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Detailed Clinical Phenotyping in Precision Medicine

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Acknowledgments

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Aims

To confer basic knowledge of the description of physical characteristics of patients

To describe the current state of systems for defining, categorizing and capture of these characteristics

To explain the problems faced when implementing a clinically usable data capture system and to provide a working

Introduction

Which data of phenotyping to rely on?

How to capture and store clinical data?

How to enable contextual assignments, categorization and analytic evaluation of the data

How to use the data to answer clinically decisive questions for achieving optimal outcomes?

What is a phenotype? – Peter Robinson, Charité, Berlin

- At least five definitions of phenotype in use in the biology literature
- The collection of observable traits of an organism, comprising its morphology, its physiology at the level of the cell, the organ, and the body, and its behaviour, comprising even characteristics such as the gene expression profiles in response to environmental cues

Robinson P Human Mutation 2012;33:778

Phenotype for purely clinical purposes

- Collection of traits elicited from the health history and physical findings of a given patient

Precision medicine

- Using the comprehensive phenotype and all available, validated medical knowledge to tailor patient care with the aim of achieving an optimal outcome

Systems for Clinical Phenotyping

Clinical data from diagnostic classification systems of diseases

Standardized nomenclature systems

- SNOMED
- ICD (International Classification of Diseases)
- ICF (International Classification of Functioning)

DECIPHER (Database of genomic variation and Phenotype in Humans using Ensembl Resources)

Human Phenotype Ontology (HPO)

Background

Many patients suffering from Rare Disease harbour genomic variants (sequence variants or copy number variants) that by disrupting normal gene expression lead to disease. However, many variants are novel or extremely rare, making clinical interpretation problematic and genotype-phenotype correlations uncertain. Identification of patients sharing variants in a given gene and having phenotypic features in common leads to greater certainty in the pathogenic nature of the gene and enables to the role of novel genes in development and disease to be defined. Furthermore, analysis of the type of genomic variant and of its consequence (eg. Loss of function or gain of function) enables insight into the mechanism of disease and potential therapeutic targets.

DECIPHER Project Proposal 

DECIPHER

DECIPHER (Database of genomic Variation and Phenotype in Humans using Ensembl Resources) is an interactive web-based database which incorporates a suite of tools designed to aid the interpretation of genomic variants.

DECIPHER enhances clinical diagnosis by retrieving information from a variety of bioinformatics resources relevant to the variant found in the patient. The patient's variant is displayed in the context of both normal variation and pathogenic variation reported at that locus thereby facilitating interpretation.

The DECIPHER Community

Contributing to the DECIPHER database is an international community of academic departments of clinical genetics and rare disease genomics now numbering more than 270 centres and having uploaded more than 36,000 cases. Each contributing centre has a nominated rare disease clinician or clinical geneticist who is responsible for overseeing data entry and membership for their centre. DECIPHER enables a flexible approach to data-sharing. Each centre maintains control of its own patient data (which are password protected within the centre's own DECIPHER project) until consent is given to share the data with chosen parties in a collaborative group or to allow anonymous genomic and phenotypic data to become freely viewable within Ensembl and other genome browsers (see below). Once data are shared, consortium members are able to gain access to the patient report and contact each other to discuss patients of mutual interest.

Public Data Access

With patient consent, positional genomic information together with a brief description of the associated phenotype becomes viewable without password protection, for example, via the DECIPHER track in Ensembl. This is of benefit not only to clinicians advising patients with similar findings but also to researchers working on specific phenotypes, Rare Diseases, drug targets or the role of genes in health and development.

DECIPHER (**D**atabas**E** of genom**iC** variat**i**on and **P**henotype in **H**umans using **E**nsembl**R**esources)


- Interactive web-based database which incorporates a suite of tools designed to aid the interpretation of genomic variants
- **DECIPHER enhances clinical diagnosis by retrieving information from a variety of bioinformatics resources relevant to the variant found in the patient**
- Patient's variant displayed in the context of both normal variation and pathogenic variation reported at that locus, thereby facilitating interpretation



(a)


Patient 4 Mother 0 Father 0 Add...



Patient phenotypes


Show simple term list



Abnormality of the eye 

Hypertelorism  


Abnormality of head or neck 



Depressed nasal bridge  

Abnormality of the musculoskeletal system 

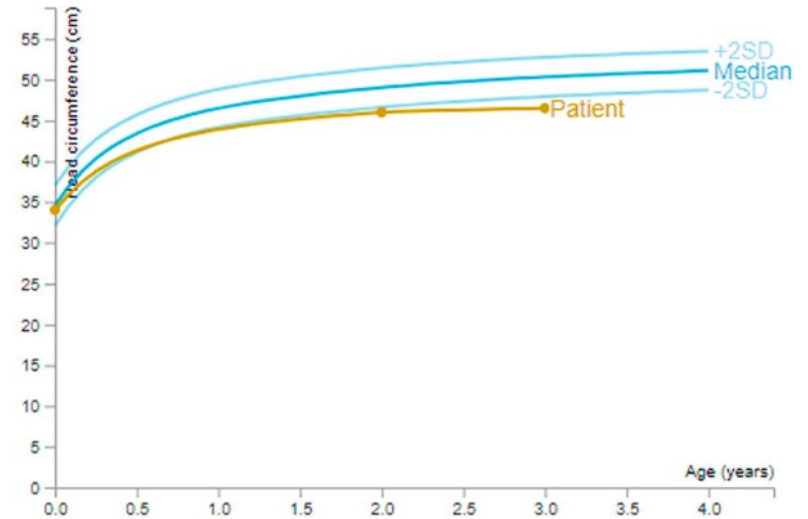
Microcephaly  

- Progressive

Abnormality of the nervous system 

Global developmental delay  

(b)



