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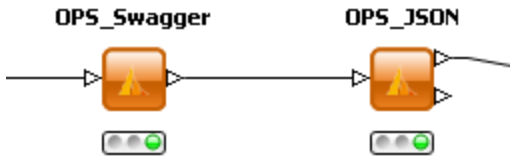
Open Pharmacological Space

Characteristics of KNIME Nodes

Daniela Digles
support@openphacts.org

Drug Discovery Workflow Workshop: Using Open PHACTS



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 for Innovation
KNIME

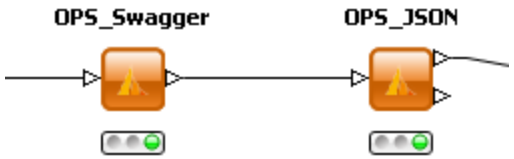
OPS-Knime nodes

- Created by Ronald Siebes, VU Amsterdam.
- No predefined set of nodes for each API call.

- OPS_Swagger:
  - creates the API call
  - Swagger file is used to automatically provide available API calls and parameters

- OPS_JSON:
  - executes the API call
  - transforms the output into a flattened spreadsheet format

- available from https://github.com/openphacts/OPS-Knime



Installing the Open PHACTS KNIME nodes

- https://github.com/openphacts/OPS-Knime
- Download the latest version of the KNIME nodes:
  - Click on the zip file (currently the latest version is org.openphacts.utils.json_1.1.0.zip
  - Click on Raw to start the Download (save it anywhere on your computer).
  - Unzip it into a folder called org.openphacts.utils.json_1.1.0 in the plugins folder of your KNIME installation.

- Start KNIME

Swagger

- Structured format for the generation of API documentation. (https://helloreverb.com/developers/swagger)
- https://raw.githubusercontent.com/openphacts/OPS_LinkedDataApi/1.5.0/api-config-files/swagger.json


```
{
  "basePath": "https://beta.openphacts.org/1.3",
  "apiVersion": "v1.3",
  "apis": [
    {
"path": "/compound" ,
      "operations": [
        {
          "httpMethod": "GET",
          "summary":  "Compound Information" ,
          "description":  "Information about a single compound.
   ...

          "group": "Compound" ,
          "parameters": [
            {
              "name":  "uri" ,
              "description":  "A compound URI. e.g.: http://www.conceptwiki.org/concept/38932552-111f-4a4e-a46a-4ed1c
              "dataType": "string",
              "required": true,
              "paramType": "query"
            },
```

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https://dev.openphacts.org/docs/1.5

OpenPHACTS API v1.5

Compound Information /compound GET

Description

Returns information about a single compound including (but not limited to): molecular weight, biotransformation, protein binding and toxicity.

...

PARAMETER	VALUE	DESCRIPTION
uri	(required)	A compound URI. e.g.: http://www.conceptwiki.org/concept/38932552-111f-4a4e-a46a-4ed1d7bdf9d5
app_id		Your access application id
app_key		Your access application key
_format		The desired result format.

