

Computer Aided Drug Design

2015/16

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Organizacyjne

- Zaliczenie
- Materiały na:
<https://github.com/filipsPL/CADD-PW/wiki>





Background





BUJNICKI LAB

FUNDED
BY:



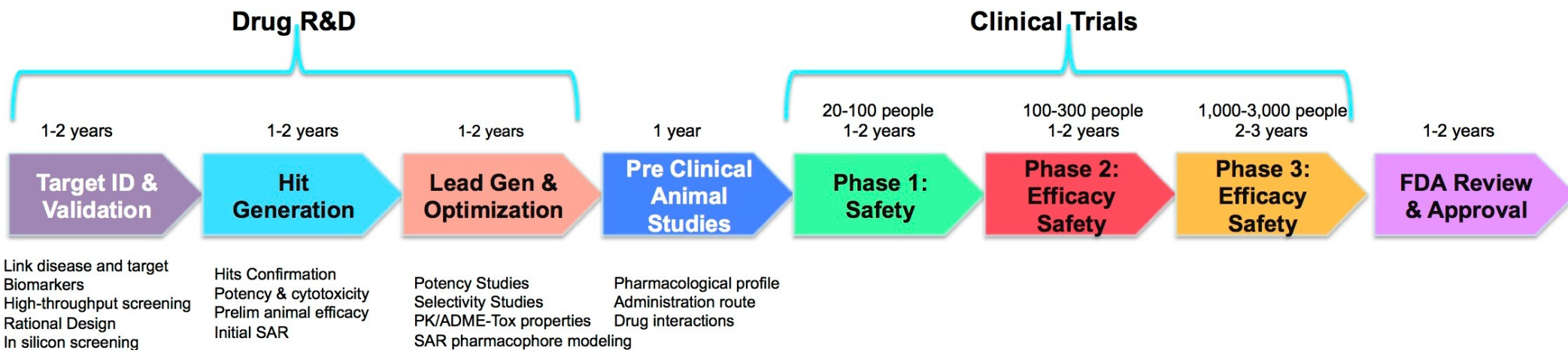
OncoArendi
Therapeutics

<http://genesilico.pl/>
<https://www.oncoarendi.com/>

Chemia medyczna

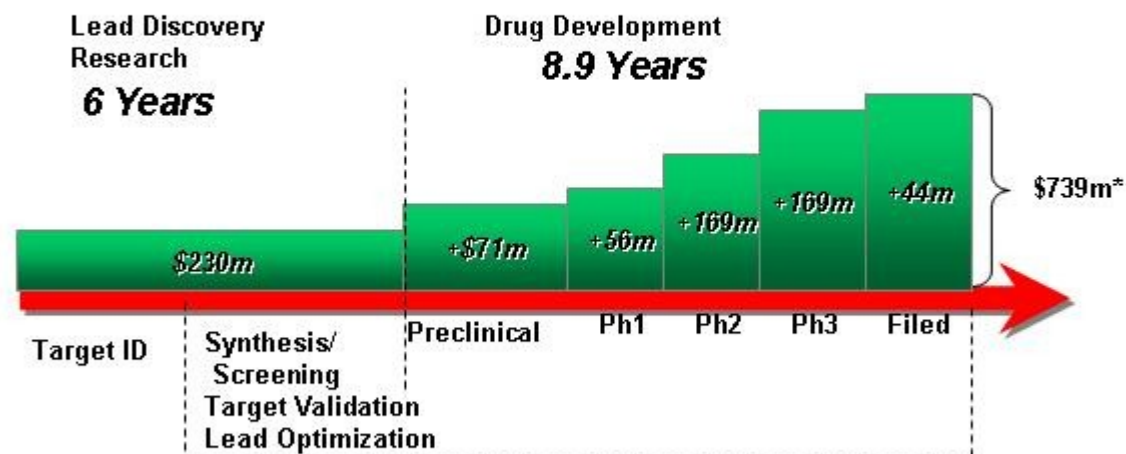


Drug discovery pipeline

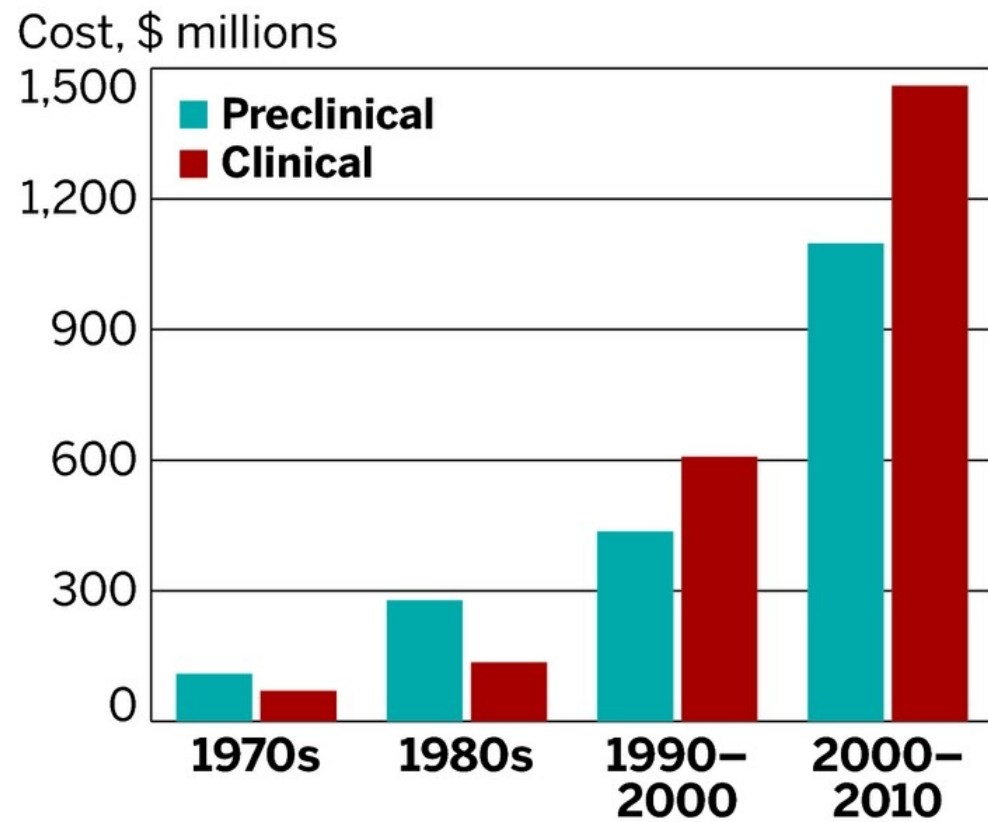


Koszty R&D

Traditional Pharmaceutical R&D *Costly* and Time Consuming***



*Lehman Brothers, 1997; ** Tufts CSDD



Drug R&D

Clinical Trials

1-2 years

Target ID & Validation

Link disease and target
Biomarkers
High-throughput screening
Rational Design
In silicon screening

