

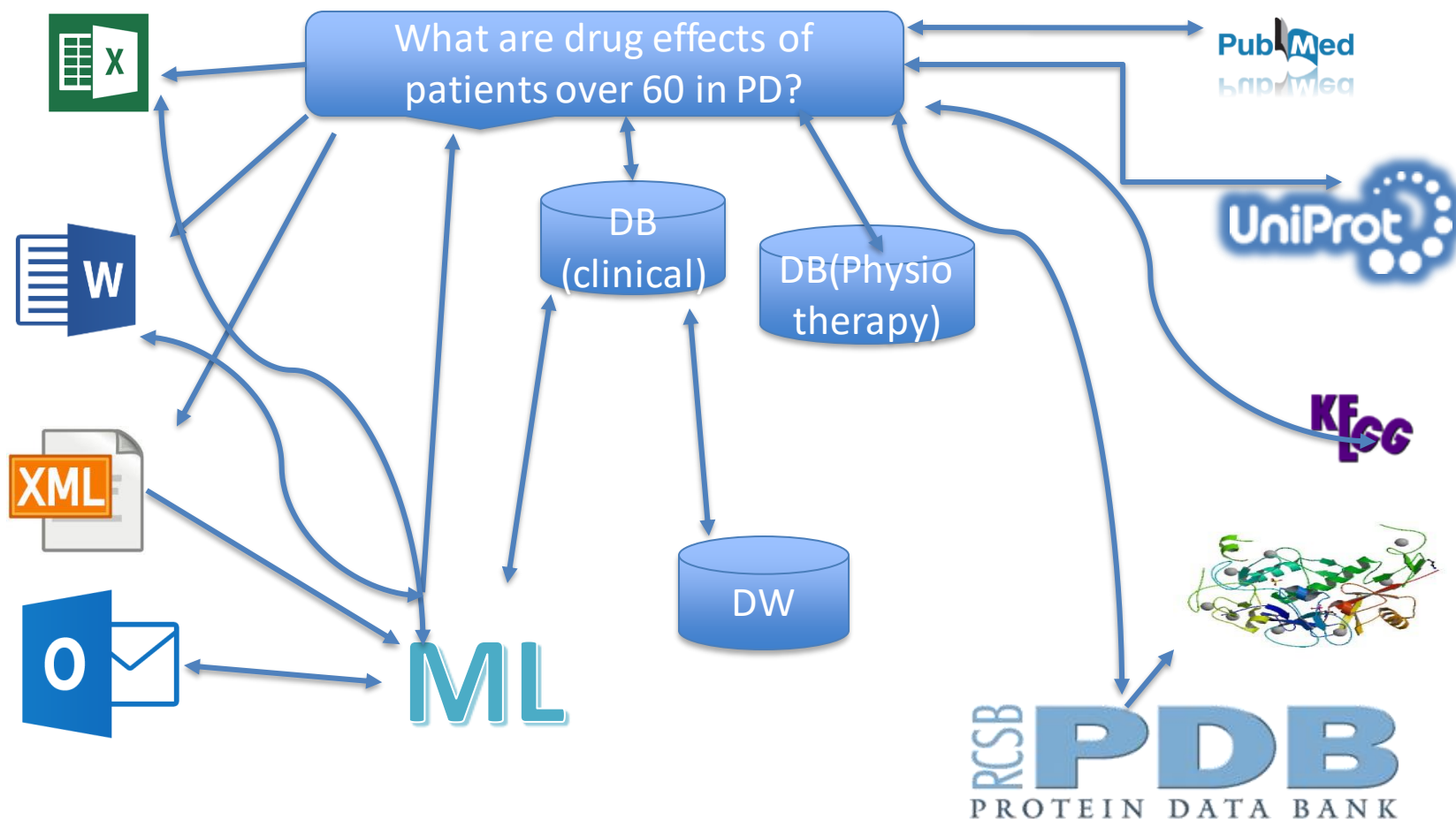
Applying New Methods to Biomedical Data to Provide Critical Insights. Case Study: Parkinson's Disease Ontology

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What is Ontology

- Explicit specification of a shared conceptualization
- “Explicit specification” describes the concepts and the relations that exist between the concepts. Cogently, this permits the concepts to be arranged in a hierarchical manner.
“conceptualization” refers to the knowledge domain that is being addressed
- “shared” refers to the confluence of tacit and explicit knowledge.

