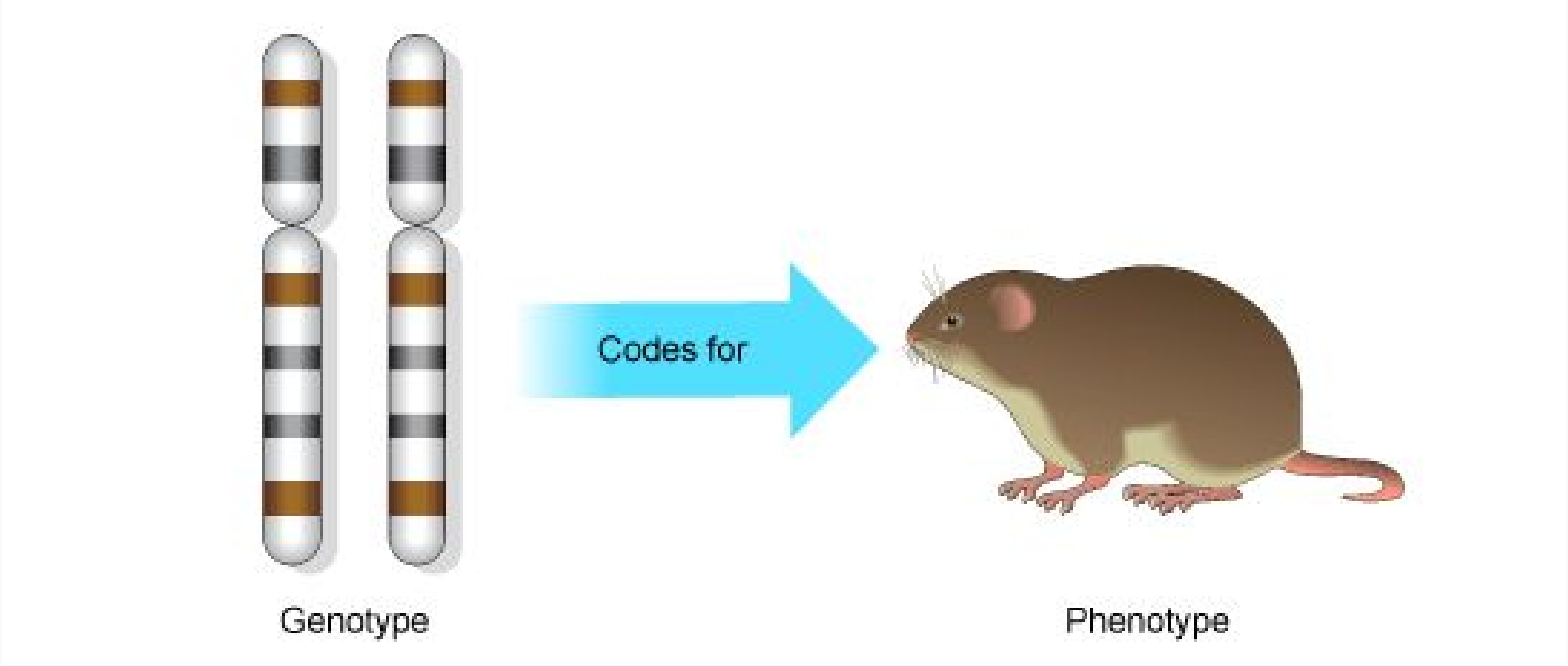
PhenoBlocks:
Phenotype Comparison Visualizations

Glueck, Michael, et al. "PhenoBlocks: Phenotype Comparison Visualizations." (2016).

As presented by Mike

What: Patient Phenotype Comparisons (as defined by an ontology)

What is a phenotype?

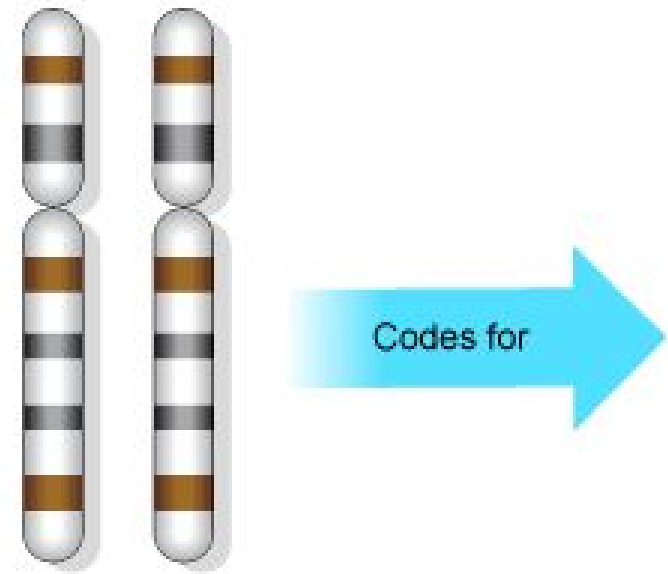


What?
Why?
How?

http://www.bbc.co.uk/staticarchive/eec1f8601eb06daafb0dbbd56924abb12344b1d4.gif

What is a phenotype?

