O
OH
O
CH3
O
SMILES
CC(=O)Oc1ccccc1C(=O)O
CHEMBL ID
CHEMBL25
INCHI Key
BSYNRYMUTXBXSQ-UHFFFAOYSA-N
Structure
Compound's name
Activity
Group
Save

Резюме:

- БД по лекарственным препаратам, зарегистрированных U.S. FDA;
- база данных по более чем 1400 субстанций лекарственных препаратов, зарегистрированных в Российской Федерации;
- база знаний по лекарственным мишеням, воздействие на которые используется/изучается для терапии исследуемых заболеваний;
- гипертекстовые ссылки, обеспечивающие связи между более чем 1200 фармакологическими мишенями, с базами данных UniProt, KEGG, PDB;
- программное обеспечение SAR Creator, которое позволяет создавать online обучающие выборки для построения (Q)SAR моделей;
- разработанные нами веб сервисы обеспечивают прогноз взаимодействий с ~80% молекулярных мишеней, которые изучаются в целевой фармакотерапевтической области.

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Support by

РНФ Российский научный фонд

Спасибо за внимание!

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