

# Outline

- BIONT Goals
- Work so Far
- Collaborative BIONT – BIORDF use case
- Next Steps

# BIONT Goals

- Develop best practices around crucial questions related to creation and use of ontologies:
  - What is an ontology?
  - How should one represent information in an ontology?
  - Ontology lifecycle: How should ontologies be created, used, accessed, maintained and evolved?
- Develop a use case spanning the Bench to Bedside Spectrum
- Demonstrate the feasibility and value proposition of using ontologies to integrate biomedical data in the context of the use case

# Work so Far

- Developed a use case for Parkinson's Disease spanning the Bench to Bedside Spectrum, from Biomedical Research to Clinical Practice.
- Developed a Seed Ontology for Parkinson's Disease based on the Cellular and Molecular Biologist Perspective
- Identification of pre-existing ontologies for “cross-linking” into the seed ontology
- Refinement of Parkinson's Disease Use Case

# Use Case: Parkinson's Disease

- Description of Parkinson's Disease and Information Needs from different perspectives:
  - Systems Physiology View
  - Cellular and Molecular Biologist View
  - Clinical Researcher View
  - Clinical Guideline Formulator View
  - Clinical Decision Support Implementer View
  - Primary Care Clinical View
  - Neurologist View
- Available at:
  - <http://esw.w3.org/topic/HCLS/ParkinsonUseCase>
- Developed by:
  - Don Doherty
  - Ken Kawamoto

# Use Case: Systems Physiology View

What chemicals (neurotransmitters) are used by each circuit element (neuron) to communicate with the next element (neuron)? What responses do they elicit in the neurons?

# Use Case: Cellular and Molecular Biologist View

What proteins are implicated in Parkinson's disease? How are protein expression patterns, protein processing, folding, regulation, transport, protein-protein interactions, protein degradation, etc. affected?

# Use Case: Clinical Researcher View

Can a certain diagnostic test (e.g., a blood test for a biomarker or an imaging study) provide an approach to diagnosing Parkinson's disease that is superior to or can complement existing diagnostic approaches?

# Use Case: Clinical Guideline Formulator View

What have been the results of clinical trials that have evaluated the benefits and costs associated with diagnostic or therapeutic interventions for Parkinson's disease?



# Use Case: Clinical Decision Support Implementer View

Which clinical guideline(s) should be used as the basis for implementing the CDS functionality?

# Use Case: Primary Care Clinician View

If a patient is not currently diagnosed with Parkinson's disease, do the patient's current symptoms indicate the need for a referral to a neurologist for further evaluation? If so, what are the referral criteria?

# Use Case: Neurologist View

What is the differential diagnosis for this patient given his/her symptoms, signs, and diagnostic test results?

# Step 1: Identify concepts and subsumption hierarchies

The screenshot displays the TopBraid Eclipse SDK interface for the Parkinson's Disease ontology. The main window shows a class hierarchy under the 'Classes' tab. The root node is 'rdfs:Resource', which contains 'owl:Thing'. Under 'owl:Thing', there are several classes: 'AllelicVariant', 'AnatomicalEntity', 'BioMarker', 'Disease', 'Gene', 'Pathway', 'Protein', 'Sample', and 'Study'. The 'Disease' class is highlighted in blue. Under 'Disease', there are 'Dementia' and 'ParkinsonsDisease'. Under 'Gene', there are 'AlphaSynuclein', 'LRRK2', 'ParkinGene', 'Tau', and 'UCHL-1'. Under 'Pathway', there are 'CellularPathway' and 'ProteosomalPathway'. Under 'Protein', there are 'Dardarin', 'DJ-1', 'E3Ligase', 'Parkin', 'PINK-1', and 'Synuclein'. Under 'Sample', there is 'CellularStudy'. The 'rdfs:Property', 'rdfs:Statement', and 'rdfs:Class' nodes are also visible at the bottom of the hierarchy.