https://s-media-cache-ak0.pinimg.com/736x/da/96/57/da965747c97fab4d174a9b3de9a6403c.jpg



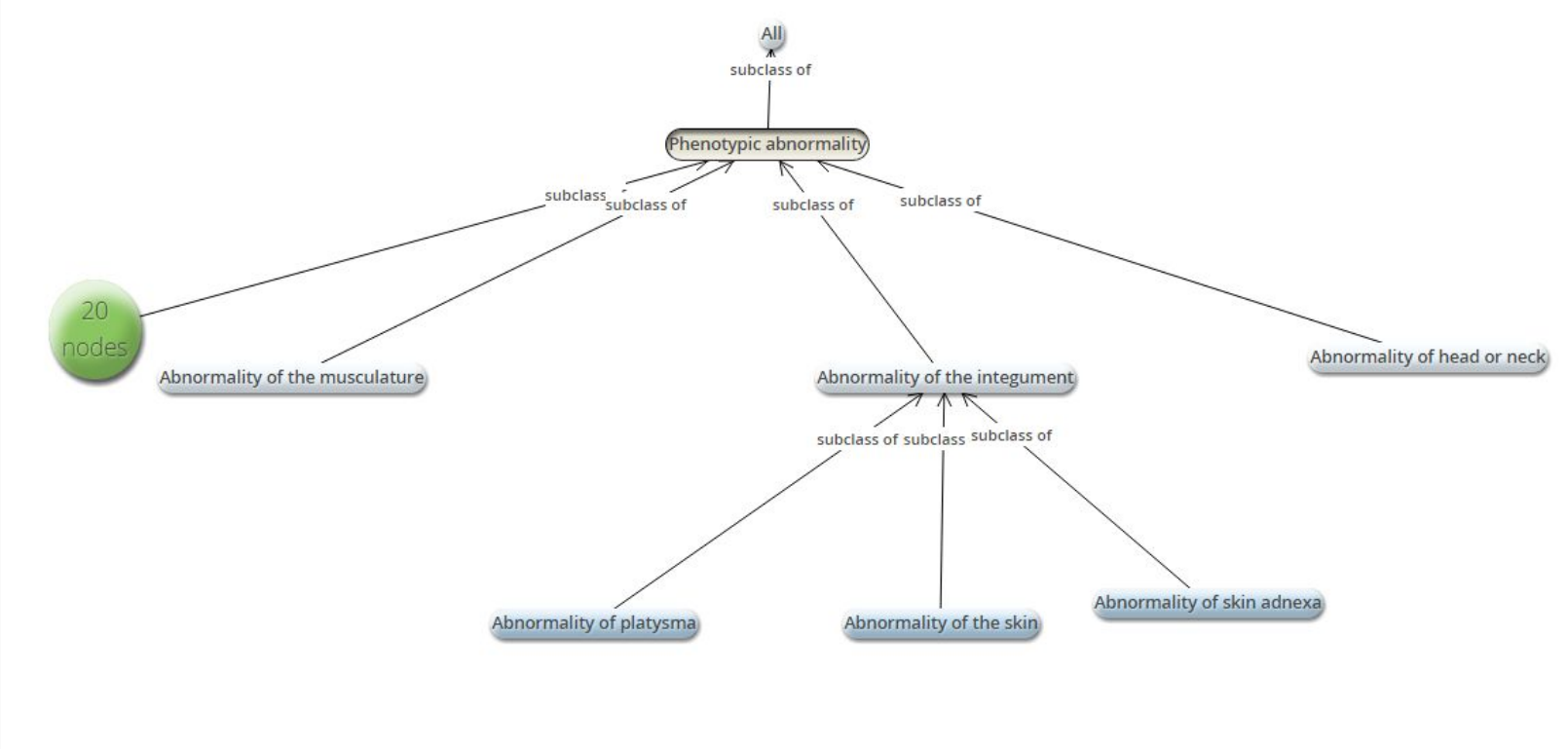
Genotype

Phenotype

What?
Why?
How?

http://www.bbc.co.uk/staticarchive/eec1f8601eb06daafb0dbbd56924abb12344b1d4.gif

What is an ontology?

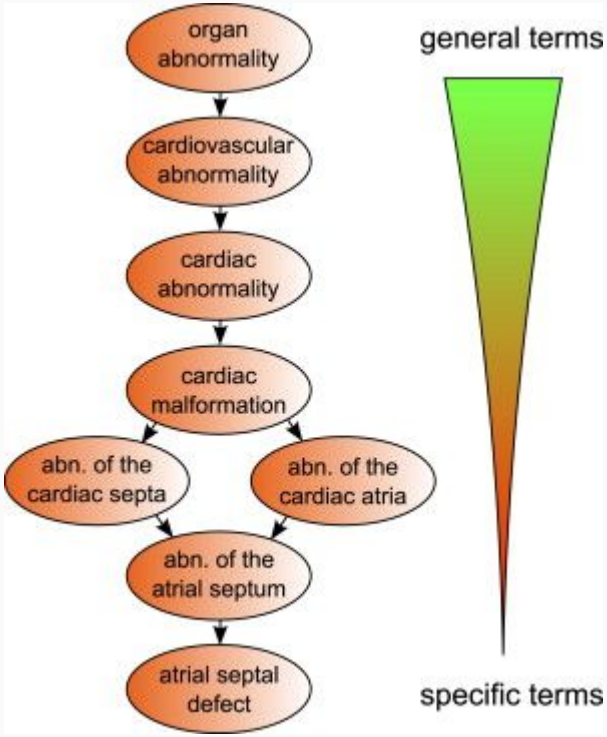


What?
Why?
How?

http://compbio.charite.de/hpoweb/showterm?id=HP:0000118

What is an ontology?