1-2 years

Hit Generation

Hits Confirmation
Potency & cytotoxicity
Prelim animal efficacy
Initial SAR

1-2 years

Lead Gen & Optimization

Potency Studies
Selectivity Studies
PK/ADME-Tox properties
SAR pharmacophore modeling

1 year

Pre Clinical Animal Studies

Pharmacological profile
Administration route
Drug interactions

20-100 people
1-2 years

Phase 1: Safety

100-300 people
1-2 years

Phase 2: Efficacy Safety

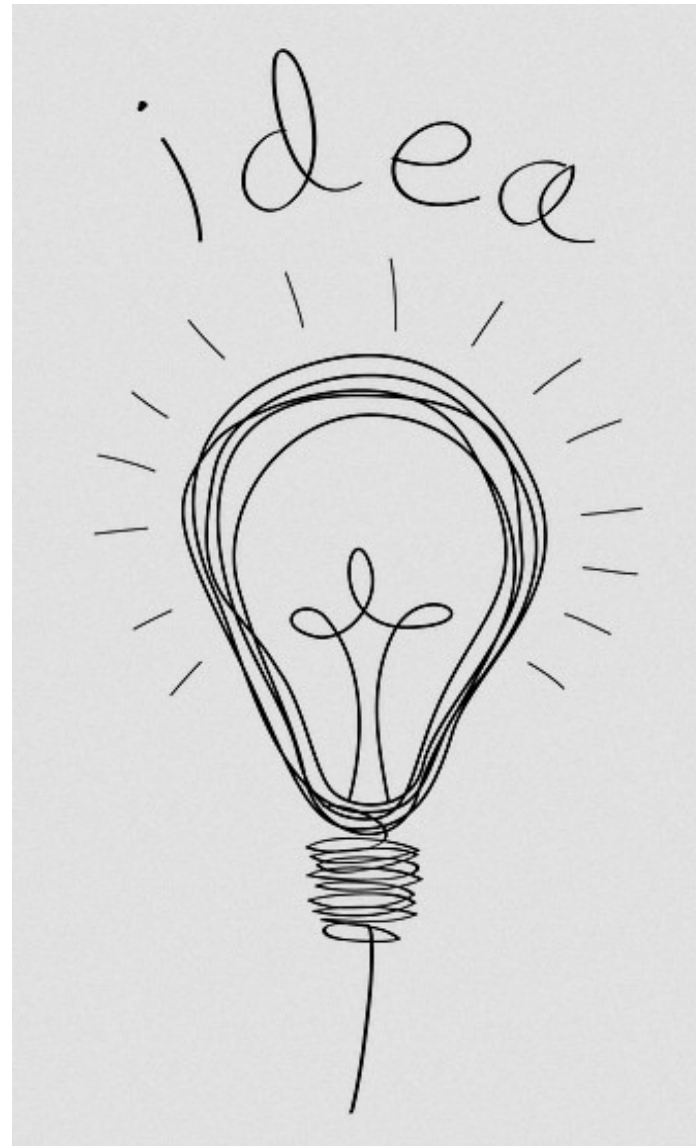
1,000-3,000 people
2-3 years

Phase 3: Efficacy Safety

1-2 years

FDA Review & Approval

Pomysł



Target?

☐ [The role of JAK/STAT signalling in the pathogenesis, prognosis and treatment of solid tumours.](#)

1. Thomas SJ, Snowden JA, Zeidler MP, Danson SJ.
Br J Cancer. 2015 Jul 7. doi: 10.1038/bjc.2015.233. [Epub ahead of print]
PMID: 26151455

☐ [B7-H3 promotes cell migration and invasion through the **Jak2**/Stat3/MMP9 signaling pathway in colorectal cancer.](#)

2. Liu F, Zhang T, Zou S, Jiang B, Hua D.
Mol Med Rep. 2015 Jul 7. doi: 10.3892/mmr.2015.4050. [Epub ahead of print]
PMID: 26151358

☐ [miR-216a may inhibit pancreatic tumor growth by targeting **JAK2**.](#)

3. Hou BH, Jian ZX, Cui P, Li SJ, Tian RQ, Ou JR.
FEBS Lett. 2015 Jul 3. pii: S0014-5793(15)00570-0. doi: 10.1016/j.febslet.2015.06.036. [Epub ahead of print]
PMID: 26149212

☐ [Sodium tanshinone IIA sulfonate ameliorates ischemia-induced myocardial inflammation and lipid accumulation in Beagle dogs through NLRP3 inflammasome.](#)

4. Hu Q, Wei B, Wei L, Hua K, Yu X, Li H, Ji H.
Int J Cardiol. 2015 May 29;196:183-192. doi: 10.1016/j.ijcard.2015.05.152. [Epub ahead of print]
PMID: 26143630

☐ [\[Effect of PM2.5 on oxidative stress-JAK/STAT signaling pathway of human bronchial epithelial cells\].](#)

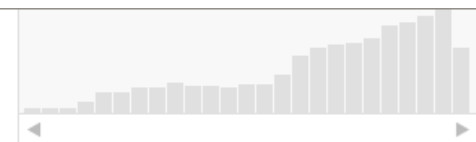
5. Xu Z, Zhang Z, Ma X, Ping F, Zheng X.
Wei Sheng Yan Jiu. 2015 May;44(3):451-5. Chinese.
PMID: 26137628

☐ [Advances and challenges in the management of essential thrombocythemia.](#)

6. Birgegård G.
Ther Adv Hematol. 2015 Jun;6(3):142-56. doi: 10.1177/2040620715580068. Review.
PMID: 26137205 **Free PMC Article**

☐ [Expression mechanism of tryptophan hydroxylase 1 in mouse islets during pregnancy.](#)

7. Iida H, Ogiwara T, Min MK, Hara A, Kim YG, Fujimaki K, Tamaki M, Fujitani Y, Kim H, Watada H.
J Mol Endocrinol. 2015 Jul 1. pii: JME-14-0299. [Epub ahead of print]
PMID: 26136513



[Download CSV](#)

Related searches

[jak2 v617f](#)