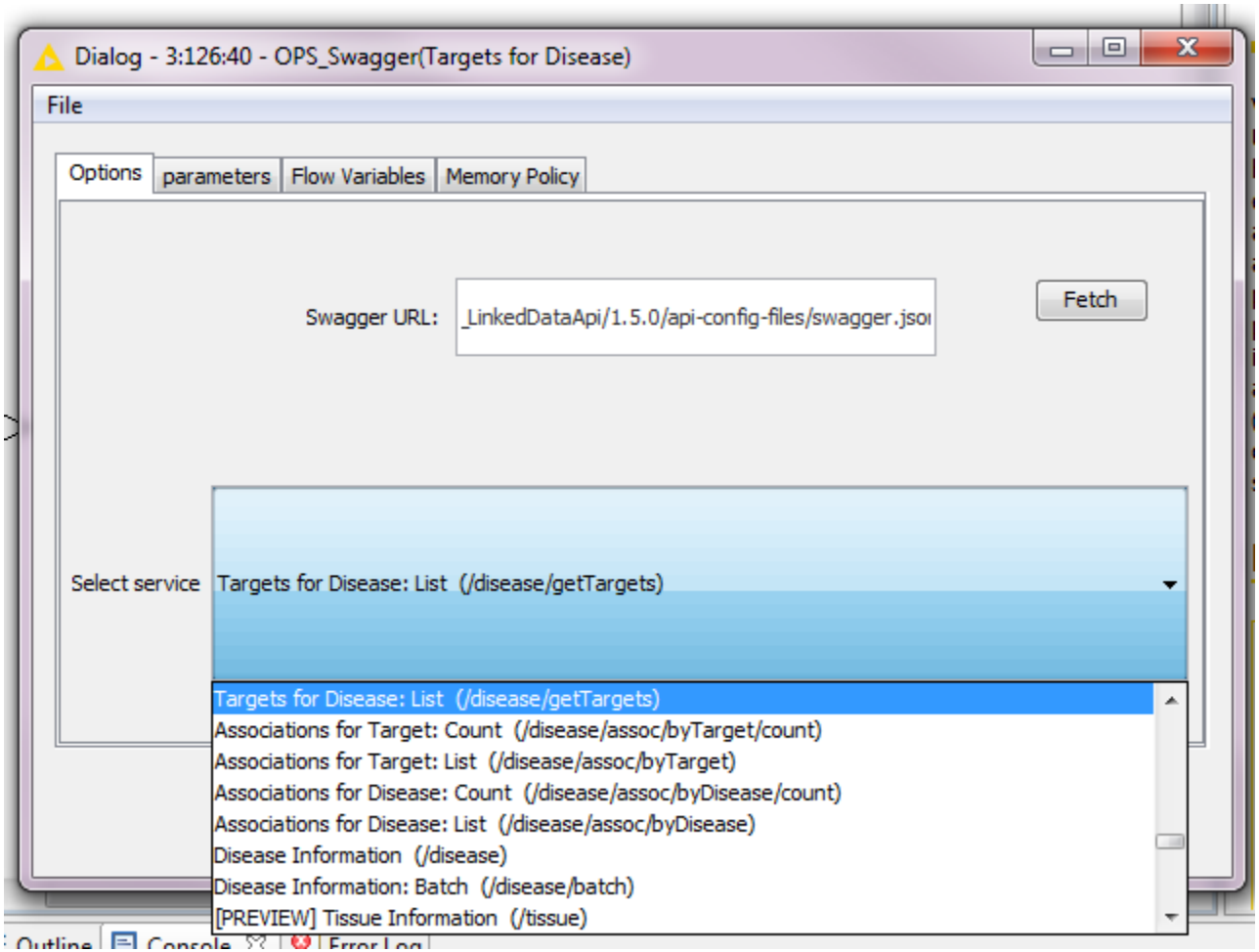
OPS_Swagger details

- Knime node where the user provides a url to a Swagger file (default: current Open PHACTS API)
- File is parsed and provides a list of the available API calls.
- Parameters tab is updated to the available parameters.
- Parameters can be set in the parameters tab or in the input table.
- Output of the node is an executable API call.

