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# From biomedical information integration to knowledge discovery through the Semantic Web

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# Semantic Web

- Extract information from structured and unstructured sources
  - From text: text mining
  - From ontologies and knowledge bases
- Integrate information
  - From structured and unstructured sources
- Aggregate information
  - Subsumption reasoning
- Use the extracted information for a meaningful purpose
  - Hypothesis generation / knowledge discovery
  - Better information retrieval
  - Question answering

# Outline

- Knowledge, integration and aggregation
- Biomedical Knowledge Repository
- Towards a biomedical Semantic Web

# KNOWLEDGE, INTEGRATION AND AGGREGATION

# Definitional knowledge

- Definitional knowledge
  - Universally true
  - Examples
    - Lung cancer *has_location* Lung
    - Myocardial infarction *isa* Cardiovascular disease
    - Liver *part_of* Abdomen (canonical anatomy, in a given species)
  - Typically found in ontologies
  - Useful as background knowledge

# Assertional knowledge

- Assertional knowledge
  - True in a given context
  - Examples
    - Aspirin *treats* headache
    - IL-13 *inhibits* COX2
    - Chest pain *manifestation_of* Myocardial infarction
    - Ciprofloxacin *causes* Tendon rupture
  - Typically found in knowledge bases (and in text)
  - Useful for knowledge discovery, question answering, biocuration support, etc.

# Definitional vs. assertional knowledge

- Definitional knowledge
  - Universally true
  - Typically found in ontologies
  - Useful as background knowledge
- Assertional knowledge
  - True in a given context
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# Why integrate assertional and definitional knowledge?

- To increase statistical power
  - Low frequency for individual, fine-grained assertions
  - Higher frequency when frequencies are aggregated at a coarser level
- To bridge the granularity mismatch
  - Differences in granularity between
    - What is expressed in in text (or structured sources)
    - What is needed in “semantic mining” applications

# Aggregating frequencies

fluoroquinolone *causes* Tendon rupture [12]

*isa*

Ciprofloxacin *causes* Tendon rupture [3]

Levofloxacin *causes* Tendon rupture [2]

Moflifloxacin *causes* Tendon rupture [7]

# Bridging the granularity mismatch

- A researcher is interested in glycosylation and its implications for one disorder: congenital muscular dystrophy.

Link between glycosyltransferase activity and congenital muscular dystrophy?

NCBI Entrez Gene

All Databases | PubMed | Nucleotide | Protein | Genome | Structure | PMC

Search Gene for 9215[uid] Go Clear Save Search

Limits | Preview/Index | History | Clipboard | Details

Display Full Report Show 20 Send to

All: 1 | Current Only: 1 | Genes Genomes: 1 | SNP GeneView: 1

1: LARGE like-glycosyltransferase [ *Homo sapiens* ]

GeneID: 9215

updated 02-Jul-2007

LARGE (GeneID: 9215)

**Phenotypes** → *has_associated_disease*

Muscular dystrophy, congenital, type 1D
MIM: 608840

Congenital muscular dystrophy, type 1D

**GeneOntology** Provided by GOA

| Function | Evidence | |
|---|---|---|
| acetylglucosaminyltransferase activity | TAS | PubMed |

| Process | Evidence | |
|---|---|---|
| N-acetylglucosamine metabolic process | TAS | PubMed |
| carbohydrate biosynthetic process | IEA | |
| glycosphingolipid biosynthetic process | TAS | PubMed |
| muscle maintenance | ISS | |
| protein amino acid glycosylation | TAS | PubMed |

| Component | Evidence | |
|---|---|---|
| integral to Golgi membrane | TAS | PubMed |
| integral to membrane | IEA | |
| membrane | IEA | |

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LARGE (GeneID: 9215)

1: LARGE like-glycosyltransferase [ *Homo sapiens* ]

GeneID: 9215 updated 02-Jul-2007

## Phenotypes

Muscular dystrophy, congenital, type 1D
MIM: 608840

## GeneOntology

Provided by GOA

*has_molecular_function*

| Function | Evidence | |
|---|---|---|
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acetylglucosaminyltransferase activity

