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An Open PHACTS Knime workflow to collect compound data from public databases

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650 JAHRE universität wien

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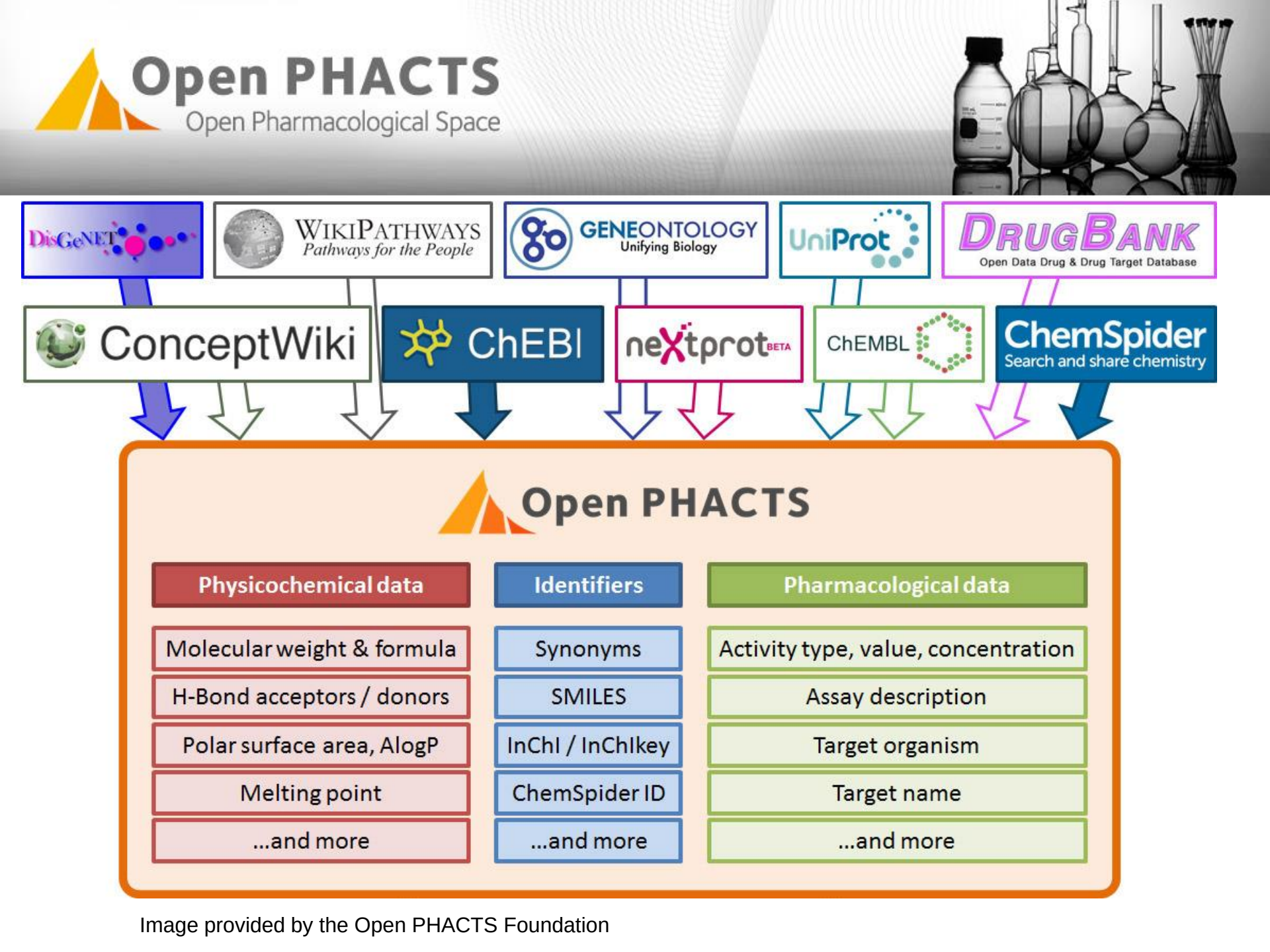