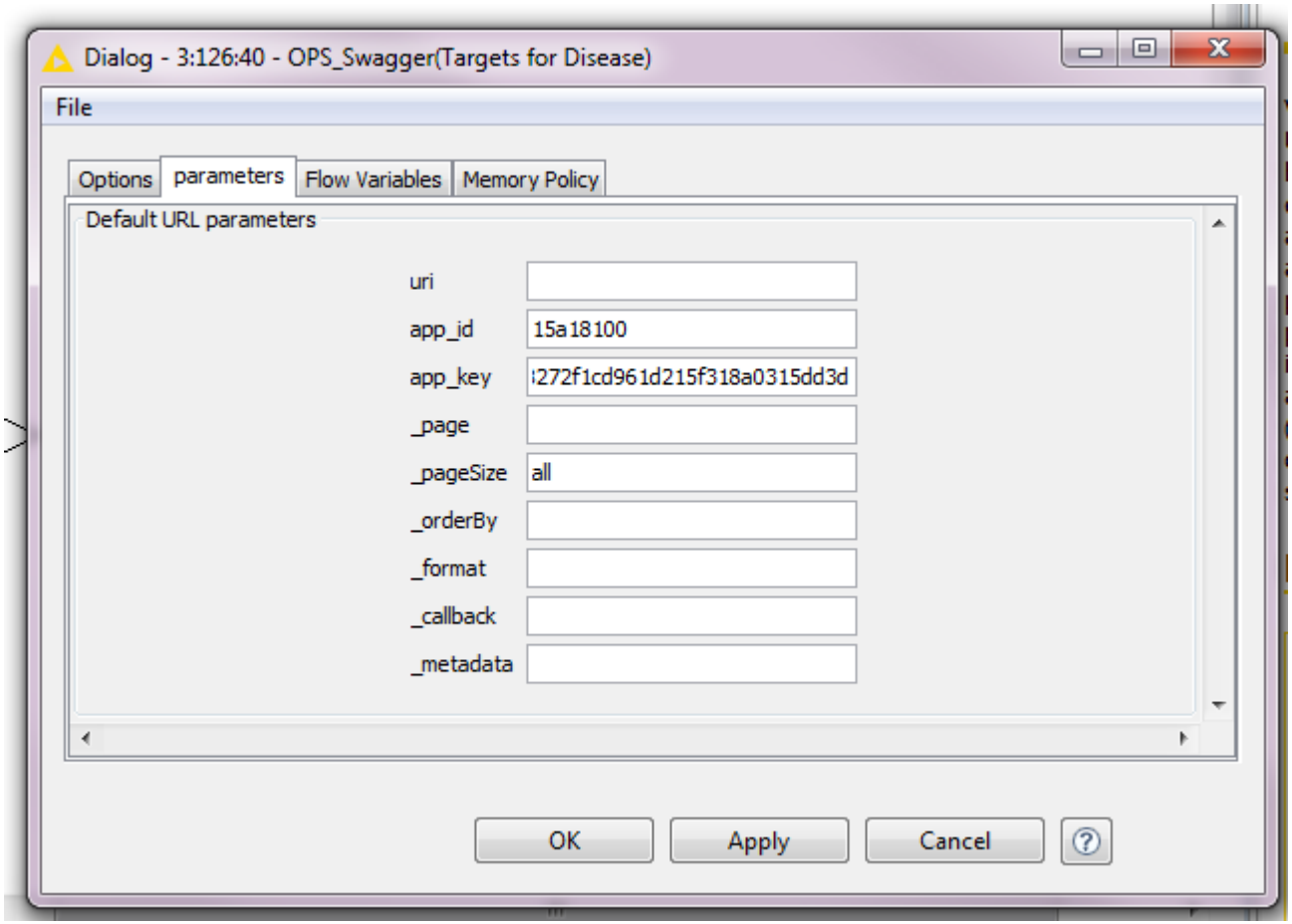
- Advantages
  - Updates to Swagger file are automatically shown in the node interface.
  - Descriptions of the parameters are available.
  - Nodes remember the configuration and can be re-used and shared.
  - Can be used for any API which uses Swagger.

- Disadvantage
  - Some familiarity with the Open PHACTS API necessary.

