Collecting compound data from public databases using Open PHACTS and KNIME

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Introduction

The Open PHACTS project [1] integrates several public databases, thus allowing answering questions relevant for research in the drug-discovery process [2]. The data collected in the project can be accessed with web tools, such as the Open PHACTS Explorer (www.openphacts.org/explorer) or by using the programming interface (API, available from dev.openphacts.org). To answer questions requiring several different queries in an automated way, workflow tools such as KNIME or Pipeline Pilot are a valuable resource. Such KNIME workflows were used for several use-cases [3] and to provide answers to drug-discovery research questions [4].

Aim of the work

In the current work, a workflow to easily generate a summary of known data connected to a compound of interest is presented.

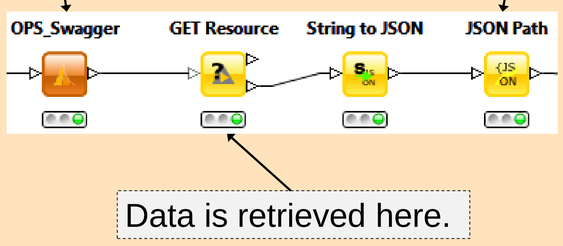
Methods

The workflow was generated using KNIME, with the Open PHACTS nodes available from the github repository (https://github.com/openphacts/OPS-Knime).

General implementation of API calls with KNIME nodes

OPS_Swagger generates the API call.

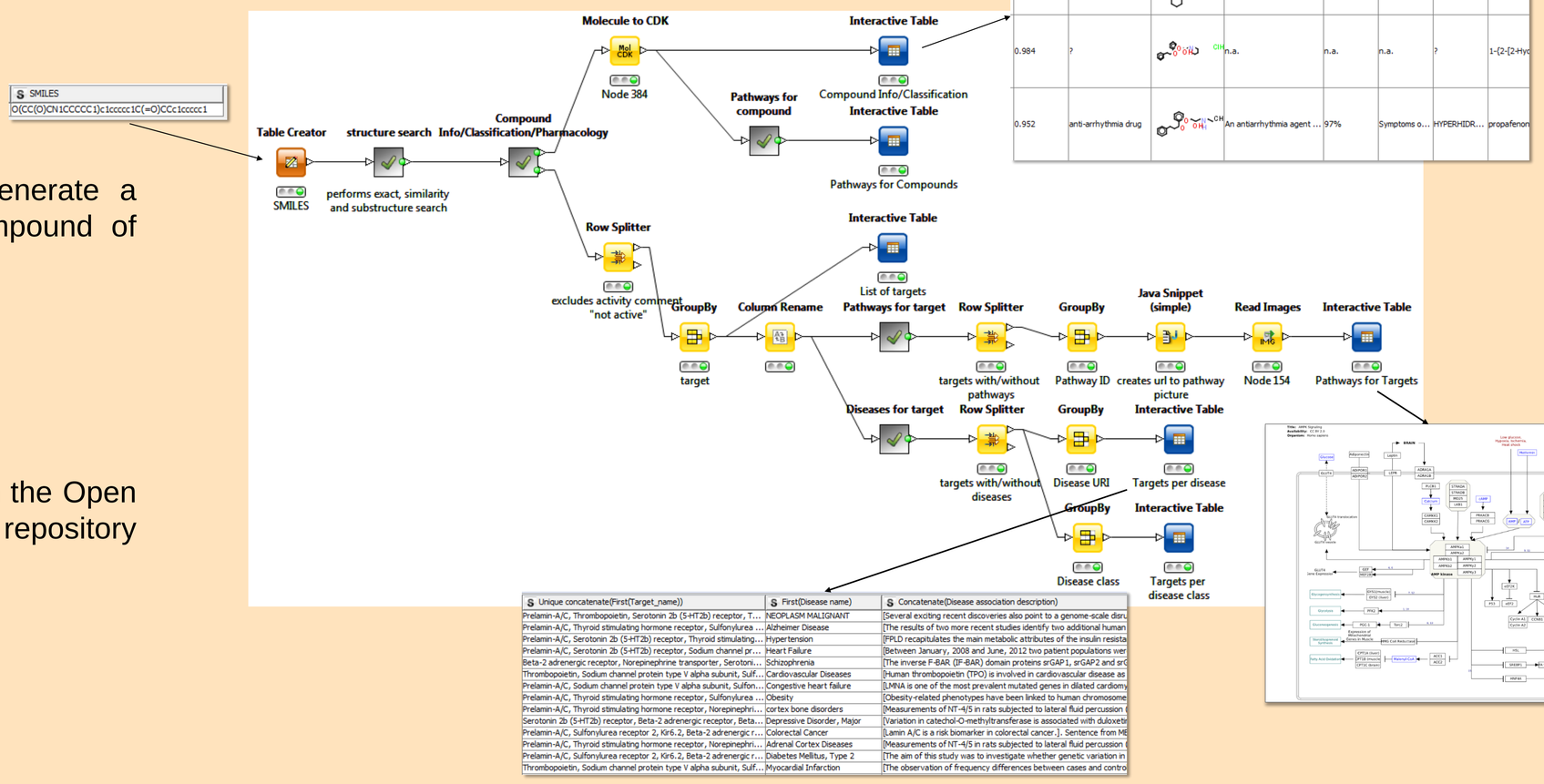
Columns which should be included in the tabular output are specified here.