- Network dataset type (xml like format)
- Similar to trees and DAGs
- Is-a relationships (hierarchical)
- Multiple inheritance
- And so much more!

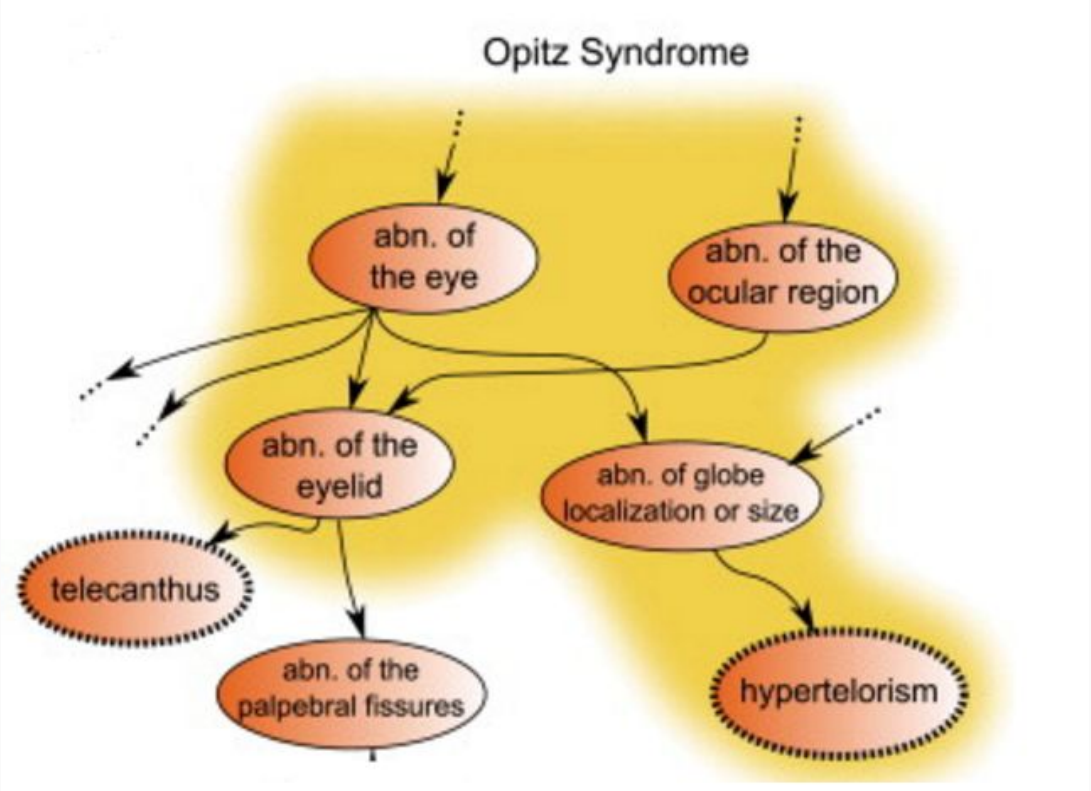


Köhler et al, 2009 (doi:10.1016/j.ajhg.2009.09.003)

What is a patient phenotype?