(a) DECIPHER enables the deposition of phenotypes using HPO terms. (b) DECIPHER supports the deposition of developmental milestones and anthropometric measurements, for example, occipitofrontal (head) circumference

Phenotypic abnormality in open-access patients in DECIPHER

Hide redundant paths

Simple view

About



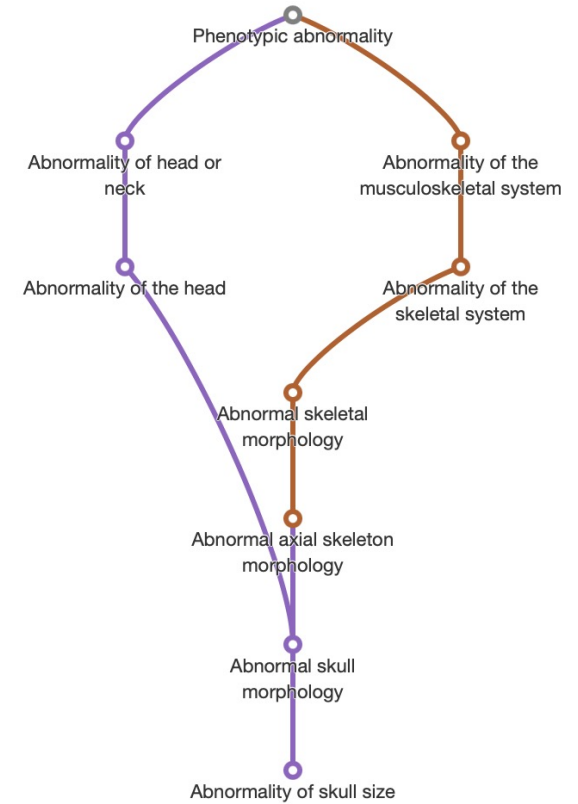
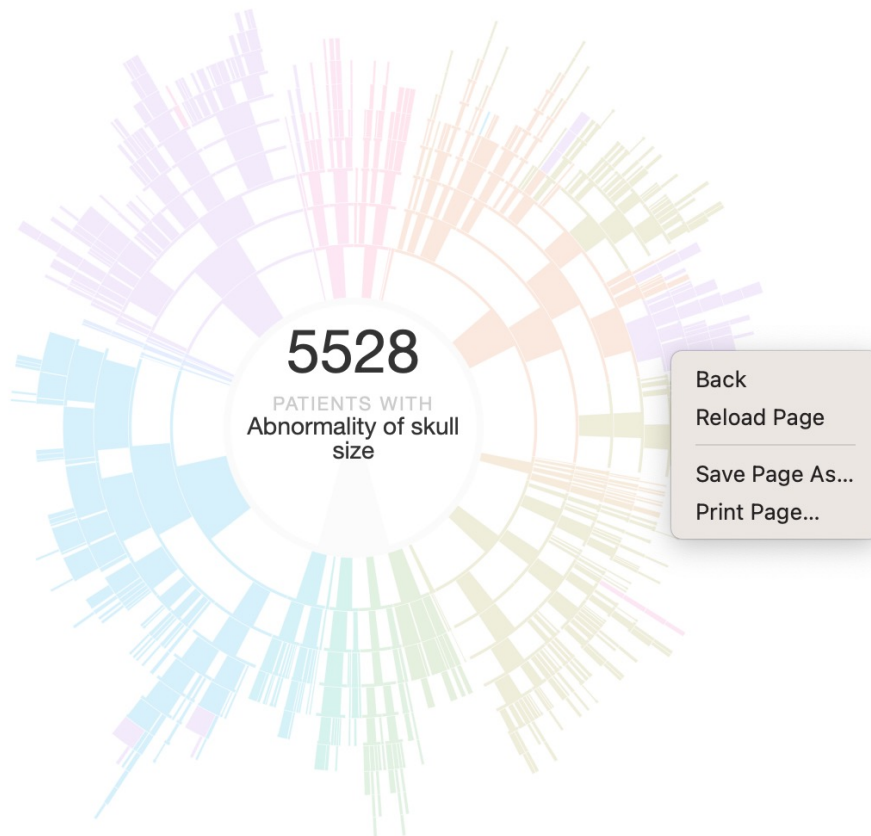
- Abnormality of the cardiovascular system
- Abnormality of blood and blood-forming tissues
- Abnormality of the endocrine system
- Abnormality of the musculoskeletal system
- Abnormality of the digestive system
- Abnormality of limbs
- Abnormality of prenatal development or birth
- Growth abnormality
- Abnormality of the genitourinary system
- Abnormality of the ear
- Abnormality of metabolism/homeostasis
- Abnormal cellular phenotype
- Abnormality of the eye
- Abnormality of the nervous system
- Neoplasm
- Constitutional symptom
- Abnormality of the immune system
- Abnormality of the voice
- Abnormality of the respiratory system
- Abnormality of head or neck
- Abnormality of the breast
- Abnormality of the integument

Phenotypic abnormality in open-access patients in DECIPHER

Hide redundant paths

Simple view

About



Patients **1417**
CNV syndromes **1**
DDD research variants **0**
Genes **0**

Results
Browser

Patients: 11 to 20 of 1417

Filter...