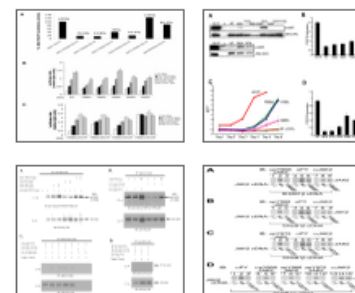
[jak2 stat3](#)

[jak2 exon 12](#)

[jak2 inhibitors](#)

[jak2 mpl](#)

PMC Images search for JAK2



[See more \(3228\)...](#)

Titles with your search terms

Somatic CALR mutations in myeloproliferative neoplasms with nonmutated **JAK2** [N Engl J Med. 2013]

JAK2 or CALR mutation status defines subtypes of essential thrombocythemia with **JAK2** [Blood. 2014]

Analiza rynku



Analiza patentowa

United States Patent [19]
Kemper

[11] **3,922,730**
[45] **Dec. 2, 1975**

[54] **RECIRCULATING TOILET SYSTEM FOR USE IN AIRCRAFT OR THE LIKE**
[75] Inventor: **James M. Kemper**, Sherman Oaks, Calif.
[73] Assignee: **Monogram Industries, Inc.**, Santa Monica, Calif.
[22] Filed: **Mar. 11, 1974**
[21] Appl. No.: **449,619**

3,431,563 3/1969 Rascov..... 4/1
3,673,614 7/1972 Clauch..... 4/10
3,829,909 8/1974 Rod et al..... 4/10
3,835,478 9/1974 Molus..... 4/11

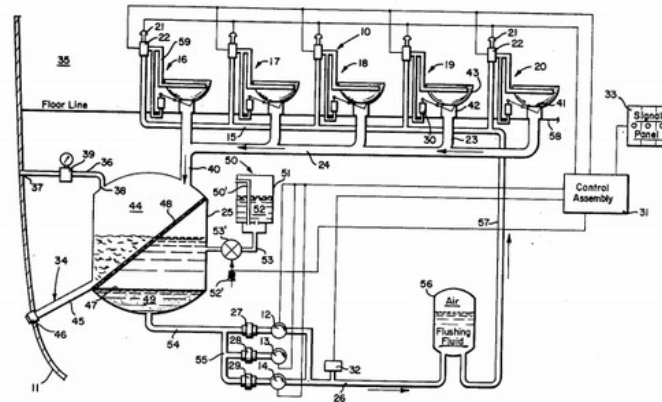
Primary Examiner—John W. Huckert
Assistant Examiner—Stuart S. Levy
Attorney, Agent, or Firm—Poms, Smith, Lande & Glenn

[52] U.S. Cl. 4/10; 4/77; 4/79;
4/115; 4/DIG. 11; 210/167
[51] Int. Cl.² E03D 5/016
[58] Field of Search 4/1, 10, 11, 12, 17, 76,
4/79, 89, 90, 82, 115, 131, DIG. 3, DIG. 11,
77; 210/152, 167

[56] **References Cited**
UNITED STATES PATENTS
2,749,558 6/1956 Lent et al. 4/10
3,032,776 5/1962 Obert et al. 4/131 X
3,079,612 3/1963 Corliss 4/10

[57] **ABSTRACT**
A recirculating toilet system for use in an aircraft or the like having at least one toilet with a valve-controlled drain line and a waste tank connected to the drain line having a flushing fluid therein. A valve-controlled flushing line is in fluid communication with both the tank and the toilet and at least one pump is provided for pumping the flushing fluid from the tank to the toilet. Means are provided for forming a vacuum in the tank so that when the toilet is flushed, waste products are sucked into the tank while the toilet is flushed with the flushing fluid.

11 Claims, 3 Drawing Figures



Analiza literatury ...