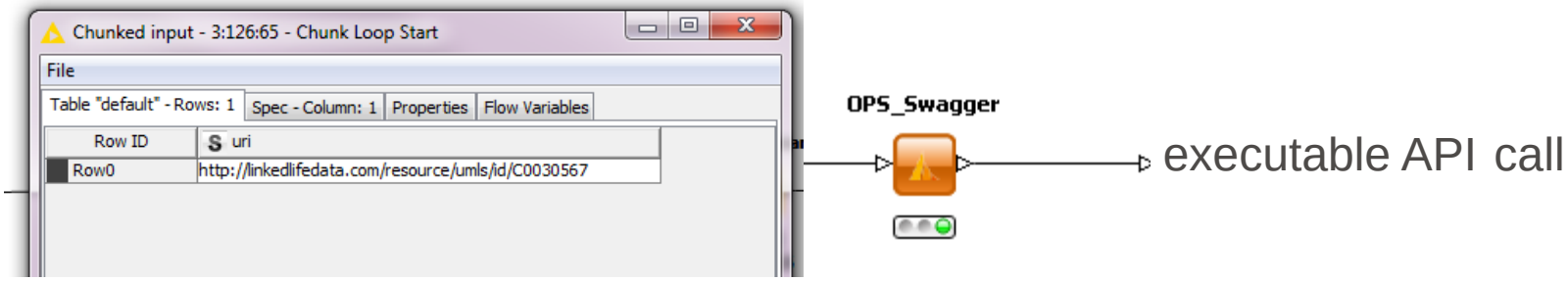
OPS_Swagger details



OPS_Swagger details



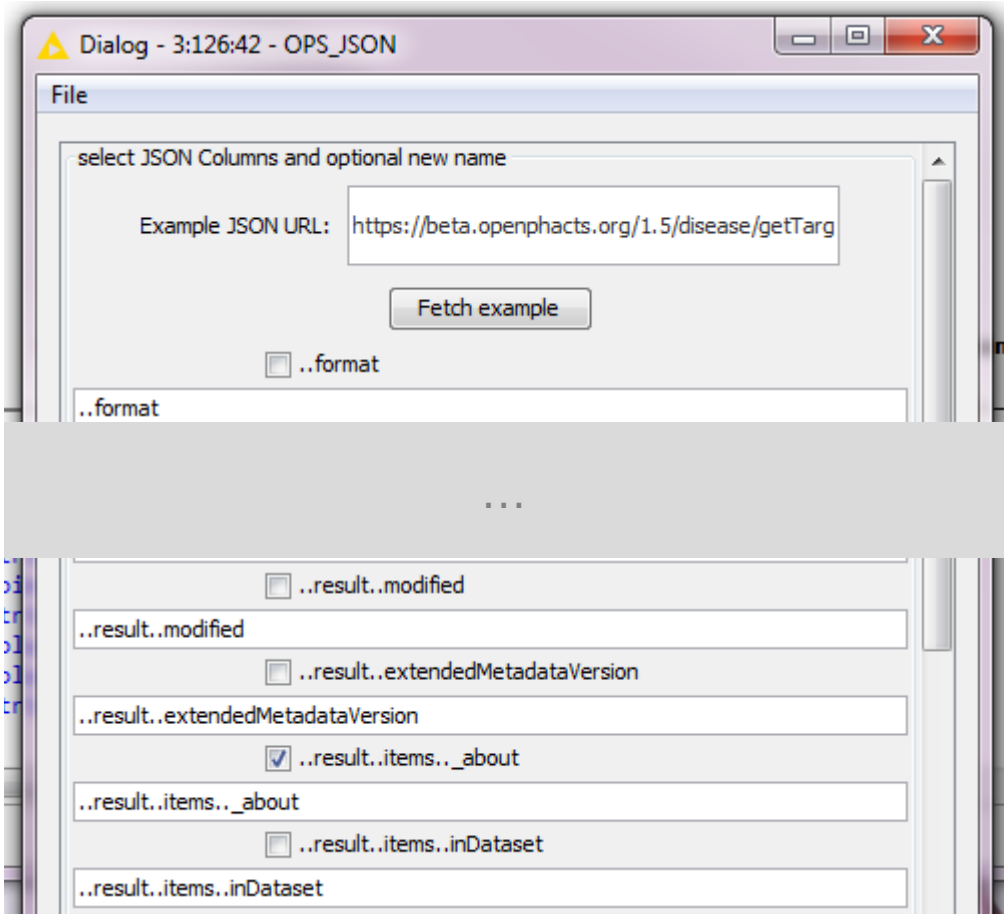
OPS_Swagger details



OPS_JSON details

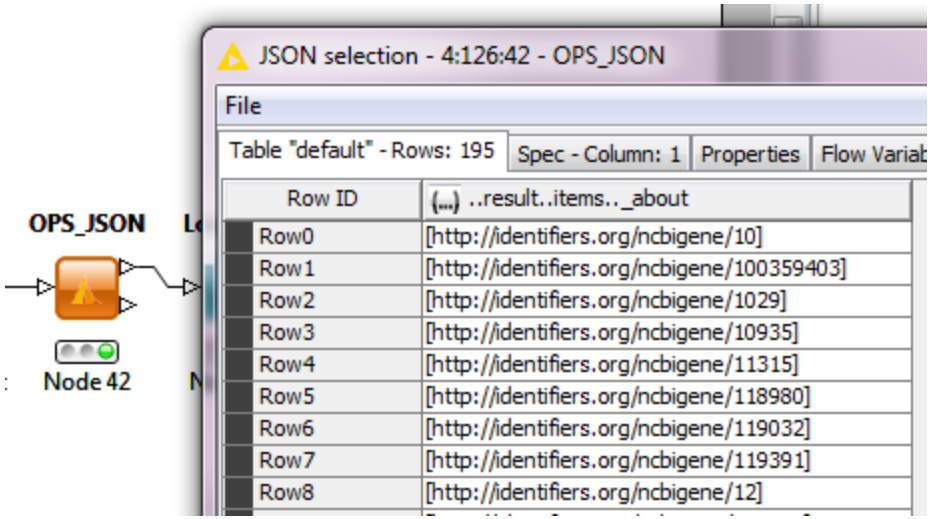
- Executes API call
- Hierarchical json structure is flattened:
  - Traverse recursively through JSON hierarchy
  - Concatenate the JSON keys which become column headers for the tables
  - The cells are the values from the current JSON key in the path
