

Analysis of Cancer Omics Data In A Semantic Web Framework

Matt Holford

Yale University

12/10/10

ySPORE

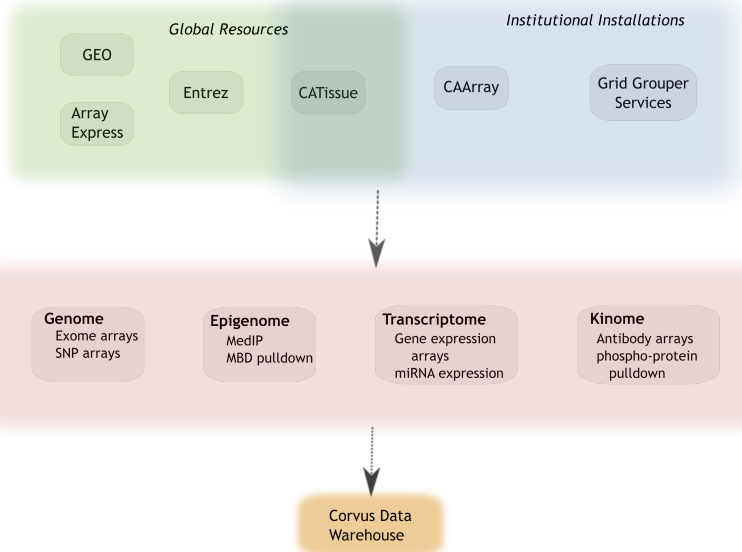
- Specialized Program in Research Excellence in skin cancer
- Large translational cancer research project
- Next generation sequencing of melanoma transcriptome and exome
- 1505 specimens - normal/melanoma cells, melanoma tumors, nevi, blood from healthy/unhealthy
- Collaborates with other SPOREs across the country

Motivation

- Integrate quantitative Omics data with functional information
- Find predictive biomarkers

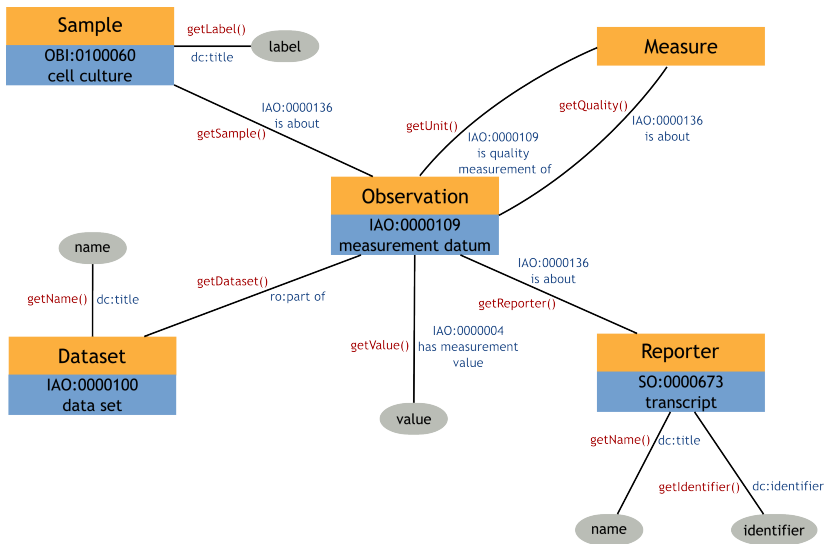
Semantic Web Tools

- Unified model to represent diverse data
- Derive new inferences using reasoning
- Share information as part of global network



Current Corvus Content

Name	Details	Data type	Samples	Obs/Samp	Total data points
Gene Expression	Normal/Tumor	continuous	43	31,842	1,369,206
Gene Expression	Pre/Post demeth.	continuous	18	30,079	541,422
Copy Number	Normal/Tumor	enumeration	29	45,758	1,326,982
Methylation	Absolute	continuous	7	19,736	138,152
Methylation	CpG, normalized	continuous	7	19,736	138,152
Phosphorylation	Intracellular/Pathways	discrete	37	114	4,218
Phosphorylation	Receptors	discrete	32	42	1,344
Phosphorylation	pY	discrete	29	737	21,373
Phosphorylation	pAKT	discrete	29	628	18,212

