



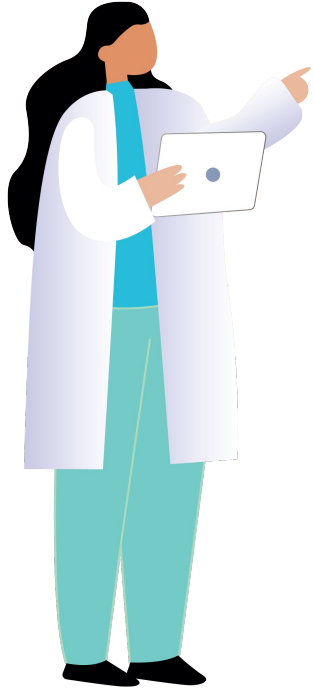
Integrating Phenotypic and Genomic Data

Orion Buske, PhD

CORD Conference
30 Apr 2025



Overview



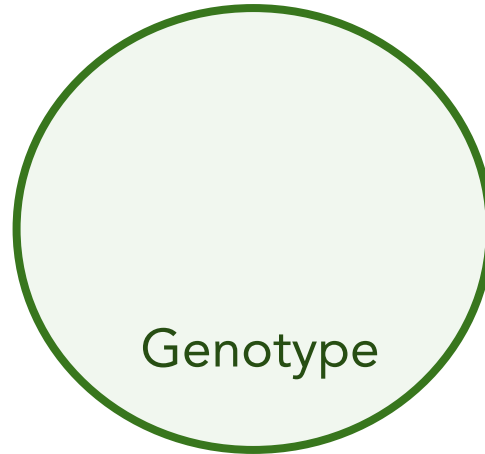
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- What is PhenoTips, and how it's being used across Canada?
- How does matchmaking help find answers for those that are undiagnosed after initial testing?
- What are some current innovations?

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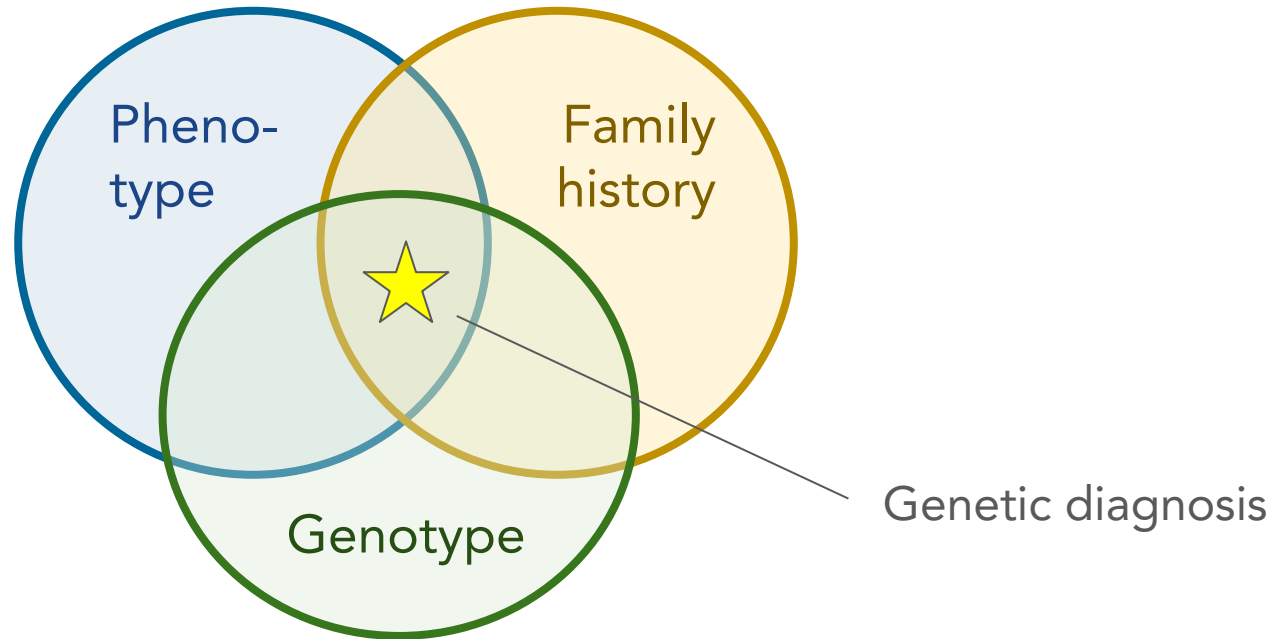
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The Need for Integrated Data in Rare Disorders