| Process | Evidence | |
|---|---|---|
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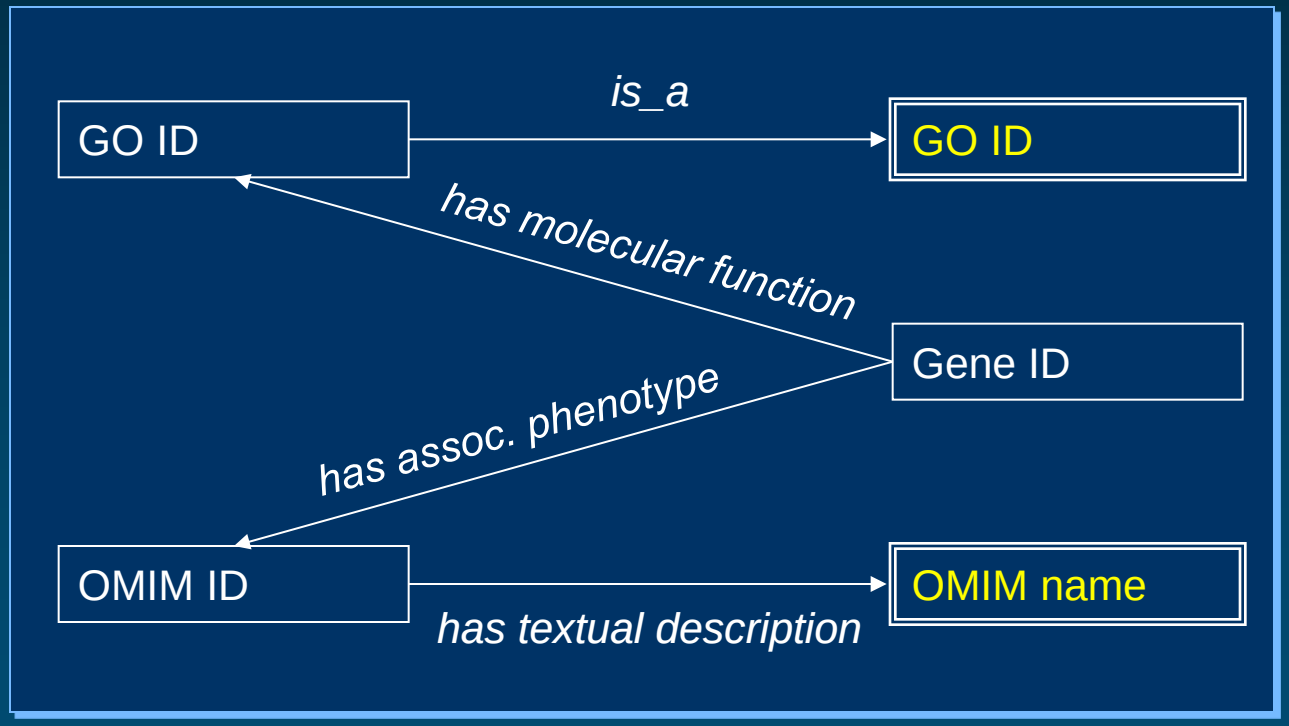
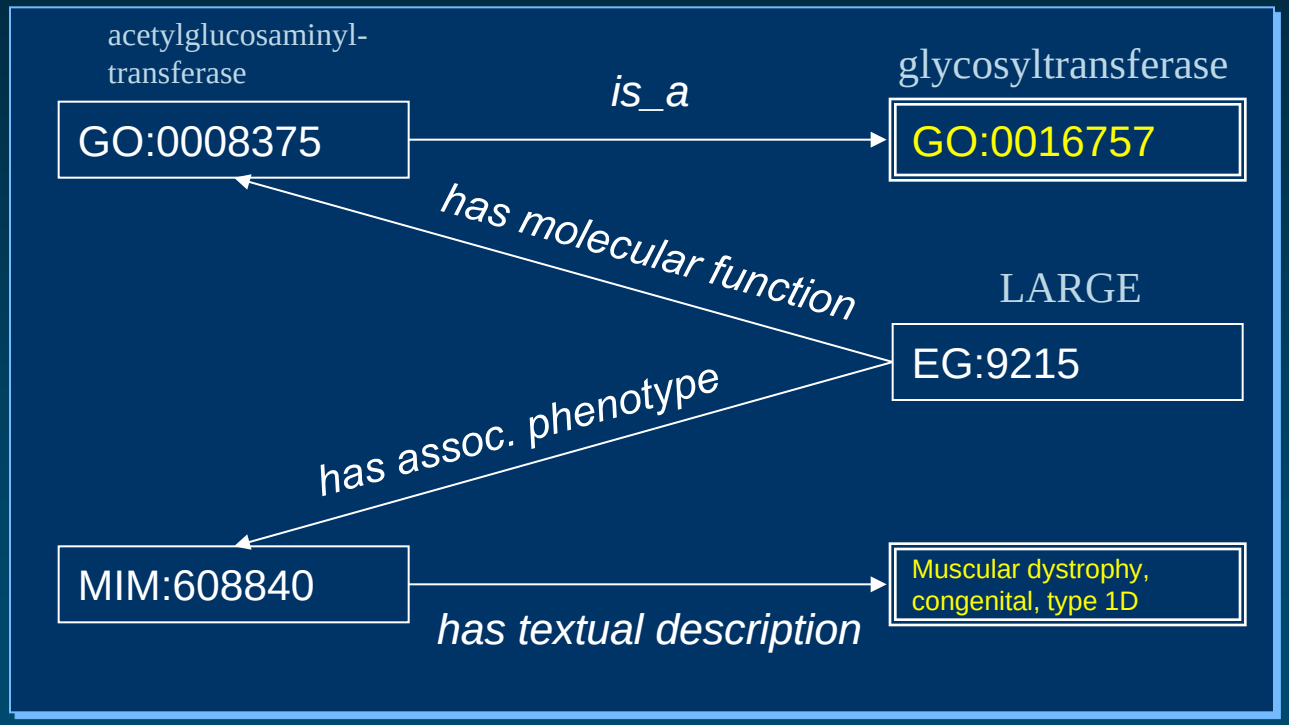
| membrane | IEA | |

