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 Kawamato

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?
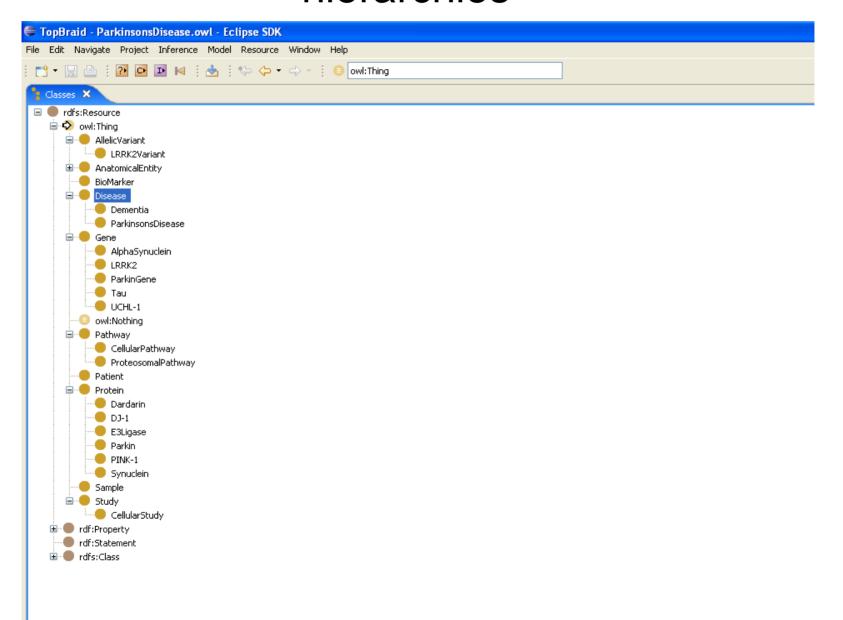
Use Case: Primary Care Clinician View

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?
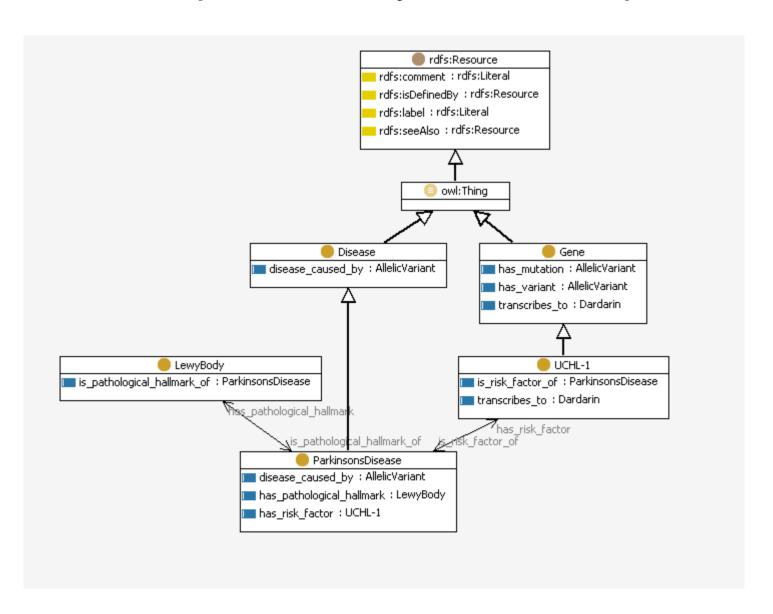
Use Case: Neurologist View

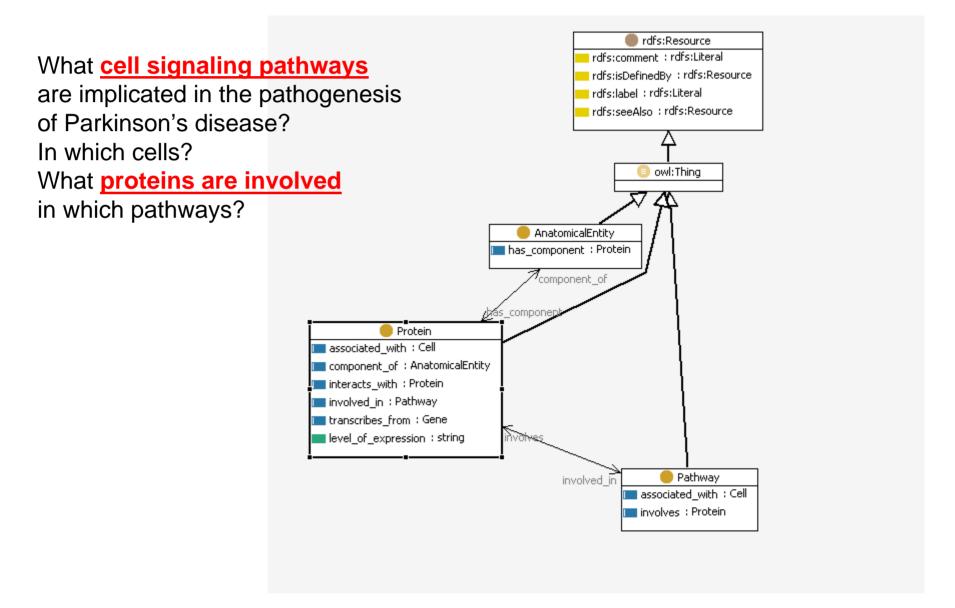What is the differential diagnosis for this patient given his/her symptoms, signs, and diagnostic test results?

Step 1: Identify concepts and subsumption hierarchies

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
  - <u>Property:</u> associated_with, <u>Domains:</u> Pathway, Protein, <u>Ranges:</u> 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