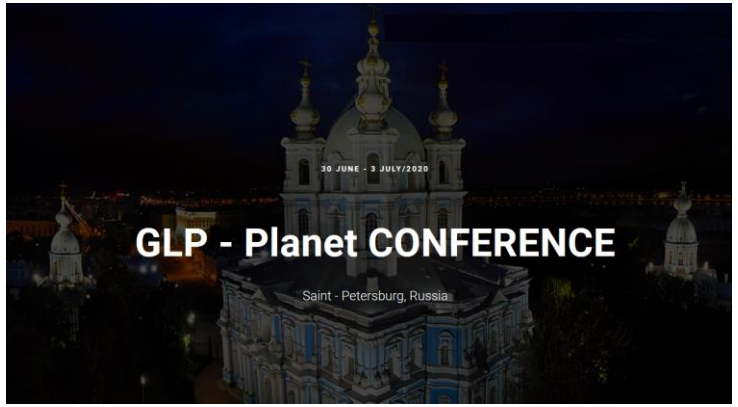
Computer-aided predictions in drug research and development

Vladimir Poroikov, Prof. Dr.

Institute of Biomedical Chemistry

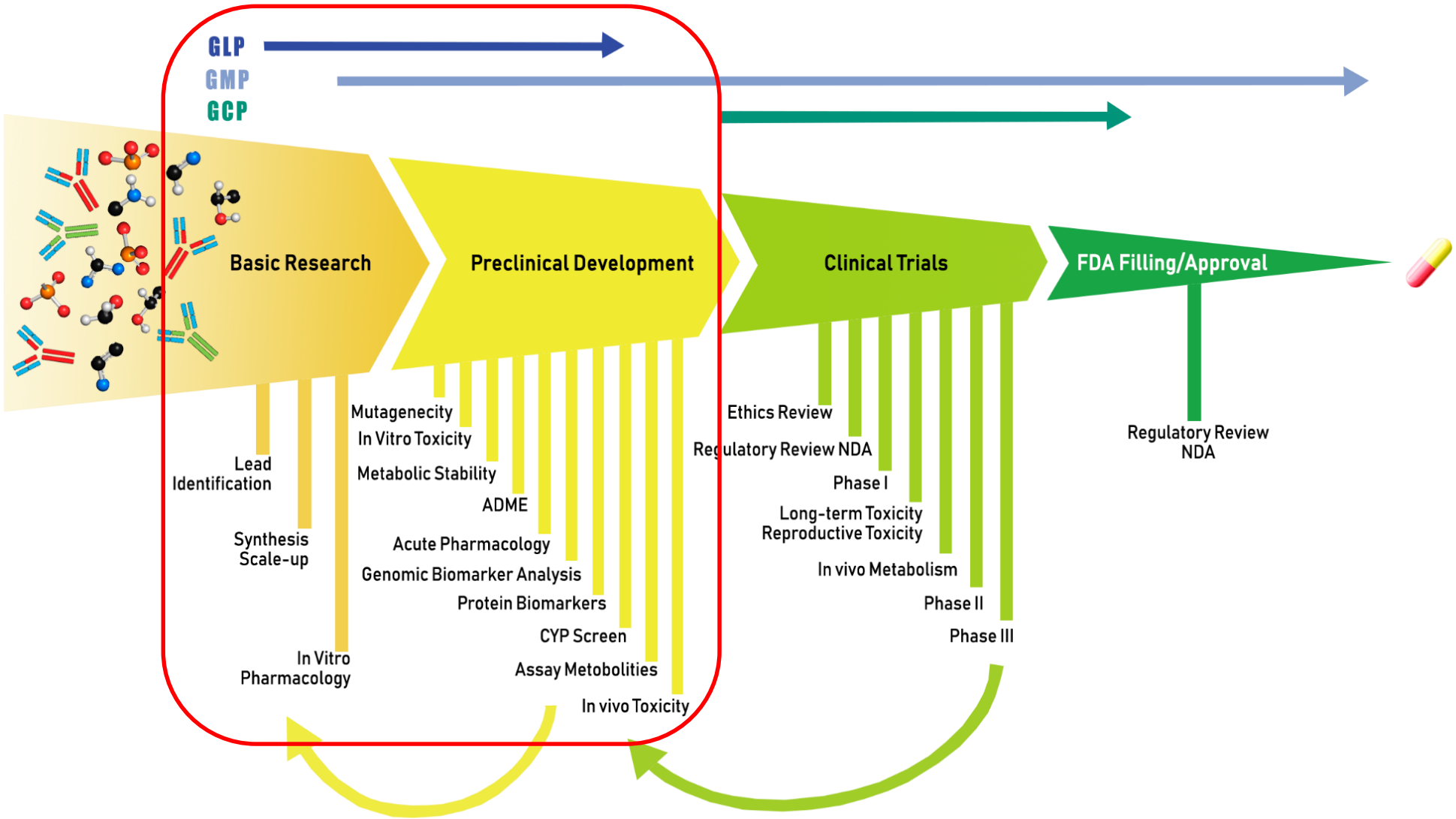
119121, Moscow, Pogodinskaya str., 10 bldg. 8

E-mail: vladimir.poroikov@ibmc.msk.ru



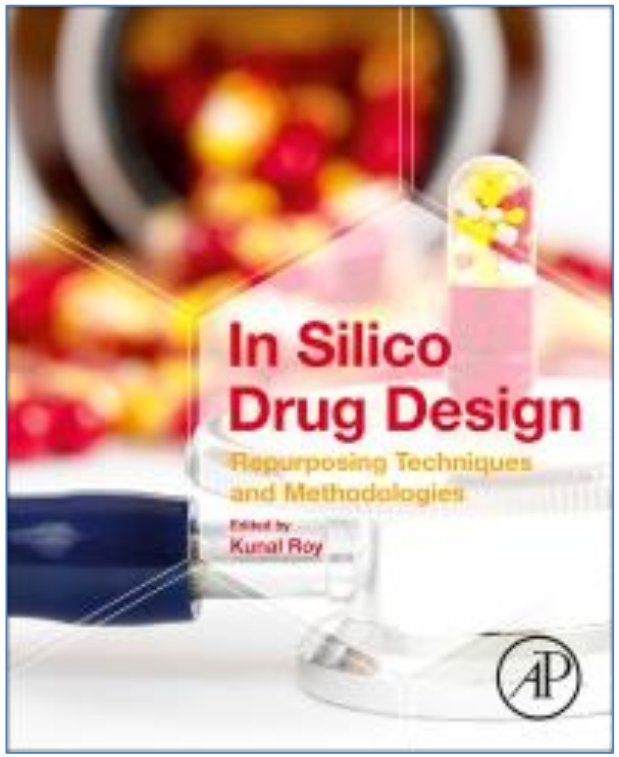
http://glp-planet.com/

Drug Research and Development: From Idea to Pharmacy



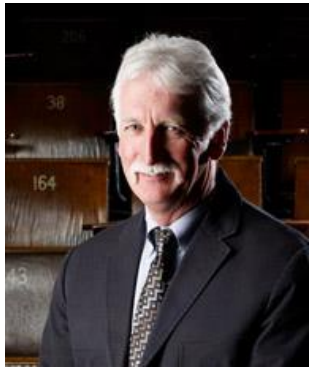
Mohsa R.C., Greig N.H. Drug discovery and development: Role of basic biological research. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, 2017, 3: 651-657.

Drug Repositioning: Time, Costs, Risks estimates



Poroikov V., Druzhilovskiy D. Drug Repositioning: New Opportunities for Older Drugs. In: In Silico Drug Design, 1st Edition. Repurposing Techniques and Methodologies. Chapter 1. Editors: Kunal Roy. Elsevier, Academic Press, 2019, p. 3-17.

How to increase the chances for development of new drugs?