# Using SPARQL to test a hypothesis

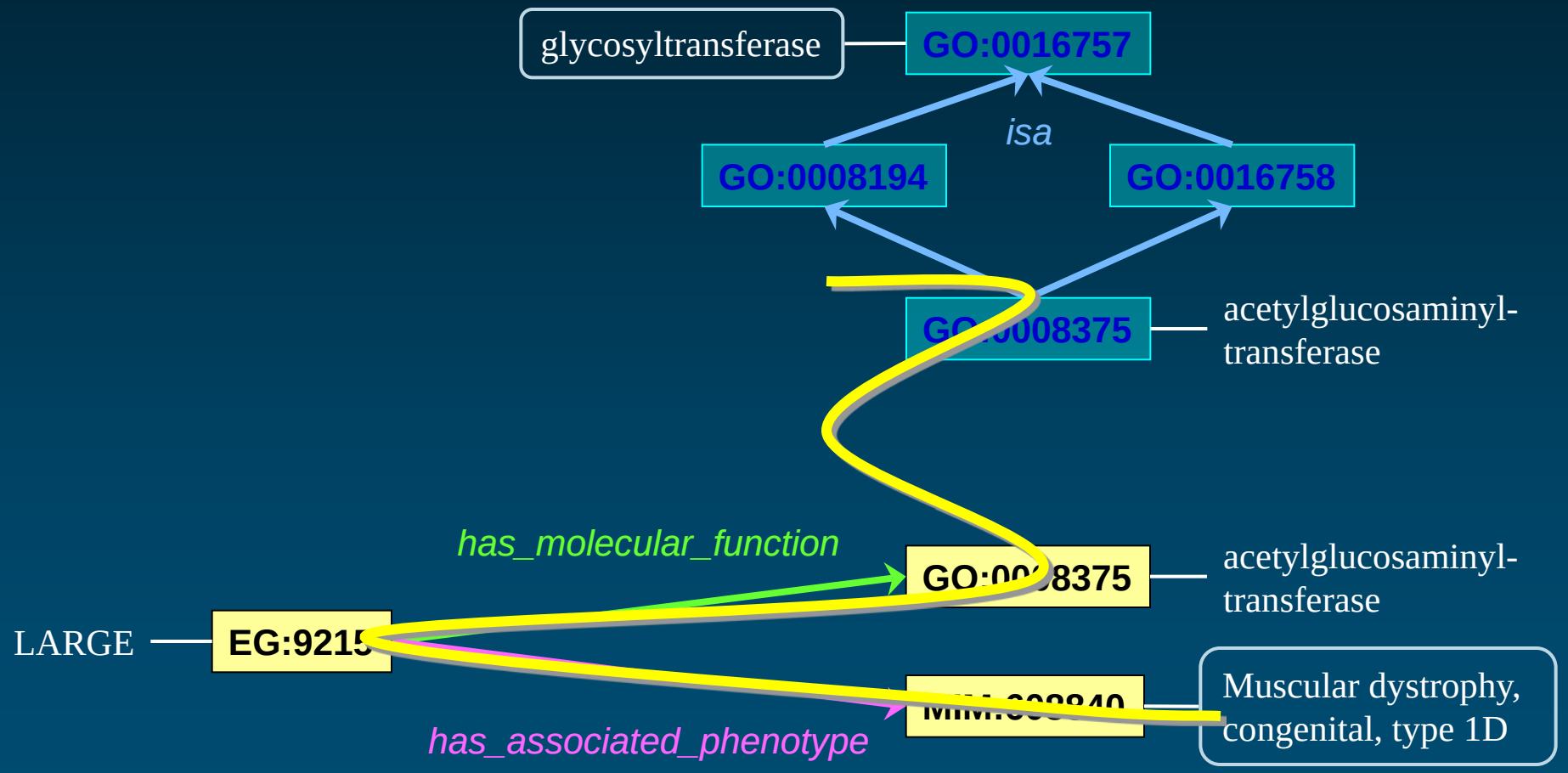
*Find all the genes annotated with the GO molecular function glycosyltransferase or any of its descendants and associated with any form of congenital muscular dystrophy*



# Results Instantiated graph



# From *glycosyltransferase* to *congenital muscular dystrophy*



# NLM BIOMEDICAL KNOWLEDGE REPOSITORY

# Biomedical Knowledge Repository

- Experimental resource
- Integrated set of relations
  - From the UMLS Metathesaurus
  - Extracted from MEDLINE by SemRep
- Together with metadata
  - Source of the relations (provenance)
- Semantic Web technologies
  - RDF store (Virtuoso)

# Knowledge sources

- Ontologies – definitional knowledge (mostly)
  - Terminology integration systems
    - Unified Medical Language System (NLM)
    - BioPortal (NCBO)
- Relations extracted from text – assertional knowledge (mostly)
  - Text corpus
    - MEDLINE
  - Relation extraction system
    - SemRep (NLM), MedLEE (Columbia)
    - Commercial systems, specialized systems

# Unified Medical Language System

- SPECIALIST Lexicon
  - 460,000 lexical items
  - Part of speech and variant information
- Metathesaurus
  - 8.3M names from over 160 terminologies
  - 2.9M concepts
  - 16M relations
- Semantic Network
  - 133 high-level categories
  - 7000 relations among them