- An example API call is used to fetch the available columns
- User can select and rename the columns he is interested in
- Output:
  - table with user selected columns
  - table with full flattened json output

OPS_JSON details



OPS_Swagger details

executable API call



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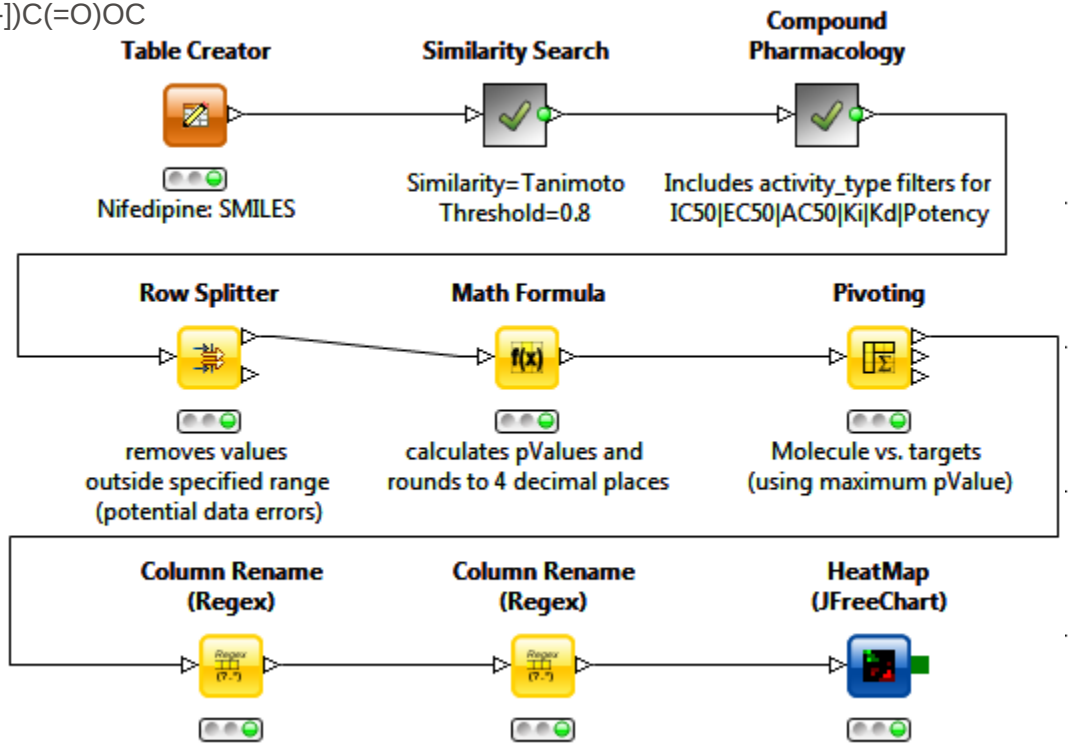
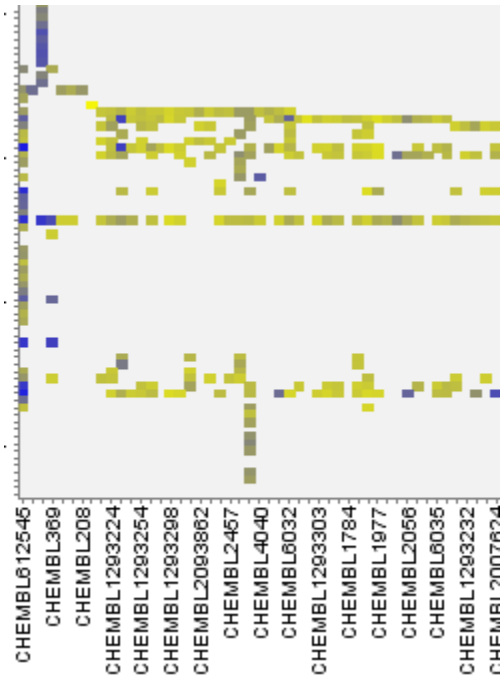
Example workflow