Currently, a multi-step approach is necessary to retrieve data from the API. A simplified node to retrieve the data directly is currently under development.

The workflow

- Query: SMILES of the molecule of interest.
- Exact or similarity/substructure search.
- Data for retrieved molecules:
  - Function and toxicity annotation (Drugbank)
  - Role of the molecule (ChEBI)
  - Pharmacology data, pChEMBL >= 5 (ChEMBL)
- Data for retrieved targets:
  - Pathways (WikiPathways)
  - Diseases (DisGeNET)
- Simple counts generated by GroupBy node.



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 disru
Prelamin-A/C, Thyroid stimulating hormone receptor, Sulfonylurea …	Alzheimer Disease	[The results of two more recent studies identify two additional human
Prelamin-A/C, Serotonin 2b (5-HT2b) receptor, Thyroid stimulating…	Hypertension	[FPLD recapitulates the main metabolic attributes of the insulin resista
Prelamin-A/C, Serotonin 2b (5-HT2b) receptor, Sodium channel pr…	Heart Failure	[Between January, 2008 and June, 2012 two patient populations wer
Beta-2 adrenergic receptor, Norepinephrine transporter, Serotoni…	Schizophrenia	[The inverse F-BAR (IF-BAR) domain proteins srGAP1, srGAP2 and srG
Thrombopoietin, Sodium channel protein type V alpha subunit, Sulf…	Cardiovascular Diseases	[Human thrombopoietin (TPO) is involved in cardiovascular disease as
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 cardiomy
Prelamin-A/C, Thyroid stimulating hormone receptor, Sulfonylurea …	Obesity	[Obesity-related phenotypes have been linked to human chromosome
Prelamin-A/C, Thyroid stimulating hormone receptor, Norepinephri…	cortex bone disorders	[Measurements of NT-4/5 in rats subjected to lateral fluid percussion (
Serotonin 2b (5-HT2b) receptor, Beta-2 adrenergic receptor, Beta…	Depressive Disorder, Major	[Variation in catechol-O-methyltransferase is associated with duloxetir
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 MB
Prelamin-A/C, Thyroid stimulating hormone receptor, Norepinephri…	Adrenal Cortex Diseases	[Measurements of NT-4/5 in rats subjected to lateral fluid percussion (
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
Thrombopoietin, Sodium channel protein type V alpha subunit, Sulf…	Myocardial Infarction	[The observation of frequency differences between cases and contro

Results

Example: O(CC(O)CN1CCCCC1)c1ccccc1C(=O)CCc1ccccc1
(a propafenone derivative)

- Structure search: 96 molecules (including the query)
- 1 known drug (propafenone)
- 191 activity values (< 10µM) against 33 targets
- 98 pathways
- >2000 diseases in 25 disease classes

Conclusions

The workflow allows the preparation of a first overview on data known for a potential compound of interest, including data for similar compounds. Links to the original data sources are retained, allowing manual curation of the collected associations.

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References:
[1] Williams A J, Harland L, Groth P, *et al.* (2012) Drug Discov. Today 17: 1188 – 1198.
[2] Azzaoui K, Jacoby E, Senger S, *et al.* (2013) Drug Discov. Today 18: 843 – 852.
[3] Ratnam J, Zdrazil B, Digles D, *et al.* (2014) PloS One: e115460. doi: 10.1371/journal.pone.0115460.
[4] Chichester C, Digles D, Siebes R, *et al.* (2015) Drug Discov. Today 20: 399 – 405.