Search Query from Pubmed (1) on Parkinson's Disease ontology

pubmed_result (3).csv - Excel

Only 1 exact query from 76 results

Rest 73 items are irrelevant

2 are relevant

Title	URL
PDON: Parkinson's disease ontology for representation and modeling of the Parkinson's disease knowledge domain.	/pubmed/26395080
Towards an expert system for accurate diagnosis and progress monitoring of Parkinson's disease.	/pubmed/25416985
Using the Gene Ontology to Annotate Key Players in Parkinson's Disease.	/pubmed/26825309
Gene expression profiling predicts pathways and genes associated with Parkinson's disease.	/pubmed/26269422
Meta-analysis of genetic and environmental Parkinson's disease models reveals a common role of mitochondrial protection pathways.	/pubmed/22198569
Efficient and biologically relevant consensus strategy for Parkinson's disease gene prioritization.	/pubmed/26961748
Bioinformatic analysis of microRNA expression in Parkinson's disease.	/pubmed/25371140
Brain transcriptomic profiling in idiopathic and LRRK2-associated Parkinson's disease.	/pubmed/22634372
Quantitative proteomics of a presymptomatic A53T alpha-synuclein Drosophila model of Parkinson disease.	/pubmed/18353766
Gene expression profiling analysis of the putamen for the investigation of compensatory mechanisms in Parkinson's disease.	/pubmed/24256571
The cybrid model of sporadic Parkinson's disease.	/pubmed/19328199
Advanced microarray analysis highlights modified neuro-immune signaling in nucleated blood cells from Parkinson's disease patients.	/pubmed/18692253
Integrative analyses of proteomics and RNA transcriptomics implicate mitochondrial processes, protein folding pathways and GWAS loci in Parkinson's disease.	/pubmed/26793951
Characterisation of a novel NR4A2 mutation in Parkinson's disease brain.	/pubmed/19429166
Proteome response to the panneuronal expression of human wild-type alpha-synuclein: a Drosophila model of Parkinson's disease.	/pubmed/18683964
A semantically enabled formalism for the knowledge management of Parkinson's disease.	/pubmed/16777785
Mortalin: a protein associated with progression of Parkinson disease?	/pubmed/18219256
Disease Ontology 2015 update: an expanded and updated database of human diseases for linking biomedical knowledge through disease data.	/pubmed/25348409
Protein Clustering and Interactome Analysis in Parkinson and Alzheimer's Diseases.	/pubmed/26838080

pubmed_result (3)

Ready Average: 26395080 Count: 11 Sum: 26395080 100%

Search query in SCAVIEW (2)

SCAView Version 1.6.0-S X

academia.scaiview.com/academia//

1 documents found, displaying 1 to 1

Export All

Exactly 1 result returned

1. PDON: **Parkinson's disease** ontology for representation and modeling of the **Parkinson's disease** knowledge domain.