- 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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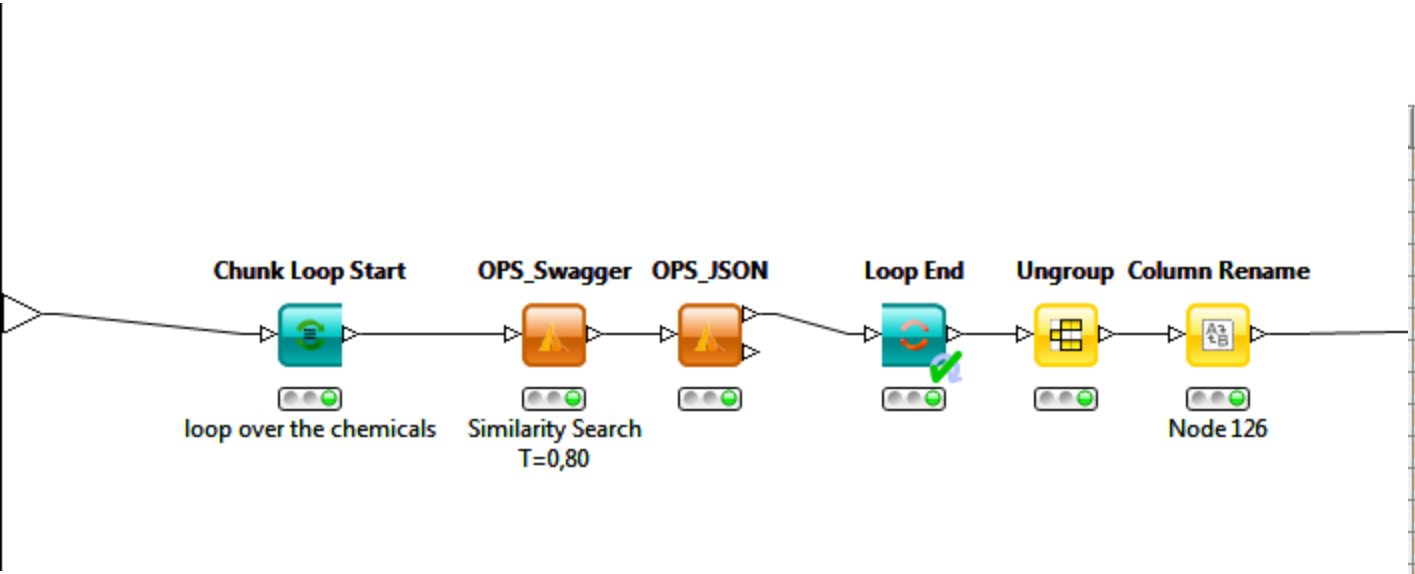
Similarity Search Metanode