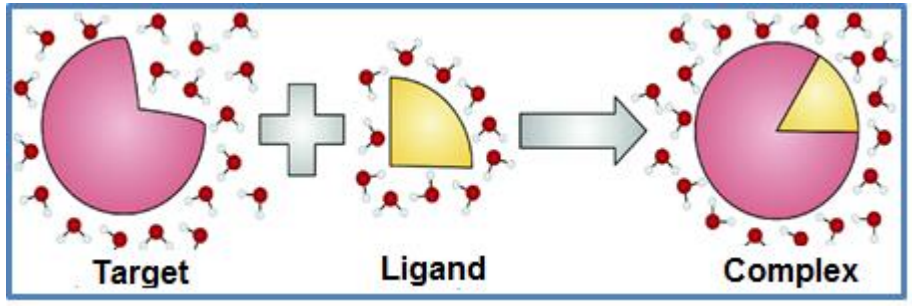


If any new drug exists that has been discovered without computations?

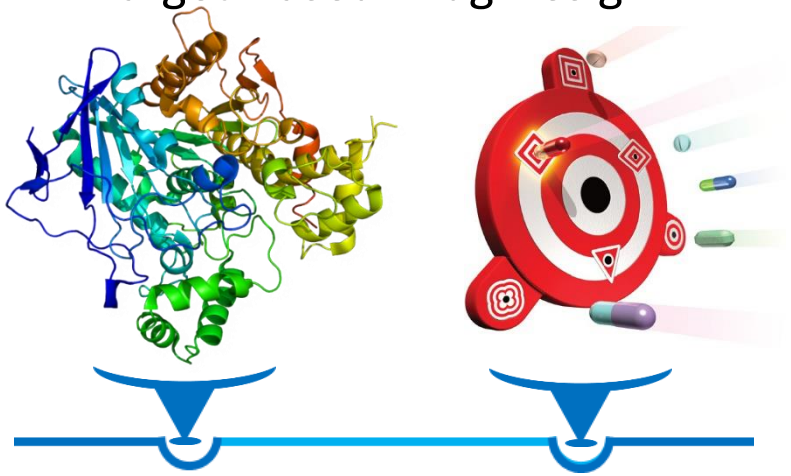
The Many Roles of Computation in Drug Discovery

William L. Jorgensen

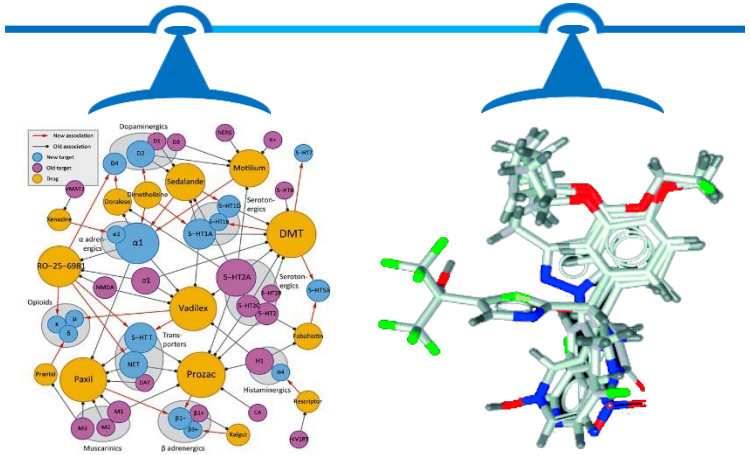
SCIENCE VOL 303 19 MARCH 2004



Target-Based Drug Design



Network Pharmacology



Ligand-Based Drug Design

PASS 2019 version (launched in July, 2019)

Dmitry Filimonov

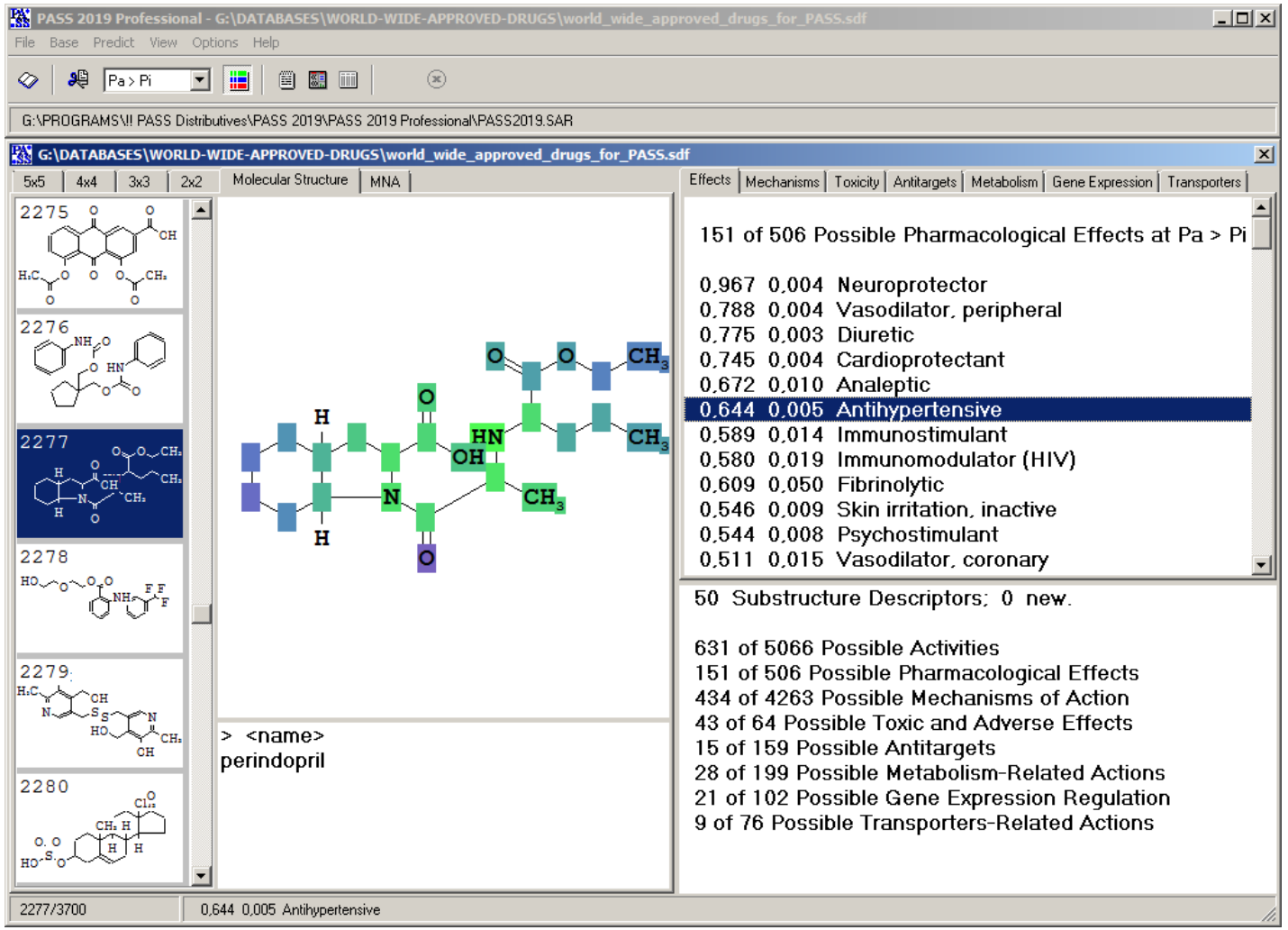
Way2Drug PREDICTIVE SERVICES
Understanding Chemical-Biological Interactions

Prediction of Activity Spectra for Substances

2019

30 Years Anniversary of PASS

SAR Base Information	1989	2019
Substances	9 314	1 025 468
Descriptors		106 816
Activity Types	114	8 054
Selected Activity Types		5 066
Average IAP	0.74	0.96



Burov Yu.V., Poroikov V.V., Korolchenko L.V. National system for registration and biological testing of chemical compounds: facilities for new drugs search. Bulletin of the National Center for Biologically Active Compounds, **1990**, No. 1, p.4-25 (Rus.).