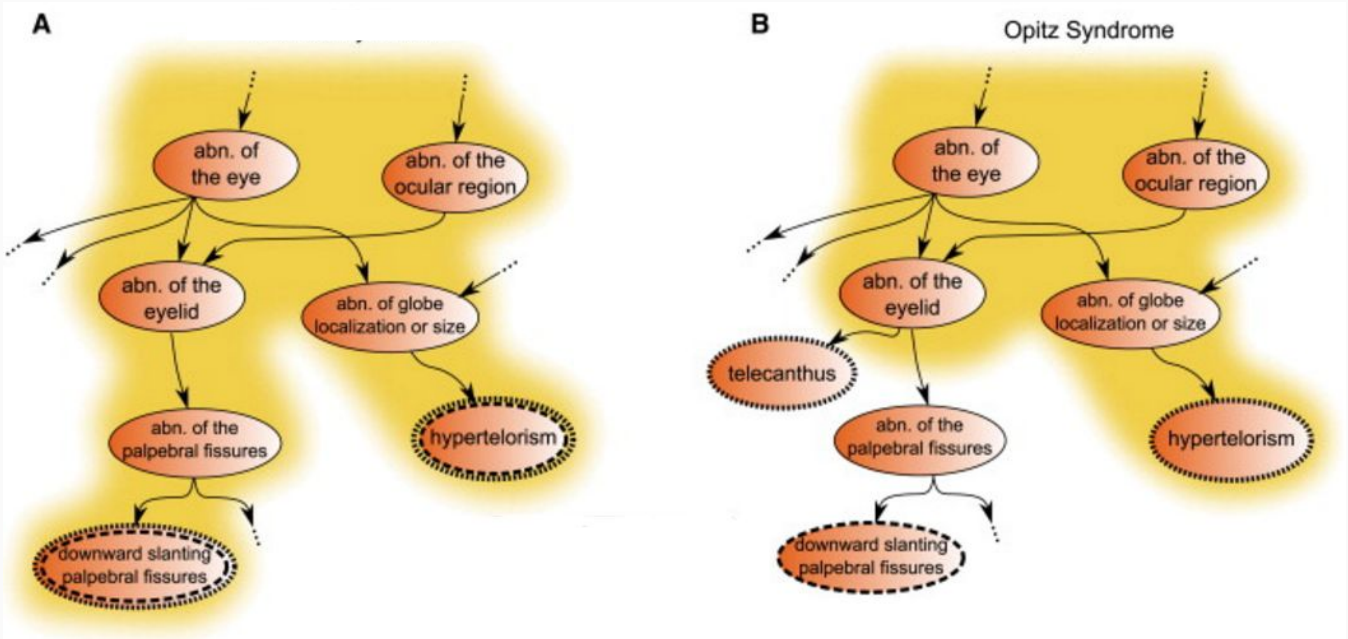
- Defined by assigning ontology terms to
  - {Present}
  - {Absent}
  - Unknown

```
{
   "id": "q1",
   "present": [
      "HP:0000492",
      "HP:0000316"
   ],
   "absent": [
     "HP:0000506"
]
}
```



Köhler et al, 2009 (doi:10.1016/j.ajhg.2009.09.003)

What is a phenotype comparison?



"Query case" (undiagnosed)

"Reference case" (in database)

Köhler et al, 2009 (doi:10.1016/j.ajhg.2009.09.003)

What?
Why?
How?

Why: Phenotype Comparison

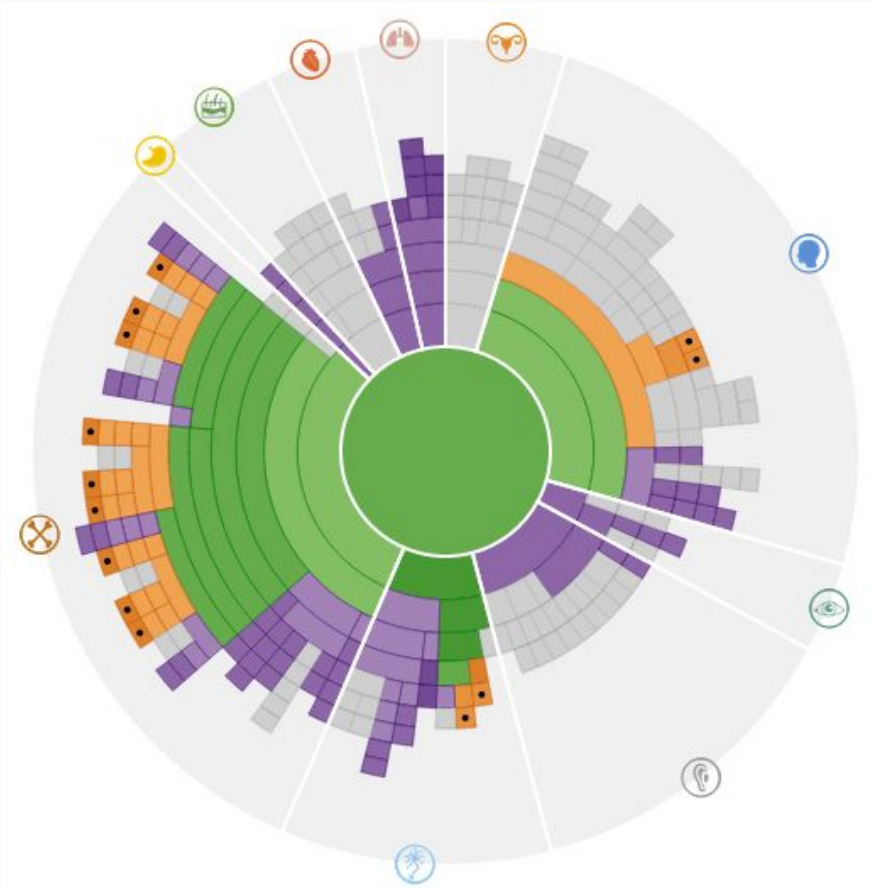
Why: Task Abstraction

- Analyse
  - Discover
    - Discover potential diagnoses
    - Verify existing diagnoses
- Query
  - Identify
    - Find similar cases
  - Compare
    - Examine similarities and differences between comparisons
  - Summarize
    - Understand case comparison profiles at a glance

How?