PubMed 26395080 Authors: Younesi, Erfan; Malhotra, Ashutosh; Gündel, Michaela; Scordis, Phil; Kodamullil, Alpha Tom; Page, Matt; Müller, Bernd; Springstube, Stephan; Wülfner, Ulrich; Scheller, Dieter; Hofmann-Apitius, Martin Date: 2015 Journal: Theoretical biology & medical modelling Affiliation: Department of Bioinformatics, Fraunhofer Institute for Algorithms and Scientific Computing, 53754, Sankt Augustin, Germany, erfany.younesi@scai.fraunhofer.de, Department of Bioinformatics, Fraunhofer Institute for Algorithms and Scientific Computing, 53754, Sankt Augustin, Germany, ashutosh.malhotra@scai.fraunhofer.de, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn-Aachen International Center for IT, 53113, Bonn, Germany, ashutosh.malhotra@scai.fraunhofer.de, Department of Bioinformatics, Fraunhofer Institute for Algorithms and Scientific Computing, 53754, Sankt Augustin, Germany, michaela.guendel@scai-extern.fraunhofer.de, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn-Aachen International Center for IT, 53113, Bonn, Germany, michaela.guendel@scai-extern.fraunhofer.de, Informatics group, UCB Pharma, 208 Bath Road, Slough, UK, phil.scordis@ucb.com, Department of Bioinformatics, Fraunhofer Institute for Algorithms and Scientific Computing, 53754, Sankt Augustin, Germany, alpha.tom.kodamullil@scai.fraunhofer.de, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn-Aachen International Center for IT, 53113, Bonn, Germany, alpha.tom.kodamullil@scai.fraunhofer.de, Informatics group, UCB Pharma, 208 Bath Road, Slough, UK, matt.page@ucb.com, Department of Bioinformatics, Fraunhofer Institute for Algorithms and Scientific Computing, 53754, Sankt Augustin, Germany, bernd.mueller@scai.fraunhofer.de, Department of Bioinformatics, Fraunhofer Institute for Algorithms and Scientific Computing, 53754, Sankt Augustin, Germany, stephan.springstube@scai.fraunhofer.de, Department of Neurology, University of Bonn, 53105, Bonn, Germany, ulrich.wuelfner@ukb.uni-bonn.de, Pharmacology Parkinson's Disease and Movement Disorders, UCB Pharma S.A., Chemin du Foriest, B-1420, Braine-l'Alleud, Belgium, dieter.scheller@ucb.com, Department of Bioinformatics, Fraunhofer Institute for Algorithms and Scientific Computing, 53754, Sankt Augustin, Germany, martin.hofmann-apitius@scai.fraunhofer.de, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn-Aachen International Center for IT, 53113, Bonn, Germany, martin.hofmann-apitius@scai.fraunhofer.de.

Statistics

BACKGROUND: Despite the unprecedented and increasing amount of data, relatively little progress has been made in molecular characterization of mechanisms underlying **Parkinson's disease**. In the area of **Parkinson's** research, there is a pressing need to integrate various pieces of information into a meaningful context of presumed **disease** mechanism(s). **Disease** ontologies provide a novel means for organizing, integrating, and standardizing the knowledge domains specific to **disease** in a compact, formalized and computer-readable form and serve as a **reference** for knowledge exchange or systems modeling of **disease** mechanism.

METHODS: The **Parkinson's disease** ontology was built according to the life cycle of ontology building. Structural, functional, and expert evaluation of the ontology was performed to ensure the quality and usability of the ontology. A novelty metric has been introduced to measure the gain of new knowledge using the ontology. Finally, a cause-and-effect model was built around **PINK1** and two **gene expression** studies from the **Gene Expression** Omnibus database were re-annotated to demonstrate the usability of the ontology.

RESULTS: The **Parkinson's disease** ontology with a subclass-based taxonomic hierarchy covers the broad spectrum of major biomedical concepts from molecular to clinical features of the **disease**, and also reflects different views on **disease** features held by molecular biologists, clinicians and drug developers. The current version of the ontology contains 632 concepts, which are organized under nine views. The structural evaluation showed the balanced dispersion of concept classes throughout the ontology. The functional evaluation demonstrated that the ontology-driven literature search could gain novel knowledge not present in the **reference Parkinson's** knowledge map. The ontology was able to answer specific questions related to **Parkinson's** when evaluated by experts. Finally, the added value of the **Parkinson's disease** ontology is demonstrated by ontology-driven modeling of **PINK1** and re-annotation of **gene expression** datasets relevant to **Parkinson's disease**.