S uri
http://ops.rsc.org/OPS980348
http://ops.rsc.org/OPS1864091
http://ops.rsc.org/OPS1299748
http://ops.rsc.org/OPS1306882
http://ops.rsc.org/OPS1188404
http://ops.rsc.org/OPS16172
http://ops.rsc.org/OPS1872614
http://ops.rsc.org/OPS1298823
http://ops.rsc.org/OPS1322374
http://ops.rsc.org/OPS95449
http://ops.rsc.org/OPS1864790
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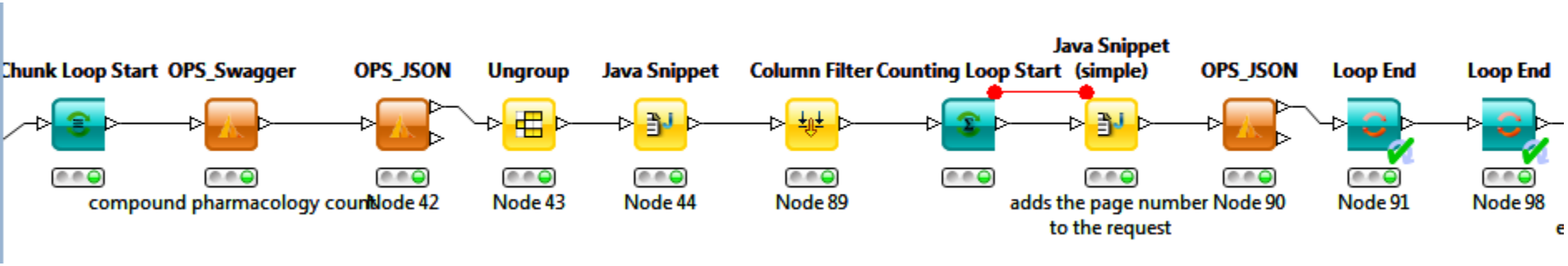
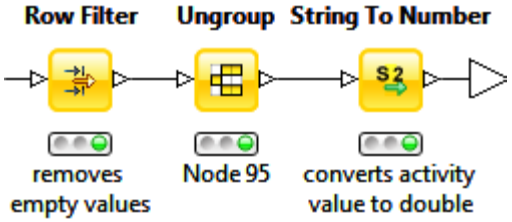
Compound Pharmacology Metanode





Coffee break

Cluster 1 use cases (Q1-Q11): Answers require mainly compound-target pharmacology data		
ID	Use case question	Sequence of API calls with filters used and link to the workflow
Q1	Give me all oxidoreductase inhibitors active <100 nM in human and mouse.	**Target Class Pharmacology** (*target_organism=Homo sapiens|Mus musculus; minEx-pChembl=7*) http://www.myexperiment.org/workflows/4504.html
Q2	For a given compound what is its predicted secondary pharmacology?	**Compound Information> Chemical Structure Search: Similarity> *Compound adverse events***
Q3	Given a target find me all actives against that target. Find/predict polypharmacology of actives.	**Target Pharmacology** (*minEx-pChembl=5*) > **Compound Pharmacology** (*minEx-pChembl=0*) http://www.myexperiment.org/workflows/4505.html
Q4	For a given interaction profile, give me similar compounds.	**Compound Information > Compound Information (Batch) > Chemical Structure Search: Similarity** (*searchOptions.Threshold=0.85*)> **Compound Information** http://www.myexperiment.org/workflows/4516.html
Q5	For molecules that contain substructure X, retrieve all bioactivity data in serine protease assays.	**Chemical Structure Search: Substructure> Compound Pharmacology**, **Target Class Members** http://www.myexperiment.org/workflows/4478.html
Q6	For a specific target family, retrieve all compounds in specific assays	**Target Class Pharmacology** http://www.myexperiment.org/workflows/4506.html
Q7	For a target, give me all active compounds	**Target Pharmacology** (*minEx-pChembl=5*)