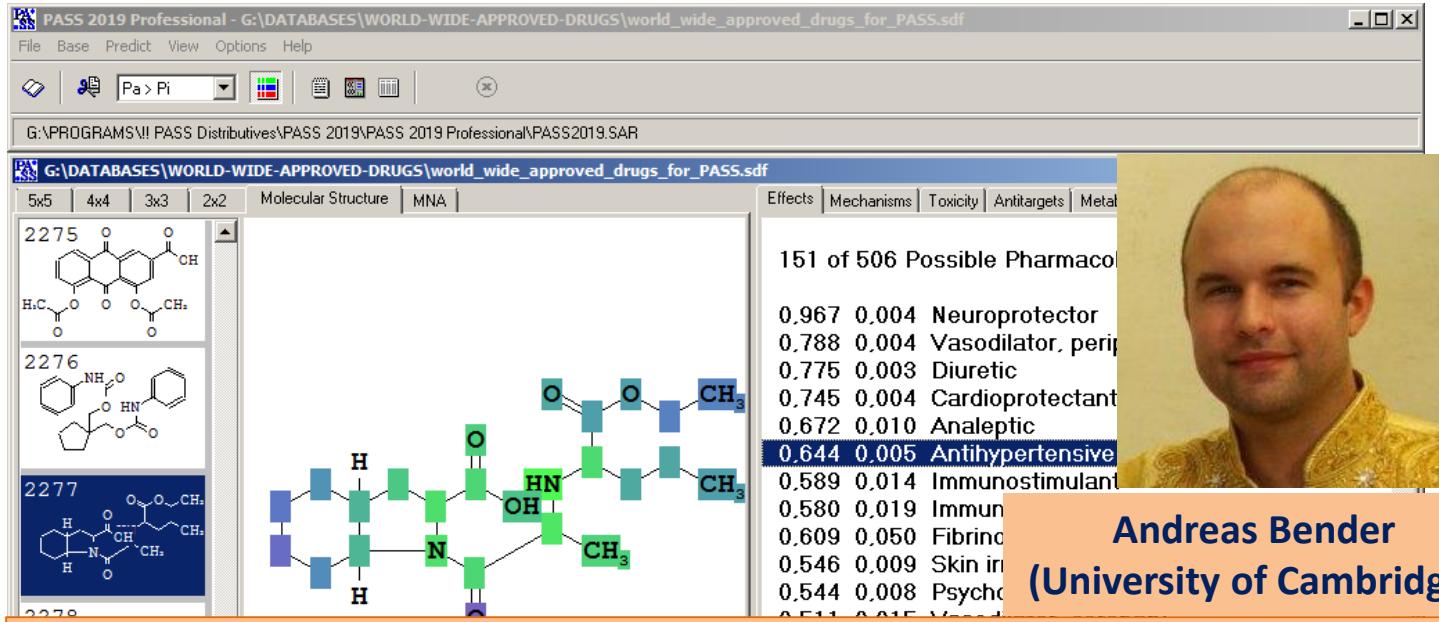
Poroikov V.V., Filimonov D.A., Gloriozova T.A., et al. Computer-aided prediction of biological activity spectra for organic compounds: the possibilities and limitations. *Russ. Chem. Bull.*, **2019**, 68 (12), 2143-2154. DOI: 10.1007/s11172-019-2683-0

PASS 2019 version (launched in July, 2019)

Dmitry Filimonov

Way2Drug PREDICTIVE SERVICES
Understanding Chemical-Biological Interactions

Prediction of Activity Spectra for Substances



Andreas Bender
(University of Cambridge)

2019

30 Years Anniversary of PASS

SAR Base Information	1989	2019
Substances	9 314	1 025 468
Descriptors		106 816
Activity Types	114	8 054
Selected Activity Types		5 066
Average IAP	0.74	0.96

"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. Journal of Cheminformatics, ***2015****, 7: 51.*

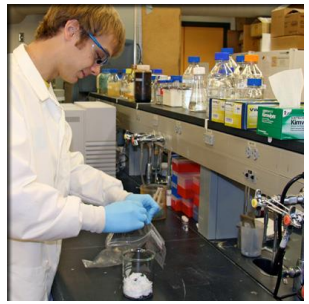
Burov Yu.V., Poroikov V.V., Korolchenko L.V. National system for registration and biological testing of chemical compounds: facilities for new drugs search. Bulletin of the National Center for Biologically Active Compounds, **1990**, No. 1, p.4-25 (Rus.).

Poroikov V.V., Filimonov D.A., Gloriozova T.A., et al. Computer-aided prediction of biological activity spectra for organic compounds: the possibilities and limitations. *Russ. Chem. Bull.*, **2019**, 68 (12), 2143-2154. DOI: 10.1007/s11172-019-2683-0

Important remarks regarding the starting point of this project

(seventies – eighties of the XX century)



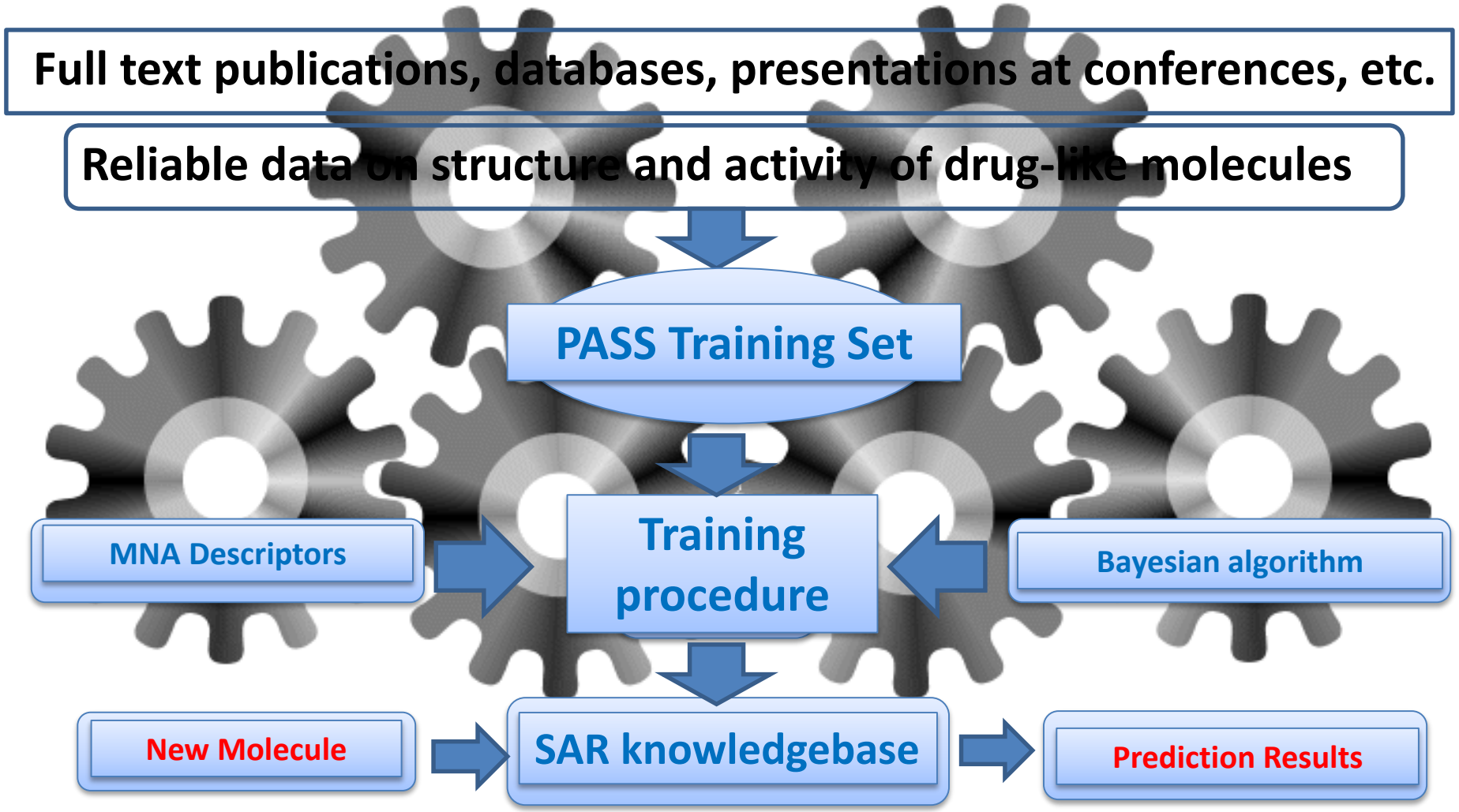

Chemical compounds were synthesized by different chemists, in different institutions, for different purposes.

