Way2Drug Cheminformatics Platform for Drug Repurposing

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Disclaimer. This document provides an outline of a presentation and is incomplete without the accompanying oral commentary and discussion.
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 reprefiling.”

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
A New Journal for the Drug Repurposing Community

Hermann A.M. Muecke, 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
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.
Web of Science statistics on drug repurposing (01.07.2017)

- Drug repurposing
  - OR
  - Drug repositioning
  - OR
  - Drug reformulating
  - OR
  - Drug redirecting
DRP: Time/Cost/Risk values

- **NCEs**
  - 10-12 years
  - $1-2 Bln
  - 0.1-1% success

- **Repurposing**
  - 1-2 years
  - $2-10 mln
  - 25+% success

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DRP: How it happens?

1. Identify new drug-target interactions, e.g.: Methotrexate
2. Observe unexpected side effects, e.g.: Sildenafil
3. Find new disease pathways
4. Define new role of existing targets, e.g.: Finasteride
5. Identify compounds that modulate specific disease phenotypes
6. Serendipity, and text mining, e.g.: Thalidomide
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

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)

Predicts (ideally) all known activities

Prediction on the basis of structural formulae (MOL or SDF)

Possibility of training with new data

User-friendly interface

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

PASS Training Set

MNA Descriptors

Training procedure

New Molecule

SAR knowledgebase

Bayesian algorithm

Prediction Results
Example of prediction for Clopidogrel

45 of 464 Possible Pharmacological Effects at Pa > Pi

0.951 0.004 Neutropenic
0.889 0.005 Acute neurologic disorders treatment

0.723 0.006 Antithrombotic

0.712 0.004 Platelet aggregation inhibitor
0.618 0.013 Antiangiogenic
0.593 0.013 Atherosclerosis treatment
0.463 0.046 Analgesic
0.385 0.003 Platelet antagonist
0.361 0.027 Stroke treatment
0.352 0.026 Angiogenesis stimulant
0.332 0.017 Anticoagulant
0.366 0.003 Diabetic neuropathy treatment
0.292 0.013 Analgesic, opiod
0.324 0.043 Antiinflammatory, ophthalmic
0.341 0.116 Spasmolytic, urinary
0.290 0.102 Cell adhesion molecule inhibitor
0.301 0.135 Neurodegenerative diseases treatment
0.261 0.396 Antiinflammatory
0.167 0.005 Acetylcholine release stimulant
0.228 0.104 Amyotrophic lateral sclerosis treatment
0.202 0.075 Pancreatic disorders treatment
0.375 0.254 Vasodilator, cerebral
0.176 0.056 Lipoprotein disorders treatment
0.156 0.047 Diabetic neuropathy treatment
0.257 0.150 Psychotropic

42 Substructure Descriptors: 0 new.

246 of 6400 Possible Activities
45 of 464 Possible Pharmacological Effects
79 of 3850 Possible Mechanisms of Action
106 of 321 Possible Toxic and Adverse Effects
5 of 118 Possible Antitargets
12 of 195 Possible Metabolism-Related Actions
17 of 1610 Possible Gene Expression Regulation
4 of 66 Possible Transporters-Related Actions
### Clopidogrel: predicted vs. known activities