DECIPHER Patient ID	Sex	Phenotype(s)	Variants	Contact
1375	46XY	Accessory oral frenulum, Alveolar ridge overgrowth, Delayed cranial suture closure, Diastasis recti, Feeding difficulties in infancy, Frontal bossing, Generalized hirsutism, High palate, Hoarse voice, Hyperactivity, Hypotonia, Intellectual disability, Low-set ears, Midface retrusion, Pes planus, Recurrent infections, Ridged cranial sutures, Strabismus	1	
1593	46XX	Abnormal heart morphology, Abnormal pinna morphology, Abnormality of the tarsal bones, Abnormality of the upper respiratory tract, Blepharophimosis, Blue sclerae, Feeding difficulties in infancy, Hypertelorism, Hypotonia, Intellectual disability, Microcephaly, Micrognathia, Patent ductus arteriosus, Recurrent infections, Seizure, Short stature, Single transverse palmar crease, Sleep disturbance, Wide nasal bridge	4	
1721	Other	Atopic dermatitis, Ichthyosis	3	
1925	46XY	Abnormal pinna morphology, Dolichocephaly, Exaggerated cupid's bow, Hypermetropia, Intellectual disability, Posteriorly rotated ears, Recurrent infections	1	
1993	Other	Cleft of alveolar ridge of maxilla, Constipation, Hypoglycemia, Lipodystrophy, Recurrent infections, Small nail, Sparse hair	2	
1995	Other	Abnormal hair pattern, Abnormality of the forehead, Arachnodactyly, Constipation, Multiple renal cysts, Recurrent infections, Tapered finger	3	
2068	46XX	Atopic dermatitis, Clinodactyly of the 5th finger, Delayed speech and language development, Fine hair, Intellectual disability, Microcephaly, Prominent nose, Short hallux, Short nail, Short palm, Short thumb, Tetralogy of Fallot, Tooth malposition	3	
2069	46XX	Atopic dermatitis, Autism, Behavioral abnormality, Bilateral tonic-clonic seizure, Brachycephaly, Constipation, Delayed speech and language development, Echolalia, Hypertelorism, Intellectual disability, Low anterior hairline, Strabismus, Widely spaced teeth	1	
2126	46XX	Abnormality of the periorbital region, Ataxia, Constipation, Delayed speech and language development, Intellectual disability, Microcephaly, Recurrent infections, Recurrent urinary tract infections, Short stature, Stridor	2	
2154	46XX	Abnormal dental enamel morphology, Atopic dermatitis, Bulbous nose, Congenital diaphragmatic hernia, Feeding difficulties in infancy, Hypermetropia, Hypotonia, Intellectual disability, Macrotia, Microcephaly, Scoliosis, Small for gestational age, Thin upper lip vermilion	1	

10



All

Search for phenotypes, diseases or genes...

e.g. [Arachnodactyly](#) | [Marfan syndrome](#) | [FBN1](#)

The Human Phenotype Ontology

The Human Phenotype Ontology (HPO) provides a standardized vocabulary of phenotypic abnormalities encountered in human disease. Each term in the HPO describes a phenotypic abnormality, such as [Atrial septal defect](#). The HPO is currently being developed using the medical literature, Orphanet, DECIPHER, and OMIM. HPO currently contains over 13,000 terms and over 156,000 annotations to hereditary diseases. The HPO project and others have developed software for phenotype-driven differential diagnostics, genomic diagnostics, and translational research. The HPO is a flagship product of the [Monarch Initiative](#), an NIH-supported international consortium dedicated to semantic integration of biomedical and model organism data with the ultimate goal of improving biomedical research. The HPO, as a part of the Monarch Initiative, is a central component of one of the [13 driver projects](#) in the [Global Alliance for Genomics and Health \(GA4GH\) strategic roadmap](#).

[Learn More About HPO](#)

Exomiser

Evaluate variants based on the predicted pathogenicity.

Genomiser

Analyze genome sequence data for non-coding variants.

Phenomizer

Rank disease differential diagnosis by clinical features.

Profile Search

Discover diseases with a phenotype profile.

News & Updates

[April 2023 HPO release & updates](#)

April 6, 2023

[June 2022 HPO release](#)

June 12, 2022

[HPOA release](#)

April 15, 2022

[View All News](#)

Phenopackets

A Global Alliance for Genomics and Health (GA4GH) international standard for phenotypic data exchange.

Human phenotype ontology

Standardized vocabulary of phenotypic abnormalities in human disease

In development using

- Medical literature
- Orphanet (<https://www.orpha.net/consor/cgi-bin/index.php>)
- DECIPHER (<https://www.deciphergenomics.org>)
- OMIM (Online Mendelian Inheritance in Man; <https://www.omim.org>)

HPO currently contains over 13,000 terms and over 156,000 annotations to hereditary diseases



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Phenopackets

A Global Alliance for Genomics and Health (GA4GH) international standard for phenotypic data exchange.

Phenomizer

April 2023

- 11'442 features
- 8'057 diseases

Features. Diseases. Ontology.

Patient's Features.

Enter feature...

HPO.	Feature. ▲	Modifier.	Num diseases.
------	------------	-----------	---------------

HPO id.	
HP:0010704	
HP:0005767	
HP:0010711	
HP:0010706	
HP:0001459	
HP:0010707	
HP:0010712	
HP:0006088	
HP:0010708	
HP:0010713	
HP:0030300	
HP:0000878	
HP:0030306	11 thoracic vertebrae
HP:0001233	2-3 finger syndactyly
HP:0005709	2-3 toe cutaneous syndactyly
HP:0004691	2-3 toe syndactyly
HP:0010709	2-4 finger syndactyly
HP:0005768	2-4 toe cutaneous syndactyly
HP:0010714	2-4 toe syndactyly
HP:0010692	2-5 finger syndactyly
HP:0010715	2-5 toe syndactyly
HP:0008083	2nd-5th toe middle phalangeal hypoplasia
HP:0011939	3-4 finger cutaneous syndactyly
HP:0006097	3-4 finger syndactyly
HP:0009779	3-4 toe syndactyly
HP:0010710	3-5 finger syndactyly
HP:0010716	3-5 toe syndactyly

Info

- The Phenomizer is developed and maintained by [Sebastian Köhler](#) (see [group website](#) for more info).
- The [Phenomizer Orphanet](#) uses the latest Orphanet date and a different algorithm for ranking the differential diagnoses.