- Significant heterogeneity of chemical classes of the compounds submitted for the state registration.

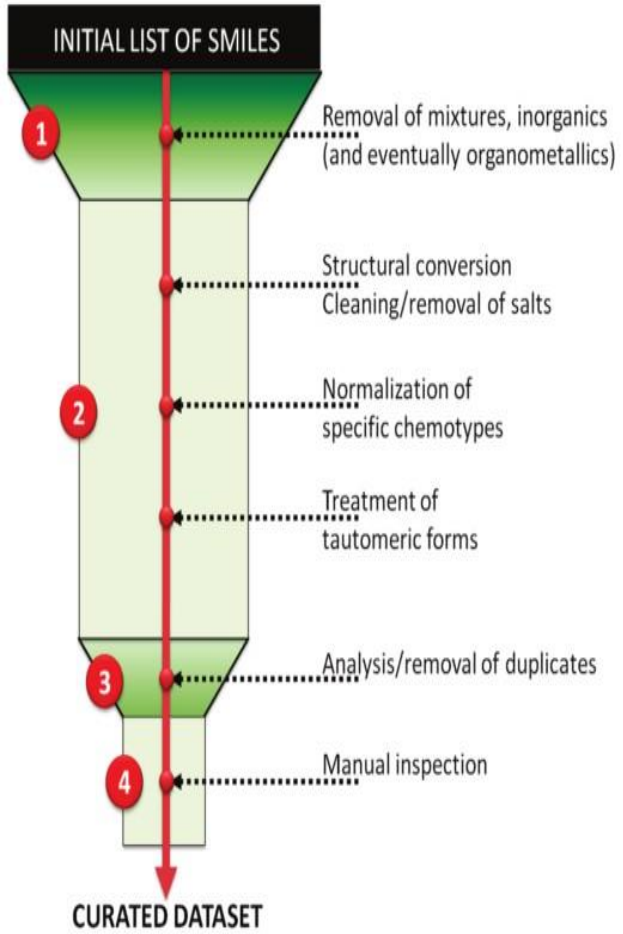
Most of the pharmacological experiments were performed *in vivo/ex vivo.*

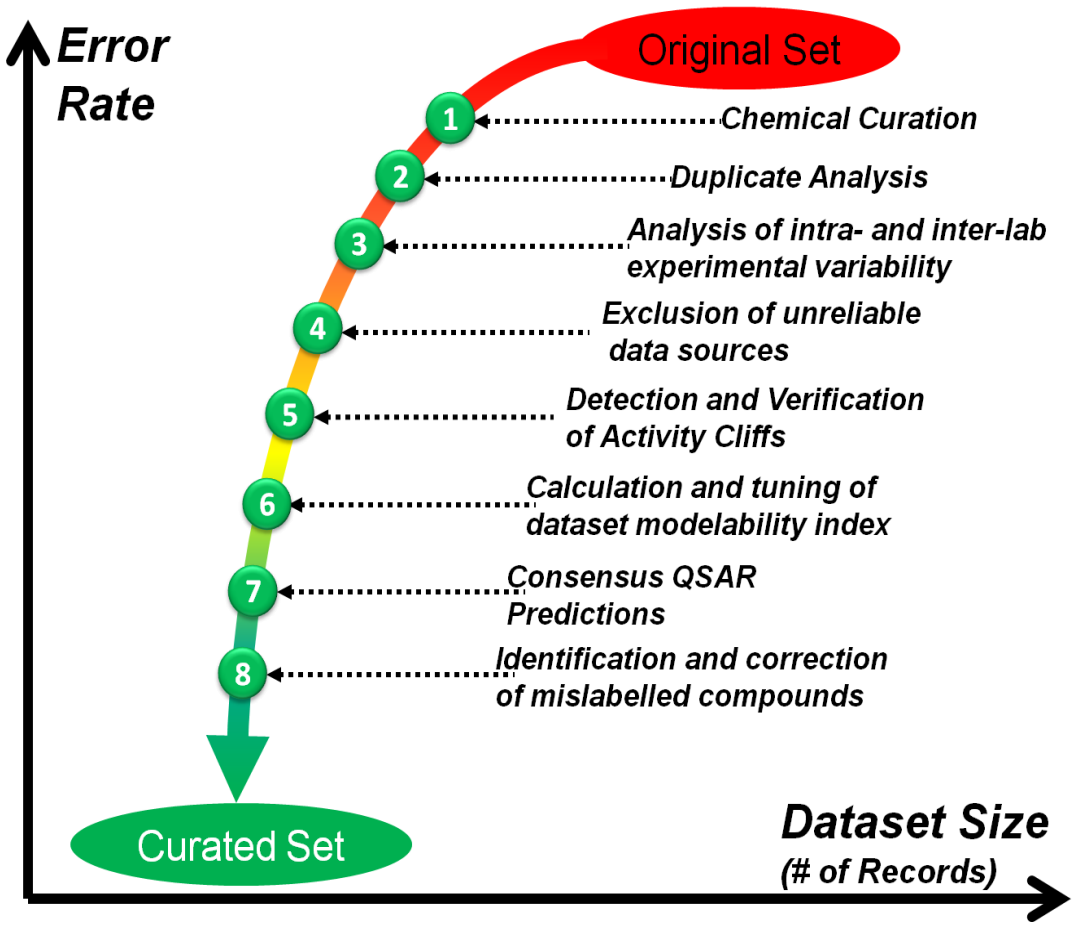
- Pharmacological effects were observed at the organism's level that leaded to the potential variety of molecular mechanisms of action.