Finding a genetic diagnosis by sequencing alone is like
“finding a needle in a stack of needles”

The Need for Integrated Data in Rare Disorders



Integrated, high-quality data is essential for accurate and timely diagnosis

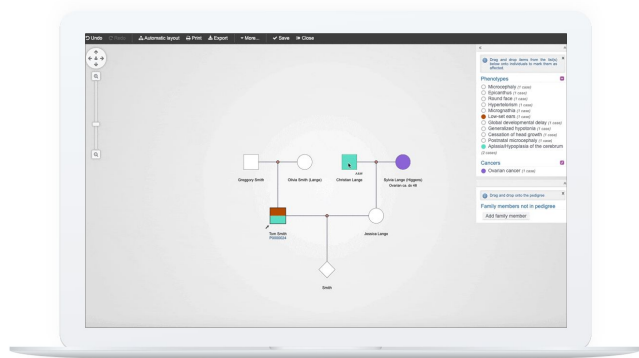
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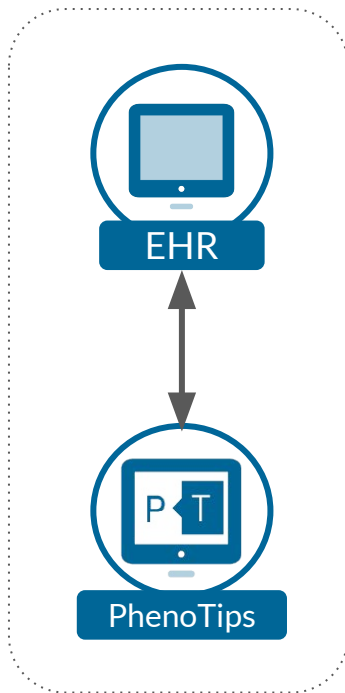
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PhenoTips: the first Genomic Health Record

Spinout from
University of Toronto and
SickKids Hospital



Goal: Help healthcare providers
deliver genomically-informed
care at scale

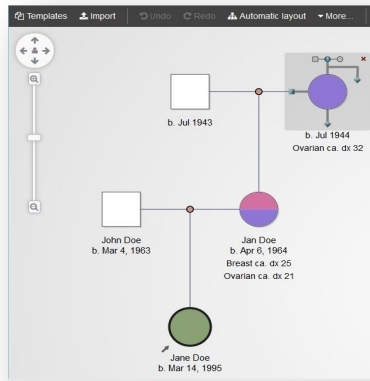


- ① **Structured** phenotype, diagnosis, genetics
- ② **Pedigree** to visualize & manage families
- ③ **Workflow** support for intake, diagnosis, test orders, research



Insights from Structured Data

Family history



Phenotype

Clinical symptoms and physical findings

GROWTH PARAMETERS

Asymmetric growth

CUTANEOUS

Maceration

Grade 1

RESPIRATORY

Pulmonary hypoplasia

BLOOD AND BLOOD-FORMING TISSUES

Anemia

Bone marrow hypocellularity

PRENATAL DEVELOPMENT OR BIRTH

Decreased fetal movement

Hydrops fetalis

Large placenta

Abnormality of the placenta

Acute intervillitis and intervillous abscesses



Suggest rare genetic conditions

Diagnosis

INSTANT OMIM SEARCH

The following terms are extracted from the phenotypic description and used automatically in searches. You can disable or re-enable their contribution in the search results by clicking on them.