How: Encode

- Ontology expanded into a tree
- Sunburst layout used
  - Shows all nodes
  - Gives more space to informative nodes
- Major branches separated
- Colour encodes overlap

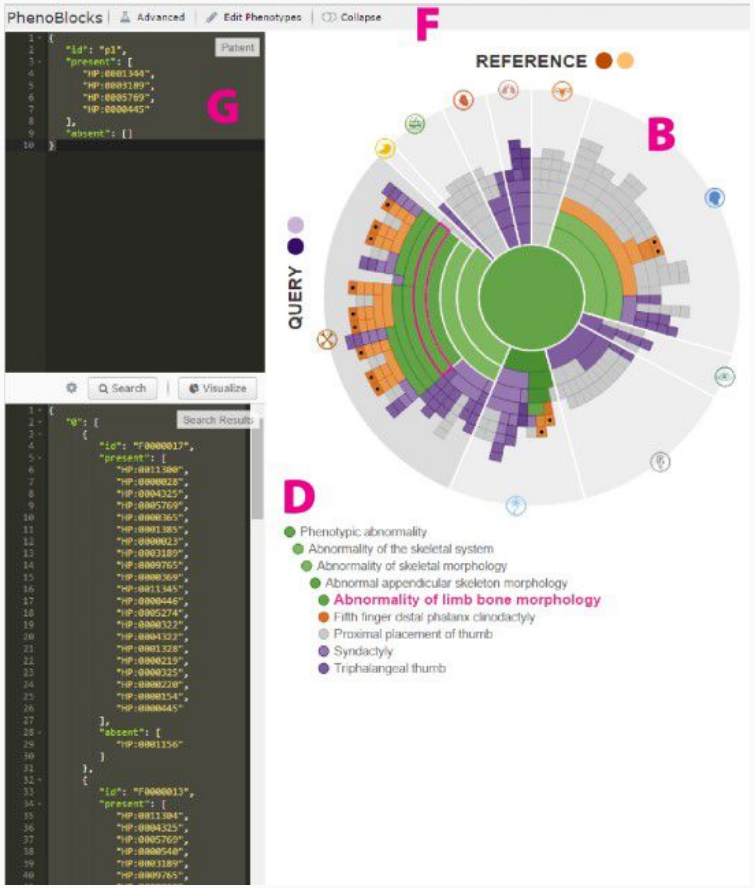


How: Manipulate Selection

How: Manipulate Selection

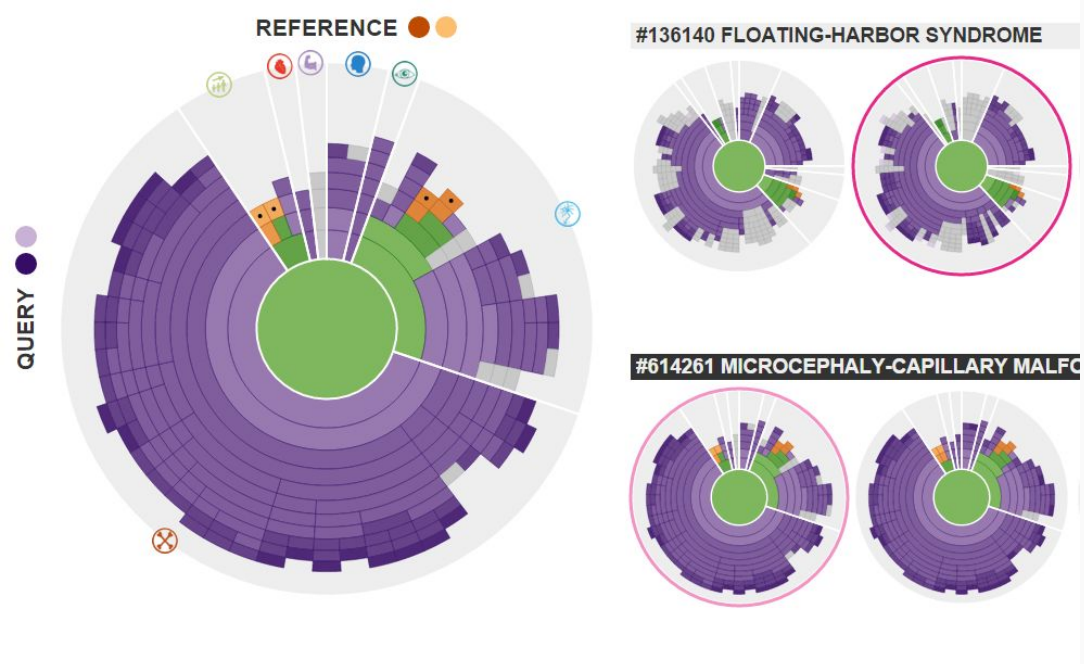
How: Manipulate

- Can change query phenotype in G
  - Will change visuals on demand
- Clicking on items in B
  - Brings up include/exclude dialog
  - Causes PhenoBlocks to freeze
- Edit Phenotype button near F
  - Also breaks PhenoBlocks