Please cite the following papers when you use this tool/HPO in your publications.

[Köhler et al., Clinical diagnostics in human genetics with semantic similarity searches in ontologies.](#)
Am J Hum Genet (2009) vol. 85 (4) pp. 457-64

[Köhler et al., The Human Phenotype Ontology in 2017.](#)
Nucleic Acids Research (2017) doi: <https://doi.org/10.1093/nar/gkw1039>

Features. Diseases. Ontology.

Enter feature...

HPO id.	Feature.
HP:0010704	1-2 finger syndactyly
HP:0005767	1-2 toe complete cutaneous syndactyly
HP:0010711	1-2 toe syndactyly
HP:0010706	1-3 finger syndactyly
HP:0001459	1-3 toe syndactyly
HP:0010707	1-4 finger syndactyly
HP:0010712	1-4 toe syndactyly
HP:0006088	1-5 finger complete cutaneous syndactyly
HP:0010708	1-5 finger syndactyly
HP:0010713	1-5 toe syndactyly
HP:0030300	10 pairs of ribs
HP:0000878	11 pairs of ribs
HP:0030306	11 thoracic vertebrae
HP:0001233	2-3 finger syndactyly
HP:0005709	2-3 toe cutaneous syndactyly
HP:0004691	2-3 toe syndactyly
HP:0010709	2-4 finger syndactyly
HP:0005768	2-4 toe cutaneous syndactyly
HP:0010714	2-4 toe syndactyly
HP:0010692	2-5 finger syndactyly
HP:0010715	2-5 toe syndactyly
HP:0008083	2nd-5th toe middle phalangeal hypoplasia
HP:0011939	3-4 finger cutaneous syndactyly
HP:0006097	3-4 finger syndactyly
HP:0009779	3-4 toe syndactyly
HP:0010710	3-5 finger syndactyly
HP:0010716	3-5 toe syndactyly

Patient's Features.

HPO.	Feature. ▲	Modifier.	Num diseases.

Features. Diseases. **Ontology.**

- ▶ Abnormality of the nervous system
- ▶ Abnormality of the respiratory system
- ▲ Abnormality of the skeletal system
 - ▶ Abnormality of cartilage
 - ▶ Abnormality of hyoid bone
 - ▶ Abnormality of limb bone
 - ▶ Abnormality of mandibular symphysis
 - ▶ Abnormality of odontoid tissue
 - ▶ Abnormality of skeletal morphology
 - ▲ Abnormality of skeletal physiology
 - ▶ Abnormality of skeletal maturation
 - ▶ Aseptic necrosis
 - ▶ Bone pain
 - ▲ Increased susceptibility to fractures
 - ▶ Bowing of limbs due to multiple fractures
 - ▶ Multiple prenatal fractures
 - ▶ Painless fractures due to injury
 - ▶ Pathologic fracture
 - ▶ Recurrent fractures
 - ▶ Fractures of the long bones
 - ▶ Fractured radius
 - ▶ Fractured ulna
 - ▶ Limb pain
 - ▶ Osteomyelitis
 - ▲ Abnormality of the nasal skeleton
 - ▶ Abnormality of cartilage of nasal septum
 - ▶ Absent nasal septal cartilage
 - ▲ Abnormality of the nasal bone
 - ▶ Aplasia/Hypoplasia of the nasal bone
 - ▶ Aplasia of the nasal bone
 - ▶ Hypoplasia of the nasal bone
 - ▶ Abnormality of the periosteum
 - ▶ Ectopic calcification
 - ▶ Abnormality of the thoracic cavity
 - ▶ Abnormality of the voice
 - ▶ Growth abnormality
 - ▶ Neoplasm

Patient's Features. Diagnosis. **Diagnosis.**

Algorithm: resnik (Unsymmetric). 2 Features.