Image provided by the Open PHACTS Foundation

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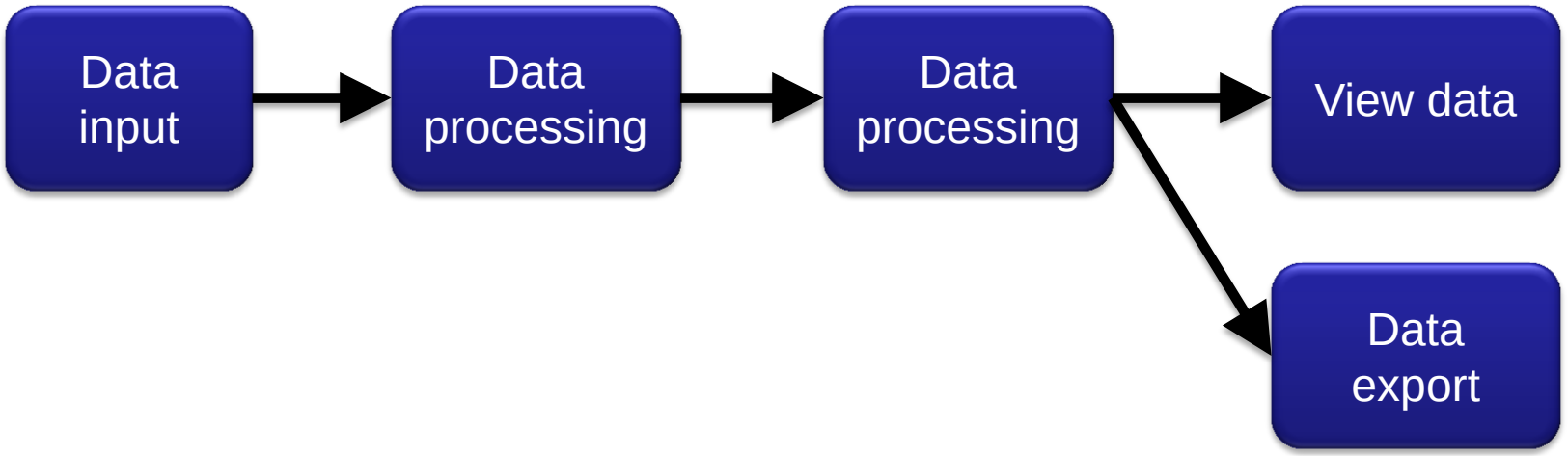
Workflow tools

- Single „blocks“ for each data processing step (e.g. data reader, calculations, visualization, …)
- Blocks are placed via drag-and-drop and connected to each other with arrows.
- Comercial (e.g. Pipeline Pilot) and free tools (e.g. KNIME) available



KNIME

- KNIME Analytics Platform
- Available from www.knime.org
- Open source data analytics, reporting and integration platform
- Workflows can be built by connecting „Nodes“
- Open PHACTS KNIME nodes available from github: https://github.com/openphacts/OPS-Knime