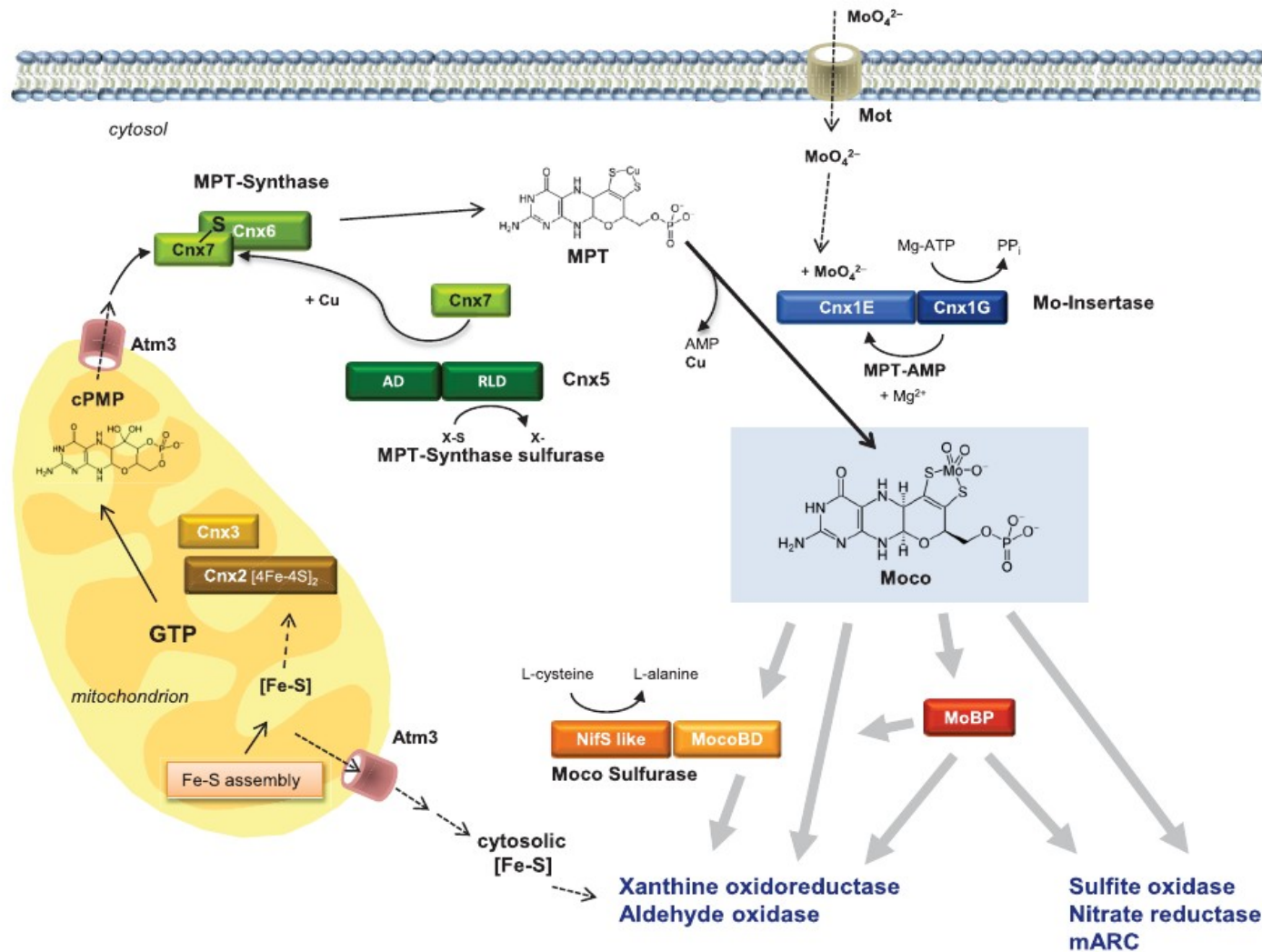
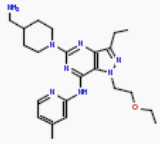
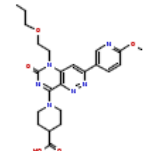
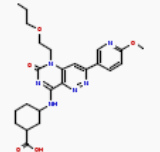
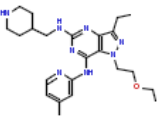
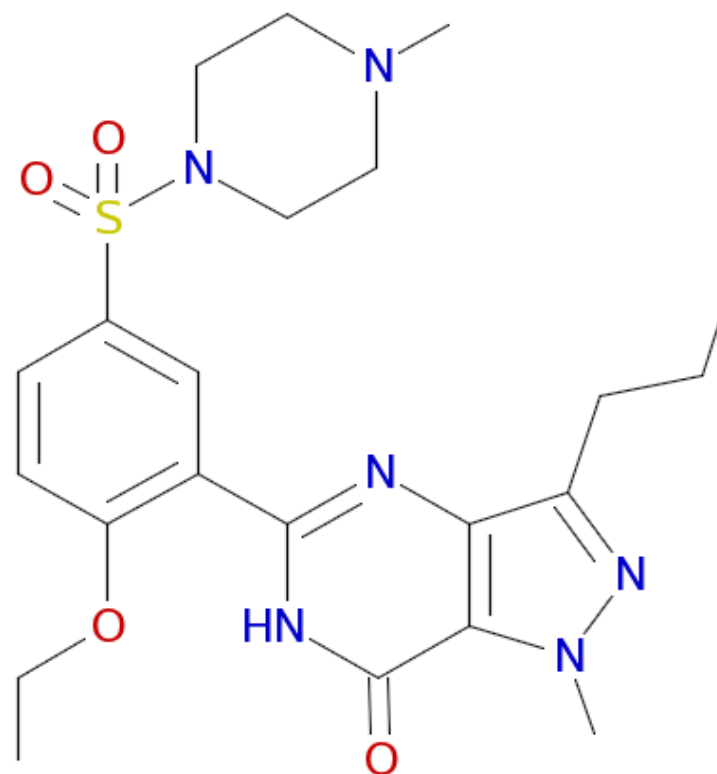


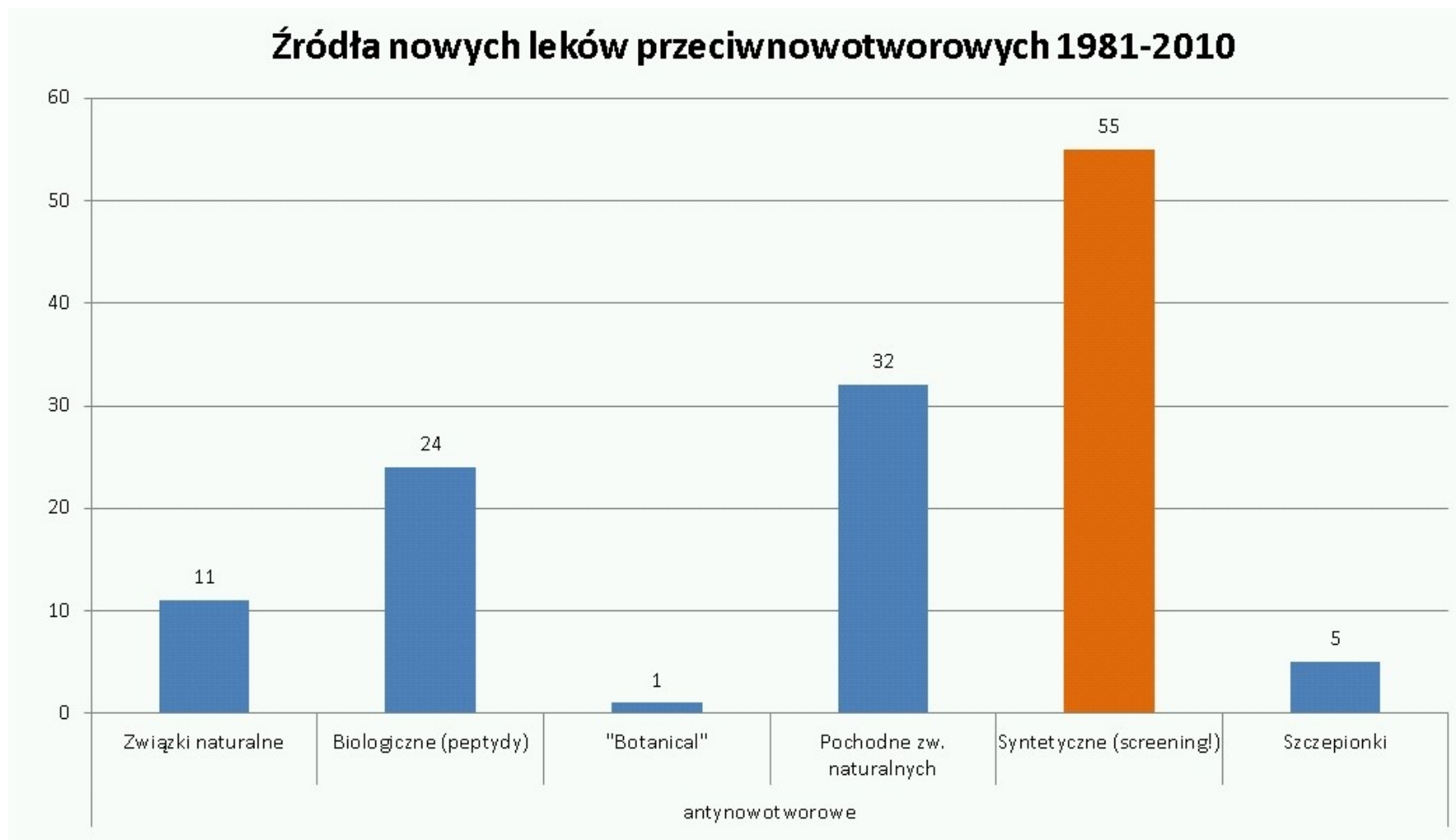
FIGURE 3. **Organization of biosynthesis and distribution of Moco in higher organisms (plants).** Moco biosynthesis starts in the mitochondria. The enzymes