<input type="checkbox"/>	p-value. ▲	Disease Id.	Disease name.	Genes.
<input checked="" type="checkbox"/>	0.0801	OMIM:61...	#615066 OSTEOGENESIS IMPERFECTA, TYPE XIV; OI14 ;;OI, TYPE XIV	SPARC (6678...
<input checked="" type="checkbox"/>	0.0801	ORPHAN...	IDIOPATHIC JUVENILE OSTEOPOROSIS	WNT3A (897...
<input checked="" type="checkbox"/>	0.2098	OMIM:16...	#167250 PAGET DISEASE OF BONE 3; PDB3	SQSTM1 (88...
<input checked="" type="checkbox"/>	0.2098	OMIM:16...	#166600 OSTEOPETROSIS, AUTOSOMAL DOMINANT 2; OPTA2;;OSTEOPETROSIS, AUTOSOMAL DOM...	CLCN7 (1186)
<input checked="" type="checkbox"/>	0.2098	OMIM:60...	#602080 PAGET DISEASE OF BONE; PDB	
<input checked="" type="checkbox"/>	0.2098	OMIM:60...	GRANGE SYNDROME	
<input checked="" type="checkbox"/>	0.2098	ORPHAN...	OSTEOPOROSIS, MYOPH...	CIAL DYSMORPHISM
<input checked="" type="checkbox"/>	0.2098	OMIM:16...		VDR (7421), ...
<input checked="" type="checkbox"/>	0.2098	OMIM:30...		18;;OSTEOPOROSIS AND ...
<input checked="" type="checkbox"/>	0.2098	OMIM:61...		15;;OSTEOPOROSIS, SUS...
<input checked="" type="checkbox"/>	0.2098	OMIM:11...		NOSMIA; HH21
<input checked="" type="checkbox"/>	0.2110	OMIM:61...		PROK2 (6067...
<input checked="" type="checkbox"/>	0.2379	OMIM:61...		NOSMIA; HH19
<input checked="" type="checkbox"/>	0.2671	ORPHAN...		PROK2 (6067...
<input checked="" type="checkbox"/>	0.2671	ORPHAN...		PLOD2 (5352...
<input checked="" type="checkbox"/>	0.2671	OMIM:25...		S FRAGILITY
<input checked="" type="checkbox"/>	0.2671	ORPHAN...		AL DISABILITY
<input checked="" type="checkbox"/>	0.2671	ORPHAN...		H CRANIOSYNOSTOSIS, O...
<input checked="" type="checkbox"/>	0.2851	OMIM:11...		P4HB (5034)...
<input checked="" type="checkbox"/>	0.2984	OMIM:11...		HISTIOCYTOMA;DMSMFH...
<input checked="" type="checkbox"/>	0.2984	ORPHAN...		MTAP (4507)
<input checked="" type="checkbox"/>	0.2984	ORPHAN...		PRKAR1A (5...
<input checked="" type="checkbox"/>	0.2984	ORPHAN...		P4HB (5034)...
<input checked="" type="checkbox"/>	0.2984	OMIM:61...		SLC9A3R1 (9...
<input checked="" type="checkbox"/>	0.2984	OMIM:12...		SLC9A3R1 (9...
<input checked="" type="checkbox"/>	0.3173	OMIM:61...		SLC4A1 (6521)
<input checked="" type="checkbox"/>	0.3310	OMIM:17...	RENAL TUBULAR ACIDOSIS, DISTAL, AUTOSOMAL DOMINANT	
<input checked="" type="checkbox"/>	0.3312	OMIM:61...	#611490 OSTEOPETROSIS, AUTOSOMAL RECESSIVE 4; OPTB4;;OSTEOPETROSIS, INFANTILE MALIG...	CLCN7 (1186...

Improve differential diagnosis using 8 diseases.

Scoring method: Binary search. **Specific search.**

HPO id.	Feature.	# Diseases.
HP:0002023	Anal atresia	1/8
HP:0002797	Osteolysis	1/8
HP:0000126	Hydronephrosis	1/8
HP:0000938	Osteopenia	1/8
HP:0002857	Genu valgum	1/8
HP:0100545	Arterial stenosis	1/8
HP:0009882	Short distal phalanx of finger	1/8
HP:0000670	Carious teeth	1/8
HP:0001646	Abnormality of the aortic valve	1/8
HP:0010628	Facial palsy	1/8
HP:0000107	Renal cyst	1/8
HP:0001643	Patent ductus arteriosus	1/8

Page 3 of 6

Improve Differential Diagnosis. Download Results.

Features. **Diseases.** Ontology.

#102500 HAJDU-CHENEY SYNDROME; HJCY Search. Reset.

Disease id.	Disease name.
OMIM:102500	#102500 HAJDU-CHENEY SYNDROME; HJCY;AC...

Annotations for #102500 HAJDU-CHENEY SYNDROME; HJCY;ACROOSTEOLYSIS WITH OSTEOPOROSIS AND CHANGES IN SKULL AND MANDIBLE;CHENEY SYNDROME;;ARTHRODENTOOSTEODYSPLASIA;;SERPENTINE FIBULA-POLYCYSTIC KIDNEY SYNDROME; SFPKS

HPO id.	Feature.
HP:0004586	Biconcave vertebral bodies
HP:0008462	Cervical instability
HP:0000280	Coarse facial features
HP:0000405	Conductive hearing impairment
HP:0006180	Crowded carpal bones
HP:0000028	Cryptorchidism
HP:0000689	Dental malocclusion
HP:0003083	Dislocated radial head
HP:0000494	Downslanted palpebral fissures
HP:0005463	Elongated sella turcica
HP:0000286	Epicanthus
HP:0001508	Failure to thrive
HP:0000293	Full cheeks
HP:0002857	Genu valgum
HP:0000218	High palate
HP:0001007	Hirsutism
HP:0000238	Hydrocephalus
HP:0000047	Hypospadias
HP:0000023	Inguinal hernia
HP:0002566	Intestinal malrotation

Patient's Features. **Diagnosis.**

Algorithm: resnik (Unsymmetric). 1 Feature.