CONCLUSIONS: **Parkinson's disease** ontology delivers the knowledge domain of **Parkinson's disease** in a compact, computer-readable form, which can be further edited and enriched by the scientific community and also to be used to construct, represent and automatically extend **Parkinson's**-related computable models. A practical version of the **Parkinson's disease** ontology for browsing and editing can be publicly accessed at <http://bioportal.bioontology.org/ontologies/PDON>.

MeSH: Animals; Databases; Genetic; Disease Models; Animal; Gene Expression Regulation; Gene Ontology; Gene Regulatory Networks; Humans; Knowledge; Molecular Sequence Annotation; Parkinson Disease, etiology, genetics; Software

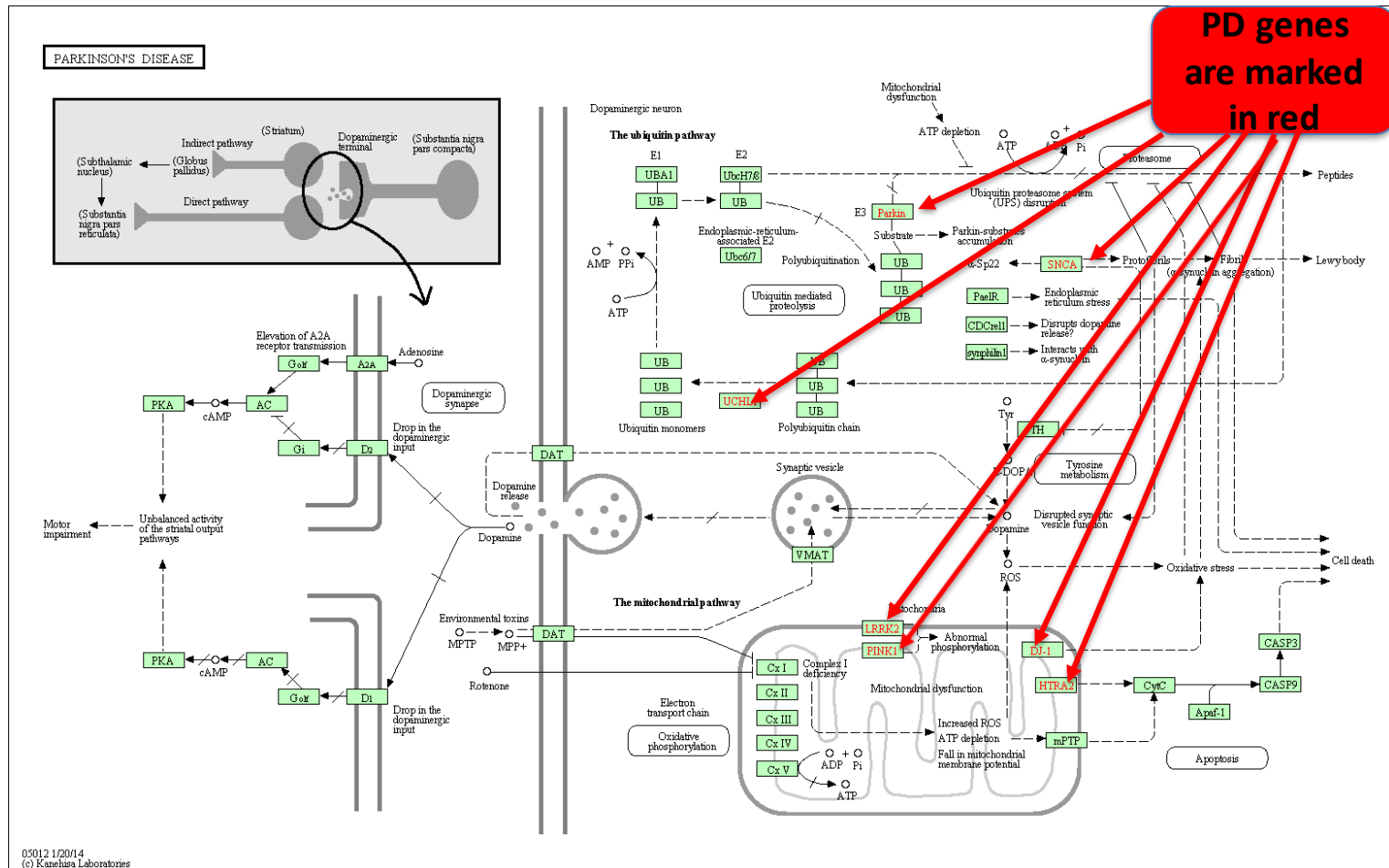
1 documents found, displaying 1 to 1

[First/ Prev] 1 [Next/ Last] 10 documents per Page

What is Parkinson's Disease(PD)

- degenerative disease that affects the Central Nervous System (CNS) due to the premature death of dopamine cells in the brain stem;
- depletion of dopamine cells leads to the reduction of the “dopamine” chemical which controls the neuromuscular movement of the body.
- 2nd most common neurodegenerative disease after Alzheimers

KEGG Pathway of PD(3) showing the depletion of dopamine



Clinical Symptoms of PD

- resting tremor on one side of the body
- slowness of movement (**bradykinesia**)