PASS: Development & Updating Workflow



Both Chemical and Biological Data Must be Curated





Alex Tropsha

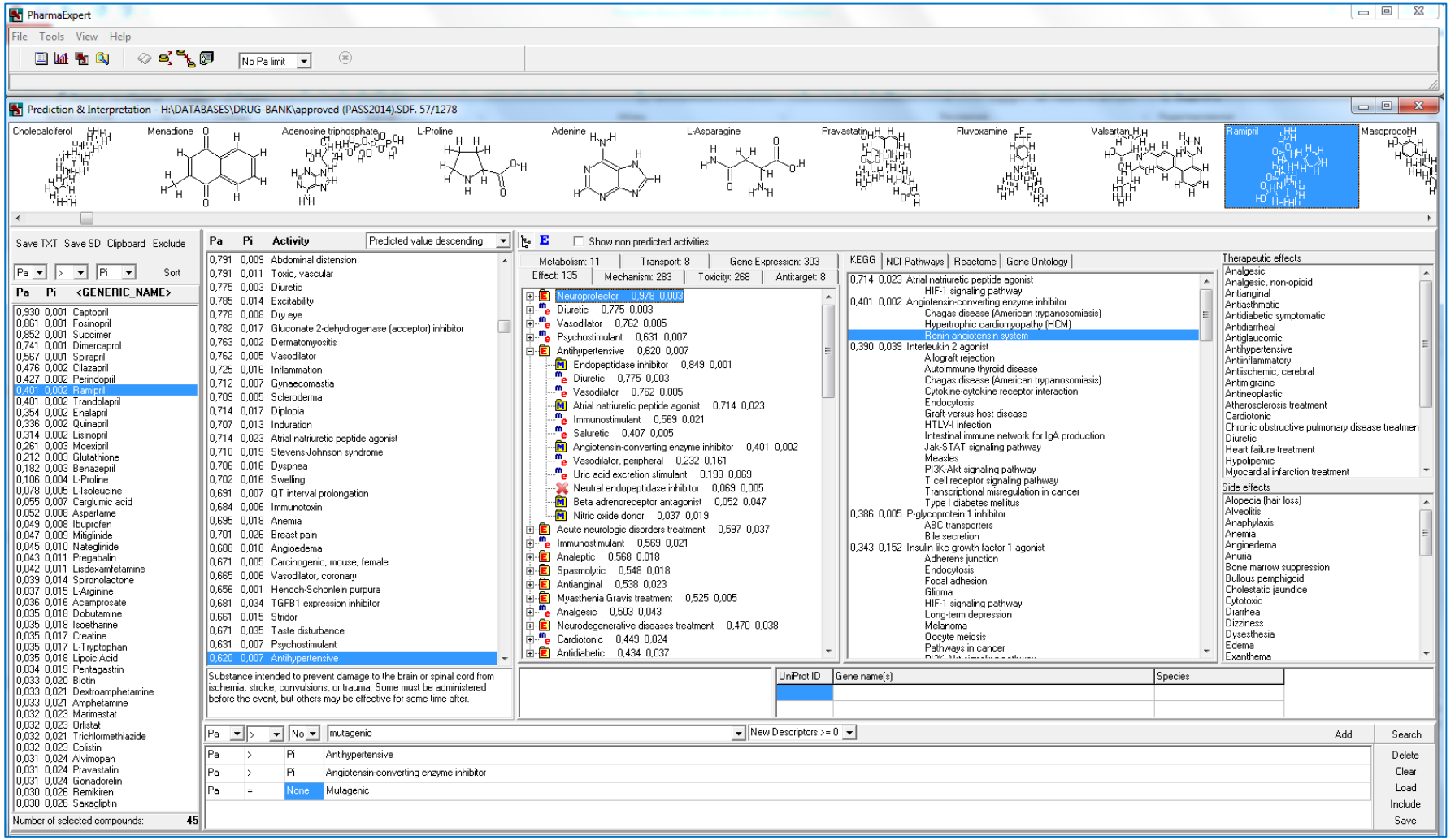
Muratov, Fourches, Tropsha. Trust but verify. *J. Chem. Inf. Model*. **2010**, 50:1189-1204.

Fourches, Muratov, Tropsha. *Nat Chem Biol.* **2015**,11:535.

Fourches, Muratov, Tropsha. Trust but verify II. *J. Chem. Inf. Model.* **2016,** 56:1243.

Thanks to the courtesy of Alex Tropsha (presentation at the XX Mendeleev Congress, Ekaterinburg, 2016).

PharmaExpert: Interpretation of the predictions

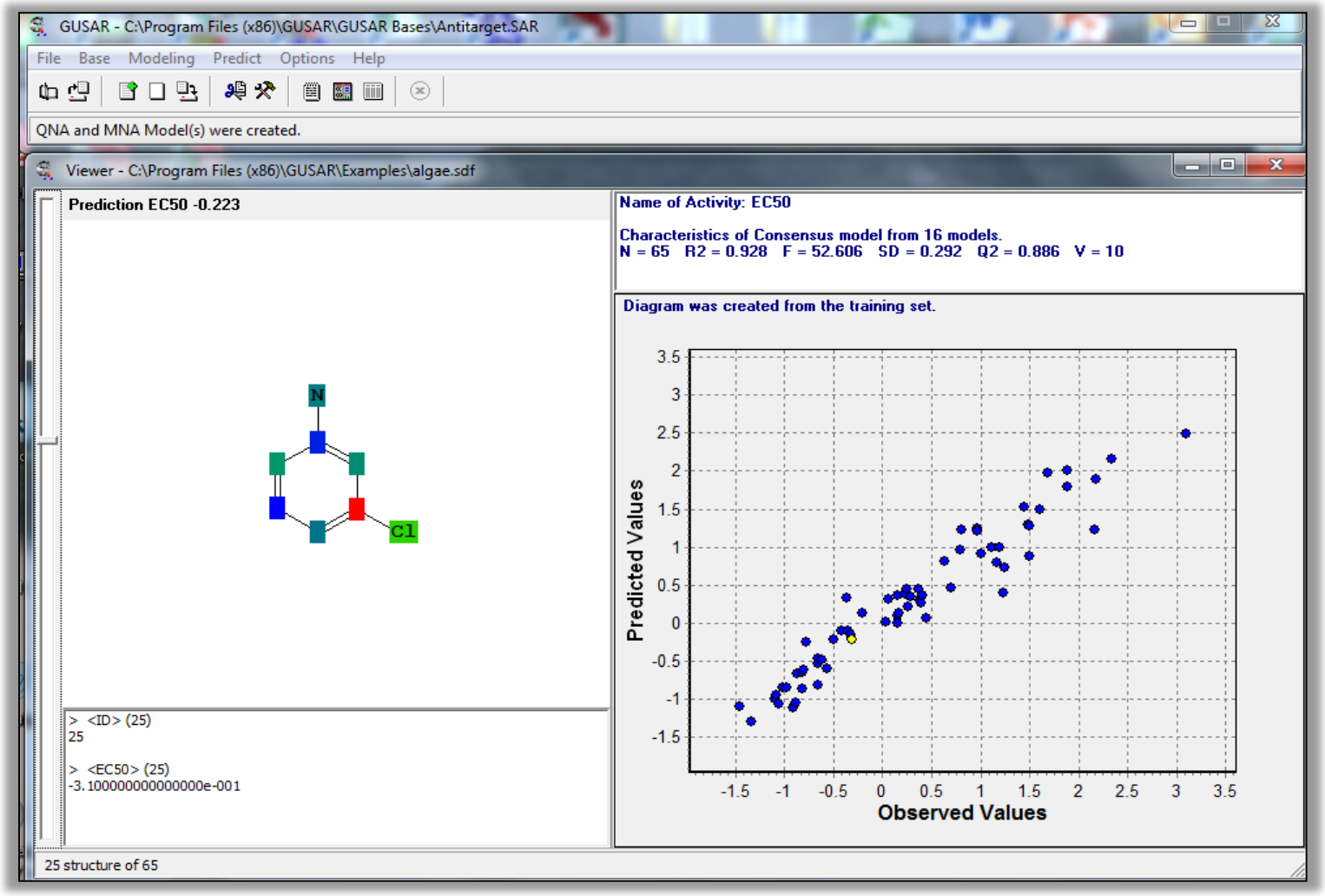


Alexey Lagunin

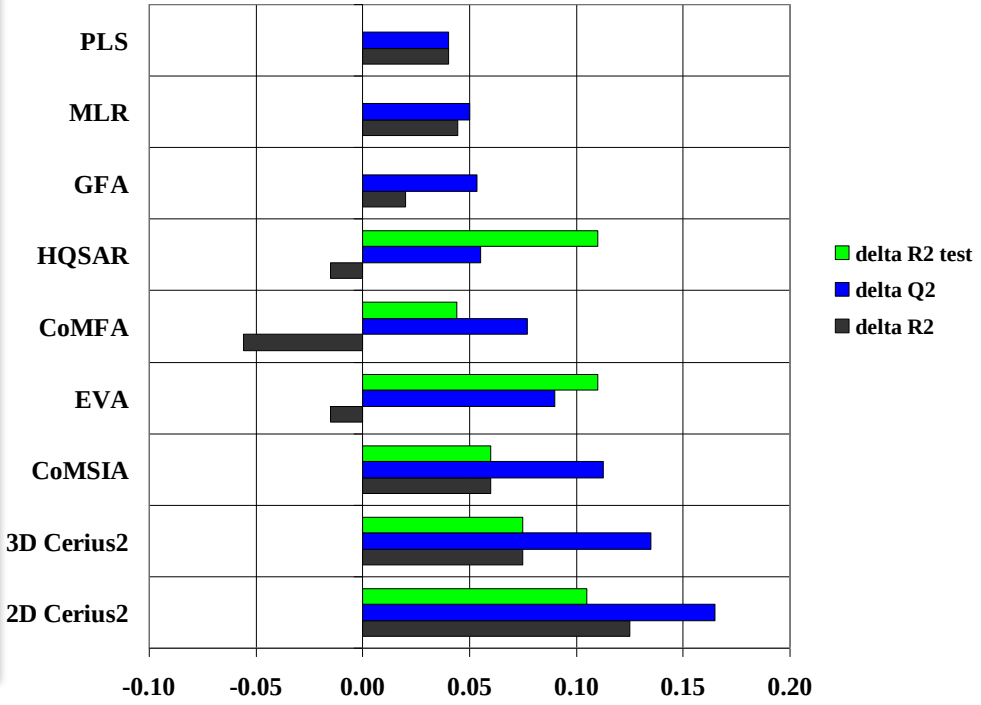
Poroikov V. et al. In: *QSAR and Molecular Modelling in Rational Design of Bioactive Molecules*. Ankara, CADD & D Society, **2005**, p.514.