<table>
<thead>
<tr>
<th>Abdominal pain</th>
<th>Conjunctivitis</th>
<th>Henoch-Schonlein purpura</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute neurologic disorders treatment</td>
<td>Consciousness alteration</td>
<td>Hepatic failure</td>
</tr>
<tr>
<td>Agranulocytosis</td>
<td>Constipation</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>Cough</td>
<td>Hepatotoxic</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>CYP2 substrate</td>
<td>Hypertensive</td>
</tr>
<tr>
<td>Anemia</td>
<td>CYP2C substrate</td>
<td>Hyperthermic</td>
</tr>
<tr>
<td>Angioedema</td>
<td>CYP2C19 inhibitor</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Angiogenesis inhibitor</td>
<td>CYP2C19 substrate</td>
<td>Infection</td>
</tr>
<tr>
<td>Antianginal</td>
<td>CYP2C9 inhibitor</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Antiarthritic</td>
<td>CYP3A substrate</td>
<td>Lassitude</td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>CYP3A4 substrate</td>
<td>Leukopenia</td>
</tr>
<tr>
<td>Antineoplastic</td>
<td>Cytochrome P450 inhibitor</td>
<td>Lichen planus</td>
</tr>
<tr>
<td>Antipsoriatic</td>
<td>Dermatitis</td>
<td>Lichenoid eruption</td>
</tr>
<tr>
<td>Antithrombotic</td>
<td>Dermatologic</td>
<td>Malaise</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>Dizziness</td>
<td>Menstruation disturbance</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Drug eruption</td>
<td>Myalgia</td>
</tr>
<tr>
<td>Artherosclerosis treatment</td>
<td>Dyspepsia</td>
<td>Nausea</td>
</tr>
<tr>
<td>Back pain</td>
<td>Emetic</td>
<td>Necrosis</td>
</tr>
<tr>
<td>Behavioral disturbance</td>
<td>Eosinophilia</td>
<td>Nephrotic</td>
</tr>
<tr>
<td>Blindness</td>
<td>Erythema</td>
<td>Neuroprotect</td>
</tr>
<tr>
<td>Bronchoconstrictor</td>
<td>Erythema multiforme</td>
<td>Neutropenia</td>
</tr>
<tr>
<td>Cardiotoxic</td>
<td>Exanthema</td>
<td>Ocular toxicity</td>
</tr>
<tr>
<td>Cataract</td>
<td>Flatulence</td>
<td>Pain</td>
</tr>
<tr>
<td>CCL4 expression enhancer</td>
<td>GP IIb/IIIa receptor antagonist</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>CCL5 expression enhancer</td>
<td>Hallucinogen</td>
<td>Pancytopenia</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Headache</td>
<td>Platelet aggregation inhibitor</td>
</tr>
<tr>
<td>Colic</td>
<td>Heart failure</td>
<td>Platelet antagonist</td>
</tr>
<tr>
<td>Colitis</td>
<td>Hematotoxic</td>
<td>Pruritus</td>
</tr>
<tr>
<td></td>
<td>Hemorrhage</td>
<td>Pulmonary embolism</td>
</tr>
</tbody>
</table>

**Blue** – predictions coincided with the experiment.

**Black** – unpredictable activities.

**Red** – unpredicted activities.
PharmaExpert: Search for multitargeted antineoplastic agents
GUSAR: General Unrestricted Structure-Activity Relationships

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


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 I 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.
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)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sertraline</td>
<td>Cocain dependency treatment</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>Antineoplastic enhancer (moderate BCRP/ABCG2 inhibitor)</td>
</tr>
<tr>
<td>Oxaprozin</td>
<td>Interleukin 1 antagonist (Inhibitor of production of Interleukin 1β)</td>
</tr>
<tr>
<td>Ramipril</td>
<td>Antiarthritic</td>
</tr>
</tbody>
</table>

Ref.
Nootropic effect in some antihypertensive drugs?

<table>
<thead>
<tr>
<th>Name</th>
<th>Pa (Nootropic effect), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>44.6</td>
</tr>
<tr>
<td>Enalapril</td>
<td>65.5</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>61.8</td>
</tr>
<tr>
<td>Perindopril</td>
<td>60.9</td>
</tr>
<tr>
<td>Quinapril</td>
<td>65.1</td>
</tr>
<tr>
<td>Ramipril</td>
<td>63.3</td>
</tr>
<tr>
<td>Monopril</td>
<td>30.9</td>
</tr>
<tr>
<td>Piracetam</td>
<td>81.7</td>
</tr>
<tr>
<td>Amlodipin</td>
<td>-</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>-</td>
</tr>
</tbody>
</table>

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).

“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 bioactivities of more than 270,000 compound-ligand pairs.”