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KNIME

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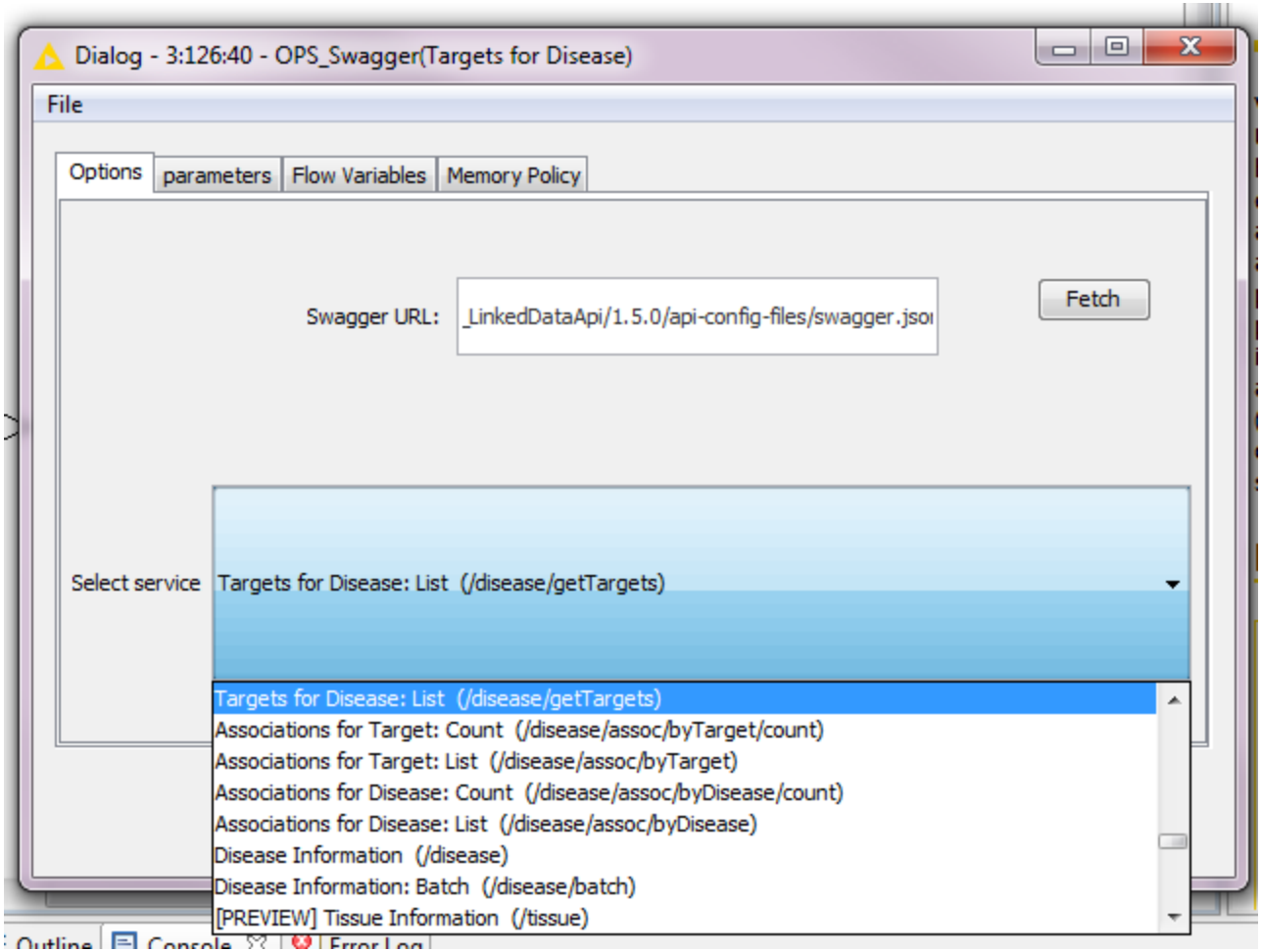
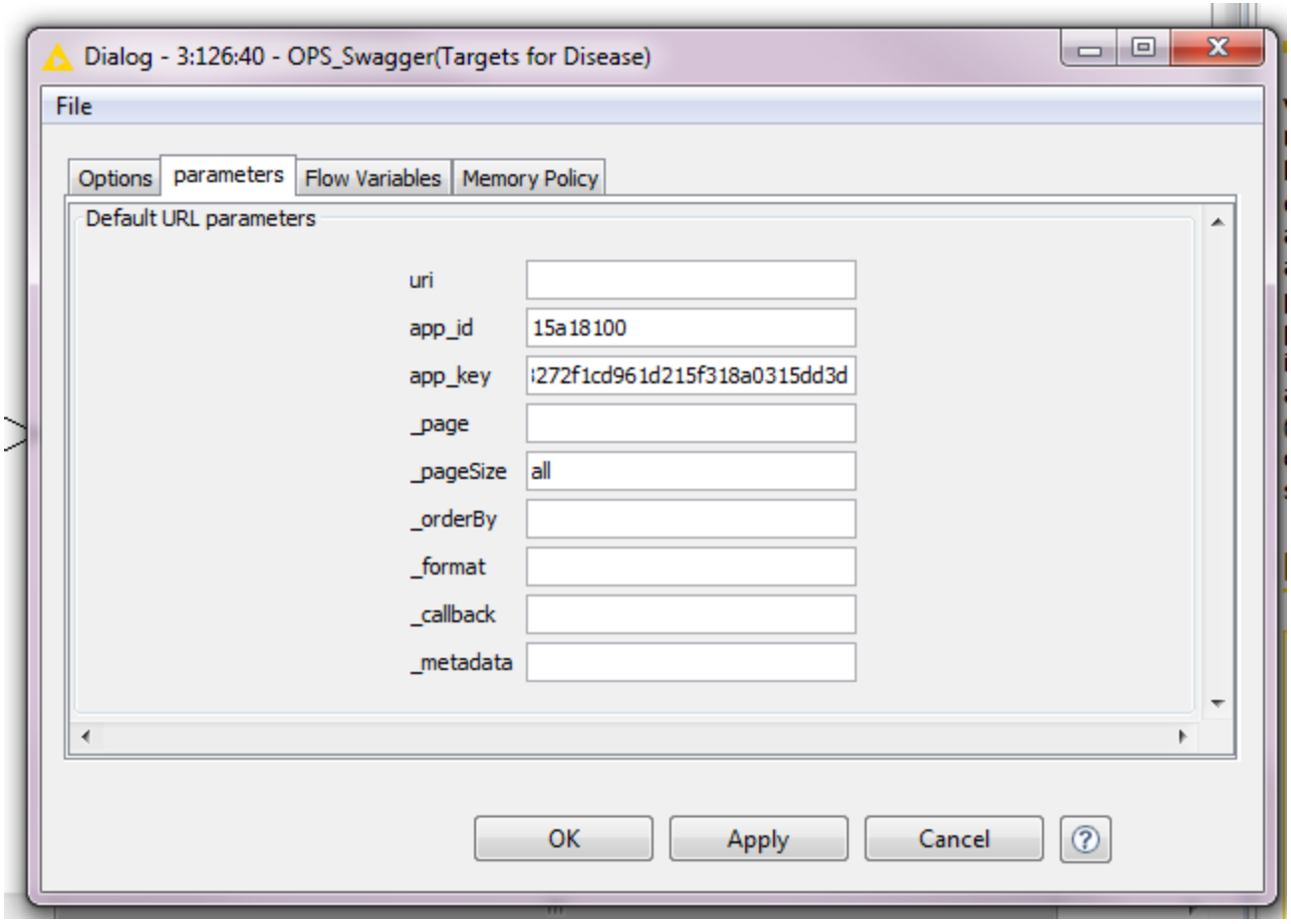
Open PHACTS KNIME node