Analiza patentów “dziury patentowe”

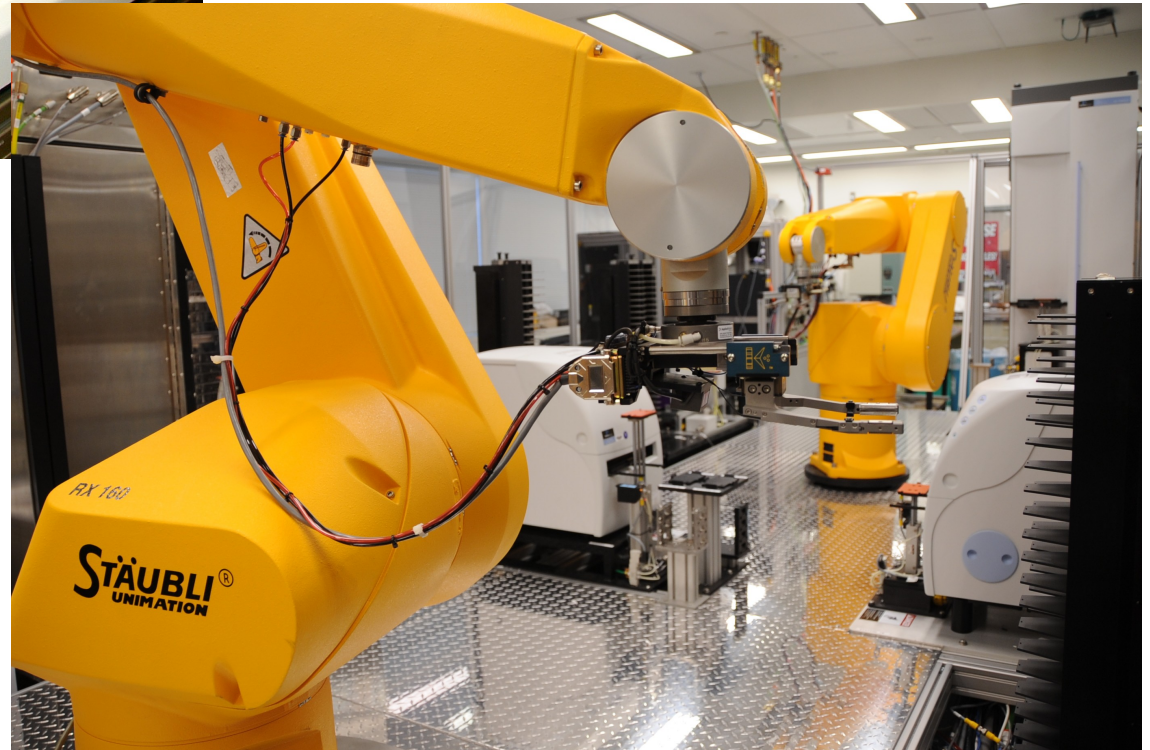
Ingredient	Molweight	Standard Type	Relation	Standard Value	Standard Units
 CHEMBL1094489	438.57	IC50	=	.007	nM
 CHEMBL1916488	468.51	IC50	=	.01	nM
 CHEMBL1916483	482.53	IC50	=	.01	nM
 CHEMBL1098465	438.57	IC50	=	.011	nM



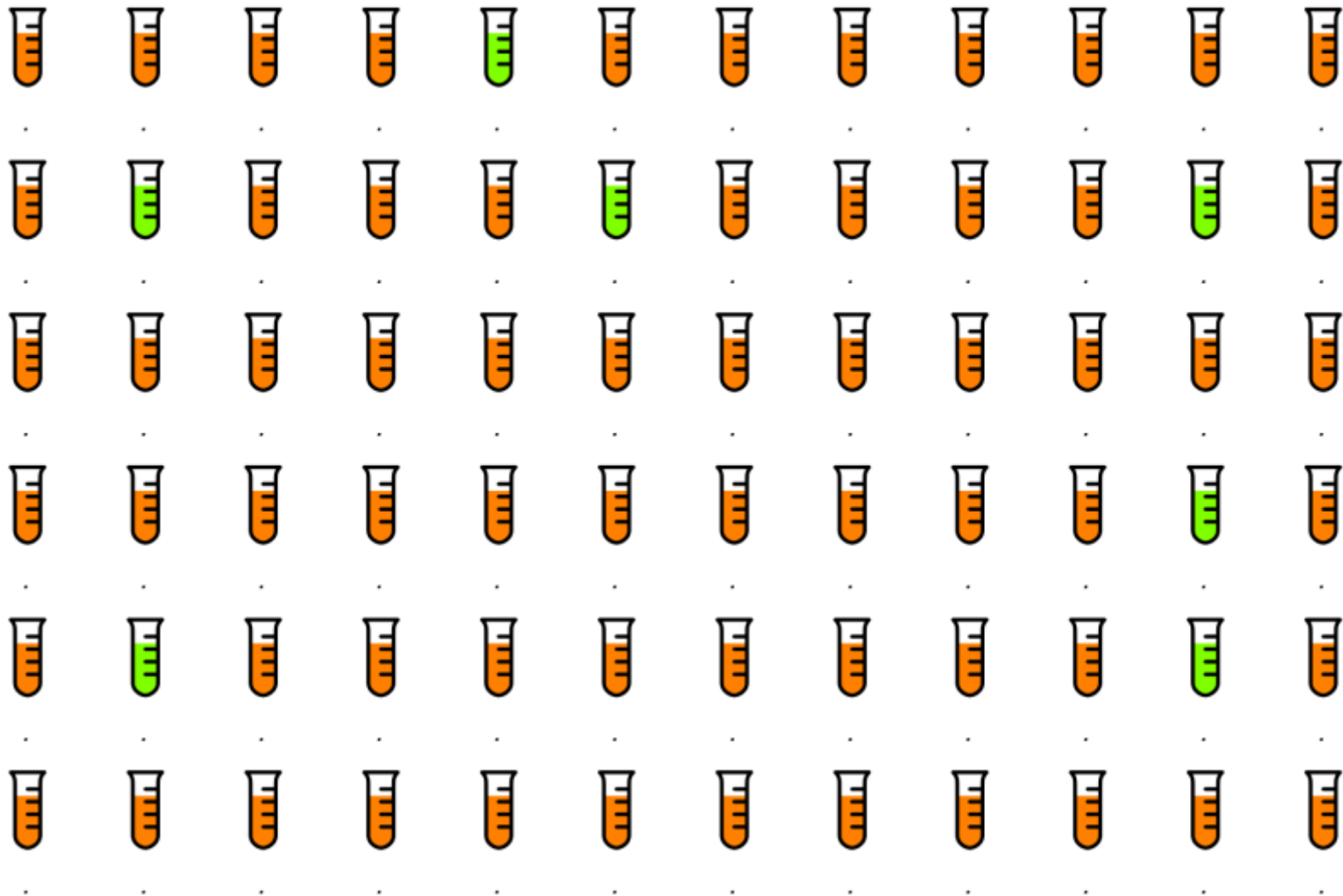
Skąd się biorą leki?











































