- stiffness of limbs (**rigidity**)
- gait problems
- small cramped handwriting (**micrographia**)
- lowered voiced volume (**dysarthia**)
- feelings of depression
- increase in dandruff or oily skin
- less frequent blinking and swallowing

Diagnosis & Treatment

- Hard to diagnose since cause is still unknown; there are no clinical tests
- Hence called Idiopathic PD compared to Juvenile-onset PD
- Communication, Palliative care
- Drug treatment like Levodopa

Canadian Statistics on PD(4)

- ~ 55,000 Canadians ≥ 18 yrs living in private households diagnosed with PD
- 0.2% of household population; 79% with Parkinson's were ≥ 65 (In industrialised countries, the prevalence of the disease is "estimated at 0.3% of the general population and about 1% of the population older than age 60 years"(5))
- 4.9%(12500) residents of long term residential care.
- In institutions, almost everyone (97%) with the condition was ≥ 65 .
- Overall, men were more likely than women to have Parkinson's disease: 0.3% versus 0.2% ($p < 0.05$) for those in private households, and 6.6% versus 4.0% ($p < 0.05$) for residents of institutions.

Charter for People with PD (PWPD) (6)

- PWPD patient has the right to consult a doctor and expect:
 - (a) receive an accurate diagnosis,
 - (b) have access to support services,
 - (c) receive continuous care and
 - (d) take part in managing the illness