Way2Drug web platform
Way2Drug available online

- India
- Russia
- Ukraine
- Mexico
- China
- United States
- Egypt
- Kazakhstan
- Brazil
- Other

- Cross-browser and cross-platform support
- 630,818 molecules
- Users relationships
- 91 countries
- 17,100 users
- Free availability 24/7/365
- Authorization/privacy
Over 300 papers published citing our web-services
(>50% with the experimental confirmation)
Way2Drug Drug Repurposing Platform

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

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

http://www.way2drug.com/dr

Supported by the RSF-DST grant (project No. 16-45-02012 - INT/RUS/RSF/12)
Way2Drug DRP: Login

http://www.way2drug.com/dr
**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.

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**DIABETES**

- **422 MILLION adults have diabetes.**
- **3.7 MILLION deaths due to diabetes and high blood glucose.**
- **1.5 MILLION deaths caused by diabetes.**

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**Epilepsy**

- **65 MILLION people worldwide currently live with epilepsy.**
- **200,000 people per year are newly diagnosed with epilepsy.**

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**TUBERCULOSIS (TB) FACTS**

- TB is a serious disease. It can infect many body parts, but is most common in the lungs.
- **1,500,000 people** died from the disease*.

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

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**MALARIA FACTS**

Malaria is a serious disease that is PREVENTABLE and TREATABLE. There are **97 countries and territories** had ongoing malaria transmission in 2015. Every 2 minutes, a child dies from malaria in Sub-Saharan Africa.

**9,000,000** people fell ill with TB.

The disease accounts for 7.4 million deaths worldwide. It’s the leading cause of death worldwide, causing around 13% of all deaths worldwide.

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**Cancer Facts**

- **97 countries and territories** had ongoing malaria transmission in 2015.
- Every 2 minutes, a child dies from malaria in Sub-Saharan Africa.

**9,000,000** people fell ill with TB.

**9,000,000** people worldwide currently live with epilepsy.

- **200,000 people per year are newly diagnosed with epilepsy.**

---

**Way2Drug DRP: Pharmacotherapeutic Areas**

- **Orphan diseases**
- **Diabetes**
- **Epilepsy**

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**RAW TEXT END**
Way2Drug DRP: Databases

http://www.way2drug.com/dr
## Way2Drug DRP: Molecular targets

### Pharmacological Targets

<table>
<thead>
<tr>
<th>Target's name</th>
<th>UniProt</th>
<th>PDB</th>
<th>Kegg</th>
<th>Pharmacotherapeutic application</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-deoxy-D-xylulose 5-phosphate reductoisomerase</td>
<td>Q8IKG4</td>
<td></td>
<td></td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase gamma-1</td>
<td>P19174</td>
<td></td>
<td></td>
<td>Malaria</td>
</tr>
<tr>
<td>11beta-Hydroxysteroid Dehydrogenase (nonspecific subtype)</td>
<td>P24385</td>
<td></td>
<td></td>
<td>Cancer</td>
</tr>
<tr>
<td>14-3-3 protein epsilon</td>
<td>P62258</td>
<td></td>
<td></td>
<td>Diabetes</td>
</tr>
<tr>
<td>15-hydroxyprostaglandin dehydrogenase (NAD+) (isoform 1)</td>
<td>P15428</td>
<td></td>
<td></td>
<td>Cancer</td>
</tr>
<tr>
<td>17beta-Hydroxysteroid dehydrogenase (nonspecific subtype)</td>
<td>P24864</td>
<td></td>
<td></td>
<td>Cancer</td>
</tr>
<tr>
<td>2-amino-3-carboxymuconate-6-semialdehyde</td>
<td>Q8TDX5</td>
<td></td>
<td></td>
<td>Diabetes</td>
</tr>
<tr>
<td>3-oxoacetyl-(acyl-carrier protein) reductase</td>
<td>Q8I257</td>
<td></td>
<td></td>
<td>Cancer</td>
</tr>
<tr>
<td>2-phosphoinositide-dependent protein kinase 1 (isoform 1)</td>
<td>O15530</td>
<td></td>
<td></td>
<td>Leishmaniasis</td>
</tr>
<tr>
<td>3-phosphoinositide-dependent protein kinase 1 (isoform 1)</td>
<td></td>
<td></td>
<td></td>
<td>Malaria</td>
</tr>
<tr>
<td>4F2 cell-surface antigen heavy chain</td>
<td>P08195</td>
<td></td>
<td></td>
<td>Cancer</td>
</tr>
</tbody>
</table>