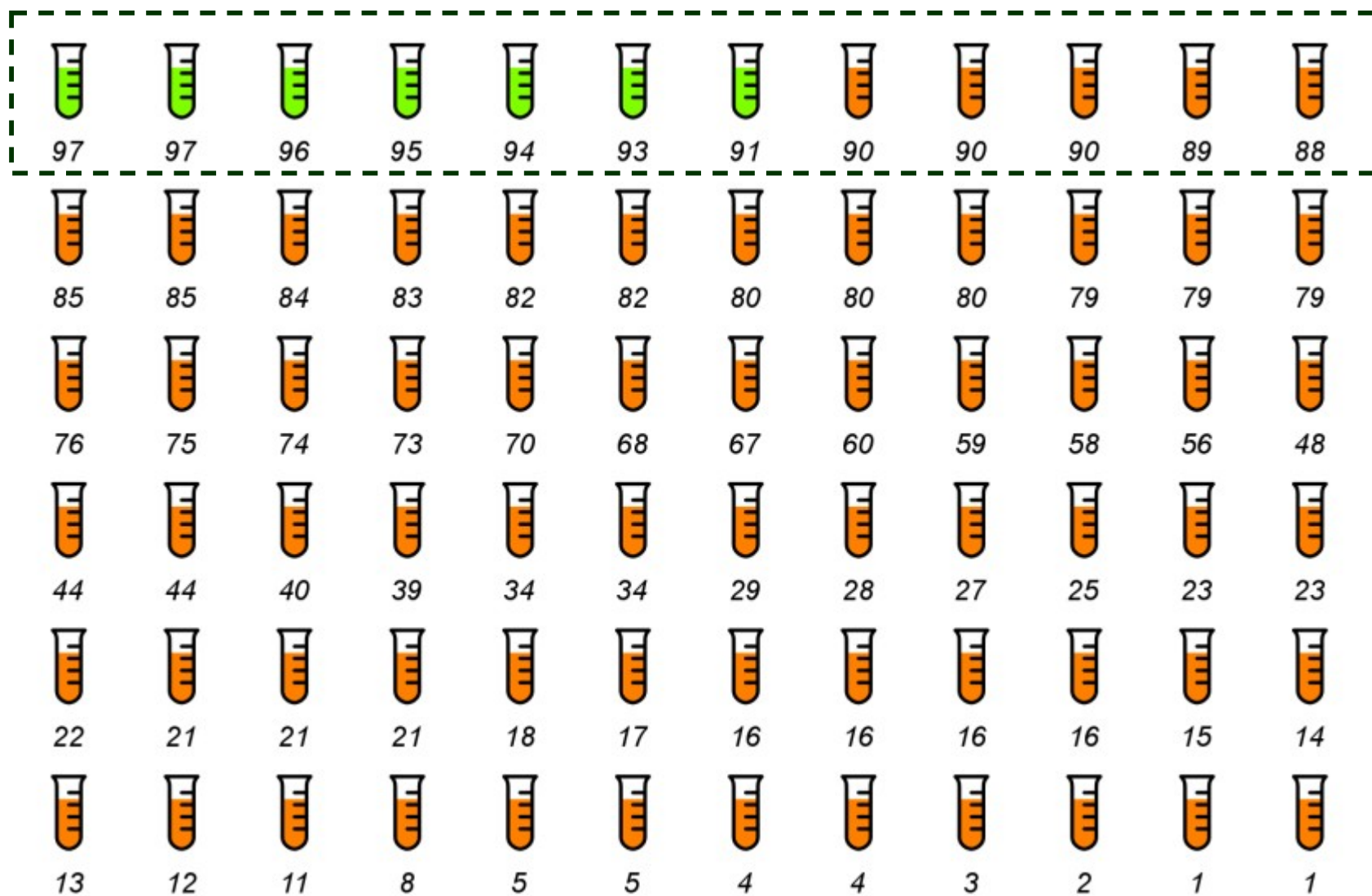
Screening bibliotek

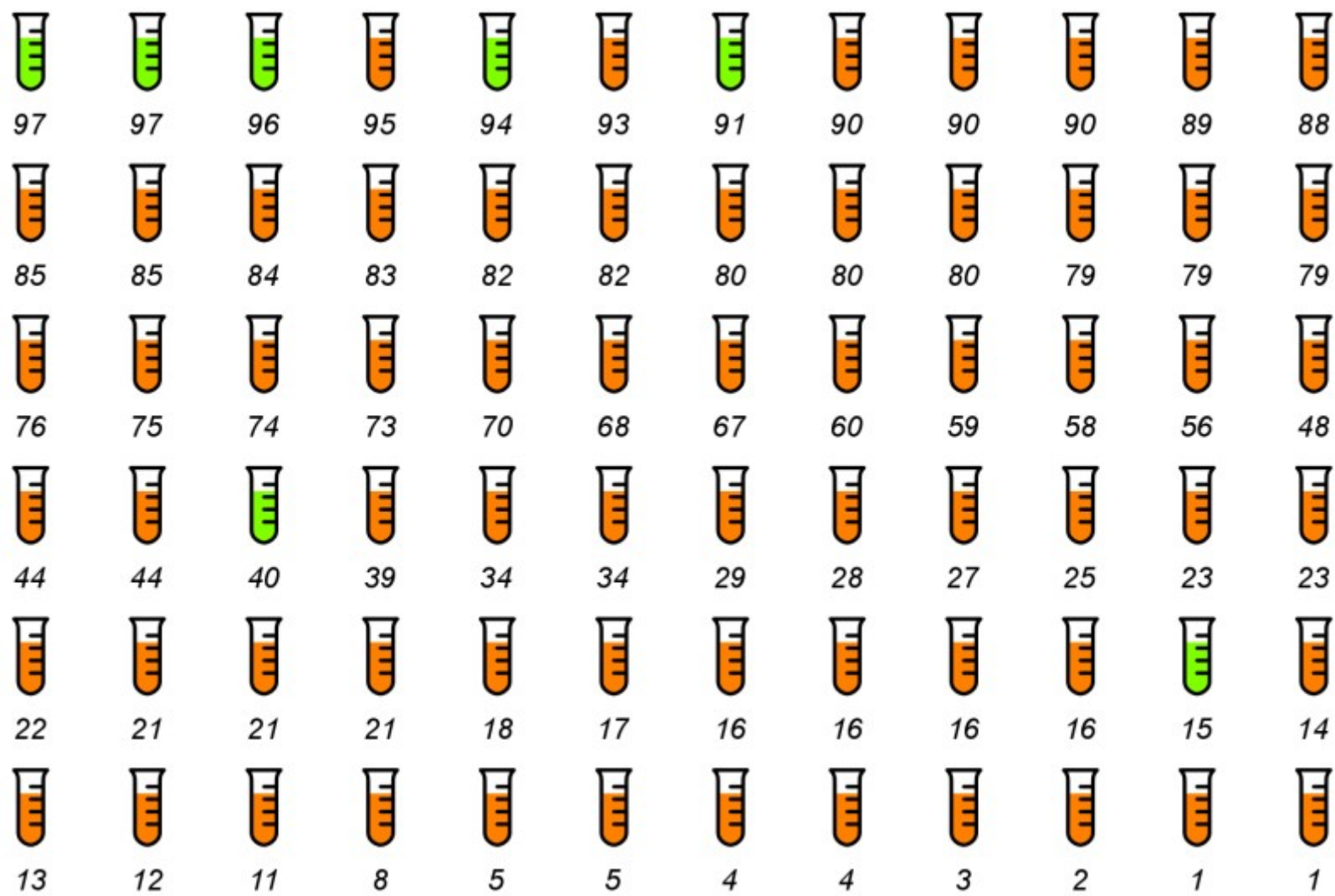


Wirtualny screening bibliotek

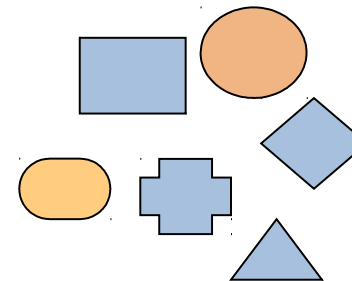
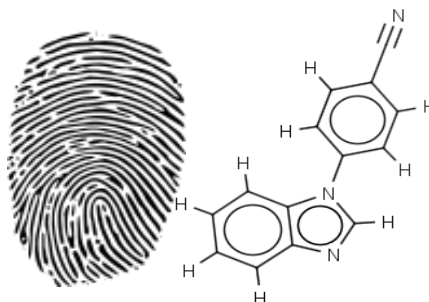
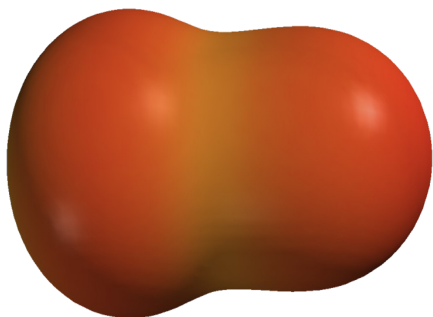
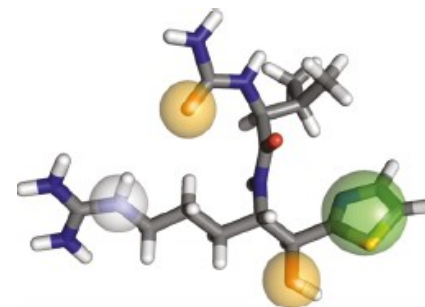
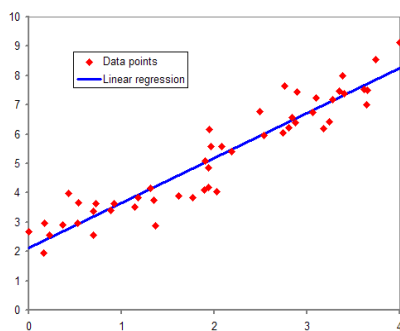
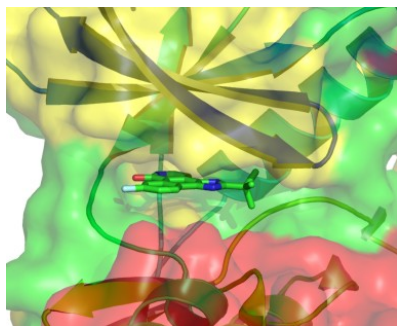


											