Arthritis Conjunctivitis Fever Headache Hearing impairment Skin rash

Matching disorders in OMIM

[MIM:120100] #120100 FAMILIAL COLD AUTOINFLAMMATORY SYNDROME 1

[MIM:142680] #142680 PERIODIC FEVER, FAMILIAL, AUTOSOMAL DOMINANT

[MIM:124950] 124950 DEAFNESS, SENSORINEURAL, WITH PERIPHERAL NEUROPATHY AND ARTERIAL DISEASE

[MIM:191900] #191900 MUCKLE-WELLS SYNDROME

[MIM:108050] 108050 ARTERITIS, FAMILIAL GRANULOMATOUS, WITH JUVENILE POLYARTHRITIS

[MIM:145590] 145590 HYPERTHERMIA, CUTANEOUS, WITH HEADACHES AND NAUSEA

Genotype

Call... count	RefG...	Chr	Pos	Ref	Alt	Variant class
1	GRCh37	1	109824680	C	T	SNP
1	GRCh37	1	111743036	G	A	SNP
1	GRCh37	1	1248329	G	A	SNP
1	GRCh37	1	145323656	A	T	SNP

Gene panels

MATCHING GENES [DOWNLOAD](#)

The following terms are extracted from the phenotypic description and used automatically in searches. You can disable or re-enable their contribution in the search results by clicking on them.

Childhood onset **NO Abnormal delivery** Abnormality of the nasal dorsum Abnormality of the pinna Abnormality of the testis Absent axillary hair Absent eyebrow Absent eyelashes Absent facial hair Absent testis Asymmetry of the ears Delayed eruption of teeth Dental malocclusion Depressed nasal ridge Dry skin Freckling Generalized hypotrichosis Hypohidrosis Midface retrusion Milia Numerous pigmented freckles Phimosis **NO Premature birth** Pterygium Scoliosis Scrotal hypoplasia Soft skin Sparse eyelashes Sparse hair White hair

LMNA

Abnormality of the nasal dorsum; Abnormality of the pinna; Abnormality of the testis; Absent eyebrow; Absent eyelashes; Absent facial hair; Delayed eruption of teeth; Hypohidrosis; Midface retrusion; Scoliosis; Sparse eyelashes; Sparse hair

MBTP52

Abnormality of the nasal dorsum; Abnormality of the pinna; Abnormality of the testis; Absent eyebrow; Absent eyelashes; Absent facial hair; Dry skin; Hypohidrosis; Scoliosis; Sparse eyelashes; Sparse hair

BRAP

Abnormality of the pinna; Abnormality of the testis; Absent eyebrow; Absent eyelashes; Absent facial hair; Dental malocclusion; Dry skin; Freckling; Midface retrusion; Scoliosis; Sparse hair

TWIST2

PhenoTips Adoption Across Canada



634,300
patient records



398,700
family records



2,100
users

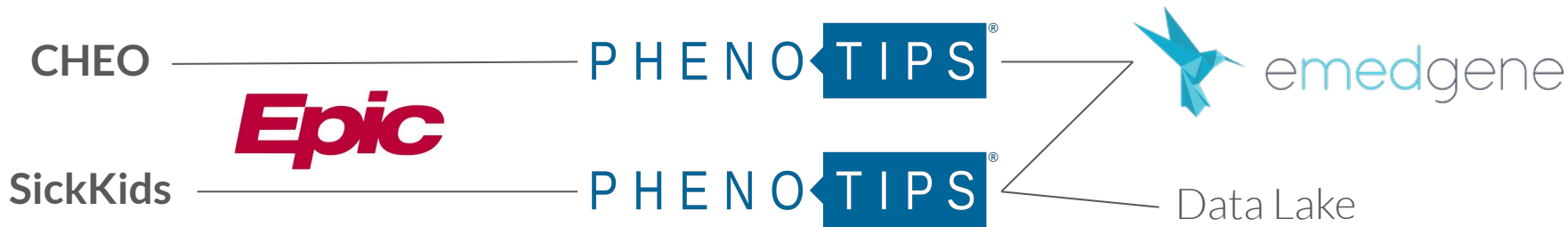
Examples:

- Alberta Health Services
- Genome Sequencing Ontario
- Genomics4RD

Example: Genome Sequencing Ontario



Supporting a coordinated multi-site clinical genome sequencing program



Sequencing 3,000+ people per year and growing rapidly

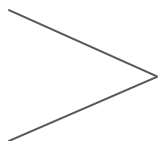
Example: Alberta Health Services



Supporting structured data workflows across provincial health system

Edmonton

Calgary



Epic

P H E N O

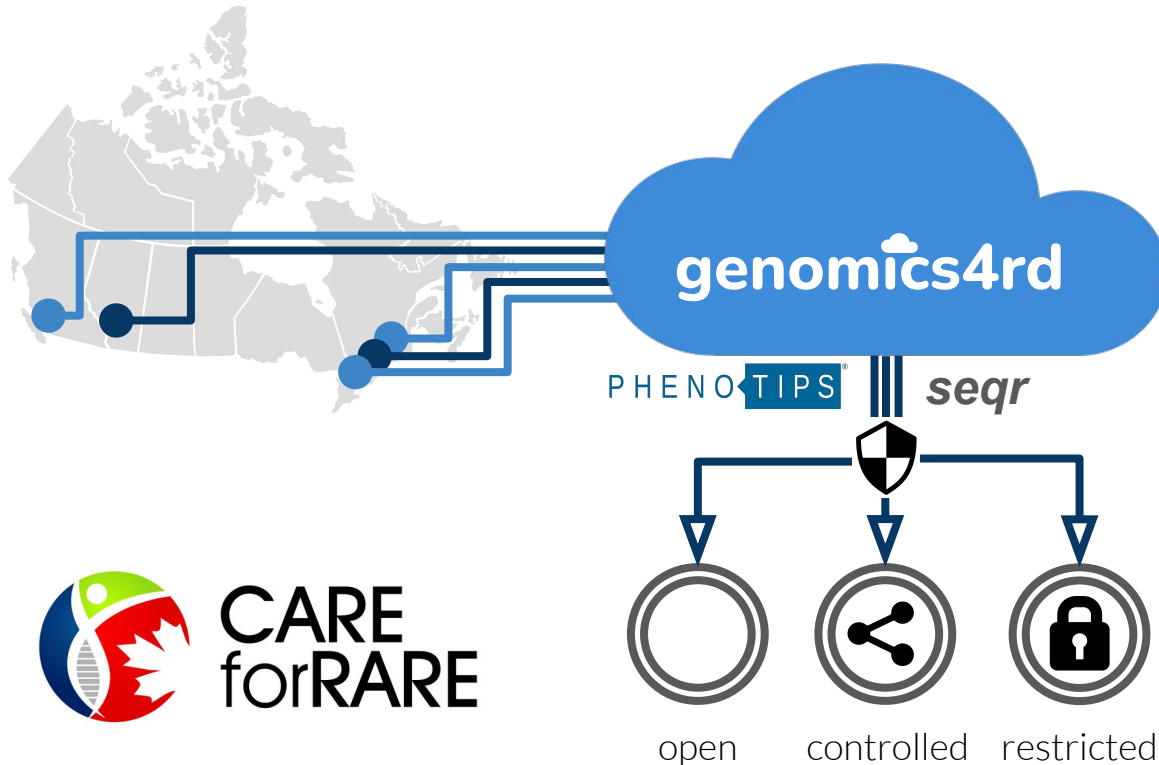
TIPS[®]

Research
Projects

Currently project to improve the management of prenatal records, avoid data gap when transition from mother's record

