

Using HPO in genomic medicin



VEP course 2019

Jeroen van Reeuwijk
Researcher Translational Genomics



Radboudumc

Lecture objectives & outline

Objectives

- Next-generation phenotyping: Human Phenotype Ontology
- HPO tools for variant/disease gene prioritization

Outline

Part 1: Introduction to HPO

- Use of phenotypic information in clinical genetics
- Standardized phenotyping using HPO
- HPO structure

Part 2: Applications using HPO

- Capturing patient clinical data in HPO format
- Using HPO-profiles in variant-disease interpretation
- Phenotype matching tools
- Outlook

Use of phenotypic information

- Pre-genetic testing:
 - differential diagnosis
 - choice of genetic testing: single gene, genepanel(s), exome/genome, SNP array
- Post-genetic testing:
 - genotype-phenotype correlation
 - candidate disease gene/variants analysis
 - disease processes and biochemical pathways
 - clinically similar patients
 - animal disease models

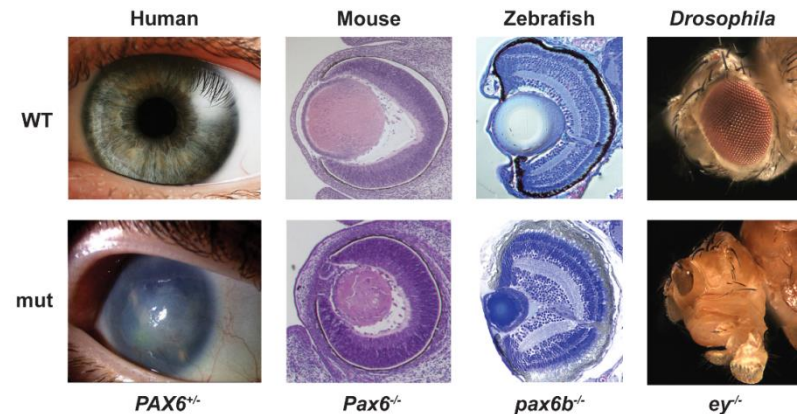
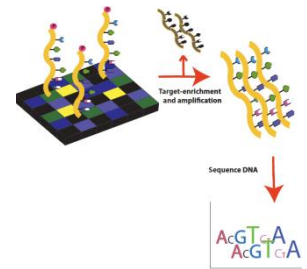


Figure 1 of Washington et al. PLoS Biol 7(11): e1000247

Use of phenotypic information

in exome/genome diagnostics:

Variant Effect Predictions

Clinical symptoms



Clinical molecular diagnosis

Computational use of phenotypic info

Computable data:

- Standardized terminology
- Relationship between terms

➔ “Next-generation phenotyping”



Human Phenotype Ontology: HPO

Am J Hum Genet. 2008 Nov;83(5):610-5. doi: 10.1016/j.ajhg.2008.09.017. Epub 2008 Oct 23.

The Human Phenotype Ontology: a tool for annotating and analyzing human hereditary disease.

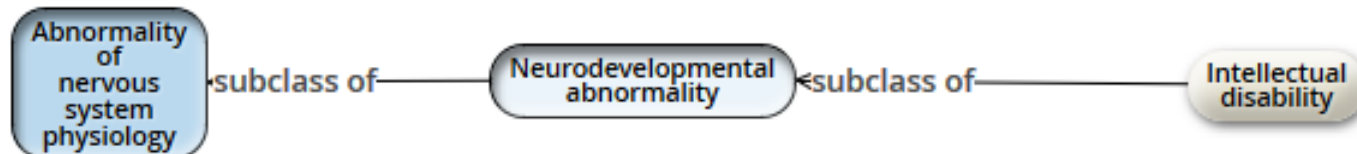
Robinson PN¹, Köhler S, Bauer S, Seelow D, Horn D, Mundlos S.

*Peter Robinson
& Sebastian Köhler*

- Standardized clinical terminology
- Ontology data model: entities, attributes and relations



UNIVERSITÄTSMEDIZIN BERLIN



Expansion of the Human Phenotype Ontology (HPO) knowledge base and resources

HPO Today: the standard for electronic clinical phenotyping in medical genetics

- Standardized clinical terminology for ~14.000 clinical features
- Annotation of 7000+ disorders with HPO terms
- Algorithms for diagnostics & translational research

Part of



monarch
INITIATIVE



Global Alliance
for Genomics & Health
Collaborate. Innovate. Accelerate.

International recognition core resource



Standardized phenotyping using HPO

Table 1. A selection of public-facing clinical databases using HPO to annotate patient data for disease-gene discovery projects

Name	URL
PhenomeCentral	phenomecentral.org
DDD (Deciphering Developmental Disorders)	www.ddduk.org
DECIPHER (DatabasE of genomiC variation and Phenotype in Humans using Ensembl Resources)	decipher.sanger.ac.uk
ECARUCA (European Cytogeneticists Association Register of Unbalanced Chromosome Aberrations)	http://umcecaruca01.extern.umcn.nl:8080/ecaruca/ecaruca.jsp
The 100 000 Genomes Project	https://www.genomicsengland.co.uk/
Geno2MP (Exome sequencing data linked to phenotypic information from a wide variety of Mendelian gene discovery projects)	http://geno2mp.gs.washington.edu
NIH UDP (Undiagnosed Diseases Program)	available via phenomecentral.org
NIH UDN (Undiagnosed Diseases Network)	available via phenomecentral.org
HDG (Human Disease Gene Website series)	www.humandiseasegenes.com
Phenopolis (An open platform for harmonization and analysis of sequencing and phenotype data)	https://phenopolis.github.io
GenomeConnect (Patient portal developed by ClinGen (67))	www.genomeconnect.org
FORGE Canada & Care4Rare Consortium	available via phenomecentral.org
RD-Connect	platform.rd-connect.eu
Genesis	thegenesisprojectfoundation.org

Standardized phenotyping using HPO

Commercial software for variant interpretation such as

- FDNA: Face2Gene
- Cartagenia BENCH
- GEPADO – Software Solutions for Genetics – GmbH
- BioDiscovery's NxClinical
- Diploid: Diagnosing rare diseases: Moon
- Centogene
- SimulConsult
- Fabric Genomics
- Qiagen
- Congenica

The diagram illustrates the clinical, genetic, and molecular aspects of Fanconi anemia (FA). It shows the relationship between FA and acquired aplastic anemia, their shared phenotypes, and the genetic subtypes of FA. The diagram also details the molecular pathway of FA, showing the role of various proteins in DNA repair.

Genetic and Clinical Features:

- Fanconi anemia** is a disease that can be caused by DNA interstrand cross-linking agents and aldehydes. It is a genetic condition that can be inherited (FA-A, FA-B, FA-V) or caused by variants in other genes (FANCL, FANCD2).
- Acquired aplastic anemia** is a disease that can be caused by environmental risk factors (Parvovirus B19, Radiation, Benzene, Pesticides, Unknown).
- Both diseases share a common phenotype, which includes: Microcephaly, Radial-ray deformities, Short stature, Neutropenia, Thrombocytopenia, and Anemia.
- Both diseases are associated with **Precision stratification and treatment**.
- FA is an **Autosomal recessive** condition.