Lexical resources

Terminological resources

Ontological resources

# UMLS Metathesaurus

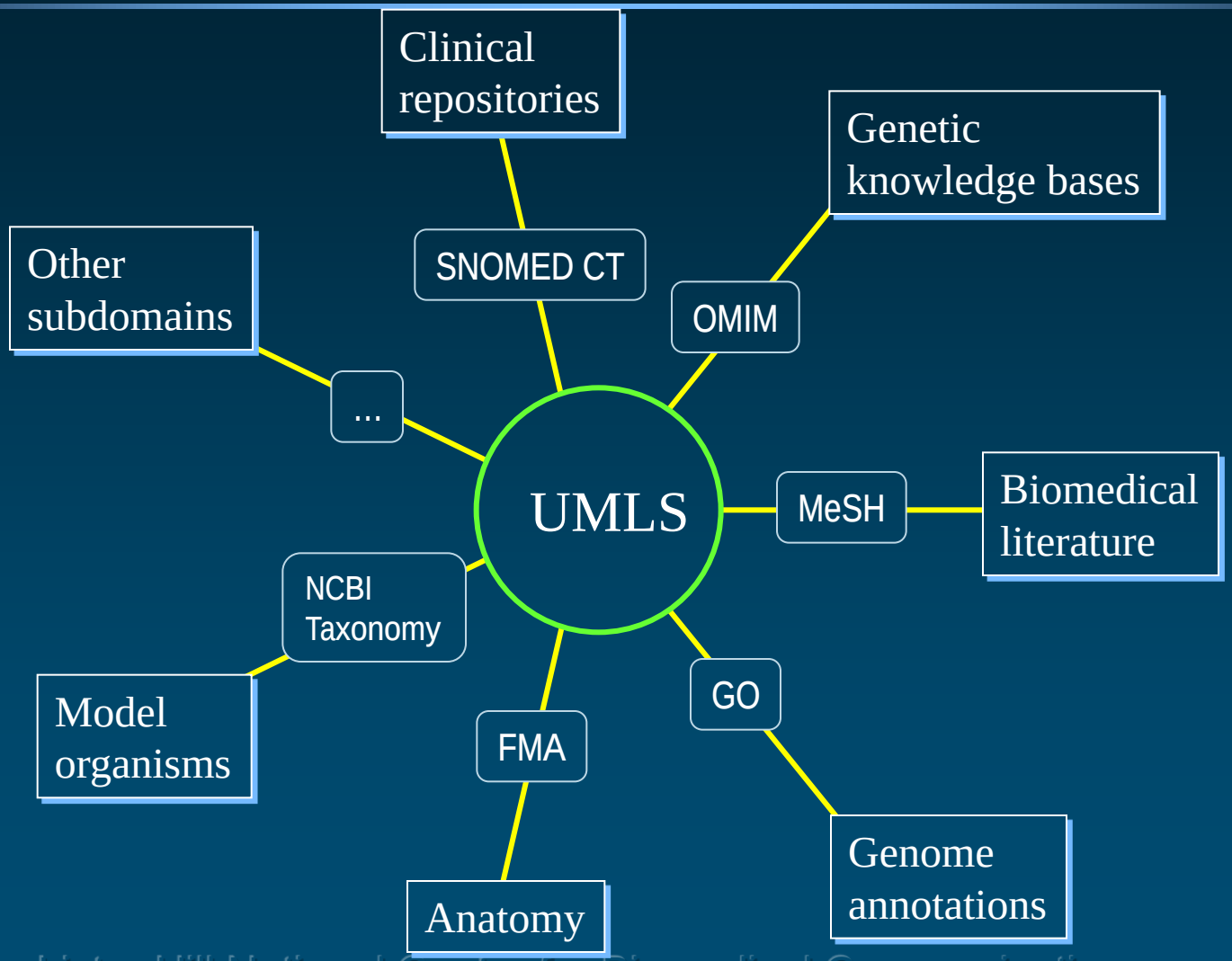
- Synonymous terms clustered into a concept
- Preferred term
- Unique identifier (CUI)

| | | |
|---|---|---|
| Addison Disease | MeSH | D000224 |
| Primary hypoadrenalism | MedDRA | 10036696 |
| Primary adrenocortical insufficiency | ICD-10 | E27.1 |
| Addison's disease (disorder) | SNOMED CT | 363732003 |