TopBraid - ParkinsonsDisease.owl - Eclipse SDK

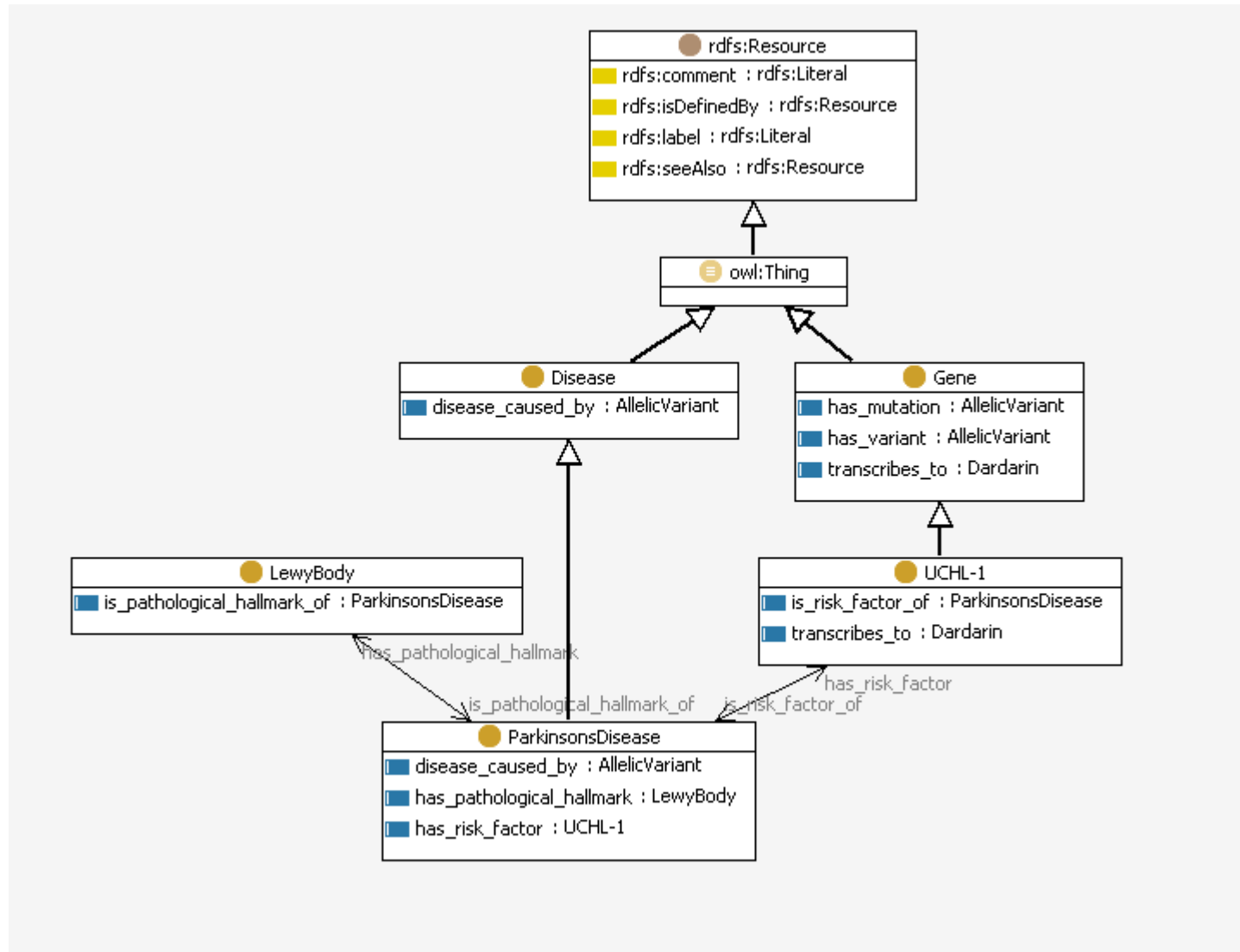
File Edit Navigate Project Inference Model Resource Window Help