Open PHACTS KNIME node



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Answering „scientific competency questions“

- 20 questions defined at the beginning of the project.
- Azzaoui K, Jacoby E, Senger S, *et al.* (2013) Drug Discov. Today 18: 843 – 852.
- Example: Give me all oxidoreductase inhibitors active <100 nM in human and mouse.
- Many questions need a combination of queries to the Open PHACTS Platform.
- Workflows published: Chichester C, Digles D, Siebes R, *et al.* (2015) Drug Discov. Today 20: 399 – 405.

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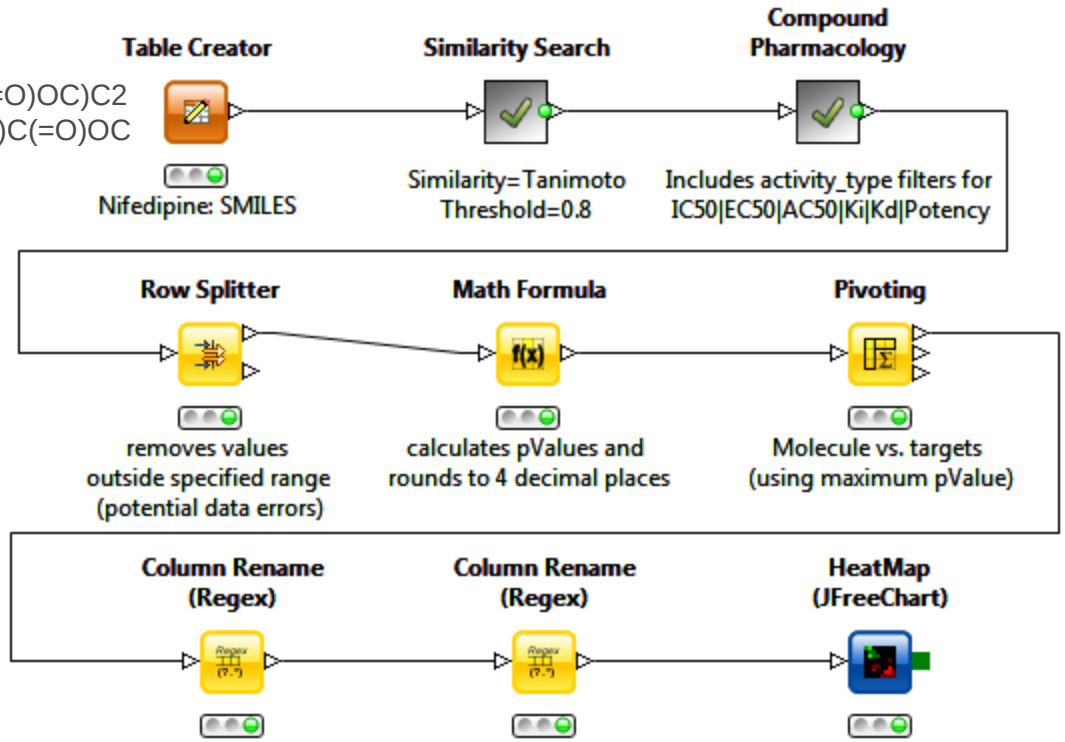
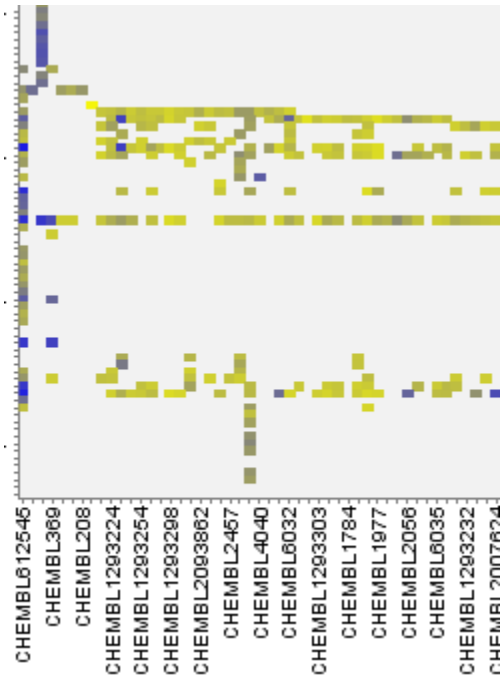
Example workflow

- Q10: For a given compound, summarize all similar compounds and their activities