Molecular Pathway:

The **Fanconi anemia pathway** is a complex molecular pathway involved in DNA repair. It shows the role of various proteins, including FANCD1, FANCD2, FANCD3, FANCD4, FANCD5, FANCD6, FANCD7, FANCD8, FANCD9, FANCD10, FANCD11, FANCD12, FANCD13, FANCD14, FANCD15, FANCD16, FANCD17, FANCD18, FANCD19, FANCD20, FANCD21, FANCD22, FANCD23, FANCD24, FANCD25, FANCD26, FANCD27, FANCD28, FANCD29, FANCD30, FANCD31, FANCD32, FANCD33, FANCD34, FANCD35, FANCD36, FANCD37, FANCD38, FANCD39, FANCD40, FANCD41, FANCD42, FANCD43, FANCD44, FANCD45, FANCD46, FANCD47, FANCD48, FANCD49, FANCD50, FANCD51, FANCD52, FANCD53, FANCD54, FANCD55, FANCD56, FANCD57, FANCD58, FANCD59, FANCD60, FANCD61, FANCD62, FANCD63, FANCD64, FANCD65, FANCD66, FANCD67, FANCD68, FANCD69, FANCD70, FANCD71, FANCD72, FANCD73, FANCD74, FANCD75, FANCD76, FANCD77, FANCD78, FANCD79, FANCD80, FANCD81, FANCD82, FANCD83, FANCD84, FANCD85, FANCD86, FANCD87, FANCD88, FANCD89, FANCD90, FANCD91, FANCD92, FANCD93, FANCD94, FANCD95, FANCD96, FANCD97, FANCD98, FANCD99, and FANCD100.

The pathway shows the role of these proteins in DNA repair, with FANCD1 and FANCD2 being the core proteins. The pathway is involved in the repair of DNA damage, particularly in the context of DNA interstrand cross-links.

HPO: structure & ontologies

- HPO structure

- Terms (~14.000)
- Term relationship (subclass of ..)



Intellectual disability

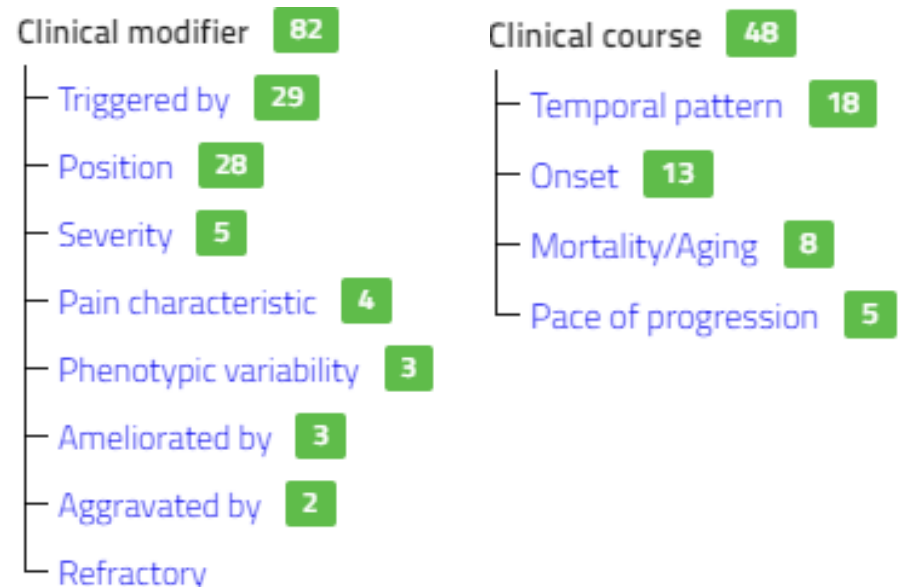
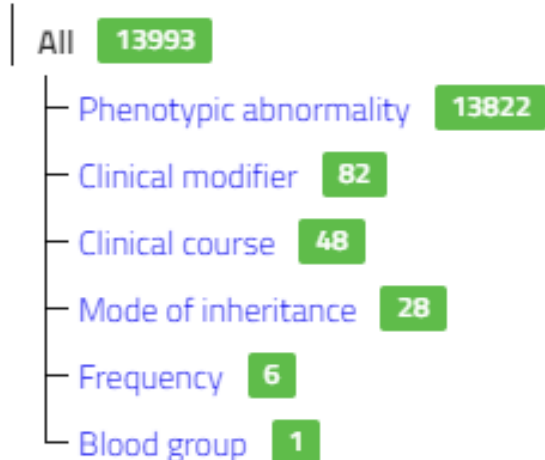
Primary ID: HP:0001249

Synonyms: mental retardation, ...

Textual definition: Subnormal intellectual functioning ...

...defined as an IQ score below 70.

- HPO subontologies:




HPO-browser: <https://hpo.jax.org/app/>

HPO-subontology Phenotypic abnorm.