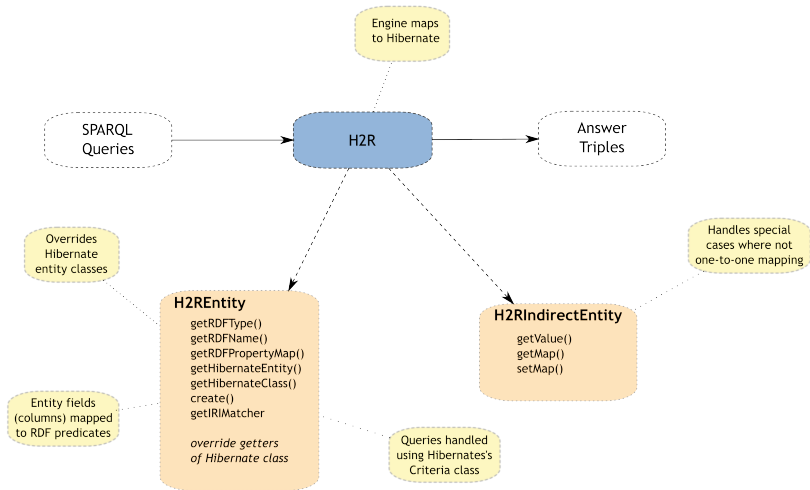


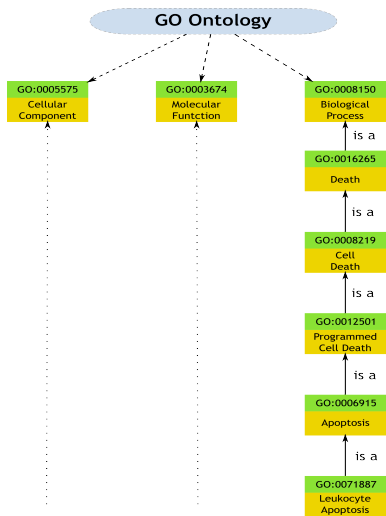
RDF Access

- Need to retrieve only a portion of dataset as RDF graph
- RDB-RDF mappings: generic vs. custom

Our approach

- Map SPARQL to existing object-relational model (Hibernate)
- Already have flexible object model
- Take advantage of Hibernate's query optimization and caching