Showing 1 to 10 of 2,322 entries
Molecular targets: Links to the external resources

http://www.way2drug.com/dr
Way2Drug DRP: FDA Approved Drug Substances

FDA approved drugs

<table>
<thead>
<tr>
<th>Structure</th>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Mechanism of Action</th>
<th>Pharmacotherapeutic application</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Structure" /></td>
<td>Adenuric Febucic Febucic Uloric</td>
<td>Febuxostat (USAN; Rec INN)</td>
<td>Xanthine Oxidase Inhibitors</td>
<td>Gout; Hyperuricosuria; Cancer therapy associated disorders; Angina pectoris, stable Hematologic-blood cancer</td>
</tr>
<tr>
<td><img src="image2.png" alt="Structure" /></td>
<td>Edecrin Hydemedine</td>
<td>Aminopyrine (Rec INN; JAN)</td>
<td>Wnt Signaling Inhibitors</td>
<td>Hypertension</td>
</tr>
<tr>
<td><img src="image3.png" alt="Structure" /></td>
<td>Potiga Trobalt</td>
<td>Gabapentin (USAN) Retigabine (Prop USAN)</td>
<td>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</td>
<td>Epilepsy; Lennox-Gastaut syndrome; Neuralgia, postherpetic (PHN); Amyotrophic lateral sclerosis; Epilepsy, partial seizures</td>
</tr>
</tbody>
</table>

Neoplastic disorders (234 drugs)  
Malaria (12 drugs)  
Tuberculosis (20 drugs)  
Epilepsy (41 drugs)  
Diabetes (84 drugs)
Way2Drug DRP: Search for Clopidogrel

A Knowledge Based Approach to Drug Repurposing for Socially Important and Rare Diseases
RSF - DST Project # 16-45-02012 - INT/RUS/RSF/12

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.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Mechanism of Action</th>
<th>Pharmacotherapeutic application</th>
<th>PASSOnline prediction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Iscover Plavix</td>
<td>Clopidogrel bisulfate (USAN)</td>
<td>Purinergic P2T antagonist</td>
<td>Arrhythmia</td>
<td>Stroke</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clopidogrel hydrogensulfate</td>
<td>Signal transduction modulator</td>
<td>Disorders of hemostasis</td>
<td>Fibrillation, atrial</td>
</tr>
</tbody>
</table>
Way2Drug DRP: PASS Prediction for Clopidogrel Bisulfate

<table>
<thead>
<tr>
<th>Structure</th>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Mechanism of Action</th>
<th>Pharmacotherapeutic application</th>
<th>PASSOnline prediction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Iscover Plavix</td>
<td>Clopidogrel bisulfate (USAN)</td>
<td>Purinergic P2Y12 antagonist</td>
<td>Arrhythmia</td>
<td>PASS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clopidogrel hydrogensulfate</td>
<td></td>
<td>Stroke</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Components: 2

Atherosclerosis
Thrombosis
Systemic lupus
erythematosus
Angina pectoris, stable
Acute coronary syndrome

http://www.way2drug.com/dr
### Way2Drug DRP: Drug Substances Registered in Russia

#### Pharmaceutical Substances Registered in Russia

<table>
<thead>
<tr>
<th>Structure</th>
<th>Trade name</th>
<th>Substance name</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Structure" /></td>
<td>Фосфаден</td>
<td>ADENOSINE PHOSPHATE</td>
<td>Торговое название: Фосфаден Международное название: Аденозин фосфат Страна: Россия. дата актуализации: 17.05.1999 (РПС)</td>
</tr>
<tr>
<td><img src="image2.png" alt="Structure" /></td>
<td>Пентамин</td>
<td>AZA-TEMATON-BROMID</td>
<td>Торговое название: Пентамин Международное название: Азаметония бромид Страна: Россия. В нескольких препаратах, несколько дат регистрации.</td>
</tr>
<tr>
<td><img src="image3.png" alt="Structure" /></td>
<td>Азатиоприн</td>
<td>AZAN</td>
<td>Торговое название: Азатиоприн Международное название: Азатиоприн Страна: Россия</td>
</tr>
<tr>
<td><img src="image4.png" alt="Structure" /></td>
<td>СКИНОРЕН</td>
<td>AZELAIC ACID</td>
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</tbody>
</table>

New opportunities for drug repurposing?