Lagunin A. et al. Chemo- and bioinformatics resources for in silico drug discovery from medicinal plants beyond their traditional use: a critical review.. *Nat. Prod. Rep.*, **2014**, *31*: 1585.

GUSAR: General Unrestricted Structure-Activity Relationships



Alexey Zakharov



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

Our Software Registration by the Russian State Patent Agency

METAPREDICT
No. 2004610666 of 12.03.2004

PASS
No. 2006613275 of 15.09.2006

PreTox
No. 2006613276 of 15.09.2006

PharmaExpert
No. 2006613590 of 16.10.2006

GUSAR
No. 2006613591 of 16.10.2006

BIOGENPHARM
No. 2006614395 of 15.02.2007

BIOGENERATOR
No. 2006614396 of 15.02.2007

NetFlowEx
No. 2011617330 of 26.05.2011

Net2Target
No. 2014660877 of 17.10.2014

PASS CLC Pred
No. 2016610382 of 11.01.2016

PASS Targets
No. 2016610846 of 20.01.2016

PASS SMP
No. 2016663627 of 13.11.2016

РОССИЙСКАЯ ФЕДЕРАЦИЯ

СВИДЕТЕЛЬСТВО

об официальной регистрации программы для ЭВМ

№ 2006613275

PASS (Prediction of Activity Spectra for Substances)

Правообладатель(ли): *Филимонов Дмитрий Алексеевич (RU), Пройков Владимир Васильевич (RU), Глориозова Татьяна Андреевна (RU), Лагунин Алексей Александрович (RU)*

Автор(ы): *Филимонов Дмитрий Алексеевич, Пройков Владимир Васильевич, Глориозова Татьяна Андреевна, Лагунин Алексей Александрович (RU)*

Заявка № 2006612815
Дата поступления 17 августа 2006 г.
Зарегистрировано в Реестре программ для ЭВМ
15 сентября 2006 г.

Руководитель Федеральной службы по интеллектуальной собственности, патентам и товарным знакам

Б.П. Симонов

Our freely available predictive web-services

Dmitry Druzhilovskiy

Anastassia Rudik

HOME | ABOUT | SERVICES | ACTIVITIES | PUBLICATIONS | RESULTS | Already have an account? LOGIN

- Predictors
- Databases
- SAR Creator
- PASS Online Total
- PASS Online Selector
- MNA/QNA Similarity
- FDA PCP Search
- MPDS Search

- PASS Online
- PASS Targets
- KinScreen
- DIGEP-Pred
- PASS CLC Pred
- AntiHIV-Pred
- AntiBac-Pred
- SOMP: Sites of Metabolism Prediction
- SMP: Substrate/Metabolite Specificity Prediction
- RA: Reacting Atoms
- MetaTox
- Acute rat toxicity
- Antitarget prediction
- Ecotoxicity
- ROSC-Pred
- ADVER-Pred
- DDI-Pred
- Resistance
- SprOS
- . . .

20 predictive web services

PASS, PharmaExpert and GUSAR: Some Applications

Drug Discovery Today • Volume 00, Number 00 • August 2015 REVIEWS

Teaser In silico approaches reveal mechanisms of adverse drug reactions and predict them at the earliest stages of drug development.

In silico assessment of adverse drug reactions and associated mechanisms

Sergey M. Ivanov[1,2], Alexey A. Lagunin[1,2] and Vladimir V. Poroikov[1,2]

[1] Institute of Biomedical Chemistry, 10/8, Pog
[2] Pirogov Russian National Research Medical
117997 Moscow, Russia

During recent years, various *i*
estimate chemical and biolog
fragments, protein targets, pa
adverse drug reactions (ADRs
These features have also been
that enable estimation of AD
development. In this review,
predict these features for a ce

Chemical Research in Toxicology

Article

pubs.acs.org/crt

Quantitative Prediction of Antitarget Interaction Profiles for Chemical Compounds

Alexey V. Zakharov,*[,†,‡] Alexey A. Lagunin,[‡] Dmitry A. Filimonov,[‡] and Vladimir V. Poroikov[‡]

[†]National Cancer Institute, National Institu

JOURNAL OF CHEMICAL INFORMATION AND MODELING

Application Note

pubs.acs.org/jcim

MetaTox: Web Application for Predicting Structure and Toxicity of Xenobiotics' Metabolites

Anastasia V. Rudik,*[,†] Vladislav M. Bezhentsev,[†] Alexander V. Dmitriev,[†] Dmitry S. Druzhilovskiy,[†] Alexey A. Lagunin,[†,‡] Dmitry A. Filimonov,[†] and Vladimir V. Poroikov[†]

[†]Institute of Biomedical Chemistry, 119121, Russia
[‡]Pirogov Russian National Research Medical University, 1 Ostrovityanova Str., Moscow, 117997, Russia

DE GRUYTER Drug Metabol Pers Ther 2018; 33(2): 65–73

Dmitriy V. Ivashchenko*, Anastasia V. Rudik, Andrey A. Poloznikov, Sergey V. Nikulin, Valeriy V. Smirnov, Alexander G. Tonevitsky, Eugeniy A. Bryun and Dmitriy A. Sychev

Which cytochrome P450 metabolizes phenazepam? Step by step *in silico*, *in vitro*, and *in vivo* studies

Лабораторные животные для научных исследований
Научно-практический журнал. eISSN 2618723X / DOI 10.29296/2618723X

Russian English

Альтернативные методы исследования. Компьютерная оценка острой токсичности для грызунов

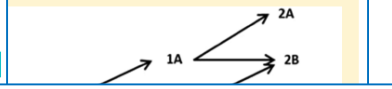
Поиск

В.С. Сухачев[1,2], лаборант Института
технологий имени М.В. Ломоносова
С.М. Иванов[1], канд. биол. наук, научн
имени В.Н. Ореховича, ORCID ID: 000
Д.А. Филимонов[1], канд. физ.-мат. на
0000-0002-0339-8478,
В.В. Поройков[1], профессор, д-р биол.
имени В.Н. Ореховича, заведующий
0000-0001-7937-2621

[1]Научно-исследовательский институ
Россия, 119121, Москва, Погодинска
[2]Российский технологический униве
Россия, 119571, Москва, пр-т Вернад
E-mail: withstanding@yandex.ru

Резюме

Определение значений полуле
доклинических исследований
4 способах введения веществ
использованием компьютерно
версии (для крыс и мышей), та



ehp Environmental Health Perspectives

OPEN ACCESS

HOME CURRENT ISSUE ARCHIVES COLLECTIONS 中文翻译 AUTHORS ABOUT

Vol. 128, No. 2 | Research

CoMPARA: Collaborative Modeling Project for Androgen Receptor Activity

Kamel Mansouri, Nicole Kleinstreuer, Ahmed M. Abdelaziz, Domenico Alberga, Vinicius M. Alves, Patrik L. Andersson, Carolina H. Andrade, Fang Bai, Ilya Balabin, Davide Ballabio, Emilio Benfenati, Barun Bhhatarai, Scott Boyer, Jingwen Chen, Viviana Consonni, Sherif Farag, Denis Fourches, Alfonso T. García-Sosa, Paola Gramatica, Francesca Grisoni, Chris M. Grulke, Huixiao Hong, Dragos Horvath, Xin Hu, Ruili Huang, ... See all authors

Published: 7 February 2020 | CID: 027002 | https://doi.org/10.1289/EHP5580

Sections PDF Supplemental Materials Tools Share

Abstract

Background: Endocrine disrupting chemicals (EDCs) are xenobiotics that mimic the interaction of natural hormones and alter synthesis, transport, or metabolic pathways. The prospect of EDCs causing adverse health effects in humans and wildlife has led to the development of scientific and regulatory approaches for evaluating bioactivity. This need is being addressed using high-throughput screening (HTS) *in vitro* approaches and computational modeling.