All 13993

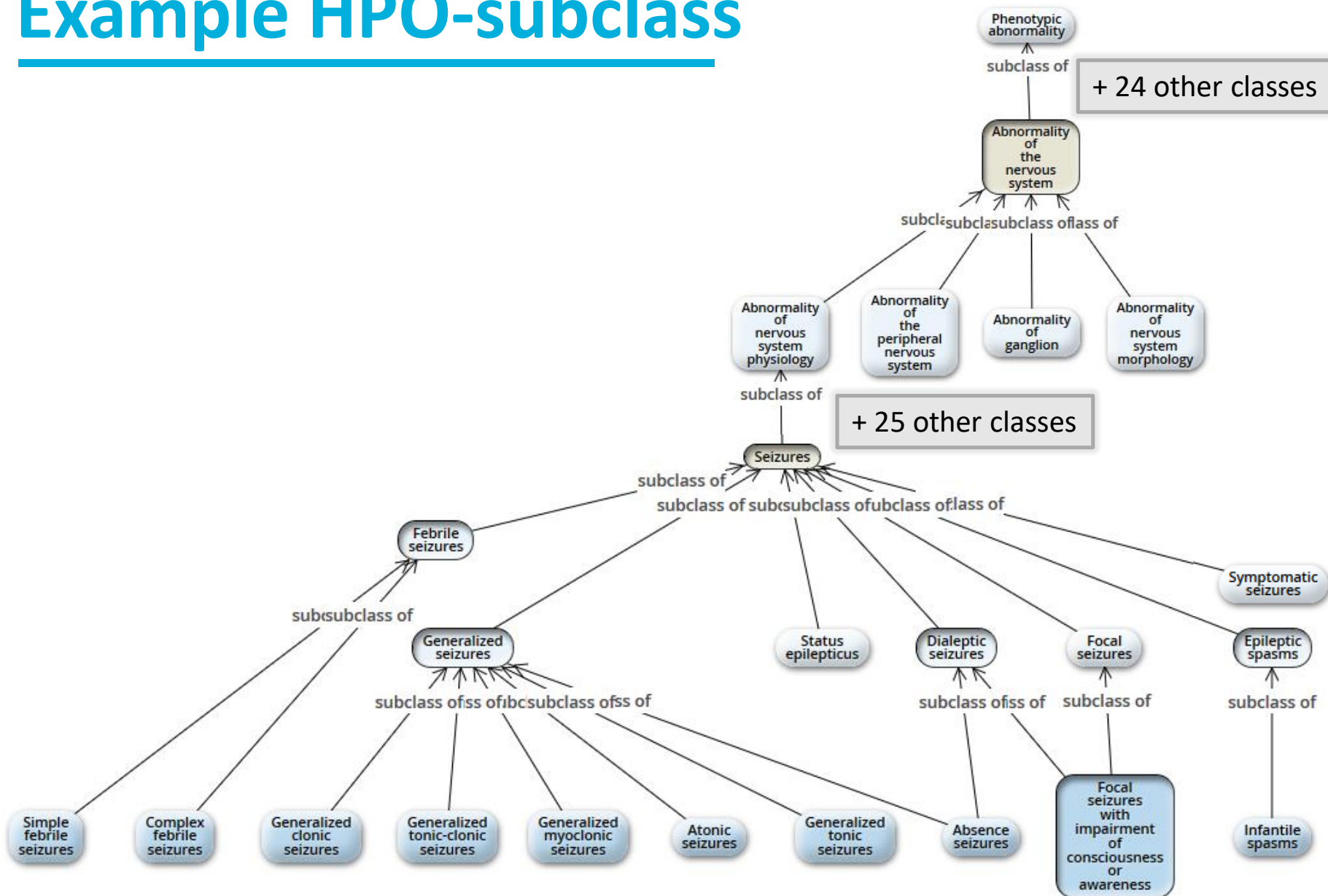
Phenotypic abnormality 13822



Abnormality of the skeletal system	3627
Abnormality of limbs	2740
Abnormality of the nervous system	1762
Abnormality of head or neck	1317
Abnormality of metabolism/homeostasis	1153
Abnormality of the cardiovascular system	1144
Abnormality of the eye	1112
Abnormality of the integument	902
Abnormality of the genitourinary system	900
Abnormality of the immune system	757
Abnormality of the digestive system	619

Neoplasm	602
Abnormality of the musculature	595
Abnormality of blood and blood-forming tissues	567
Abnormality of the endocrine system	404
Abnormality of the respiratory system	388
Abnormality of the ear	292
Abnormal cellular phenotype	224
Abnormality of connective tissue	203
Abnormality of prenatal development or birth	143
Growth abnormality	95
Constitutional symptom	79
Abnormality of the breast	31
Abnormality of the voice	28
Abnormality of the thoracic cavity	3

Example HPO-subclass



HPO-annotation disorders

Manual by HPO-team (mainly OMIM) example:

Infopage for disease entry

COFFIN-SIRIS SYNDROME 4

30 associated HPO classes

HPO id	HPO label
▶ HP:0000152	Abnormality of head or neck
▶ HP:0000707	Abnormality of the nervous system
▶ HP:0000924	Abnormality of the skeletal system
▶ HP:0001574	Abnormality of the integument
▶ HP:0003011	Abnormality of the musculature
▶ HP:0001507	Growth abnormality

Associated genes

[SMARCA4 \(6597\)](#)

HPO-annotation disorders

Manual & semi-automated (OMIM, Orphanet, DECIPHER) example:

Infopage for disease entry

Coffin-Siris syndrome

56 associated HPO classes

HPO id	HPO label
▶ HP:0000924	Abnormality of the skeletal system
▶ HP:0000152	Abnormality of head or neck
▶ HP:0000707	Abnormality of the nervous system
▶ HP:0001574	Abnormality of the integument
▶ HP:0040064	Abnormality of limbs
▶ HP:0000478	Abnormality of the eye

Associated genes

[ARID1B \(57492\)](#)
[ARID2 \(196528\)](#)
[SMARCB1 \(6598\)](#)
[SOX11 \(6664\)](#)
[SMARCE1 \(6605\)](#)
[ARID1A \(8289\)](#)
[SMARCA4 \(6597\)](#)

➔ difference in number of HPO associated with gene
OMIM: disease subtypes ➔ more specific; Orphanet: more inclusive

HPO-annotation of genes

- Gene annotation files:
 - Source: OMIM, Orphanet or All
 - Frequent (present >50% patients) or all frequencies
 - Most specific HPO or including all “ancestors”
- Gene \longleftrightarrow Disorder(s) \longleftrightarrow HPO-term(s)
 - SMARCA4 \rightarrow COFFIN-SIRIS SYNDROME 4 (OMIM) \rightarrow 30 most specific HPO terms
 - 1220 Genes \leftarrow 1382 Disorders (OMIM) \leftarrow Intellectual disability (incl. more specific “descendants” terms)

Summary part 1

- Importance of clinical information in genetic testing
- The HPO project provides a great computable resource for clinical features that characterize diseases and associated genes

Part 2: Applications using HPO

- Capturing patient clinical data in HPO format
- Using HPO-profiles in variant-disease interpretation
- Phenotype matching tools
- Outlook

Capturing phenotypic information



- (Electronic) Patient Dossier:
 - No standardised terminology
 - Unstructured text
 - At different locations
 - Limited access

Reden van verwijzing: verstandelijke beperking
Gaarne onderzoek voor [redacted] ivm mentale retardatie eci. M
Locatie: [redacted]

Aanwezig: [redacted] en beide ouders

Medische voorgeschiedenis

- aangeboren heupluxatie/dysplasie
- blindheid (hoge myopie)
- verstandelijke beperking
- refluxoesophagitis
- kyphose/scoliose

Anamnese

Hulpvraag: diagnose ook voor de andere kinderen

Graviditeit en partus: ongecompliceerd. Apgar 9/10.

Congenitale afwijkingen: heupluxatie/dysplasie

Neonatale periode: geen voedingsproblemen; bij drie maanden
veel oorontstekingen en ook na de tweede vaccinatie had zij een

Psychomotore ontwikkeling: de ontwikkeling is traag verlopen. [redacted]
herkent de dagelijkse patronen. Structuur is sowieso belangrijk

Overige tractusanamnese: ziet slecht. De visus is -13 dpt (via [redacted])
Psychosociaal: [redacted] woont bij haar ouders. Ze gaat naar de

Versleten linker heup. Obstipatie.

Capturing phenotypic information

(Electronic) Request form genome diagnostics Radboudumc

Muscle

- ☐ atrophy
- ☐ exercise intolerance
- ☐ muscle anomalies, please specify:
 - ☐ (electrically silent) cramps
 - ☐ muscle stiffness
 - ☐ myotonia
 - ☐ rippling
- ☐ muscular dystrophy
- ☐ ocular muscle weakness (ptosis, diplopia, eye movement disorder)
- ☐ facio-bulbar muscle weakness (swallowing feeding, dysarthria, facial myopathy)
- ☐ limb-girdle muscle weakness
- ☐ distal muscle weakness
- ☐ rhabdomyolysis
- ☐ hyperCK-emia
- ☐ cardiac symptoms (cardiomyopathy, arrhythmia)
- ☐ Respiratory symptoms:.....

Immune/blood

- ☐ auto-immune disorder
- ☐ immunodeficiency
- ☐ recurrent infections:
 - viral/bacterial/fungal
- ☐ anemia
- ☐ leucopenia
- ☐ thrombocytopenia
- ☐ splenomegaly

feeding difficulties

- ☐ failure to thrive
- ☐ diarrhea
- ☐ vomiting
- ☐ constipation
- ☐ hepatomegaly
- ☐ anal atresia/stenosis
- ☐ esophagus atresia/stenosis
- ☐ omphalocele

Other:

- ☒ MRI Portin
- ☐ - periventricular leukomalacia
- ☐ - leukocephaly - pachygyria
- ☐ - callosal agonesis
- ☐
- ☐
- ☐

Clinical relevant information

Feel free to fill out the blank field with all the clinical information you want to share. Or use the standard checkboxes below.