MINISTRY OF
PRODUCTION
AND
TRADE
OF THE
RUSSIAN
FEDERATION
(Minpromtorg Rossii)

19 May 2016

MINISTRY OF
HEALTH
OF THE
RUSSIAN
FEDERATION
(Minszdrav Rossii)

ПРИКАЗ

Ob 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),

предназначаем:

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

Министра здравоохранения Российской Федерации

В.И. Скворцова
Partial statistics of PASS predictions

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<th>Pa&gt;70%</th>
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<td>73</td>
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<tr>
<td>89</td>
<td>31</td>
<td>Meprin B inhibitor</td>
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<tr>
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<td>55</td>
<td>37</td>
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<tr>
<td>45</td>
<td>23</td>
<td>Phenylalanine 4-hydroxylase inhibitor</td>
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<td>22</td>
<td>Progesterone agonist</td>
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<tr>
<td>32</td>
<td>10</td>
<td>Fibroblast growth factor 1 agonist</td>
</tr>
<tr>
<td>30</td>
<td>5</td>
<td>Fibroblast growth factor 4 antagonist</td>
</tr>
<tr>
<td>26</td>
<td>10</td>
<td>Potassium channel (Voltage-sensitive) blocker</td>
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<tr>
<td>24</td>
<td>17</td>
<td>Interleukin 6 antagonist</td>
</tr>
<tr>
<td>20</td>
<td>8</td>
<td>5 Hydroxytryptamine 2A antagonist</td>
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<td>Dopamine D2 antagonist</td>
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<td>18</td>
<td>11</td>
<td>Interleukin 5 antagonist</td>
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<td>5</td>
<td>Tumour necrosis factor alpha release inhibitor</td>
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<tr>
<td>11</td>
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<td>AMP-activated protein kinase, alpha-1 subunit inhibitor</td>
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<tr>
<td>10</td>
<td>6</td>
<td>Opioid kappa receptor agonist</td>
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<td>10</td>
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<td>Dopamine D2 agonant</td>
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<tr>
<td>9</td>
<td>2</td>
<td>Histone deacetylase SIRT1 inhibitor</td>
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<td>2</td>
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</table>

**Pa** and **Pi** are parameters used in the PharmaExpert Search tool to evaluate the affinity of compounds towards 5-HT2A receptors.
Way2Drug DRP: Selection of the desirable properties

Draw a structure:

To receive results, please, enter:
Your e-mail

Choose activities/properties which you want to predict:
- Select/unselect all
- PASS Online (all activities)
- PASS Online (Effects)
- PASS Online (Mechanism)
- PASS Online (Metabolism)
- PASS Online (Transport)
- PASS Online (Adverse Effects & Toxicity)
- SOMP (Site of metabolism prediction)
- GUSAR (Antitarget)
- GUSAR (Acute Rat Toxicity)
- GUSAR (Environmental Toxicity)
- DIGEP-Pred (mRNA Level)
- DIGEP-Pred (Protein Level)
- BBB

And finally:
Click here to predict

http://www.way2drug.com/dr
Way2Drug DRP: Total predictions for Clopidogrel

To receive results, please, enter:

vvp1951@yandex.ru

Choose activities/properties which you want to predict:

- Select/unselect all
- PASS Online (all activities)
- PASS Online (Effects)
- PASS Online (Mechanism)
- PASS Online (Metabolism)
- PASS Online (Transport)
- PASS Online (Adverse Effects & Toxicity)
- SOMP (Site of metabolism prediction)
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- DIGEP-Pred (Protein Level)
- 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:  vyp1951@yandex.ru