ROYAL SOCIETY OF CHEMISTRY

Chem Soc Rev

REVIEW ARTICLE

View Article Online
View Journal

Check for updates

Cite this: DOI: 10.1039/d0cs00098a

QSAR without borders

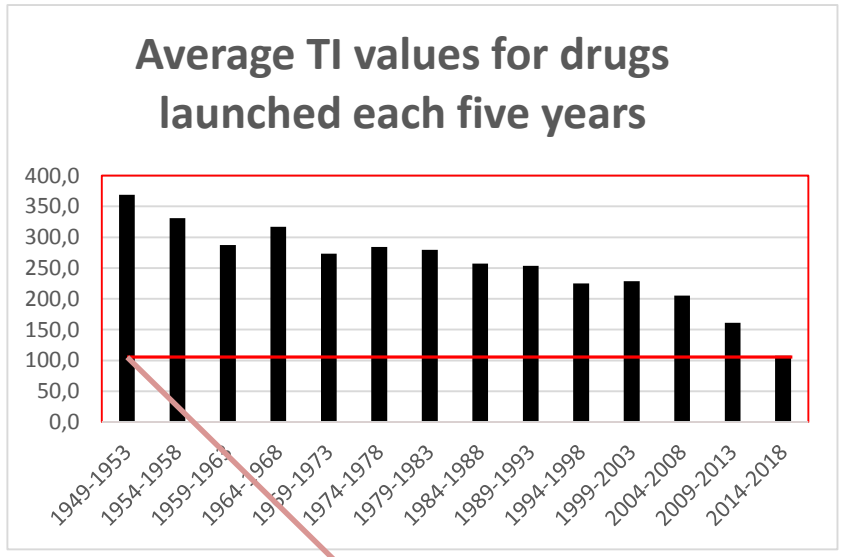
Eugene N. Muratov, [ab] Jürgen Bajorath, [c] Robert P. Sheridan, [d] Igor V. Tetko, [e] Dmitry Filimonov, [f] Vladimir Poroikov, [f] Tudor I. Oprea, [ghi] Igor I. Baskin, [jk] Alexandre Varnek, [j] Adrian Roitberg, [l] Olexandr Isayev, [a] Stefano Curtalolo, [m] Denis Fourches, [n] Yoram Cohen, [o] Alan Aspuru-Guzik, [p]

Could we estimate *in silico* which drug is not safe enough?

PASS

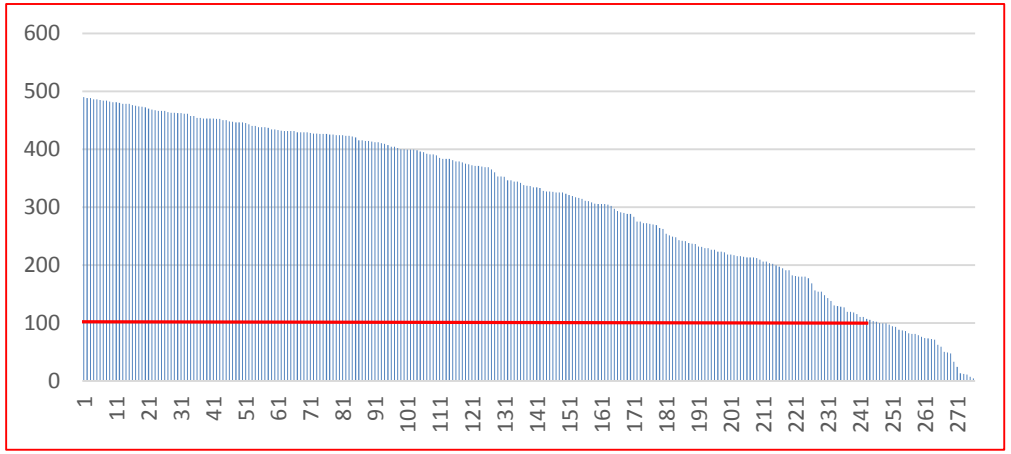
Predicts ~500 adverse and toxic effects

$$Toxicity\ Index\ (TI) = \sum N_{adv\&tox}$$

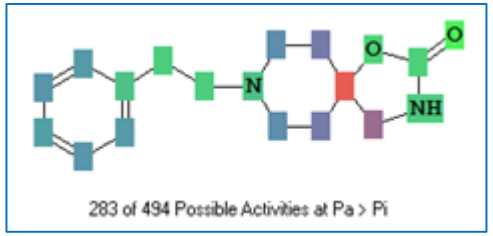


Threshold value: TI =108

For 88% of 276 withdrawn drugs TI exceeds the Threshold.



For Fenspiride TI = 293; threshold exceeded by more than twice.



Poroikov V., Filimonov D. et al., 2020. Unpublished.

Summary and further prospects

- Based on our long-term studies in bio- and chemoinformatics, we developed general computational methods predicted with reasonable accuracy many biological activities/properties using structural formula of drug-like compound as an input data.
- We developed 20 web-services that are widely used by about 24 thousand researchers from 100 countries; more than 800 independent papers published with the appropriate citations.
- Further development of these resources requires integration, curation of the information, improvement of functionality, etc.
- Active cooperation between the researchers working in the field of drug discovery will be beneficial for all parties.

Acknowledgements

Our current team

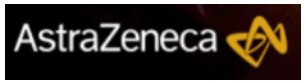
Dmitry Filimonov, Tatyana Gloriozova,
Alexey Lagunin, Dmitry Druzhilovskiy,
Anastasia Rudik, Alexander Dmitriev,
Olga Tarasova, Alexander Veselovsky,
Boris Sobolev, Oleg Gomazkov,
Sergey Ivanov, Pavel Pogodin, Leonid Stolbov,
Dmitry Karasev, Polina Savosina, Nikita Ionov,
Nadezhda Biziukova

Former team members

Yulia Borodina, Alexey Zakharov,
Varvara Dubovskaja, Anastassia Sergeiko,
Alexandra Urusova, Khalimat Murtazalieva,
Vladislav Bezhentsev, Maxim Semin