11	13	12	59	97	21	85	3	14	60	18	44
											
17	91	25	80	34	96	16	16	5	90	93	23
											
2	82	67	76	16	68	85	15	58	8	5	73
											
34	1	28	39	4	40	21	1	88	84	97	44
											
79	94	83	90	79	21	4	56	29	89	95	74
											
79	82	80	22	90	48	23	27	80	70	16	75



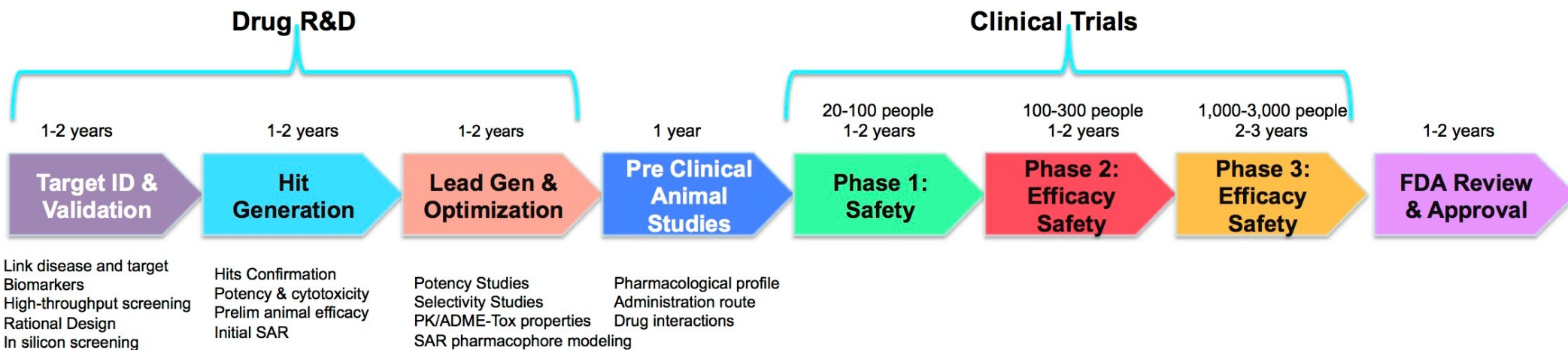


Metody screeningu wirtualnego























...