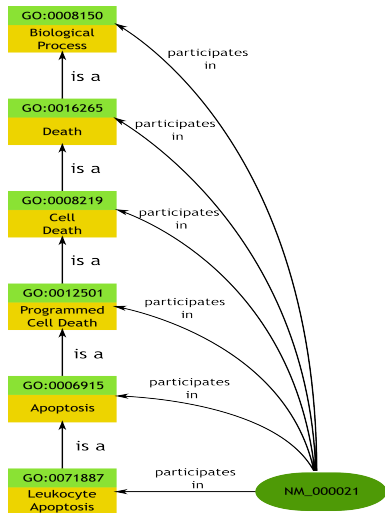


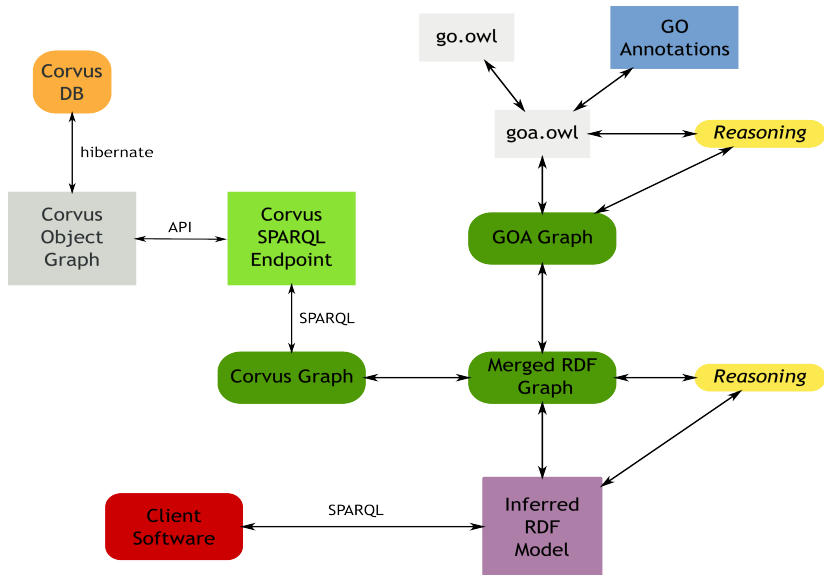
Gene Ontology (GO)

- 3 major hierarchies to annotate genes
- Class subsumption hierarchies
- Annotations for species provided separately

Reasoning on GO

- Use SKOS representation of GO
- Declare genes to be associated with GO processes (Concepts)
- Used OWL2 property chain:
 $RO:participates_in + SKOS:broader \rightarrow RO:participates_in$





Use Case

- Decitabine - a demethylating agent used for melanoma therapy
- Find genes involved in apoptosis
 - with high methylation pre-Decitabine administration
 - with increased gene expression post-Decitabine administration
- Used two datasets:
 - relative methylation prior to treatment
 - ratio of gene expression post/pre treatment
- Seven melanoma cell lines:
 - WW165, YUMAC, YUGEN8, YUSAC2, YUSIT1, YULAC, YURIF

SPARQL query

```
PREFIX dc: <http://purl.org/dc/elements/1.1/>
PREFIX ro: <http://www.obofoundry.org/ro/ro.owl#>
PREFIX obo: <http://purl.obolibrary.org/obo/>
PREFIX go: <http://purl.org/obo/owl/GO#>
```

```
SELECT (count(?rep) as ?repcount) ?samp
WHERE {
  ?ds dc:title "Methylation Relative" .
  ?obs ro:part_of ?ds .
  # IAO_0000004 = 'has_measurement_value'
  ?obs obo:IAO_0000004 ?obsVal .
  # IAO_0000136 = 'is_about'
  ?obs obo:IAO_0000136 ?rep .
  ?obs obo:IAO_0000136 ?samp .
  # OBI_0100060 = 'cell culture'
  ?samp a obo:OBI_0100060 .
  ?ds2 dc:title "AZA Pre-Post Treatment Ratios" .
  ?obs2 ro:part_of ?ds2 .
  ?obs2 obo:IAO_0000136 ?rep .
  ?obs2 obo:IAO_0000136 ?samp .
  ?obs2 obo:IAO_0000004 ?obsVal2 .
  ?rep ro:participates_in go:0006915 .

  FILTER ( ?obsVal > 2 ) .
  FILTER ( ?obsVal2 > 1 )
} GROUP BY (?samp)
```

Results

Cell Line	Gene Count	IC50 (nM)
YUMAC	22	34
YUSAC	7	91
YULAC	9	110
YUSIT1	2	132
YUGEN8	6	139
WW165	2	239
YURIF	0	255

Hypothesis

Decitabine targets apoptosis-related gene promoters predominantly in Decitabine-sensitive cell lines, thus conveying its cytotoxic effect by activating the apoptosis pathway.

Future Plans

- Omics data from other sources
 - Cancer data from caArray or caIntegrator
 - Array data from ArrayExpress/GEO
- Other types of functional information
 - Pathway data (Reactome/BioCarta)
 - Pharmacological data (PharmGKB/DrugBank)

Special Thanks

- Jim McCusker
- Kei-Hoi Cheung
- Michael Krauthammer
- Yale CBB Program

Funding

- National Cancer Institute
 - Yale SPORE in skin cancer
- National Library of Medicine
 - Yale Biomedical Informatics Research Training Program

Questions ?

Matt Holford

matthew.holford@yale.edu