ID	Use case question	Sequence of API calls with filters used and link to the workflow
Q6	For a specific target family, retrieve all compounds in specific assays	**Target Class Pharmacology** http://www.myexperiment.org/workflows/4506.html
Q7	For a target, give me all active compounds with the relevant assay data.	**Target Pharmacology** (*minEx-pChembl=5*) http://www.myexperiment.org/workflows/4507.html
Q8	Identify all known protein-protein interaction inhibitors	**Target Class Pharmacology** (*target_type=ppi*, *minEx-pChembl=5*) http://www.myexperiment.org/workflows/4508.html
Q9	For a given compound, give me the interaction profile with targets.	**Compound Pharmacology** (*activity_type=IC50|EC50|AC50|Ki|Kd|Potency)* http://www.myexperiment.org/workflows/4509.html
Q10	For a given compound, summarize all similar compounds and their activities.	**Chemical Structure Search: Similarity (***searchOptions.SimilarityType=0; searchOptions.Threshold=0.80)***> Compound Pharmacology** (*activity_type=IC50|EC50|AC50|Ki|Kd|Potency)* http://www.myexperiment.org/workflows/4510.html
Q11	Retrieve all data for a given list of compounds depicted by their chemical structure (SMILES) with options to match stereochemistry.	**Chemical Structure Search: Exact** (*searchOptions.MatchType=2*)**> Compound Pharmacology, Compound Information**, **Compound Classifications** *(tree=chebi)* http://www.myexperiment.org/workflows/4511.html

Cluster 2 use cases (Q12-Q20): Answers requiring pharmacology plus disease, pathway, and text mining data		
Q12	For a given compound, which of its targets have been patented in the context of a disease?	**Compound Pharmacology> *PatentsCalls* >Disease for Target**
Q13	For disease X, which targets have ligands in different stages of the development process with publications/patents describing these compounds?	**Targets for Disease> Target Pharmacology** (*minEx-pChembl=5*), **Target Information**>***Patents calls***
Q14	Target druggability: compounds directed against target X have what indications? Which new targets have appeared recently in the patent literature for a disease?	**Target pharmacology** (*minEx-pChembl=5*) >***Indications for Compounds*> *Patent calls* >Disease for Targets**
Q15	a) Which chemical series have been shown to be active against target X? b) Which new targets have been associated with disease Y? c) Which companies are working on target X or disease Y?	**a) Classification of Compounds for Target** (*minEx-pChembl=5*) **b) b) Associations for Disease** c) Competitive Intelligence data not available http://www.myexperiment.org/workflows/4512.html
Q16	Targets in Parkinson's disease or Alzheimer's disease are activated by which compounds?	**Target for Disease> Target Pharmacology** (*minEx-pChembl=5*) http://www.myexperiment.org/workflows/4513.html
Q17	For my specific target, which active compounds have been reported in the literature?	**Target Pharmacology** (*minEx-pChembl=5*) http://www.myexperiment.org/workflows/4507.html
Q18	For pathway X, find compounds that agonize targets assayed in only functional assays with potency <1 µM.	**Pathway Information: Get Targets>Target Pharmacology** (*activity_type=Potency*, *max-activity_value=1000*, *activity_unit=nanomolar*) http://www.myexperiment.org/workflows/4514.html
Q19	For the targets in a given pathway, retrieve the compounds that are active with more than one target.	**Pathway Information: Get Targets>Target Pharmacology** (*minEx-pChembl=5*) http://www.myexperiment.org/workflows/4515.html
Q20	For a given disease, retrieve all targets in the pathway and all active compounds hitting them.	**Targets for Disease> Target Pharmacology** (*minEx-pChembl=5*) http://www.myexperiment.org/workflows/4513.html