Cancer

Digestive tract and liver

Ear

Eye

☐ retinal dystrophy

☐ congenital stationary night blindness

☐ anophthalmia

☐ coloboma

☐ ptosis

☐ achromatopsia

☐ cataract

☐ microphthalmia

☐ hypertelorism

☐ nystagmus

Clinical Registry tool using HPO



Open source software: phenotype/genotype collection tool

- Intuitive interface for HPO phenotyping
- HPO suggestions for Differential Diagnosis / Deep phenotyping
- HPO-mining of clinical notes by concept recognition algorithms
- Suggestions on matching OMIM disorders
- Operational at CARE for RARE (Canada), Sanford Health (USA)

- Commercial support by





Quick phenotype search:

[hide suggestions](#)

BROWSE

▶ GROWTH

▶ CRANIOFACIAL

▶ EYES

▶ EARS

▶ CUTANEOUS

▶ CARDIOVASCULAR

▶ RESPIRATORY

▶ MUSCULOSKELETAL

▶ GASTROINTESTINAL

▶ GENITOURINARY

▶ BEHAVIOUR

▶ NEUROLOGICAL

☐ Y ☐ N Short stature ⓘ

☐ Y ☐ N Disproportionate short-limb short stature ⓘ

(also known as: Short stature, disproportionate short limb)

☐ Y ☐ N Disproportionate short stature ⓘ

(also known as: Short stature, disproportionate)

☐ Y ☐ N Mesomelic short stature ⓘ

(also known as: Short stature, disproportionate mesomelic)

☐ Y ☐ N Severe short stature ⓘ

(also known as: Short stature, severe)

☐ Y ☐ N Mild short stature ⓘ

(also known as: short stature, mild)

☐ Y ☐ N Moderately short stature ⓘ

(also known as: Moderate short stature)

☐ Y ☐ N Proportionate short stature ⓘ

(also known as: Short stature, proportionate)

☐ Y ☐ N Rhizomelia ⓘ

(also known as: Short stature, rhizomelic)

☐ Y ☐ N Asymmetric short stature ⓘ

[hide suggestions](#)


CURRENT SELECTION

How informative is your phenotypic description:



GROWTH PARAMETERS

Short stature

HPO-mining of clinical notes

SUGGESTIONS FROM CLINICAL NOTES

☐ Y ☐ N **High forehead** ⓘ ✕

...Affected male relatives show characteristic facies, including **high forehead**, midface hypoplasia, large mouth with long upper middle incisors, thick lips, high-arched palate, large jaw with prominent chin, and large, poorly formed ears....

☐ Y ☐ N **Incisor macrodontia** ⓘ ✕

...Affected male relatives show characteristic facies, including high forehead, midface hypoplasia, **large mouth with long upper middle incisors**, thick lips, high-arched palate, large jaw with prominent chin, and large, poorly formed ears....

☐ Y ☐ N **Midface retrusion** ⓘ ✕

...Affected male relatives show characteristic facies, including high forehead, **midface hypoplasia**, large mouth with long upper middle incisors, thick lips, high-arched palate, large jaw with prominent chin, and large, poorly formed ears....

☐ Y ☐ N **Wide mouth** ⓘ ✕

...Affected male relatives show characteristic facies, including high forehead, midface hypoplasia, **large mouth** with long upper middle incisors, thick lips, high-arched palate, large jaw with prominent chin, and large, poorly formed ears....

1 to 4 of 12 suggestions

CURRENT SELECTION

How informative is your phenotypic description:



GROWTH PARAMETERS

Short stature

DELETE

ADD DETAILS

How informative is your phenotypic description:



[What's this?](#)

GROWTH PARAMETERS

Short stature [DELETE](#) [ADD DETAILS](#)

CRANIOFACIAL

Coarse facial features [DELETE](#) [ADD DETAILS](#)

Long eyelashes [DELETE](#) [ADD DETAILS](#)

Sparse scalp hair [DELETE](#) [ADD DETAILS](#)

EYE DEFECTS

Visual impairment [DELETE](#) [EDIT DETAILS](#) [CLEAR DETAILS](#)

No additional information.

EAR DEFECTS

Hearing impairment [DELETE](#) [ADD DETAILS](#)

CARDIOVASCULAR

Malformation of the heart and great vessels [DELETE](#)

[ADD DETAILS](#)

MUSCULOSKELETAL

Aplasia/Hypoplasia of the distal phalanges of the hand

[DELETE](#) [ADD DETAILS](#)

YOU MAY WANT TO INVESTIGATE...

Phenotypes that are likely to help improve differential diagnosis

- ☐ Y ☐ N Partial agenesis of the corpus callosum [i](#)
- ☐ Y ☐ N Facial hypertrichosis [i](#)
- ☐ Y ☐ N Intussusception [i](#)
- ☐ Y ☐ N Gastric ulcer [i](#)
- ☐ Y ☐ N Aplasia/Hypoplasia of the patella [i](#)
- ☐ Y ☐ N Hypoplastic fifth fingernail [i](#)



How informative is your phenotypic description:



[What's this?](#)

CUTANEOUS

Hypoplastic fifth fingernail [DELETE](#) [ADD DETAILS](#)

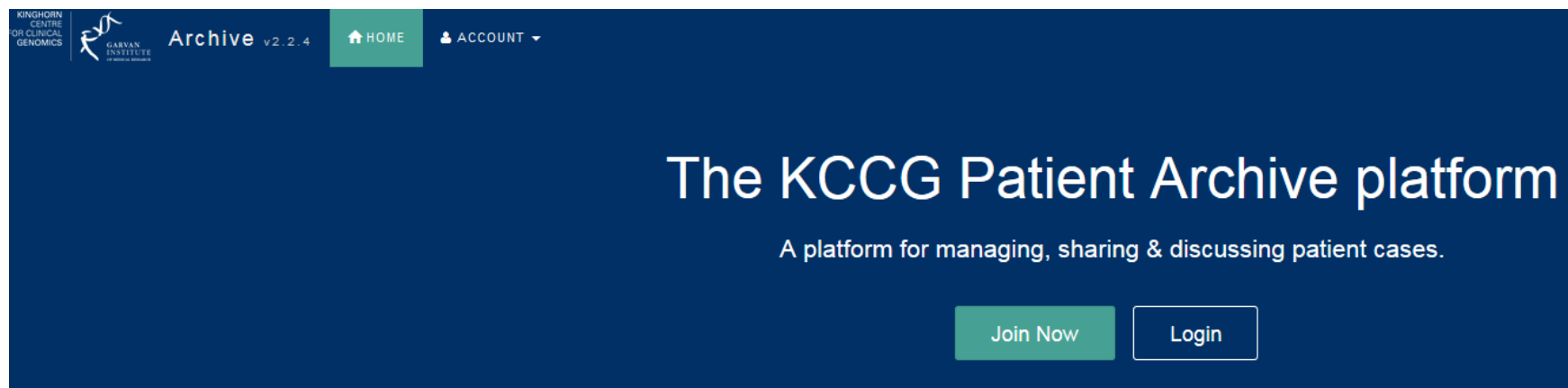
Facial hypertrichosis [DELETE](#) [ADD DETAILS](#)

CARDIOVASCULAR

Malformation of the heart and great vessels [DELETE](#)

[ADD DETAILS](#)