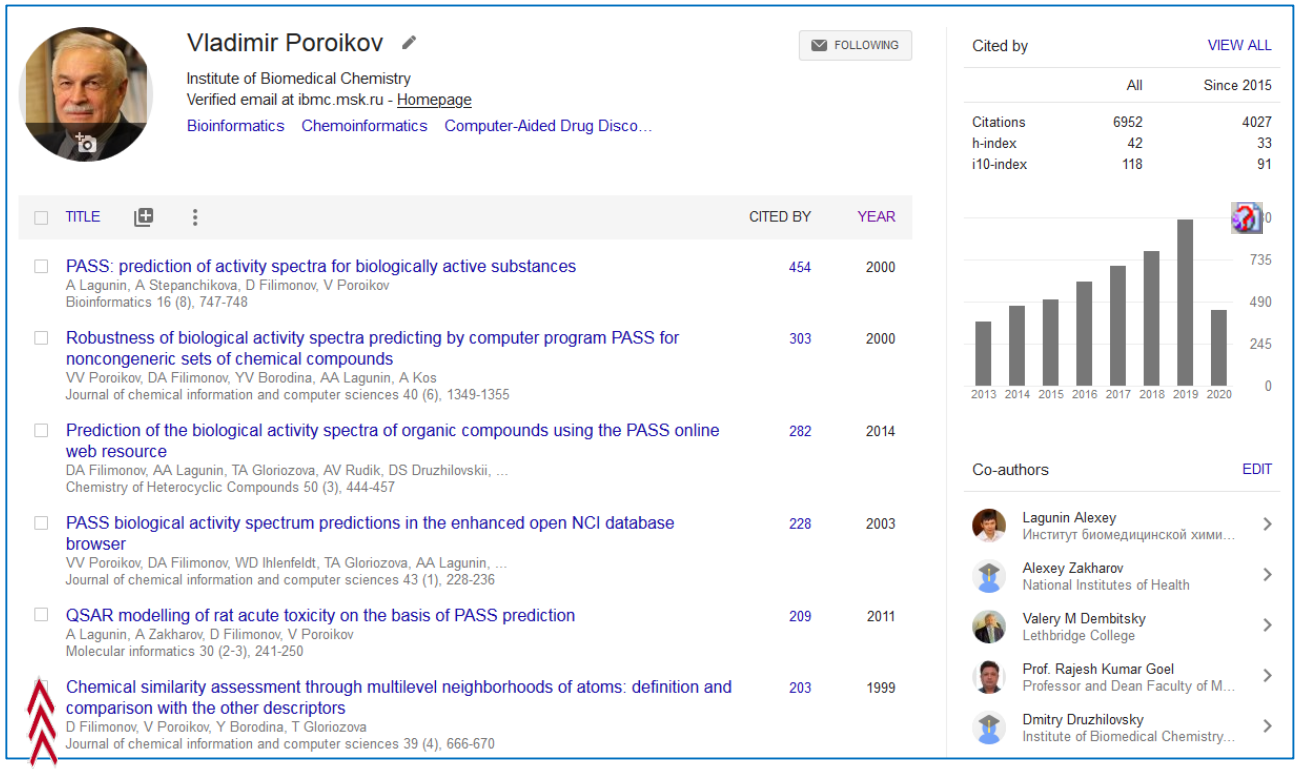
Some our collaborators

Athina Geronikaki (Greece), Marc Nicklaus (USA), Rajesh Goel (India), Alexander Kel (Germany), Alexandre Varnek (France), Valery Dembitsky (Canada), Narahari Sastry (India), . . .



Thank you for your kind attention!

Your questions, please, address to: vladimir.poroikov@ibmc.msk.ru; vvp1951@yandex.ru



Vladimir Poroikov

FOLLOWING

Institute of Biomedical Chemistry
Verified email at ibmc.msk.ru - Homepage
Bioinformatics Chemoinformatics Computer-Aided Drug Disco...

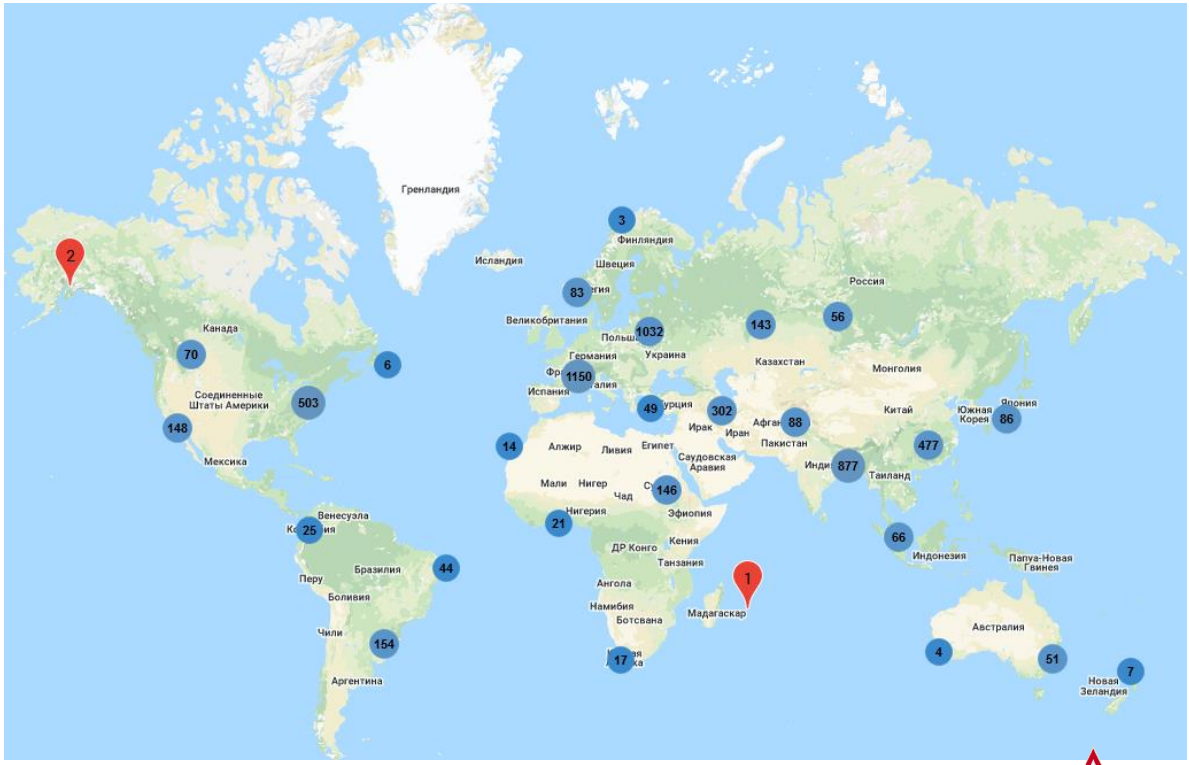
TITLE	CITED BY	YEAR
PASS: prediction of activity spectra for biologically active substances A Lagunin, A Stepanchikova, D Filimonov, V Poroikov Bioinformatics 16 (8), 747-748	454	2000
Robustness of biological activity spectra predicting by computer program PASS for noncongeneric sets of chemical compounds VV Poroikov, DA Filimonov, YV Borodina, AA Lagunin, A Kos Journal of chemical information and computer sciences 40 (6), 1349-1355	303	2000
Prediction of the biological activity spectra of organic compounds using the PASS online web resource DA Filimonov, AA Lagunin, TA Gloriozova, AV Rudik, DS Druzhilovskii, ... Chemistry of Heterocyclic Compounds 50 (3), 444-457	282	2014
PASS biological activity spectrum predictions in the enhanced open NCI database browser VV Poroikov, DA Filimonov, WD Ihlenfeldt, TA Gloriozova, AA Lagunin, ... Journal of chemical information and computer sciences 43 (1), 228-236	228	2003
QSAR modelling of rat acute toxicity on the basis of PASS prediction A Lagunin, A Zakharov, D Filimonov, V Poroikov Molecular informatics 30 (2-3), 241-250	209	2011
Chemical similarity assessment through multilevel neighborhoods of atoms: definition and comparison with the other descriptors D Filimonov, V Poroikov, Y Borodina, T Gloriozova Journal of chemical information and computer sciences 39 (4), 666-670	203	1999

Cited by VIEW ALL

	All	Since 2015
Citations	6952	4027
h-index	42	33
i10-index	118	91

Co-authors EDIT

- Lagunin Alexey — Институт биомедицинской хими...
- Alexey Zakharov — National Institutes of Health
- Valery M Dembitsky — Lethbridge College
- Prof. Rajesh Kumar Goel — Professor and Dean Faculty of M...
- Dmitry Druzhilovsky — Institute of Biomedical Chemistry...



List of our publications: https://scholar.google.ru/citations?user=F13hIJMAAAAJ&hl=en

Citation Map: https://publons.com/dashboard/tools/citation-map/