Searching for palliative care in PDON using R

20 Frequently
Used words



```
findAssocs(dtm,"palliative",corlimit=0.95)  
$palliative  
numeric(0)
```

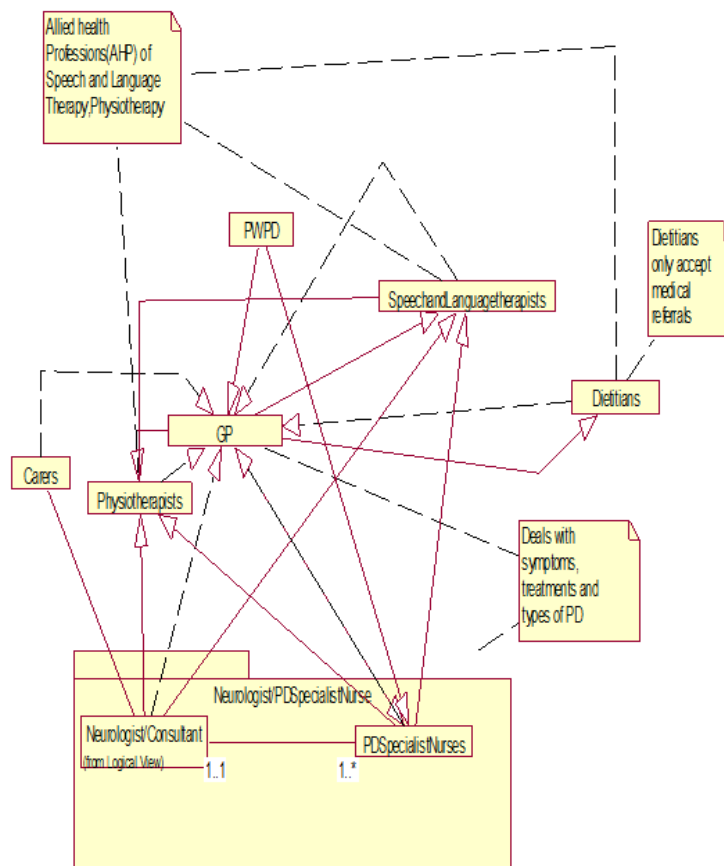
Human Disease Ontology (HDO) using OntoCat package in R

- `hdo<-getOntology("http://www.berkeleybop.org/ontologies/doid.owl")`
- `concepts<-length(getAllTerms(hdo)) – 11663`
- `NumPDconcepts<-length(searchTerm(hdo,"Parkinson")) – 10`
.....`termAccession=DOID_14330,`
`termURI=http://purl.obolibrary.org/obo/DOID_14330, label=Parkinson's`
`disease)`
- `term<-getTermById(hdo,"DOID_14330")`
- `getLabel(term)`
- `showPathsToTerm(hdo,term))`
- Path 1: `DOID_14330 <- DOID_0050890 <- DOID_1289 <- DOID_331 <-`
`DOID_863 <- DOID_7 <- DOID_4`