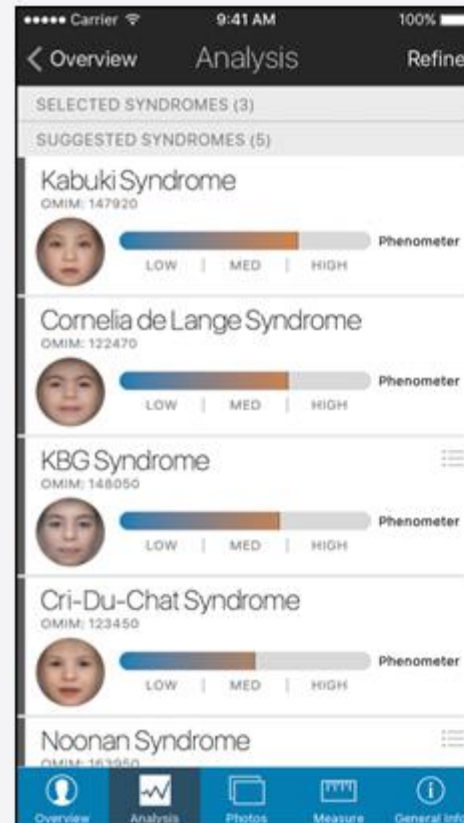
Clinical Registry using HPO



- Patient Archive (HPO-centric patient phenotyping)
 - Intuitive interface for HPO phenotyping
 - HPO-mining of clinical notes by concept recognition algorithms
 - Operational at
 - UDP, The University of Western Australia (UWA)
 - IRUD, Japan

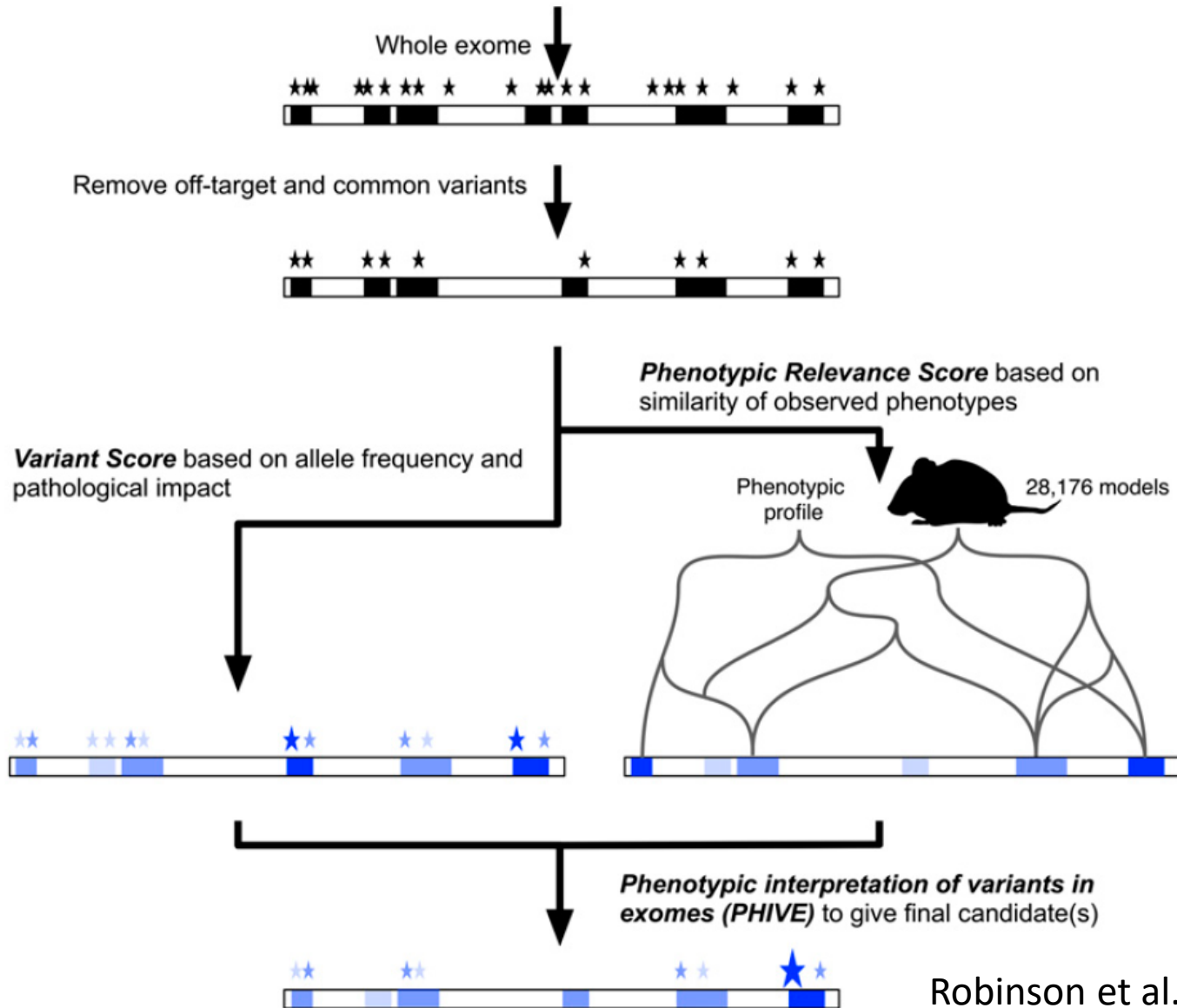
HPO in Facial Phenotyping

Create a case by uploading an image or photographing your patient.