owl:Thing

Classes

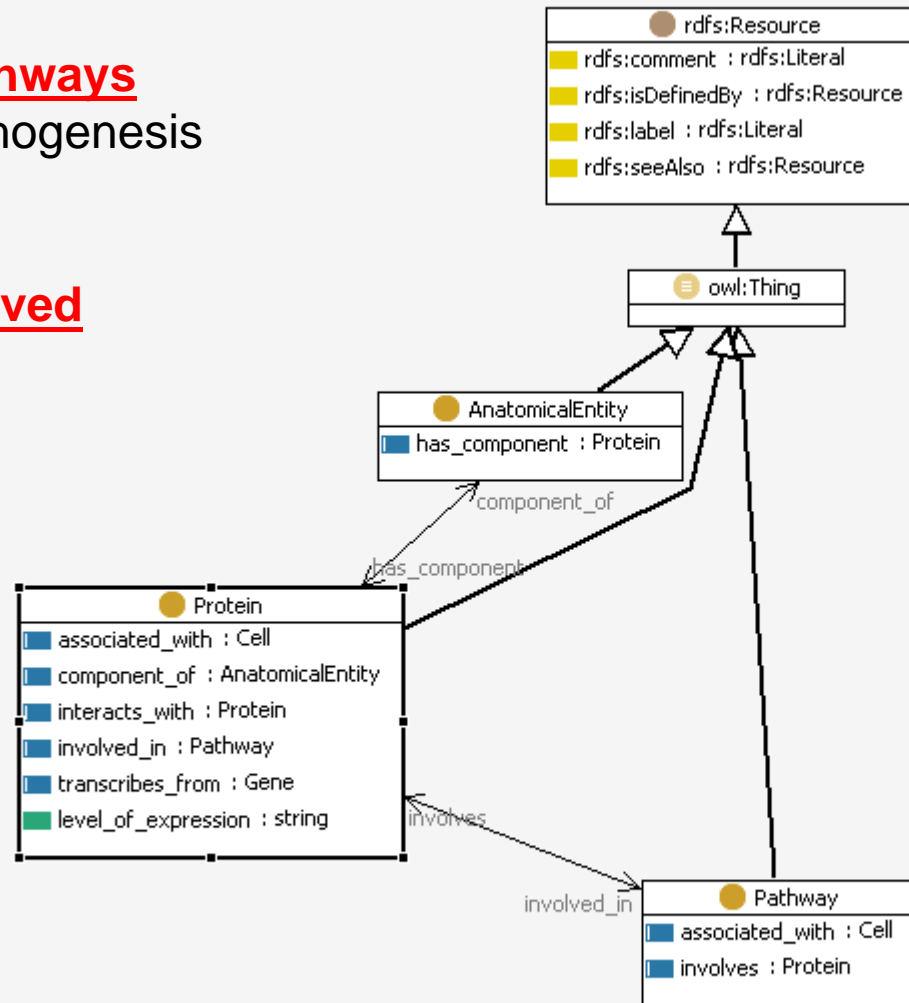
- rdfs:Resource
  - owl:Thing
    - AllelicVariant
    - LRRK2Variant
    - AnatomicalEntity
    - BioMarker
    - Disease
      - Dementia
      - ParkinsonsDisease
    - Gene
      - AlphaSynuclein
      - LRRK2
      - ParkinGene
      - Tau
      - UCHL-1
    - owl:Nothing
    - Pathway
      - CellularPathway
      - ProteosomalPathway
    - Patient
    - Protein
      - Dardarin
      - DJ-1
      - E3Ligase
      - Parkin
      - PINK-1
      - Synuclein
    - Sample
    - Study
      - CellularStudy
  - rdfs:Property
  - rdfs:Statement
  - rdfs:Class

# Step 2: Identify relationships



# Step 3: Look at Information Queries

What **cell signaling pathways** are implicated in the pathogenesis of Parkinson's disease?  
In which cells?  
What **proteins are involved** in which pathways?



# Ontology Design Issues

- Using classes vs relationships
  - UHCL-1 transcribed\_into Dardarin
- Using instance-of vs subclasses
  - UHCL-1 subclass-of Gene vs UHCL-1 instance-of Gene
- Granularity/Specificity of relationships
  - AllelicVariant causes Disease, vs LRR2KVariant causes Parkinson's Disease
- Uncertainty
  - *The discovery that genetic mutations in the alpha synuclein gene could cause Parkinson's disease in families*
- Multiple Domains/Ranges
  - Property: associated\_with, Domains: Pathway, Protein, Ranges: Cell, Biomarker
- Default Values
  - Default function of proteosomal pathway is protein degradation
- Ontology Inclusion and Modularization
  - NeuroNames, Enzyme Commission, MeSH
- Higher Order Relationships
  - Association between a Gene and a Disease in the context of a Study

# BIONT-BIORDF Use Case

- *Show me the location of receptors that bind to a ligand which is a therapeutic agent in {Parkinson's, Huntington's} disease in each of the dopaminergic neurons in the {pars compacta, pars reticularis, substantia nigra}.*
- Spans the following domains
  - Compartments of Neurons (Anatomy, Systems Physiology)
  - Receptors on Neurons (Protein, Molecular Biology)
  - Compounds that bind to Receptors (Pharmacology)
  - Ligands associated with disease (Clinical/Medical)
- Spans the following Data Sources
  - Neuron DB (SenseLab), RDF
  - KI DB, OWL
  - PubChem, TBD



# Next Steps

- Refine Parkinson's Disease Ontology based on the collaborative use case
- Specify SPARQL queries against Parkinson's Disease Ontology
- Annotate Data Sources with
  - Ontological relationships, e.g., receptor located\_in neuron
  - SPARQL queries to populate the relationships
- Populate RDF database with relevant RDF data based on refined Parkinson's Disease Ontology
- Update/refine Parkinson's Disease Ontology