CC1=C(C(C(=C(N1)C)C(=O)OC)C2
=CC=CC=C2[N+](=O)[O-])C(=O)OC





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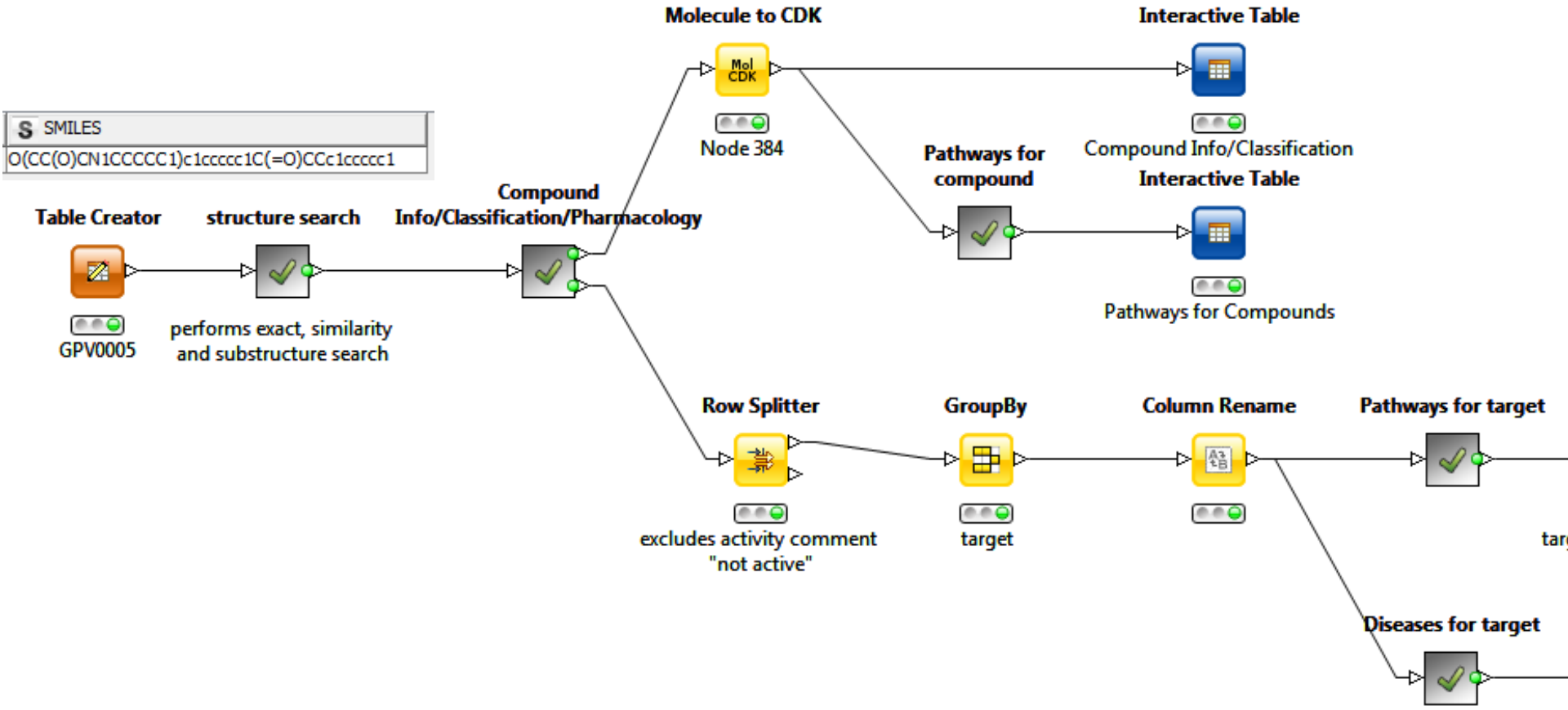
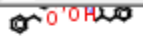
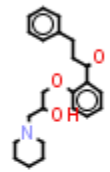
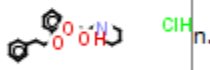
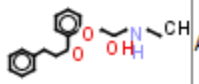
Workflow to collect compound data



Collected results: compound information

- Structure search: 96 molecules, including the molecule itself.
- Compound information/classification: 1 known drug propafenone

similarity	Chebi Class Label	SMILES	DB_description	DB_pro...	DB_toxi...	reporte...	label
0.955	?		n.a.	n.a.	n.a.	?	1-{2-[3-(4-t
1	?		n.a.	n.a.	n.a.	?	1-propanon
0.984	?		n.a.	n.a.	n.a.	?	1-{2-[2-Hyc
0.952	anti-arrhythmia drug		An antiarrhythmia agent ...	97%	Symptoms o...	HYPERHIDR...	propafenon

Collected results: bioactivity values

- 191 activity values (lower than 10 µM) against 33 targets.