<input type="checkbox"/>	p-value. ▲	Disease Id.	Disease name.	Genes.
<input checked="" type="checkbox"/>	0.3926	OMIM:60...	#602080 PAGET DISEASE OF BONE; PDB	
<input checked="" type="checkbox"/>	0.3926	OMIM:16...	#166600 OSTEOPETROSIS, AUTOSOMAL DOMINANT 2; OPTA2;;OSTEOPETROSIS, AUTOSOMAL DOM...	CLCN7 (1186)
<input checked="" type="checkbox"/>	0.3926	OMIM:61...	#613390 FANCONI ANEMIA, COMPLEMENTATION GROUP O; FANCO	FANCC (2176...
<input checked="" type="checkbox"/>	0.3926	OMIM:60...	GRANGE SYNDROME	
<input checked="" type="checkbox"/>	0.3926	OMIM:61...	#615066 OSTEogenesis IMPERFECTA, TYPE XIV; OI14 ;;OI, TYPE XIV	SPARC (6678...
<input checked="" type="checkbox"/>	0.3926	ORPHAN...	IDIOPATHIC JUVENILE OSTEOPOROSIS	WNT3A (897...
<input checked="" type="checkbox"/>	0.3926	ORPHAN...	OSTEOgenesis IMPERFECTA - RETINOPATHY - SEIZURES - INTELLECTUAL DISABILITY	
<input checked="" type="checkbox"/>	0.3926	OMIM:12...	CYSTIC ANGIOMATOSIS OF BONE, DIFFUSE	
<input type="checkbox"/>	0.4433	OMIM:27...	SPINAL MUSCULAR ATROPHY, TYPE I, WITH CONGENITAL BONE FRACTURES	
<input type="checkbox"/>	0.4838	OMIM:24...	HYPOPROTEINEMIA, HYPERCATABOLIC	B2M (567)
<input type="checkbox"/>	0.4838	OMIM:60...	RADIOULNAR SYNOSTOSIS WITH AMEGAKARYOCYTIC THROMBOCYTOPENIA	HOXA11 (3207)
<input type="checkbox"/>	0.4838	OMIM:61...	#614900 DIAMOND-BLACKFAN ANEMIA 11; DBA11	TSR2 (90121...
<input type="checkbox"/>	0.4838	OMIM:10...	ARMS, MALFORMATION OF	
<input type="checkbox"/>	0.4838	OMIM:15...	MESOMELIC DYSPLASIA, KANTAPUTRA TYPE	
<input type="checkbox"/>	0.4838	OMIM:21...	#212780 CENANI-LENZ SYNDACTYLY SYNDROME; CLSS;;CENANI SYNDACTYLISM;;CENANI-LENZ SY...	APC (324), L...
<input type="checkbox"/>	0.4838	OMIM:17...	RADIAL HYPOPLASIA, TRIPHALANGAL THUMBS, HYOSPADIAS, AND MAXILLARYDIASTEMA	
<input type="checkbox"/>	0.4838	OMIM:17...	RADIAL RAY HYPOPLASIA WITH CHOANAL ATRESIA	
<input type="checkbox"/>	0.4838	OMIM:61...	#613951 FANCONI ANEMIA, COMPLEMENTATION GROUP P; FANCP	FANCC (2176...
<input type="checkbox"/>	0.4838	OMIM:12...	127350 DYSCHONDROSTEOSIS AND NEPHRITIS	
<input type="checkbox"/>	0.4838	DECIPHE...	LERI-WEILL DYSCHONDROSTOSIS (LWD) - SHOX DELETION	
<input type="checkbox"/>	0.4838	OMIM:15...	%156230 MESOMELIC DWARFISM OF HYPOPLASTIC TIBIA AND RADIUS TYPE	
<input type="checkbox"/>	0.4838	OMIM:19...	ULNAR HYPOPLASIA	
<input type="checkbox"/>	0.4838	OMIM:11...	113470 BRACHYMESOMELIA-RENAL SYNDROME	
<input type="checkbox"/>	0.4838	OMIM:22...	FACIOCARDIOMELIC DYSPLASIA, LETHAL	
<input type="checkbox"/>	0.4838	OMIM:61...	SKELETAL DEFECTS, GENITAL HYPOPLASIA, AND MENTAL RETARDATION	ZBTB16 (7704)
<input type="checkbox"/>	0.4838	OMIM:31...	ULNAR HYPOPLASIA WITH LOBSTER-CLAW DEFORMITY OF FEET	
<input type="checkbox"/>	0.4838	OMIM:60...	VENTRICULOMEGALY WITH DEFECTS OF THE RADIUS AND KIDNEY	

Impediments to use in clinical medicine

Documentation of health history and physical findings

- Insufficient resolution
- No system for documentation or reporting

Features mostly related to genetic defects

Incomplete ontology due to

- Lacking resolution
- Binary and specific search aids insufficient
- Omission of standard diagnostic attributes

Multiple time points not possible

Curation centralized

Changes require extensive resources

Language restricted to English

Data capture for clinical medicine

How to capture and store clinical data?

How to enable contextual assignments, categorization and analytic evaluation of the data

How to operationalize our data to ask and answer decisive questions about outcomes?

Prerequisites

1. Unrestricted ability to migrate
 - Data (-base)
 - Programmes/ algorithms
2. No proprietary storage system
3. Full addressability of data at blinding speed (search engine technology)

Concept

To provide a **comprehensive basis for digital diagnostics:**

- **Structured data entry (SDE) tool** to capture clinical data as discrete items/features with references to defined properties, anatomic location and time
- Application of advanced IT tools to consolidate and analyse data from different sources to enable evaluation of large cohorts

To enable **seamless integration of existing genomic and imaging data of large cohorts of patients** with all other **modalities*** in an easy to use clinical decision support system (CDSS):

- By directly targeting the data stream of high-throughput, allelic level resolution whole genome sequencing (WGS)
- By examining the prospect for image analysis in addition to routinely collected (unstructured) data in clinical care
- By aggregating data to obtain data-driven diagnostic and prognostic information to support precise and fast clinical decision making and personalised medicine

Documentation of a health history and physical findings

Efficient and reliable electronic capture

Time-stamped, discrete data objects and their attributes

Incorporated real-time report generator

Multiple language data entry and report

Data storage system provides basis for broad analysis and inter-actability of data with other storage

The user interface is accessible in two roles, a consumer role (CR) and an administrator role (AR); designated domain experts get access in AR

In AR the domain expert has access to backend subsystems that permit

- To create, modify and delete fields
- To set field-properties, such as the type (text field, checkbox, radio-button, etc.)
- To position
- To create new forms