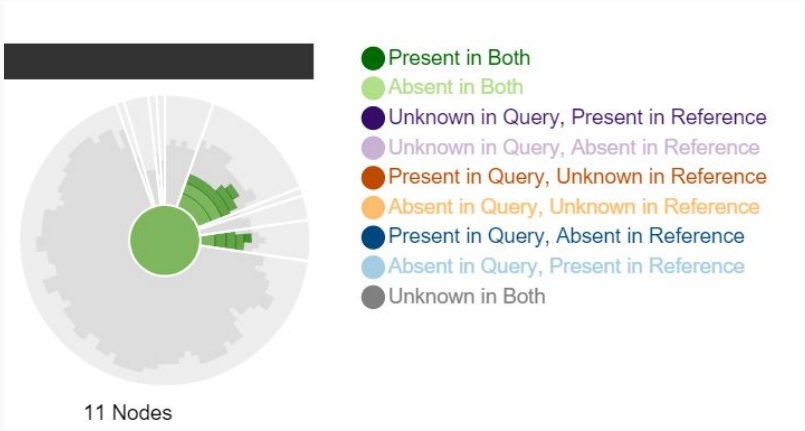
How: Facet

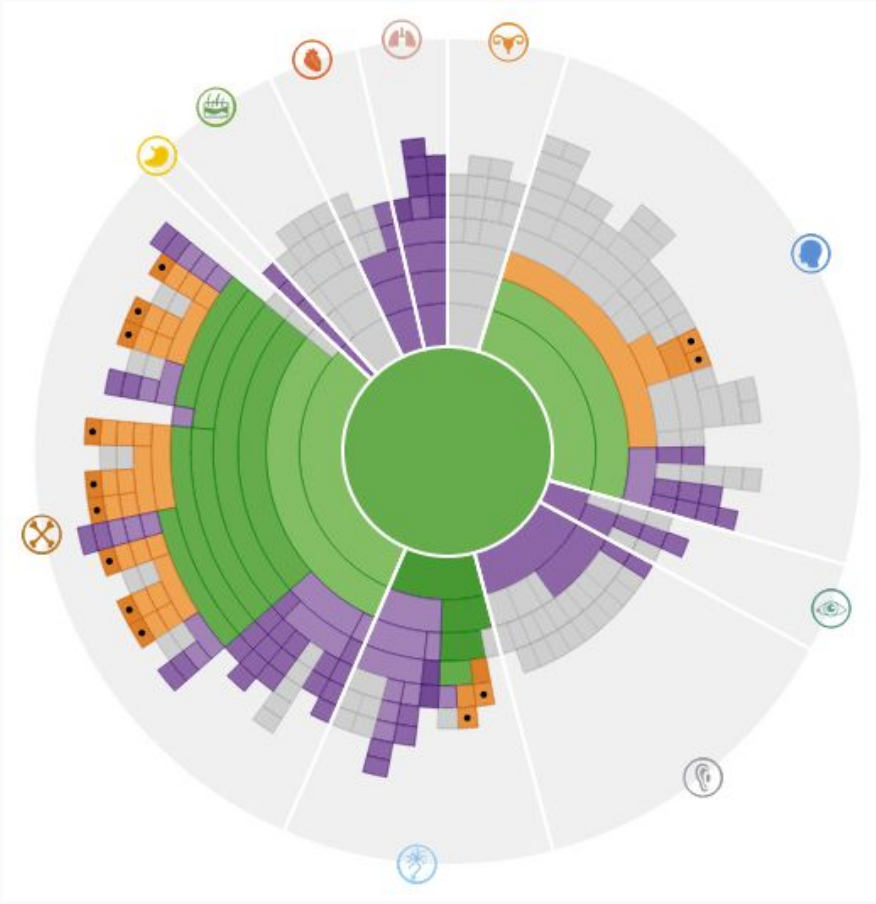
- Partitioned by main branches of phenotype ontology
- Small multiples used to juxtapose multiple cases



How: Reduce

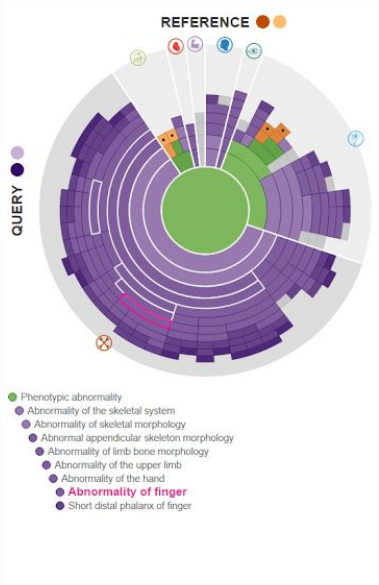
- Clicking on categories collapses
  - Not yet functional
- Can filter which nodes to display based on membership