Gdzie mogą nam pomóc komputery?

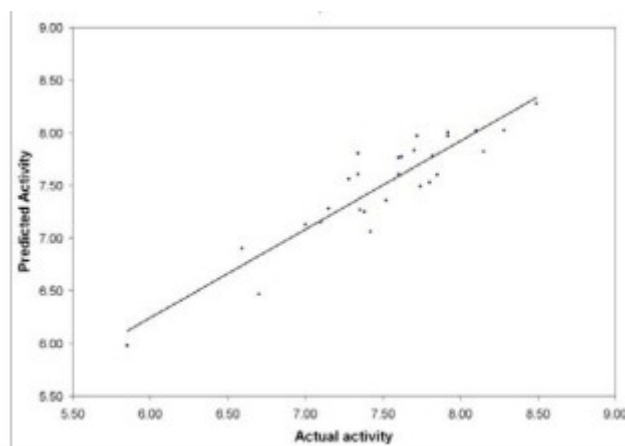


Dalsze analizy

- Structure-Activity Relationship (SAR)

Compound	Ref.	Ref.	Reference(s) (Ref(s), year)	Ref. (Ref(s), year)	Ref. (Ref(s), year)
1			1,2	1	1
2			1	1	1
3			1	1	1
4			1	1	1
5			1	1	1
6			1	1	1
7			1	1	1
8			1	1	1
9			1	1	1
10			1	1	1

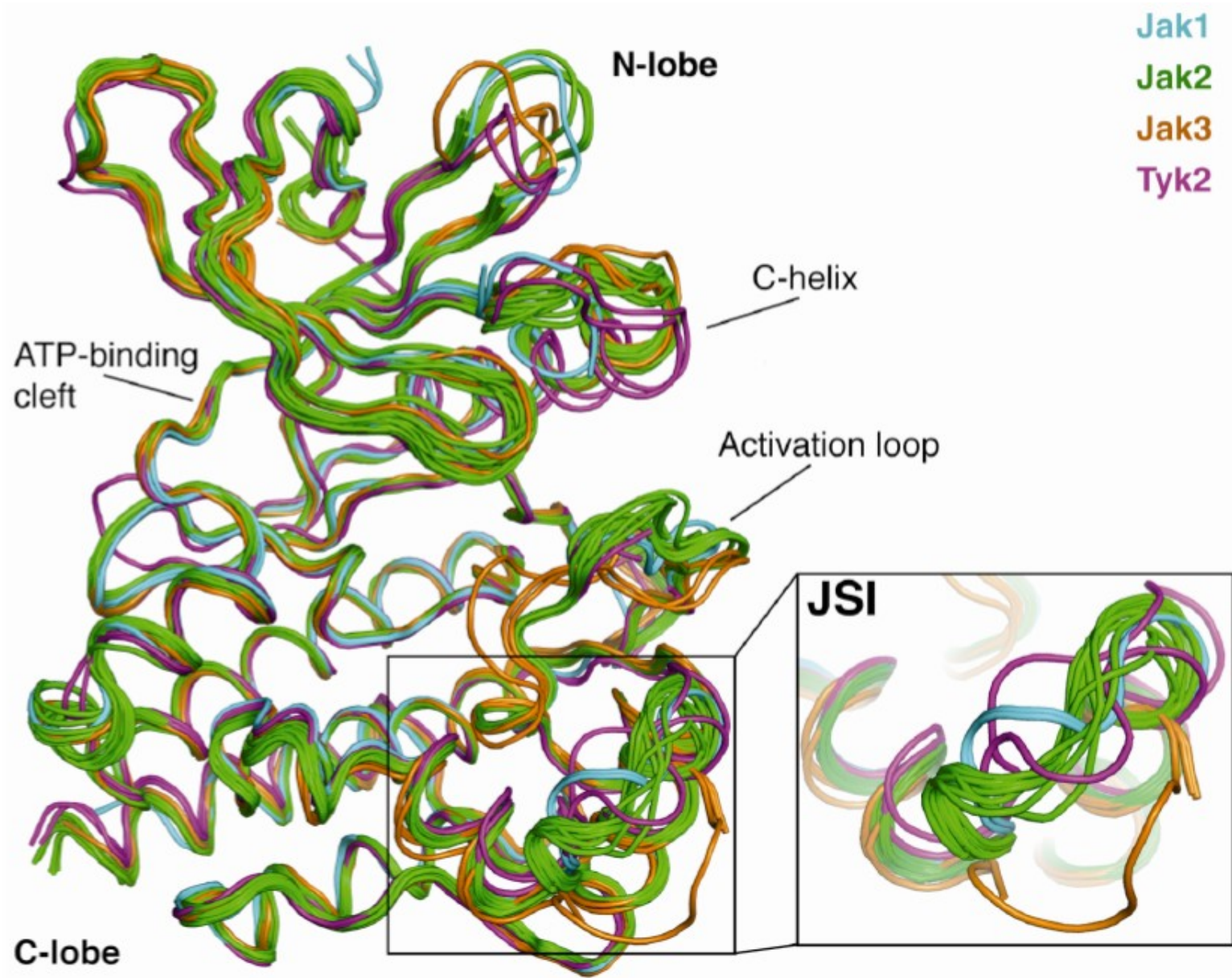
- QSAR – Quantitative SAR



ACS Chem Biol. Feb 19, 2010; 5(2):
245-253.

Curr Chem Genomics. 2008; 2:
29-39.

Activity profiling



ADMET profiling (druglikeness)

- Absorption, Distribution, Metabolism, Excretion, Toxicity
 - Solubility
 - logP
 - Blood/brain barrier penetration
 - ...
 - Metabolites prediction
 - Possible off-targets
 - ...

Badania przedkliniczne



This rat is being deprived of restful sleep using a single platform ("flower pot") technique.