Content and phrasing of the report generator can be defined in AR

Clinicians use the CR to create new content of existing forms, alter content, search for content, and generate reports

Captured content is processed in a semantically cohesive format by real-time report generation with the intention to spare physician and allied health care personnel resources

Allgemein

Haut und Nägel

Kopf und Hals

Lymphknoten

Thorax

Kreislauf

Abdomen

Neurostatus

Bewegungsapparat

Allgemeinzustand

- gut
 pathologisch

Details

Bewusstsein

- normal
 pathologisch
 somnolent
 soporös
 auf Schmerzreiz reagierend
 bewusstlos

Glasgow Coma Scale

Eye Opening Response

- Spontaneous, open with blinking at baseline
 Opens to verbal command, speech, or shout
 Opens to pain, not applied to face
 None

Verbal Response

- Oriented

Customization via Module

Entry via:

Login > Domain Routine > Customise my Modules > click on **Master** of choice, file builds

To edit:

Scroll to element of choice > click on line of interest > click on **pencil icon** > click on **Edit**

Change items available

Use **Save**, **Preview** and **Discard** as appropriate

To save changes to existing module, click **Save**

Lymphknoten				Lymphknoten				Header	Category
Okzipital	normal	pathologisch	links	Konsistenz	normal	erhöht	derb	Header	Title1
								Button	Radio
	Anzahl	grösster Durchmesser	rechts	Konsistenz	normal	erhöht	derb	Button	Radio
								Field	Measurement
Mastoid	normal	pathologisch	links	Konsistenz	normal	erhöht	derb	Header	Title2
								Button	Checkbox
	Anzahl	grösster Durchmesser	rechts	Konsistenz	normal	erhöht	derb	Button	Checkbox
								Field	Measurement
Lymphknoten	normal	pathologisch	links	Konsistenz	normal	erhöht	derb	Header	Title1
								Button	Radio
	Anzahl	grösster Durchmesser	rechts	Konsistenz	normal	erhöht	derb	Button	Radio
								Field	Measurement
Lymphknoten	normal	pathologisch	links	Konsistenz	normal	erhöht	derb	Header	Title2
								Button	Checkbox
	Anzahl	grösster Durchmesser	rechts	Konsistenz	normal	erhöht	derb	Button	Checkbox
								Field	Measurement
Lymphknoten	normal	pathologisch	links	Konsistenz	normal	erhöht	derb	Header	Title1
								Button	Radio
	Anzahl	grösster Durchmesser	rechts	Konsistenz	normal	erhöht	derb	Button	Radio
								Field	Measurement
Lymphknoten	normal	pathologisch	links	Konsistenz	normal	erhöht	derb	Header	Title2
								Button	Checkbox
	Anzahl	grösster Durchmesser	rechts	Konsistenz	normal	erhöht	derb	Button	Checkbox
								Field	Measurement

Customization via Table

Entry via:

Login > Domain Routine > Customize my Modules > click on field > choose table* for new version or new module

*For new version or module rename table before upload

For Upload:

Click on field + > Choose File > fill in new **Module Name** > **Submit** > **Back Button**

When count complete, module ready for use

Beispiel Glasgow Coma Scale (GCS)

Glasgow Coma Scale		Glasgow Coma Scale Header	Title1	
Eye Opening Response		Eye Openi	Header	Title2
	Spontaneous, open with blinking at baseline	S ₁ S ₂ S ₃ S ₄ S ₅ E ₁ E ₂ S ₁ C ₁	Spontanec	Button Radio GCS _{Eye}
	Opens to verbal command, speech, or shout	O ₁ O ₂ S ₁ S ₂ S ₃ A ₁ O ₁ O ₂	Opens to v	Button Radio GCS _{Eye}
	Opens to pain, not applied to face	O ₁ O ₂ S ₁ S ₂ S ₃ A ₁ O ₁ O ₂	Opens to p	Button Radio GCS _{Eye}
	None	N ₁ N ₂ A ₁ N ₁ G ₁ N ₁ N ₁ B ₁ H ₁	None	Button Radio GCS _{Eye}
Verbal Response		V ₁ V ₂ R ₁ R ₂ M ₁ R ₁ R ₂ Y ₁	Verbal Re:	Header Title2
	Oriented	O ₁ O ₂ O ₃ O ₄ G ₁ O ₁ Z ₁ O ₁	Oriented	Button Radio GCS _{Verbal}
	Confused conversation, but able to answer questions	C ₁ C ₂ C ₃ C ₄ V ₁ C ₁ C ₂ Z ₁ C ₁	Confused	Button Radio GCS _{Verbal}
	Inappropriate responses, words discernible	In ₁ In ₂ R ₁ R ₂ O ₁ R ₁ R ₂ Ni ₁ H ₁	Inappropri	Button Radio GCS _{Verbal}
	Incomprehensible speech	In ₁ In ₂ U ₁ D ₁ O ₁ D ₁ D ₁ Ni ₁ H ₁	Incompreh	Button Radio GCS _{Verbal}
	None	N ₁ N ₂ A ₁ N ₁ G ₁ N ₁ N ₁ B ₁ H ₁	None	Button Radio GCS _{Verbal}
Motor Response		M ₁ M ₂ R ₁ R ₂ M ₁ R ₁ R ₂ P ₁	Motor Res:	Header Title2
	Obeys commands for movement	O ₁ O ₂ O ₃ O ₄ G ₁ O ₁ W ₁ P ₁	Obeys con	Button Radio GCS _{Motor}
	Purposeful movement to painful stimulus	P ₁ P ₂ U ₁ M ₁ D ₁ M ₁ C ₁ U ₁	Purposeful	Button Radio GCS _{Motor}
	Withdraws from pain	W ₁ W ₂ S ₁ R ₁ O ₁ S ₁ R ₁ W ₁ C ₁	Withdraws	Button Radio GCS _{Motor}
	Abnormal (spastic) flexion, decorticate posture	A ₁ A ₂ F ₁ F ₂ A ₁ F ₁ F ₂ Ni ₁ H ₁	Abnormal	Button Radio GCS _{Motor}
	Extensor (rigid) response, decerebrate posture	E ₁ E ₂ R ₁ R ₂ E ₁ R ₁ R ₂ P ₁	Extensor (Button Radio GCS _{Motor}
	None	N ₁ N ₂ A ₁ N ₁ G ₁ N ₁ N ₁ B ₁ H ₁	None	Button Radio GCS _{Motor}
GCS Score		G ₁ G ₂ S ₁ P ₁ G ₁ P ₁ P ₁ W ₁ G ₁ G ₁	GCS Score	GCS Score Field Measurement