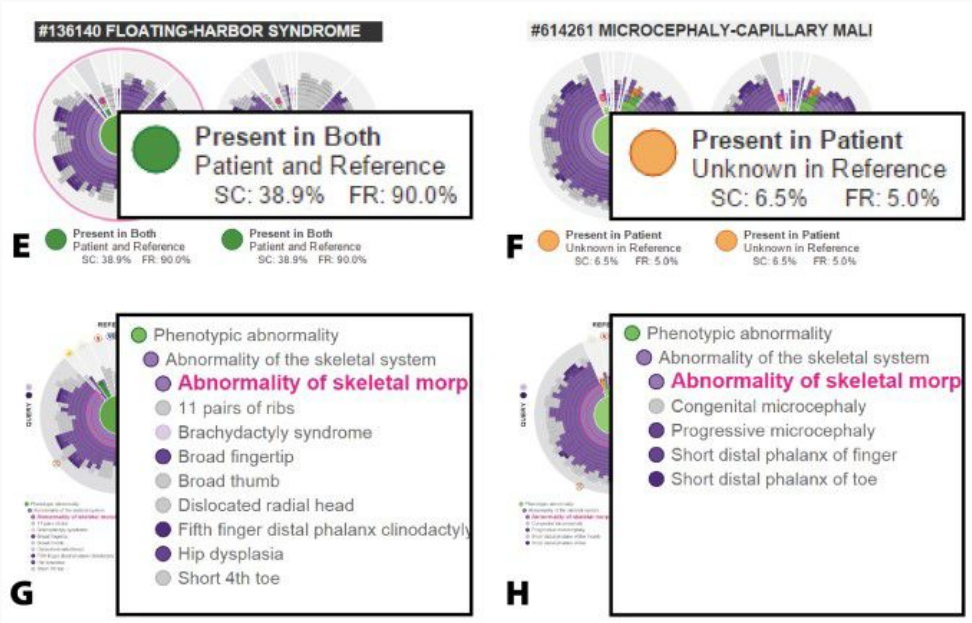




How: Embed

- Details on demand
  - Main view (linked highlighting!)
  - Small multiples view

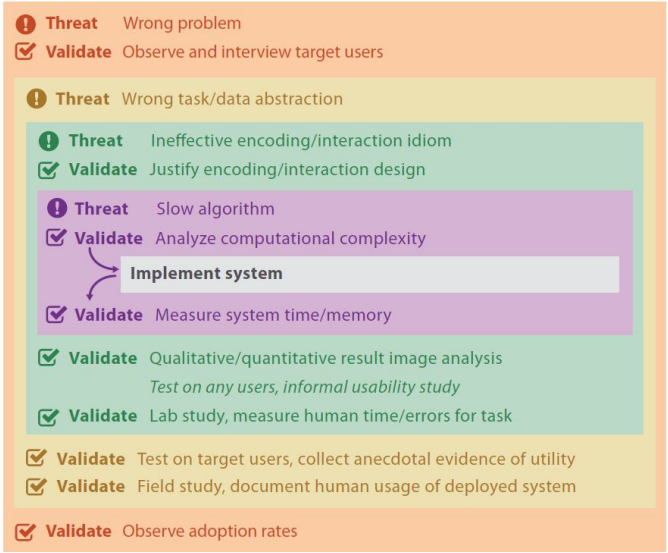




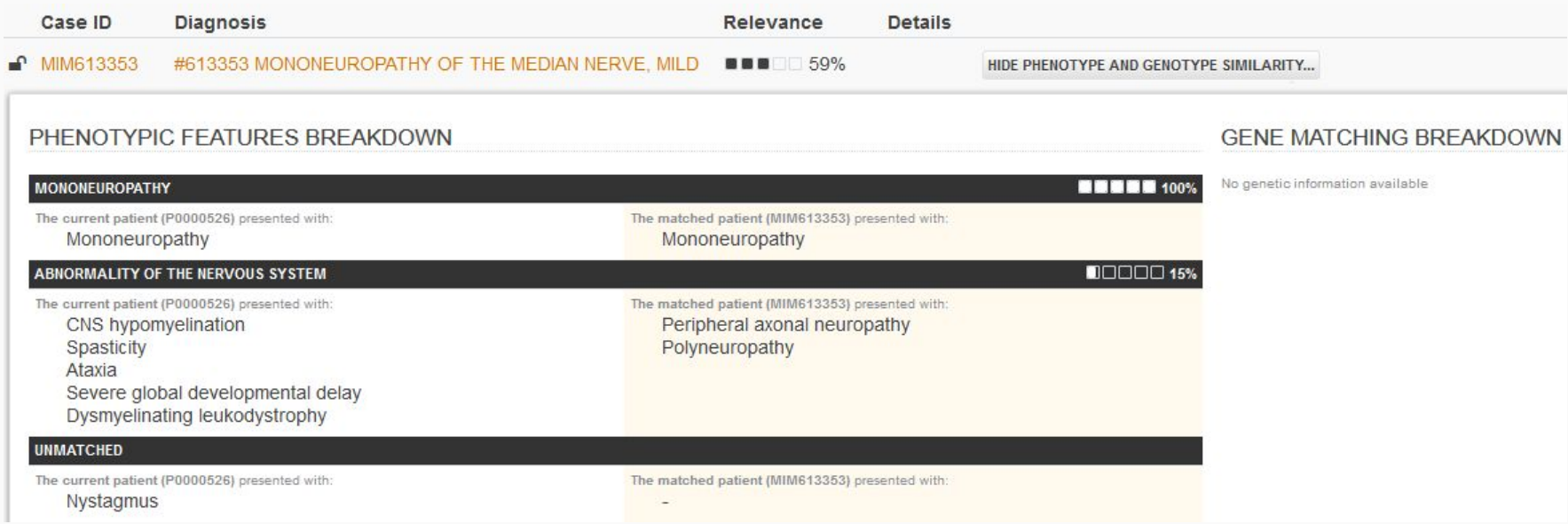
Validation

Validation

- Worked with two clinicians during and after development
  - Tailored workflow to their needs during development
  - Validated the system based on user feedback after development
- Idiom validation not provided
  - No quantitative comparison to other methods/tools
- Algorithmic validation not provided
  - Slow and buggy, but technically not yet released



Validation: PhenomeCentral



Case ID	Diagnosis	Relevance	Details
MIM613353	#613353 MONONEUROPATHY OF THE MEDIAN NERVE, MILD	59%	HIDE PHENOTYPE AND GENOTYPE SIMILARITY...