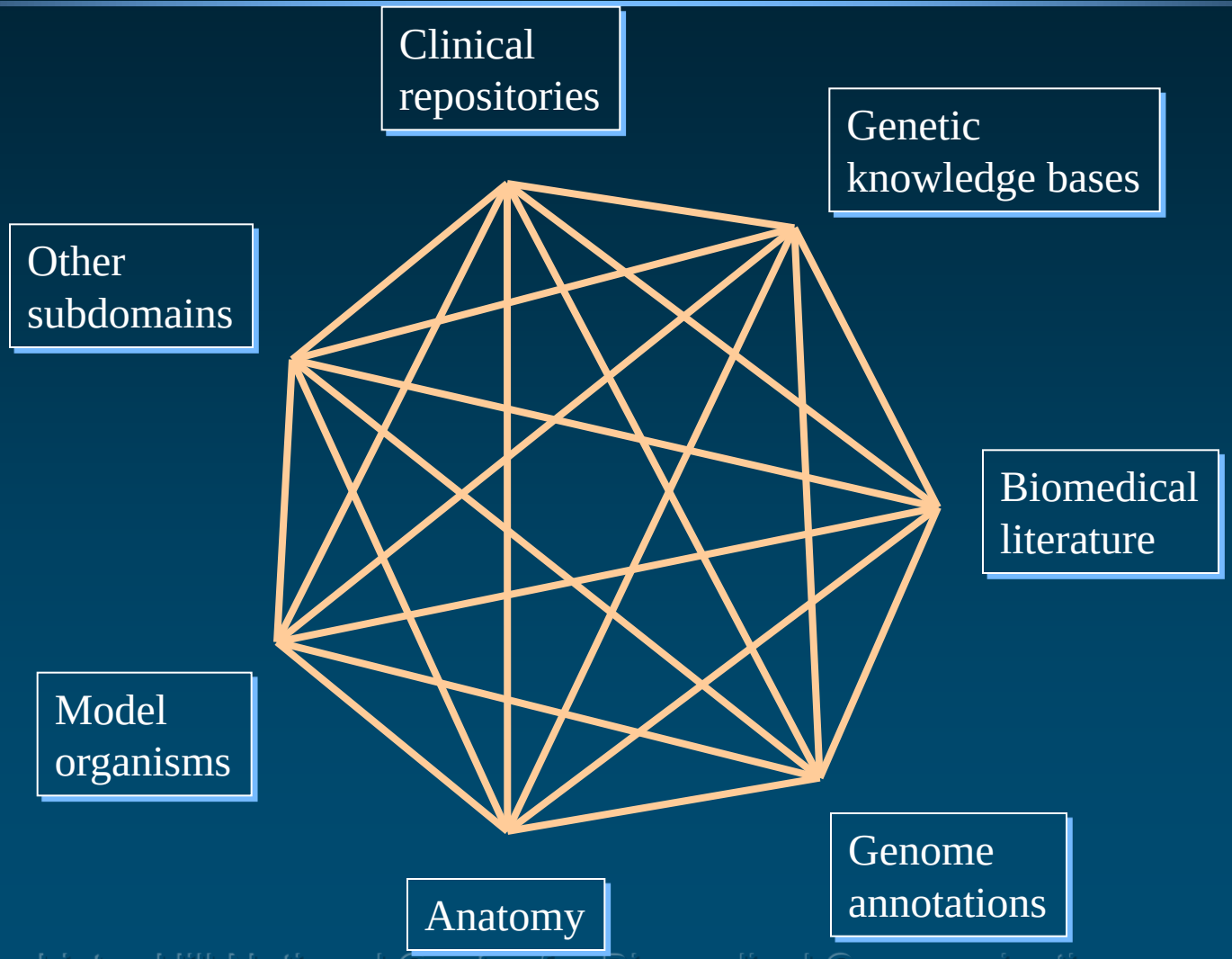
C0001403

Addison's disease

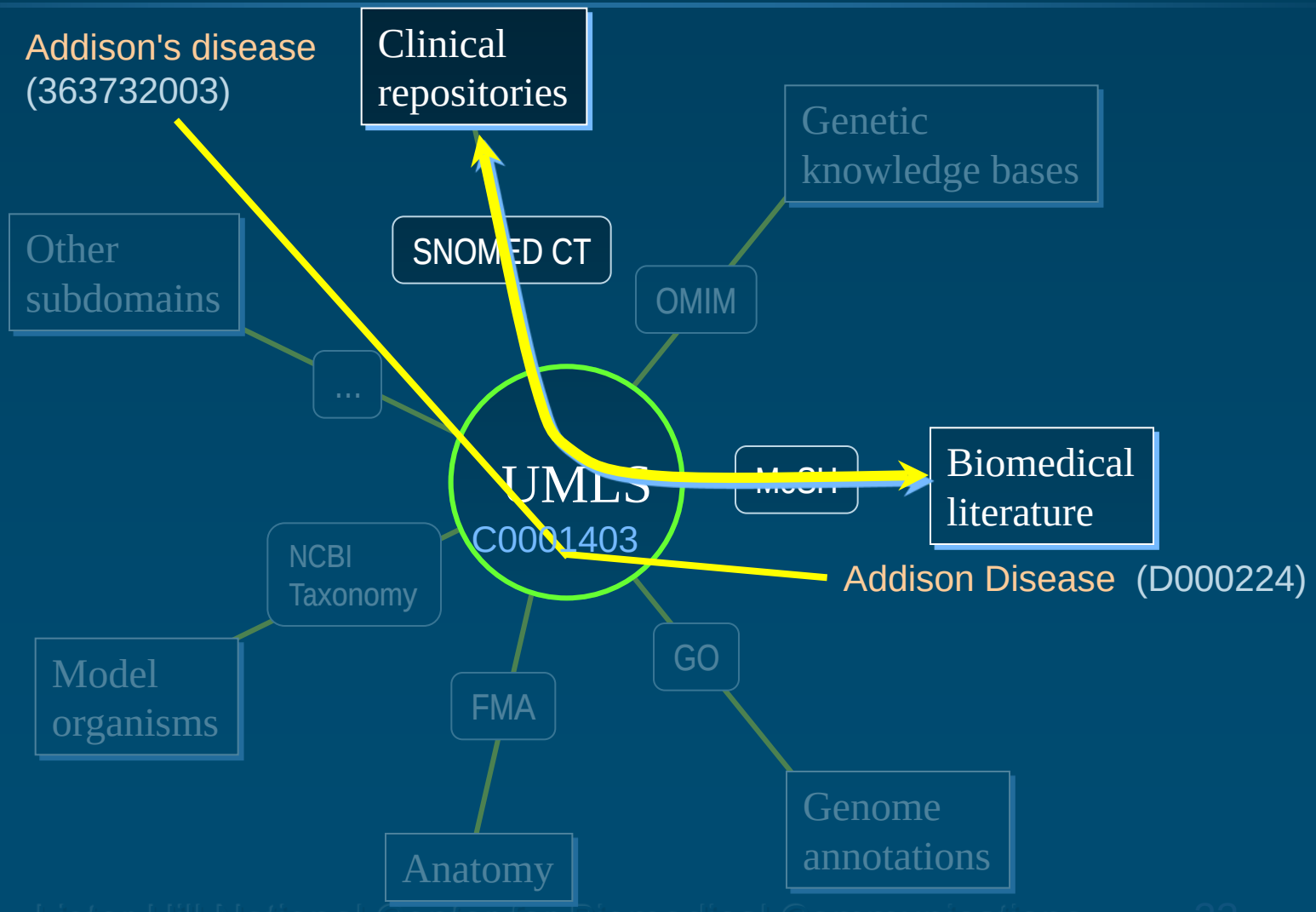
# Integrating subdomains



# Integrating subdomains



# Trans-namespace integration

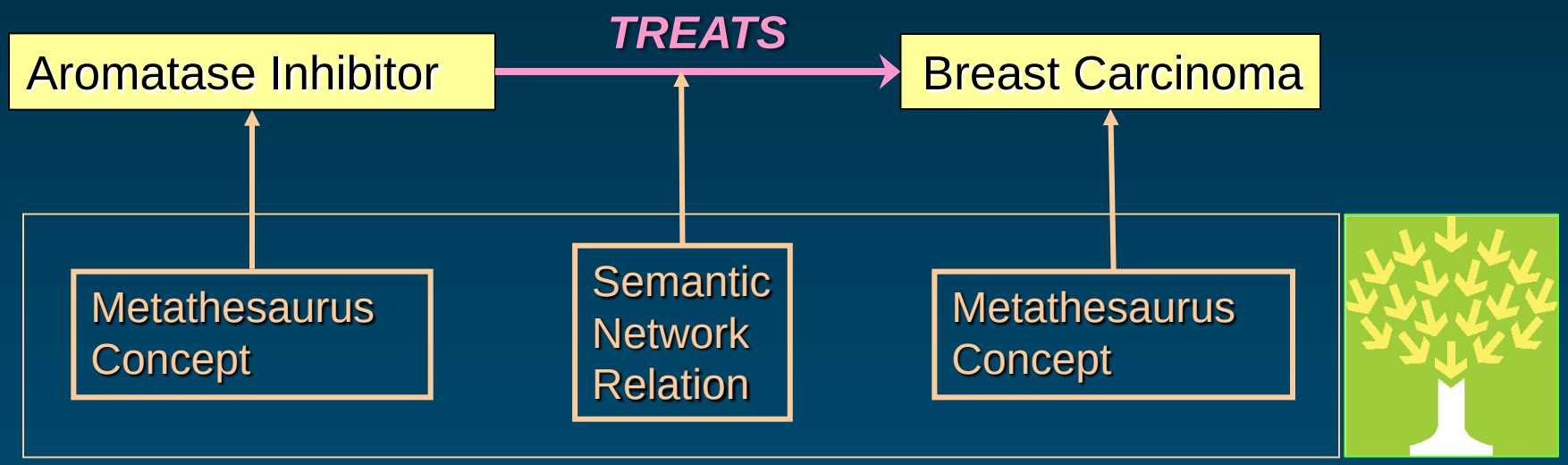


# SemRep

- Part of the Semantic Knowledge Representation project at NLM
  - Tom Rindflesch & Marcelo Fiszman
- Knowledge extraction system for the automatic summarization system SemanticMEDLINE
  - http://skr3.nlm.nih.gov/SemMedDemo/
- Extract semantic predications from biomedical research literature (MEDLINE citations)

# SemRep: Extract Predication

… Exemestane after non-steroidal aromatase inhibitor for post-menopausal women with advanced breast cancer