Example: Genomics4RD

Genomics4RD: the first centralized pan-Canadian rare disease research data lake



Harmonized, structured
phenotype-genotype data
for ~3,000 families

Most still unsolved

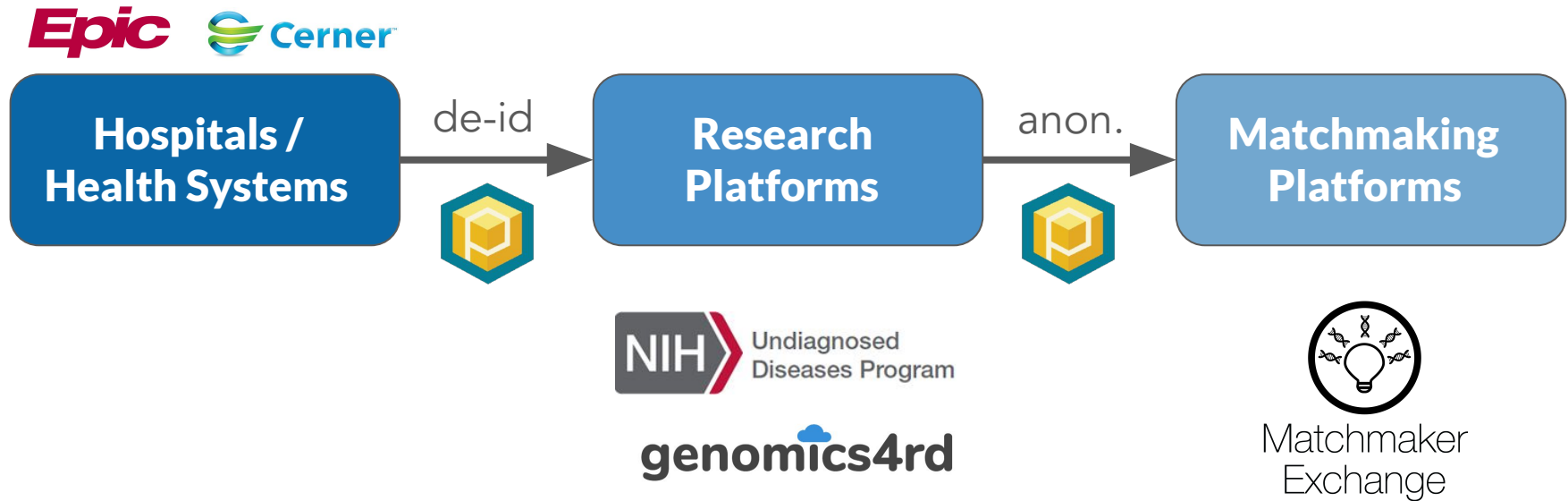
Supports collaboration,
data sharing, and gene
discovery

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Matchmaking to Find Answers for Undiagnosed Patients