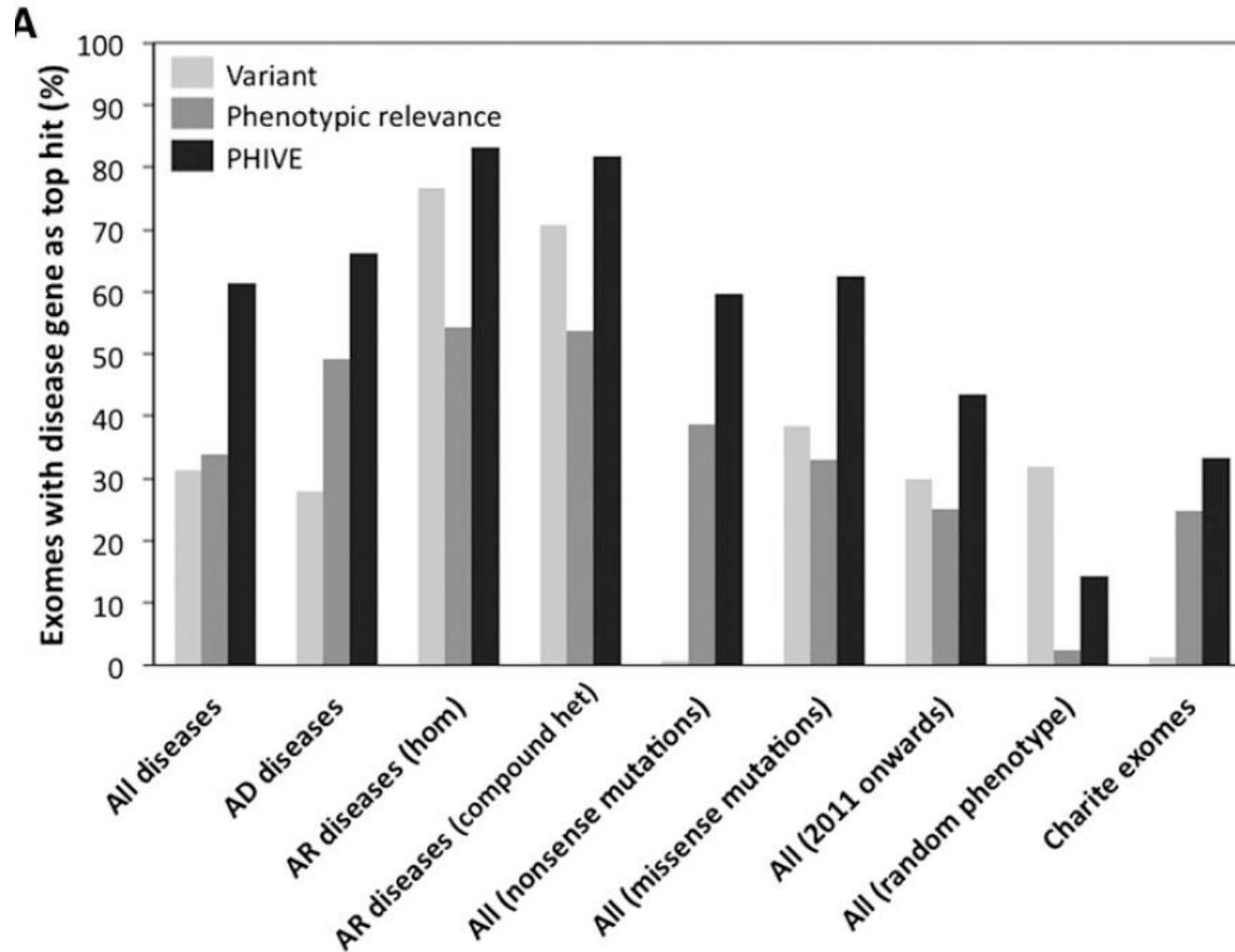


Review a prioritized list of suggested syndromes.

Phenotypic interpretation of variants

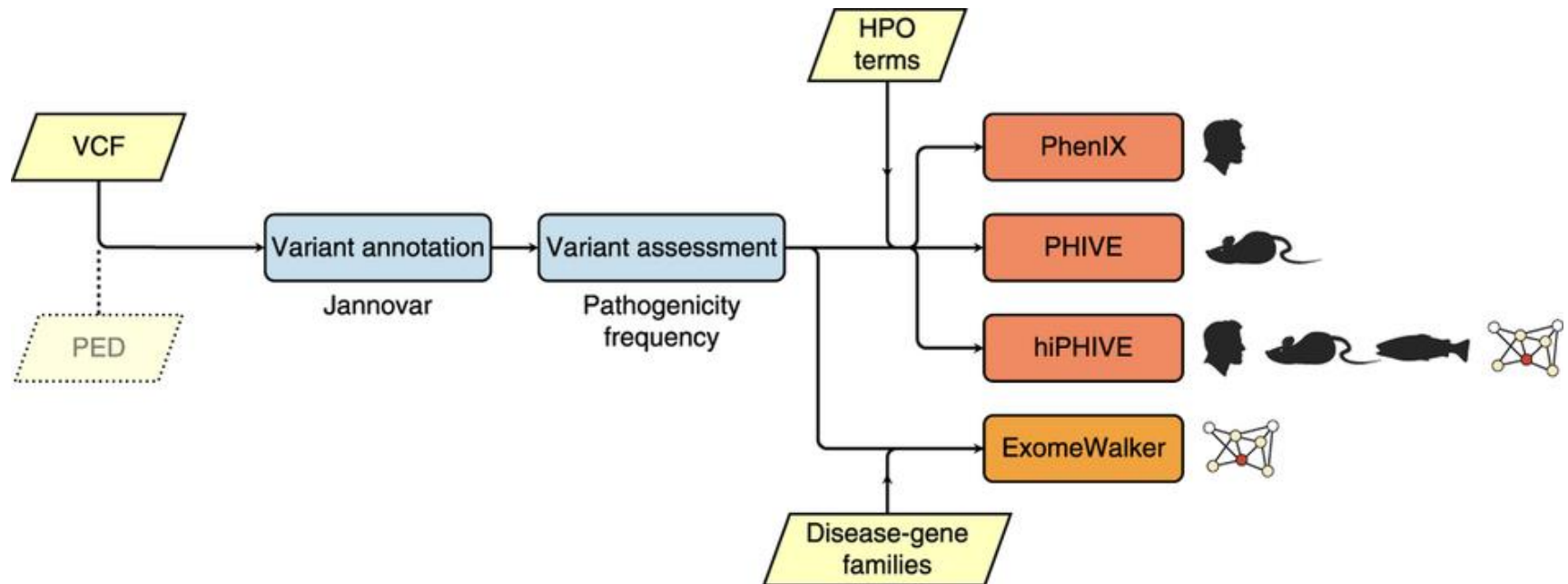


Phenotypic interpretation of variants



Exomiser

Automated phenotypic interpretation of variants in Exomes



Smedley et al., Nat Prot. 2014

Exomiser

Benchmarking of Exomiser on simulated exomes with HGMD* variants

		1000 Genomes and ESP frequency data		
		Unknown inheritance ^a	Autosomal dominant ^b	Autosomal recessive ^c
Known	Full phenotype	96.8	97.1	97.1
	Imperfect phenotype	94.0	94.3	96.0
Novel	Full phenotype	73.6	78.8	86.6
	Imperfect phenotype	61.4	68.1	78.8