Elemente aufgelistet, Berechnung hinterlegt

Im Bericht GCS Score

Auflistung der Art von Feldern

Verschiedene Sprachen hinterlegt

Allgemein

Haut und Nägel

Kopf und Hals

Lymphknoten

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Kreislauf

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Diagnoseraster für degenerative Wirbelsäulenerkrankungen

Zerviko-									
	vertebrales Syndrom								
	zephales Syndrom								
	spondylogenes Syndrom								
		bei/mit							
			Fehlhaltung/Fehlfom						
				Lordosierung/ Kopfprotraktion					
				Streckhaltung					
				Kyphosierung					
				Schiefhals/Torticollis					
					rechts				
					links				
				Beckegeradstand					
				Beckentiefstand					
					rechts	cm			
					links	cm			
				Skoliose					
					lumbale				
							links-konvexe		
							rechts-konvexe		
					thorakale				
							links-konvexe		
							rechts-konvexe		
					thorakolumbale				
							links-konvexe		
							rechts-konvexe		
					kompensiert				
							Lot	rechts	cm
								links	cm
				Schultertiefstand					
					rechts	cm			
					links	cm			
			muskulärer Dysbalance						
				insuffiziente segmentale Stabilisation					
					ventral				
					dorsal				
			Tendomyosen						

Implications of structured data entry

For patients

- Improved and personalized diagnostics
- Access to own data possible
- Structured follow-up data for outcome assessment and quality control

For physicians

- Documentation with discrete, time-stamped data points is available real-time and is paired with reporting,
- Fully addressable and analyzable data for quality control and research
- More face time with patients
- Analysis for individual care, quality control and research

For health professionals

- Structured data entry tailored for disease, as for physicians
- Suggestions for structured diagnosis

For technology

- Data from diverse sources for improved diagnosis, outcome measurement, research
- Option to expand to any other disease

For my institution

- Data to drive process organization and optimization for increased quality and cost savings

Summary

Phenotyping systems for physical characteristics available for research purposes

Not operational for clinical routine not given

- Insufficient resolution
- No system for clinical documentation or reporting
- Limited sequential input
- Adaptations resource-intensive
- Limited language editions

Structured data entry with enabled domain implemented adaptations technically feasible for embedding in a given system

What next?

Avatar for medical purposes

Structured data entry

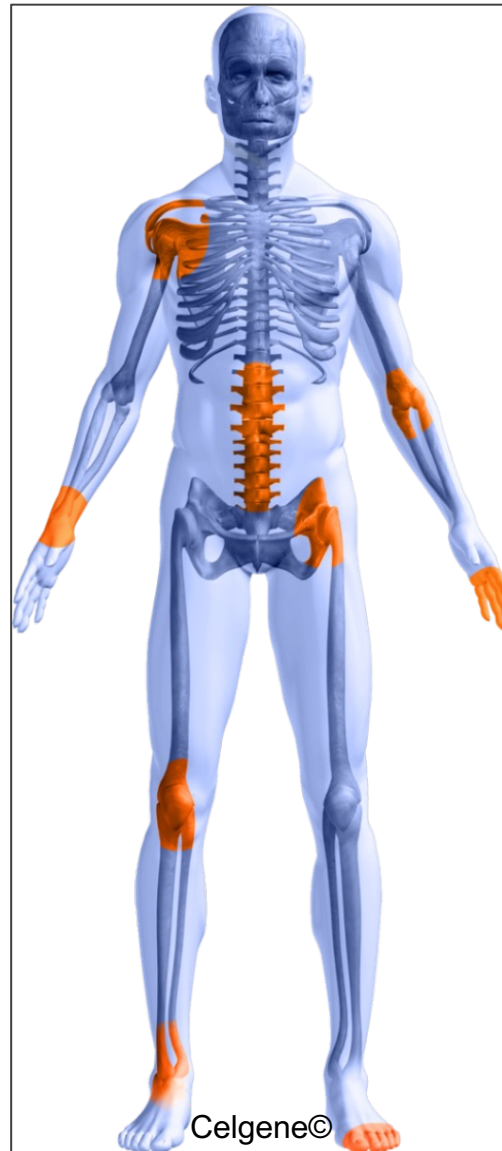
- Health history
- Physical findings

Apparative diagnostics

- Physiologic
- functional

Molecular diagnostics

- Genetics
- Epigenetics
- Other



Routine laboratory

- General
- Specialized

Imaging

- Radiation based
- Ultrasound
- MRI, others
- combined

Response to therapy

- Efficacy, Effectiveness
- Undesired effects