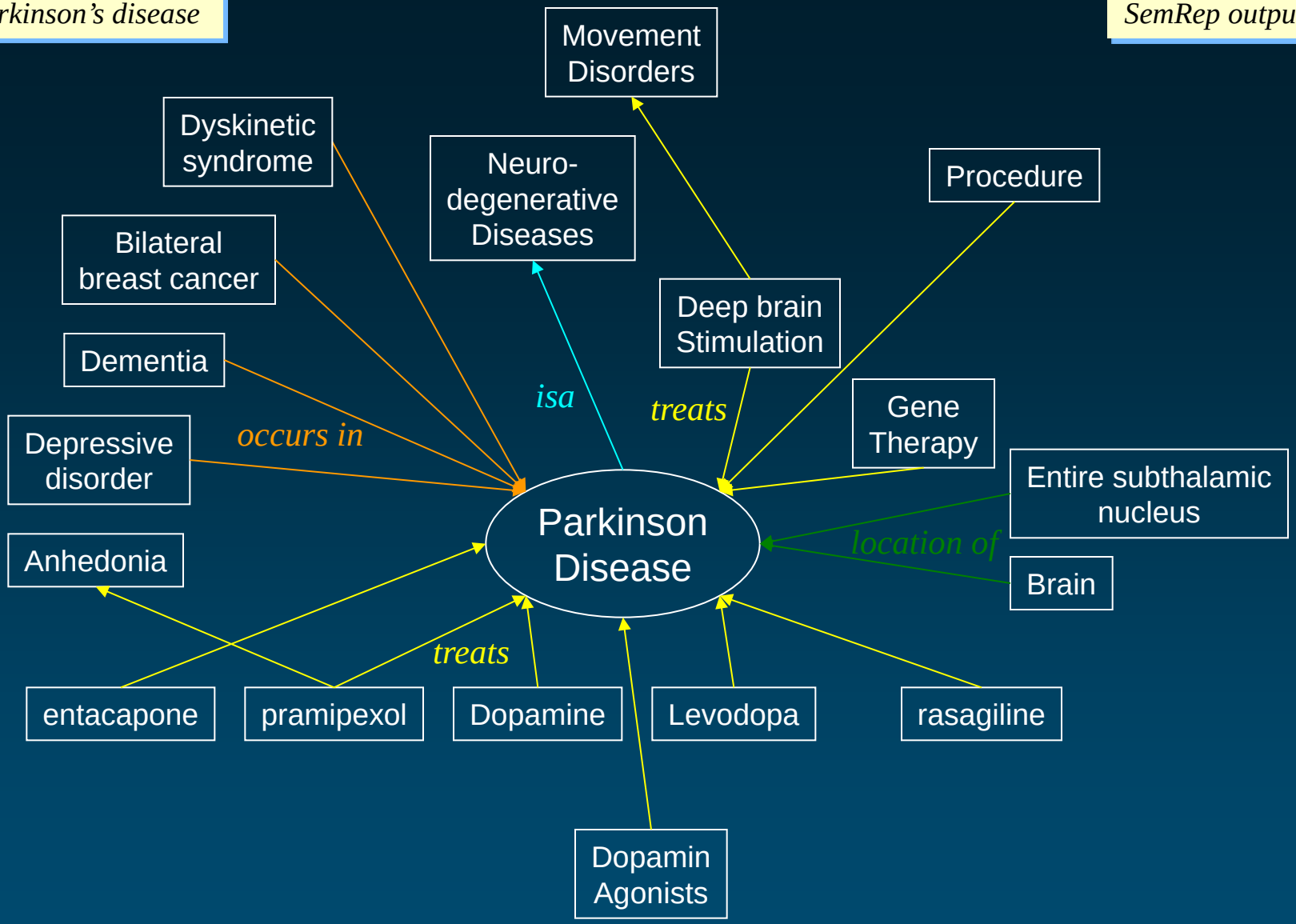

Unified Medical Language System

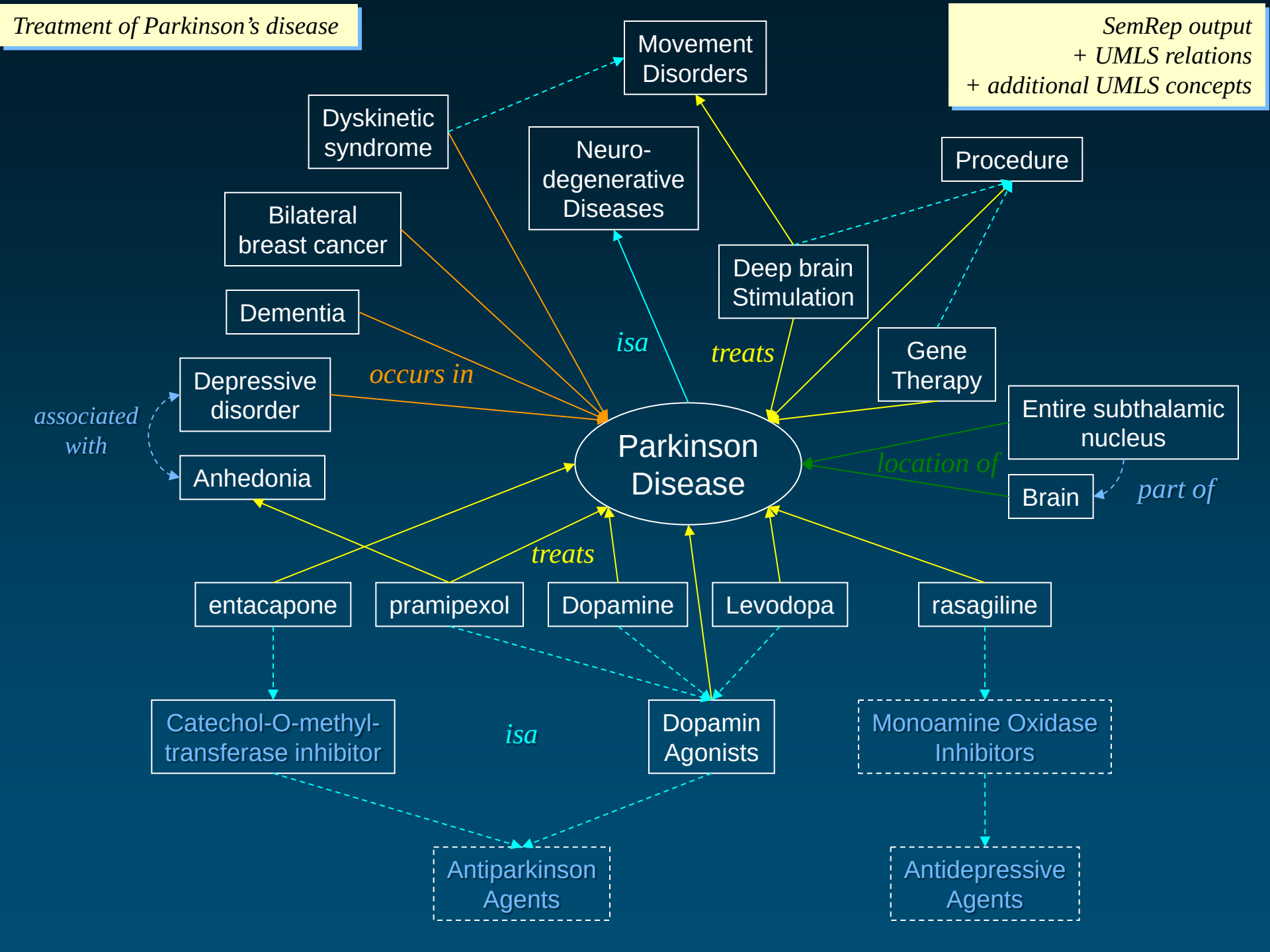
# Predication Database: SemMedDB

- Processed all of MEDLINE
  - More than 21 million citations
  - Titles and abstracts
- SemRep predications extracted
  - 57 million predications (through 06/30/2012)
- Made available to the research community
  - MySQL database
  - RDF triples

*Treatment of Parkinson's disease*

*SemRep output*




Treatment of Parkinson's disease
SemRep output
+ UMLS relations
+ additional UMLS concepts
Movement Disorders
Dyskinetic syndrome
Neuro-degenerative Diseases
Procedure
Bilateral breast cancer
Deep brain Stimulation
Dementia
isa
treats
Gene Therapy
occurs in
Depressive disorder
associated with
Entire subthalamic nucleus
Parkinson Disease
location of
Anhedonia
Brain
part of
treats
entacapone
pramipexol
Dopamine
Levodopa
rasagiline
Catechol-O-methyl-transferase inhibitor
isa
Dopamin Agonists
Monoamine Oxidase Inhibitors
Antiparkinson Agents
Antidepressive Agents

# Status

- Experimental
- Fully populated
  - UMLS 2012AA
  - 50M relations extracted from MEDLINE
- SemMedDB available for download
- UMLS in RDF not yet available for download
- Not available as a SPARQL endpoint
  - Licensing issues
  - Lack of access control in RDF stores

# Potential applications

- Multi-document summarization
  - Semantic MEDLINE “plus”
- Information retrieval of relations
  - Beyond keywords or concepts
- Simple question answering
  - Which drugs treat congestive heart failure?
- Knowledge discovery
  - Swanson’s paradigm (e.g., finding “B”s)
  - Patterns of relations

# TOWARDS A BIOMEDICAL SEMANTIC WEB

# Challenges

- Linked data vs. Linked OPEN data
  - Intellectual property restrictions on some of the data sources
    - "UMLS license"
  - Privacy issues with clinical data
- Lack of Semantic Web awareness/interest from some data source / ontology providers
  - RDF versions produced by third parties
    - Inconsistent URIs