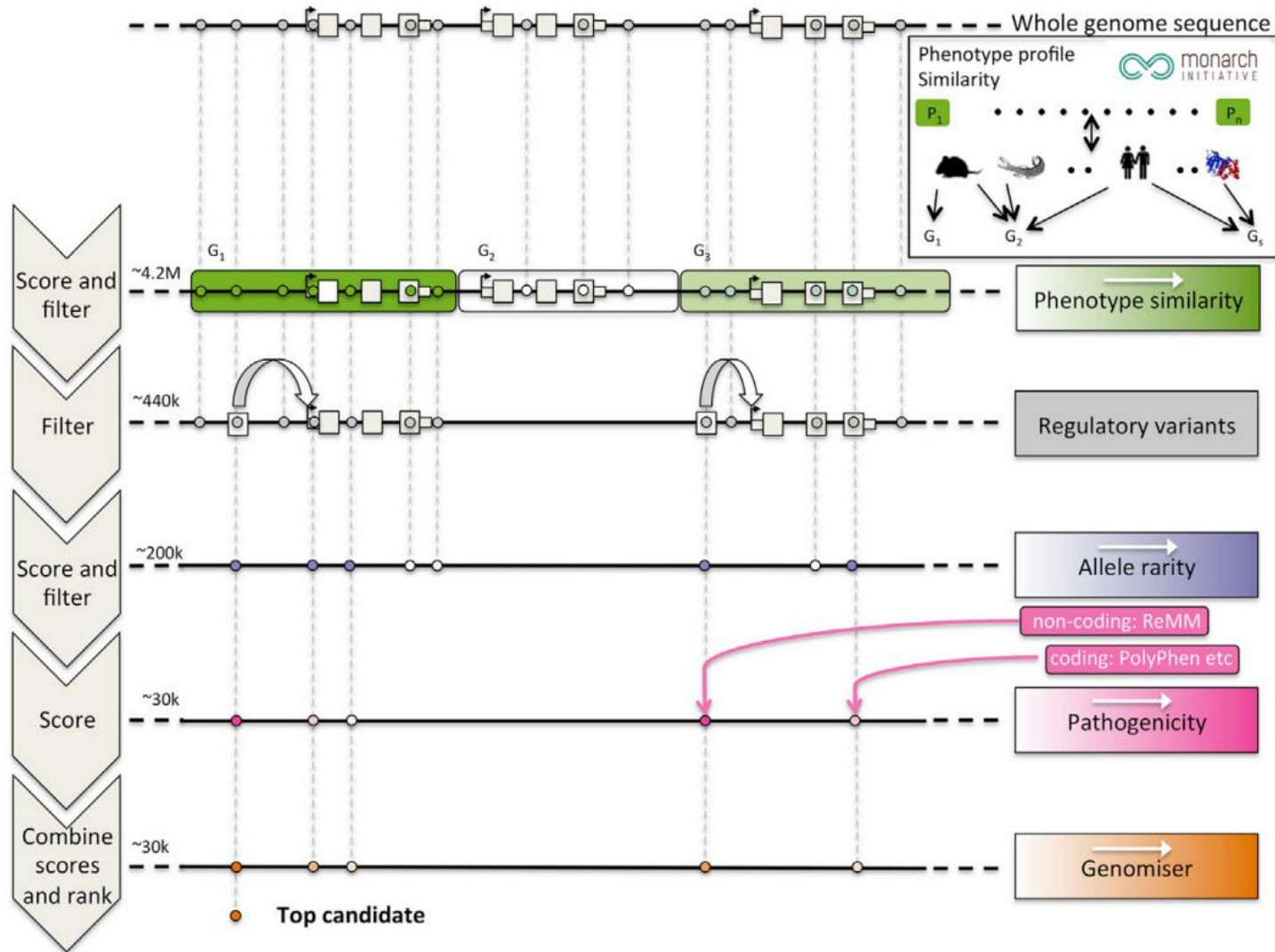
% of exomes with top-ranked variant

*HGMD: Human Gene Mutation Database

ESP: US Exome Sequencing Project collaboration

Bone et al., Genet Med 2015

Genomiser: also non-coding



<https://hpo.jax.org/app/tools/genomiser>

HPO driven variant interpretation

Integrated in commercial software:

- FDNA: Face2Gene.
- Cartagenia BENCH
- GEPADO – Software Solutions for Genetics – GmbH
- BioDiscovery's NxClinical
- Diploid: Diagnosing rare diseases: Moon
- Centogene
- SimulConsult
- Fabric Genomics
- Qiagen
- Congenica

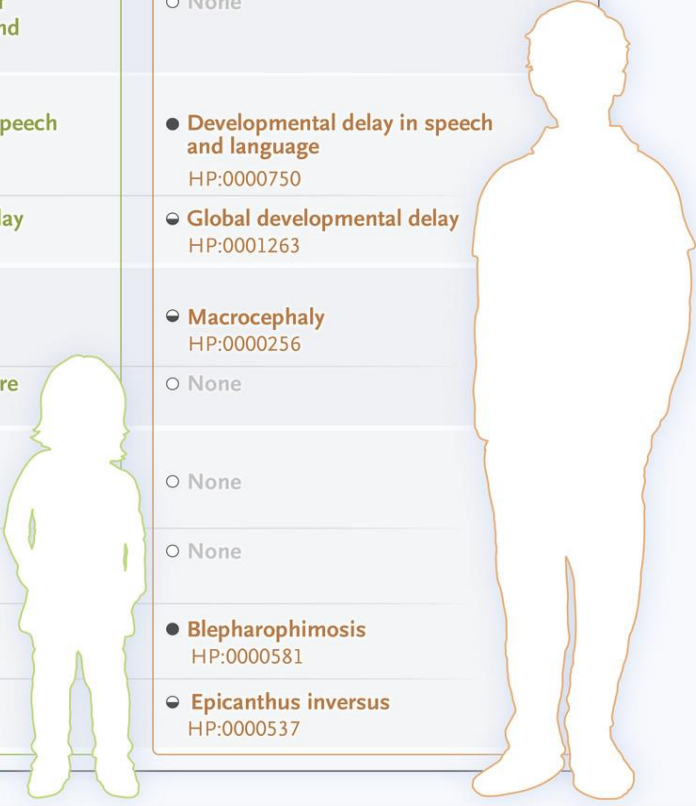
Phenotype matching tools

Matching of unrelated cases for rare disorders worldwide

- Disease gene identification
- Disease prognosis

“Fuzzy” Matching of Phenotypic Profiles.

Wiedemann–Steiner Syndrome Profile	Patient 1 Profile (3-year-old girl)	Patient 2 Profile (14-year-old boy)
DIGITS		
Short toe HP:0001831	<input type="radio"/> None	<input checked="" type="radio"/> Long toe HP:0010511
Short middle phalanx of finger HP:0005819	<input checked="" type="radio"/> Cone-shaped epiphysis of the phalanges of the hand HP:0010230	<input type="radio"/> None
DEVELOPMENT		
Developmental delay in speech and language HP:0000750	<input checked="" type="radio"/> Developmental delay in speech and language HP:0000750	<input checked="" type="radio"/> Developmental delay in speech and language HP:0000750
Intellectual disability HP:0001249	<input checked="" type="radio"/> Global developmental delay HP:0001263	<input checked="" type="radio"/> Global developmental delay HP:0001263
SKELETAL		
Microcephaly HP:0000252	<input checked="" type="radio"/> Microcephaly HP:0000252	<input checked="" type="radio"/> Macrocephaly HP:0000256
Short stature HP:0004322	<input checked="" type="radio"/> Proportionate short stature HP:0003508	<input type="radio"/> None
FACIAL		
Thin upper lip HP:0000219	<input checked="" type="radio"/> Thick upper lip HP:0000215	<input type="radio"/> None
Hypertelorism HP:0000316	<input checked="" type="radio"/> Hypertelorism HP:0000316	<input type="radio"/> None
Blepharophimosis HP:0000581	<input type="radio"/> None	<input checked="" type="radio"/> Blepharophimosis HP:0000581
Epicanthus HP:0000286	<input type="radio"/> None	<input checked="" type="radio"/> Epicanthus inversus HP:0000537



SIGN UP

LOGIN

- PhenomeCentral (phenotype/genotype matching)
 - HPO-based semantic similarity patient phenotypes
 - Genotypic & phenotypic matching of cases
 - Matching with casus from connected databases (Matchmaker Exchange)

enter patient data → see similar patients → start a collaboration

A Quick phenotype search:

Enter keywords and choose from the suggested ontology terms.

B Clinical symptoms and physical findings

GROWTH PARAMETERS

Head circumference for age
Microcephaly (<-3SD)

CRANIOFACIAL

Wide nasal bridge

EYE DEFECTS

Hypertelorism
NO Abnormal eye morphology

EAR DEFECTS

Hearing impairment

CARDIOVASCULAR

Ventricular septal defect

NEUROLOGICAL

Focal seizures

C LIST OF CANDIDATE GENES

#	GENE
1	GENECARDS: NOTCH2 OMIM: 600275 ENTREZ: 4853

D

Case ID	Diagnosis	Contact	Relevance
Undisclosed identifier	Undisclosed diagnosis	Undisclosed owner. Initiate anonymous contact	29%
Undisclosed identifier	Undisclosed diagnosis	Undisclosed owner. Initiate anonymous contact	24%
Undisclosed identifier	Undisclosed diagnosis	Undisclosed owner. Initiate anonymous contact	15%
Undisclosed identifier	Undisclosed diagnosis	Undisclosed owner. Initiate anonymous contact	14%
Undisclosed identifier	Undisclosed diagnosis	Undisclosed owner. Initiate anonymous contact	14%