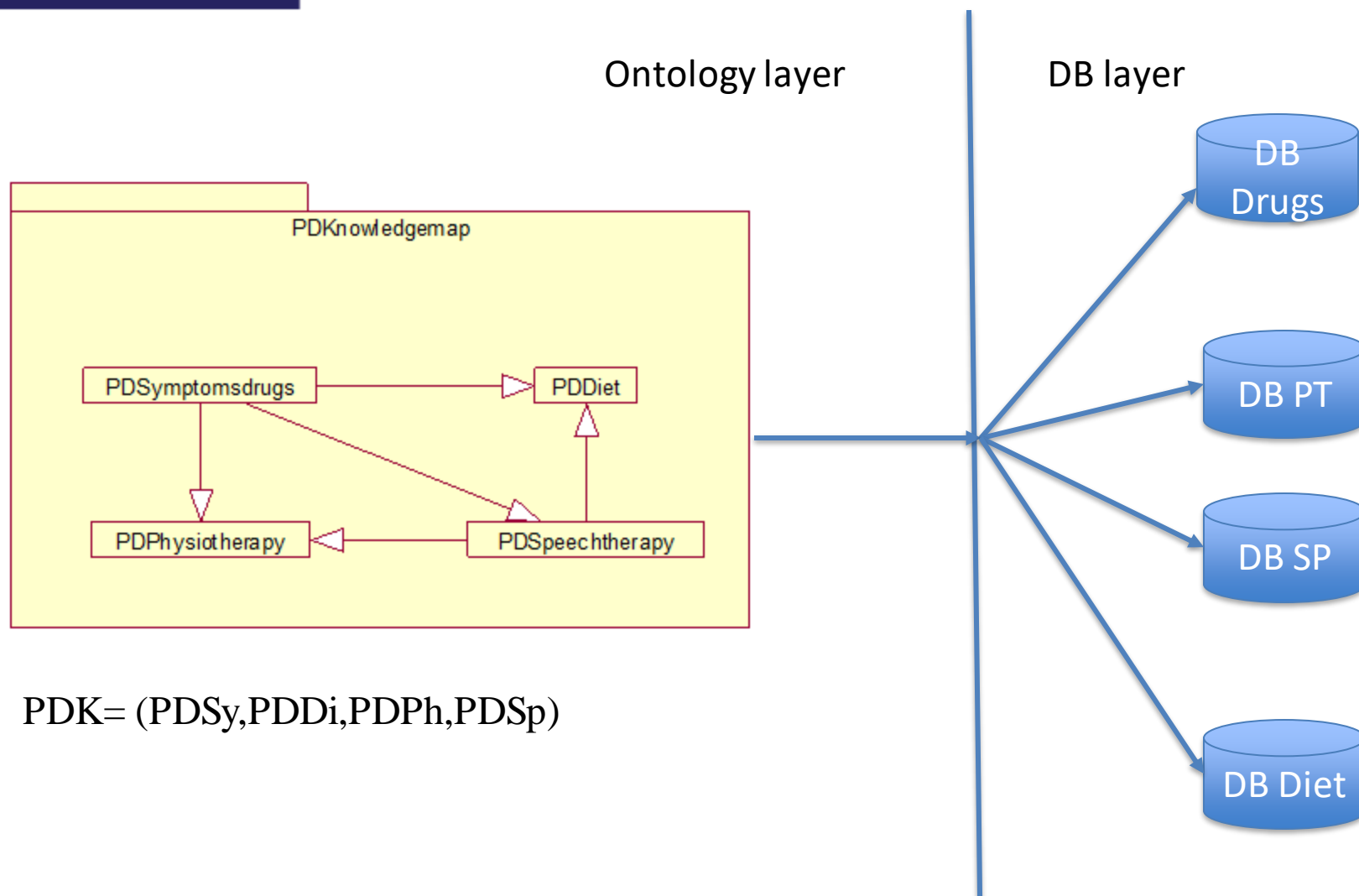
Hierarchy of HDO

- -----DROID_680 tauopathy
- -----DROID_3688 plexopathy
- -----DROID_14784 olivopontocerebellar atrophy
- -----DROID_13548 secondary Parkinson disease
- -----DROID_11870 Pick's disease
- -----**DROID_0050890 synucleinopathy**
- -----**DROID_12217 Lewy body dementia**
- -----**DROID_4752 multiple system atrophy**
- -----**DROID_14330 Parkinson's disease**
- `getTermSynonymsById(hdo,"DROID_14330")` -- no synonyms

Business Process of Knowledge Map of PD



PD Knowledge Map (7)



Ontology structure of Symptoms and synonyms between PDSy, PDSp

OntoEdit Professional

File Edit View Tools Windows Help

file://newOnto.org/C:/research/htechsight/ParkinsonsDiseaseSymptoms (C:/research/parkinsons/htechsightdoc/pddrug...)

Rule Editor General Axioms Inferencing Visualizer Debugger Domain-Lexicon Identification Metadata

Concepts & Relations General Axioms Inferencing Visualizer Debugger Domain-Lexicon Identification Metadata