First(Target_name)	First(Target_organism...	Unique count(SMILES)	Max*(similarity)
P-glycoprotein 1	Homo sapiens	27	1
CCRF-CEM/VCR-1000	Homo sapiens	23	1
Plasmodium falciparum	Plasmodium falciparum	7	1
Unchecked	?	6	1
Plasmodium falciparum (isolate K1 / Thailand)	Plasmodium falciparum K1	4	0.955
HERG	Homo sapiens	3	0.955
Cytochrome P450 2D6	Homo sapiens	2	0.952
Cytochrome P450 3A4	Homo sapiens	2	0.952
Cytochrome P450 1A2	Homo sapiens	2	0.952
Thrombopoietin	Homo sapiens	1	0.952
Serotonin 2b (5-HT2b) receptor	Homo sapiens	1	0.952
Thyroid stimulating hormone receptor	Homo sapiens	1	0.968
Beta-2 adrenergic receptor	Homo sapiens	1	0.952
Beta-1 adrenergic receptor	Homo sapiens	1	0.952
Norepinephrine transporter	Homo sapiens	1	0.952
Serotonin 2a (5-HT2a) receptor	Homo sapiens	1	0.952

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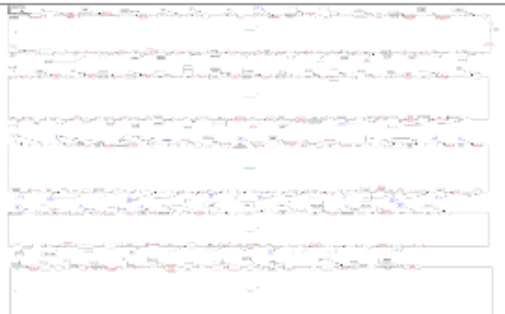
Collected results: pathways for targets

- 98 pathways

Unique concatenate(First(Target_name))	First(Pathway title)	Image from column1	Count(Pathw
Serotonin 2b (5-HT2b) receptor, Thyroid stimulating h...	GPCR downstream signaling		8
Serotonin 2b (5-HT2b) receptor, Thyroid stimulating h...	GPCR ligand binding		8

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Collected results: diseases for targets