E PHENOTYPIC FEATURES BREAKDOWN

Feature	Current Patient (P0001152)	Matched Patient
ABNORMALITY OF THE VENTRICULAR SEPTUM	presented with: Ventricular septal defect	1 undisclosed feature
ABNORMALITY OF SKULL SIZE	presented with: Microcephaly	2 undisclosed features
ABNORMALITY OF THE NERVOUS SYSTEM	presented with: Focal seizures	2 undisclosed features

F GENE MATCHING BREAKDOWN

Variant	ESTIMATED HARMFULNESS	Variant	ESTIMATED HARMFULNESS
chr1: 120611964 - 120611964	100%	Undisclosed position	97%
G → C (MISSENSE)		Undisclosed position	68%
chr1: 120672572 - 120672572	97%		
C → T (MISSENSE)			

G Contact a non-public case owner

1 Configure your message

SUBJECT: Interested in one of your non-public cases

Information about you:

☐ DISCLOSE YOUR NAME

☐ DISCLOSE YOUR EMAIL

☐ DISCLOSE YOUR MEMBERSHIP TO PHENOMECENTRAL GROUPS

Information about your case (P0001296):

☐ INCLUDE DIAGNOSIS INFORMATION

☐ INCLUDE A PHENOTYPE SUMMARY

Your requests:

☐ REQUEST MUTUAL VIEW ACCESS TO THE TWO SIMILAR CASES

If the recipient accepts, they gain view access to your case and you gain view access to theirs.

☐ REQUEST CONTACT INFORMATION

OTHER INFORMATION TO INCLUDE IN YOUR MESSAGE

2 Preview your message

This is the message the other user will receive:

SUBJECT: [PhenomeCentral] Interested in one of your non-public cases

MESSAGE: Hello <undisclosed recipient name>, A PhenomeCentral user is interested in one of your non-public cases: <undisclosed case identifier>. Please see their message below.

PhenomeCentral has identified significant similarities between one of your cases and one of mine.

I would like to grant you the rights to view my case and to obtain view access to your case, and to learn your contact information in order to further discuss these abnormalities with you.

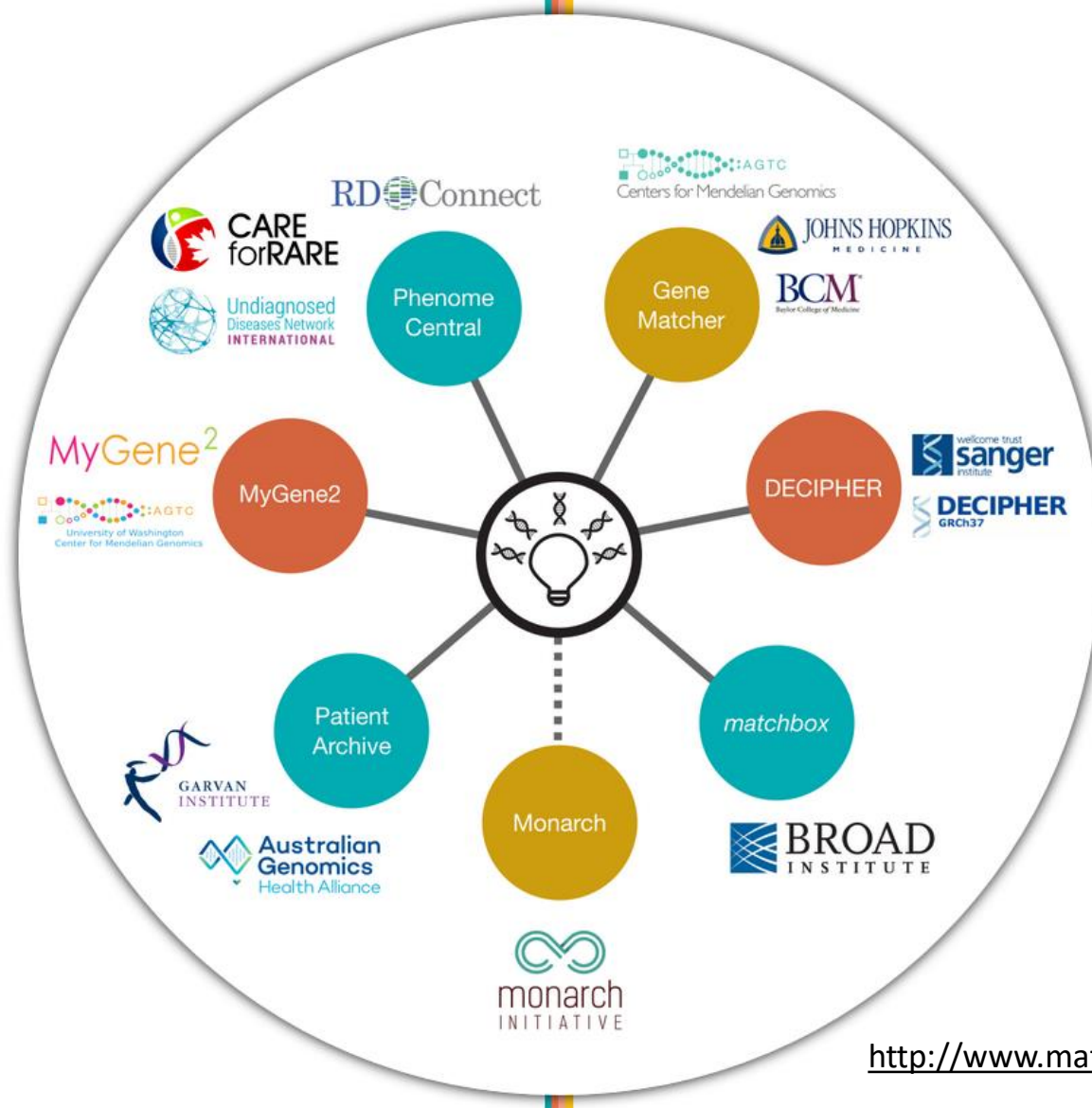
To accept view privileges from this user and to grant them view access to <undisclosed case identifier>, follow this link: <undisclosed URL>.

Best wishes,
The PhenomeCentral team

SEND CANCEL

Clinical Pheno/Genotype Matching

Matchmaker Exchange | Connected Nodes



<http://www.matchmakerexchange.org/>

Summary

Conclusion:

Structured phenotype data of patients and model organisms improves the diagnostic efficiency and prioritization of exome variants associated with known and new disorders

Critical points:

- HPO-annotation updates for disorders/genes
- completeness of coverage phenotypes by HPO-terms
- HPO-translation to other languages for use in hospital patient registries

Outlook

Integration of HPO in hospital clinical registry / diagnostic applications

HPO integrated in genome diagnostics

- HPO-based gene panels
- HPO-based genetic test selection
- HPO-based prioritization of exomic/genomic variants

HPO in genome research

- HPO-based candidate disease gene prioritization
- Cohort selection

Questions?



"My PARENTS DIED. THEIR PARENTS DIED. THEIR PARENTS DIED...
IT RUNS IN THE FAMILY."

References

HPO project/browser/tools: <https://hpo.jax.org/app/>

HPO 2018 paper: <https://www.ncbi.nlm.nih.gov/pubmed/30476213>

HPO-browser (old): <http://compbio.charite.de/hpoweb/showterm?id=HP:0000118>

Contribute to HPO annotation:

- <https://phenotate.org/>
- <https://hpo.jax.org/app/tools/workbench>

Phenotype data integration: <https://monarchinitiative.org/>