    - Inconsistent updates

# Things are changing

- Data exposed through APIs
  - E.g., http://www.nlm.nih.gov/api/
- Linked Data Service
  - Library of Congress
  - Access to authority data
  - http://id.loc.gov/
- Aggressive "data liberation" initiatives
  - E.g., http://healthdata.gov/
- Common interface to ontologies
  - CTS2

ChenMed Transforming Health Care Delivery for Seniors

**Innovative Care Models and Uses of Clinical Practice Data - the Future of Medicine**

HHS Chief Technology Officer Bryan Sivak visited ChenMed to see how they have implemented an innovative care model and how clinical data is being used to improve practice. See what he learned from his trip. Read more »

**HDI Starter Kit** - Learn about all of the HHS data available to you.

Get the Kit!

Found a great health-related dataset on another site? Tell us about it!

Suggest a Dataset

## Search the Data

Search for

Sub-Agency

Subject Area

Search

## Recent Datasets

- CMS 2008-2010 Data Entrepreneurs'...
- CMS Data Navigator
- Cross Federal Workgroup on Telehealth (...
- Child Support Enforcement Annual Data Report...
- Child Welfare Monitoring Documents Library

View more »

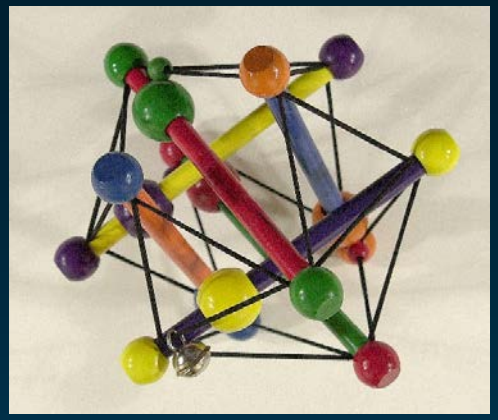
## Recent Blog Entries

- CMS Launches Medicare Claims Synthetic...
- Find the CMS data you are looking for with...
- Dwayne Spradlin joins the Health Data...
- Using CMS Data to Set Targets for ACOs
- Requesting your help with TXT4Tots Text...

View more »

# Biomedical Semantic Web

- Infrastructure for data integration
  - Definitional knowledge from ontologies
  - Assertional knowledge
    - From structured knowledge bases
    - Extracted through text mining
- Often requires semantic glue between datasets
  - UMLS, mappings
- Enabling technology for
  - Better information retrieval
  - Question answering
  - Hypothesis generation / knowledge discovery



# Medical Ontology Research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