- >2000 diseases in 25 disease classes

Unique concatenate(First(Target_name))	First(Disease name)	Concatenate(Disease association description)
Prelamin-A/C, Thrombopoietin, Serotonin 2b (5-HT2b) receptor, T...	NEOPLASM MALIGNANT	[Several exciting recent discoveries also point to a genome-scale disruption of the epigenome tha
Prelamin-A/C, Thyroid stimulating hormone receptor, Sulfonylurea ...	Alzheimer Disease	[The results of two more recent studies identify two additional human disease-associated protein
Prelamin-A/C, Serotonin 2b (5-HT2b) receptor, Thyroid stimulating...	Hypertension	[FPLD recapitulates the main metabolic attributes of the insulin resistance syndrome, including ce
Prelamin-A/C, Serotonin 2b (5-HT2b) receptor, Sodium channel pr...	Heart Failure	[Between January, 2008 and June, 2012 two patient populations were screened for the presenc
Beta-2 adrenergic receptor, Norepinephrine transporter, Serotoni...	Schizophrenia	[The inverse F-BAR (IF-BAR) domain proteins srGAP1, srGAP2 and srGAP3 are implicated in neurc
Thrombopoietin, Sodium channel protein type V alpha subunit, Sulf...	Cardiovascular Diseases	[Human thrombopoietin (TPO) is involved in cardiovascular disease as it regulates megakaryocyte
Prelamin-A/C, Sodium channel protein type V alpha subunit, Sulfon...	Congestive heart failure	[LMNA is one of the most prevalent mutated genes in dilated cardiomyopathy, and is associated v
Prelamin-A/C, Thyroid stimulating hormone receptor, Sulfonylurea ...	Obesity	[Obesity-related phenotypes have been linked to human chromosomes 1q21 and 20q13, regions
Prelamin-A/C, Thyroid stimulating hormone receptor, Norepinephri...	cortex bone disorders	[Measurements of NT-4/5 in rats subjected to lateral fluid percussion (LFP) TBI revealed two-thre
Serotonin 2b (5-HT2b) receptor, Beta-2 adrenergic receptor, Beta...	Depressive Disorder, Major	[Variation in catechol-O-methyltransferase is associated with duloxetine response in a clinical trial
Prelamin-A/C, Sulfonylurea receptor 2, Kir6.2, Beta-2 adrenergic r...	Colorectal Cancer	[Lamin A/C is a risk biomarker in colorectal cancer.]. Sentence from MEDLINE/PubMed, a databas
Prelamin-A/C, Thyroid stimulating hormone receptor, Norepinephri...	Adrenal Cortex Diseases	[Measurements of NT-4/5 in rats subjected to lateral fluid percussion (LFP) TBI revealed two-thre
Prelamin-A/C, Sulfonylurea receptor 2, Kir6.2, Beta-2 adrenergic r...	Diabetes Mellitus, Type 2	[The aim of this study was to investigate whether genetic variation in LMNA can influence the risk
Thrombopoietin, Sodium channel protein type V alpha subunit, Sulf...	Myocardial Infarction	[The observation of frequency differences between cases and controls in two independent samp
Prelamin-A/C, Thyroid stimulating hormone receptor, Sulfonylurea ...	Neoplasm Metastasis	[In conclusion, in breast carcinomas, the frequency of multiple metastasis was found to be higher
Prelamin-A/C, Thyroid stimulating hormone receptor, Beta-2 adren...	Carcinogenesis	[Using several methods we found that S100A6 interacts with lamin A/C, a protein known to be im
Prelamin-A/C, Beta-2 adrenergic receptor, Norepinephrine transp...	Carcinoma of lung	[The relationship between lung cancer phenotype and lamin expression was explored further in t
Prelamin-A/C, Thyroid stimulating hormone receptor, Sodium chan...	Recurrent Malignant Neoplasm	[Recent clinical studies report that IDC-P is associated with neoadjuvant androgen deprivation th
Prelamin-A/C, Beta-2 adrenergic receptor, Beta-1 adrenergic rece...	Adenocarcinoma	[Among the proteins that were identified, Rho GDP dissociation inhibitor 2, alpha-enolase, Lamin
Prelamin-A/C, Beta-2 adrenergic receptor, Norepinephrine transp...	Malignant neoplasm breast	[As IDC constitutes approximately 70% of breast cancers seen clinically, the level of Di12 expres
Beta-2 adrenergic receptor, Norepinephrine transporter, Serotoni...	Depression	[Using the dexamethasone/corticotrophin-releasing hormone (DEX/CRH) test, we investigated th
Norepinephrine transporter, Serotonin 2a (5-HT2a) receptor, Sero...	Parkinson Disease	[Norepinephrine transporter (NET) binding site concentration in the LC of PD subjects was signific

Conclusions

- Workflow allows the easy preparation of a first overview on known data for a compound of interest.
- New ideas for targets to test the compounds against.
  - Example: Serotonin receptor for propafenone derivatives
- Literature (Pubmed) is returned for the results.
- Methods for prioritization needed (e.g. which of the > 2000 diseases are relevant)

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