Язык письма — английский. Перевести на русский?  Перевести

PASS Online-All_Activities.pdf  PASS Online-Effects.pdf  PASS Online-Mechanism.pdf  PASS Online-Metabolism.pdf  PASS Online-Transport.pdf  PASS Online-Adverse_Effects

This is a file(s) with results from http://way2drug.com
Way2Drug DRP: Similarity search

Similarity

Cut-off value
0.4
Find structures
### Similarity

<table>
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<tr>
<th>Structure</th>
<th>Brand Name</th>
<th>Generic Name</th>
<th>Mechanism of Action</th>
<th>Pharmacotherapeutic application</th>
<th>Similarity MNA</th>
<th>Similarity QNA</th>
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<tbody>
<tr>
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<td>Iscover Plavix</td>
<td>Clopidogrel bisulfate (USAN) Clopidogrel hydrogensulfate</td>
<td>Purinergic P2T antagonist Signal transduction modulator</td>
<td>Arrhythmia Stroke Disorders of hemostasis Fibrillation, atrial Peripheral arterial disease (PAD) Angina pectoris, unstable Myocardial infarction Thrombotic Disorders Atherosclerosis Thrombosis Systemic lupus erythematosus</td>
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<td>1.000</td>
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<td>Aplaketa Ipaton Panaldine Ticlid Ticlodix Ticlodone Tiklid Tiklyd</td>
<td>Ticlopidine hydrochloride (DCF; Rec INNM; BAN; USAN)</td>
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<td>Stroke Coronary artery disease Thrombosis</td>
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Molecule Properties Prediction from Molecular Property Diagnostic Suite

**Clopidogrel**

**MPDS Unique ID Card**

**Molecular Descriptors**

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<th>Acid Group Count</th>
<th>No. of Rigid Bonds</th>
<th>No. of Rings</th>
<th>Struct. Alerts</th>
<th>No. of Aromatic Rings</th>
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**Biopharmaceutics Classification System (BCS Classification)**

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<tr>
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<th>XlogP</th>
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<th>Permeability</th>
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<td>2.732</td>
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</tbody>
</table>

**Drug-likeness Prediction (DruLiTo)**

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<tr>
<th>Filters</th>
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<th>Ghose Filter</th>
<th>CMC Filter</th>
<th>Veber Filter</th>
<th>MDDR Like Rule</th>
<th>BBB-Likeness</th>
<th>Unweighed QED</th>
<th>Weighted QED</th>
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<tbody>
<tr>
<td>mol1</td>
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<td>+</td>
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<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

**Toxicophoric Groups**

# Summary of Toxicity Filter results: #
# Date: Wed Jul 05 10:29:39 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

Structure

![Chemical Structure Image]

**SMILES**

CC(=O)Oc1ccccccc1C(=O)O

**CHEMBL ID**

CHEMBL25

**INCHI Key**

BSYNYMUTXBSQ-UHFFFAOYSA-N

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.
# Acknowledgements

**Institute of Biomedical Chemistry**
- Dmitry Druzhilovskiy, Ph.D.
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- Tatyana Gariozova
- Alexander Dmitriev, Ph.D.
- Varvara Dubovskaja, Ph.D.
- Sergey Ivanov, Ph.D.
- Olga Tarasova, Ph.D.
- Pavel Pogodin, Ph.D. Student
- Khalimat Murtazalieva, Student
- Vladislav Bezhentsev, Student
- Maxim Semin, Student

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- B. Venkateswara Rao, Ph.D.
- Sridhara Janahardan, Ph.D.
- Karunakar Tanneeru, Ph.D.
- S. Nagamani, Ph.D.
- Anamika Singh Gaur, Ph.D. Student

**Punjabi University**
- Rajesh Kumar Goel, Ph.D.
- Sandeep Kumar, Student

**Osmania Medical College & Osmania General Hospital**
- Rakesh Sahay, M.D
- Manisha Sahay, M.D.
Thank you for your kind attention!

We are open for collaboration.

Questions and suggestions:
vladimir.poroikov@ibmc.msk.ru
vvp1951@yandex.ru