select filter all all language type

synonym concept

Atypical Parkinsonism ParkinsonsPlus en synonym

complementary medicine AlternativeMedicine en synonym

Comtess COMTInhibitors en synonym

Diet Nutrition en synonym

DrugsThatShouldAvoid DrugInduced en synonym

Lesioning ThalamicStimulation en domainentry

Lesioning Pallidotomy en domainentry

Multi-SystemAtrophy ParkinsonsPlus en synonym

No known cause IdiopathicParkinsonsDisease en synonym

Instances

- brandname("Parlovel")
- dosage("initially 1 mg increasing slowly to max 10 mg tds")
- manufacturer("Sandoz")
- 1 Pergolide
 - usage("with levodopa improved control of motor fluctuations is noticed")
 - sideeffects("nausea, vomiting, confusion, hallucinations, lightheadness, fainting, rare side eff")
 - dosage("starter pack, increasing dose slowly to max 1.5 mg tds")
 - manufacturer("Lilly")
 - brandname("Celance")
- 1 Pramipexole dihydrochloride
 - brandname("Mirapexin")
 - usage("monotherapy or with levodopa")
 - dosage("start with 0.125 mg tds(3 times day) increasing slowly to a maximum of 1.5 mg tds")
 - sideeffects("nausea, vomiting, sleepiness, insomnia, dizziness, hallucinations, confusion, low t")
 - manufacturer("Pfizer")
- 1 Ropinirole hydrochloride
 - brandname("Requip")
 - usage("monotherapy or with levodopa")
 - dosage("starter pack, then increase dosage slowly to max 8 mg tds")
 - specialInstructions("introduction of dopamine agonist at a very low dose increases over time, le")
 - sideeffects("nausea, vomiting, low blood pressure, sleepiness, confusion hallucinations, swell")
 - manufacturer("GSK")
- 1 Cabergoline
- 1 Lisuride
 - brandname("Revanil")

OntoEdit Professional

File Edit View Tools Windows Help

file://newOnto.org/C:/research/parkinsons/htechsightdoc/pddiet/FoodSupplements (C:/...)

Concepts & Relations General Axioms Inferencing Visualizer Debugger Domain-Lexicon Identification Metadata

select filter all all language type

synonym concept

Balance of Good health Fluids en domainentry

Balance of Good Health DairyProducts en domainentry

Balance of Good health ProteinFoods en domainentry

Balance of Good health StarchyCarbohydrates en domainentry

balance of Good Health FattySugaryFoods en domainentry

Balance of Good Health FruitVegetables en domainentry

Drugs Medication en synonym

ETOH Alcohol en synonym

High calorie diet Foodfortification en synonym

High calorie diet Foodfortification en synonym

junk foods FattySugaryFoods en synonym

Instances

Ready. 17270.0k free

Ontological Inference

- **(1) Names of drugs of Levodopa**
- Find the brand name of the drugs of Levodopa and their corresponding manufactures that are not manufactured by Dupont, then it can be represented as:
- `FORALL X, Y <- EXISTS A`
`A:Levodopa[BrandName->>X;Manufacturer->>Y] AND NOT equal(Y, "Dupont").`
- Output:
- `Madopar (levodopa + benserazide)"; "Roche"`
- **(2) Benefits of early referral**
- `FORALL X,Y (X[benefits->>Y])`
- `<- (Y:Referral[earlyreferral->>{ "address concerns about differential diagnosis","assessment and monitoring to allow early identification of movement problems","encourage participation through optimal conditioning of cardiovascular, musculoskeletal and neuromuscular systems","preventive management of secondary complications such as joint stiffness","introduce movement strategies for use","education of individuals and carers about physical management of PD","monitor drug efficacy to optimise motor performance"}]).`
-

REFERENCES

- (1) <https://www.ncbi.nlm.nih.gov/pubmed/?term=parkinson%27s+disease+ontology>
- (2) <http://academia.scaiview.com/academia//>
- (3) http://www.kegg.jp/kegg-bin/show_pathway?hsa05012
- (4) Suzy L. Wong, Heather Gilmour and Pamela L. Ramage-Morin, Parkinson's disease: Prevalence, diagnosis and impact, Catalogue no. 82-003-X
- ISSN 1209-1367 , Nov. 19, 2014
- (5) Samli, A., Nutt, J.G., Ransom, B.R., " Parkinson's Disease", Lancet, 2004, 363:1783- 93
- (6) Kale, R., Menken, M., "Who should look after people with Parkinson's Disease?" British Medical Journal, Vol. 328, p62-63, 10 January 2004
- (7) Paul, S., *Integrating a Knowledge Management System with Database*, Marketing in the eSociety, 4th IBM eBusiness Conference UK, 2003