PHENOTYPIC FEATURES BREAKDOWN

MONONEUROPATHY 100%

The current patient (P0000526) presented with:	The matched patient (MIM613353) presented with:
Mononeuropathy	Mononeuropathy

ABNORMALITY OF THE NERVOUS SYSTEM 15%

The current patient (P0000526) presented with:	The matched patient (MIM613353) presented with:
CNS hypomyelination	Peripheral axonal neuropathy
Spasticity	Polyneuropathy
Ataxia	
Severe global developmental delay	
Dysmyelinating leukodystrophy	

UNMATCHED

The current patient (P0000526) presented with:	The matched patient (MIM613353) presented with:
Nystagmus	-

GENE MATCHING BREAKDOWN

No genetic information available

Buske et al. (2015)
10.1002/humu.22851

Validation: GeneYenta

Phenotype Tag Summary

Description	Your Importance Rating	Importance Rating
Parkinsonism	N/A	3
Macrogyria	N/A	3
Leukodystrophy	5	N/A
X-linked recessive inheritance	N/A	4
Intellectual disability, moderate	N/A	3
Delayed speech and language development	N/A	3
Nystagmus	3	4
Spasticity	3	4
Head titubation	N/A	4
Dysmyelinating leukodystrophy	5	N/A
Severe global developmental delay	3	N/A
Microcephaly	N/A	3
Athetosis	N/A	3
Ataxia	3	4
Generalized hypotonia	N/A	3
Hypomyelination	5	4
Dementia	N/A	3
Mononeuropathy	4	N/A
Progressive spastic quadriplegia	N/A	4
Optic atrophy	N/A	3

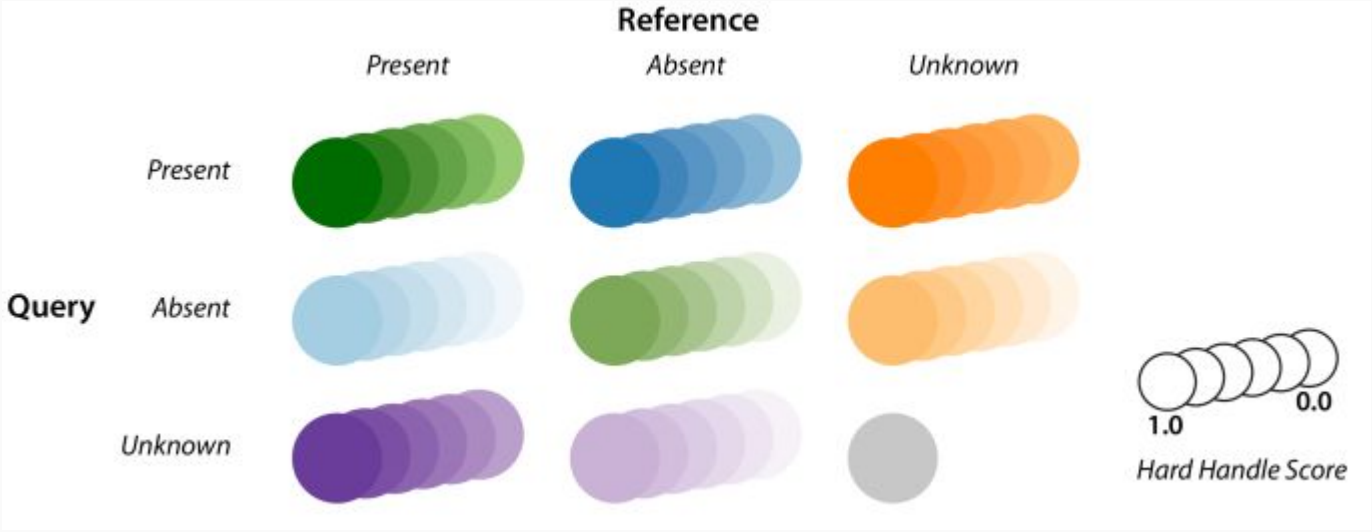
Back | Review Your Case Summary | Add Notes

Gottlieb et al. (2015)
DOI: 10.1002/humu.22772

End

Hard Handles

Informs colour, based on information content and disorder frequency



How: Encode

- Colour used to represent whether terms are in present or absent in both reference and query cases

Nine States		Reference		
		Present	*Absent*	*Unknown*
Query	*Present*	P/P	P/A	P/U
	Absent	A/P	A/A	A/U
	Unknown	U/P	U/A	U/U

Shared in Both
Divergent in Both
Missing in Query
Missing in Reference
Unknown in Both

Ontology States