Matchmaker Exchange Helps Find Additional Families



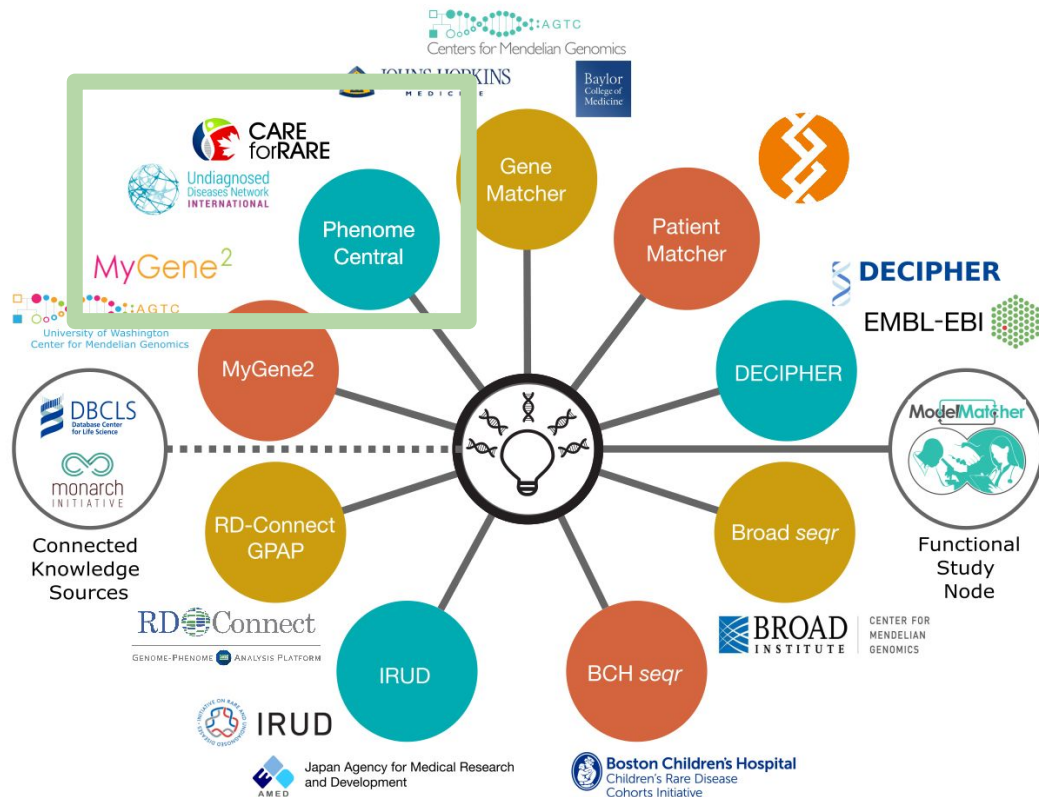
Matchmaker
Exchange

16 countries **170k** patients

500+
cases shared / week



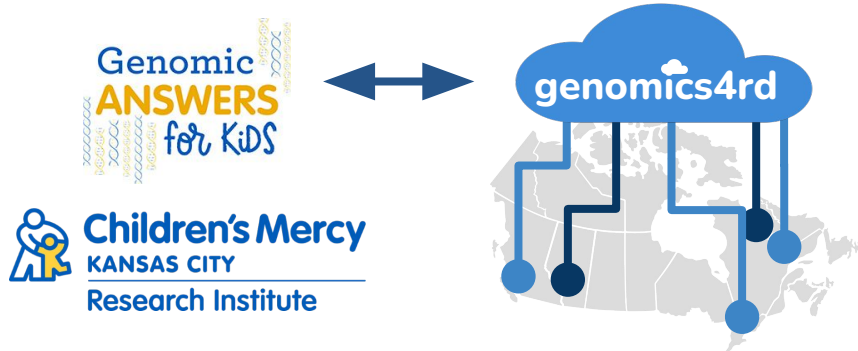
Global Alliance
for Genomics & Health



New Matchmaking Initiatives to Help Provide Answers

One-Sided Matching Platform (OSMP)

Goal: explore candidate genes by matching across internationally federated variant databases



Matt Osmond
GC, Research Coordinator
CHEO, Care4Rare

GA4GH Variant-Level Matching

Explore variants of unknown significant by matching across variant databases:

VariantMatcher
Franklin
MyGene2
Geno2MP
...



Nara Sobreira, MD, PhD
Clinical Geneticist
Johns Hopkins

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Streamlining Collection of Critical Data

Family can complete from home,
feeds directly into clinical system

The image shows two mobile app screens. The left screen is titled 'PARENTS' and contains instructions: 'Please add one or more known countries or regions of ancestry on both sides of the family:'. Below this are two search fields, one for 'Mother's ancestry' and one for 'Father's ancestry'. At the bottom, there is an information icon and a paragraph: 'Some medical conditions can be passed down in families (inherited). These inherited conditions can be more common in people from certain parts of the world. For this reason, it is important for us to know what part of the world your family is from. This information may be used in our risk assessment, as well as in planning and interpreting genetic test results. Ancestry is different from nationality or citizenship, and many people have ancestors from more than'. The right screen shows a sidebar menu with options: 'Introduction', 'Instructions', 'Parents' (highlighted), 'Your Information', 'Patient's Family', 'Mother's Family', 'Father's Family', 'Cancer Related Questions', 'Medical Conditions', 'Genetic Testing', 'Gender Identity', 'Additional Information', and 'Conclusion'.

SUGGESTIONS FROM CLINIC NOTES

☐ Y ☐ N **Depressed nasal bridge** ⓘ

Craniofacial features include flat nasal bridge, large ears, long philtrum, micrognathia, loose skin, and a triangular face.

☐ Y ☐ N **Macrotia** ⓘ

Craniofacial features include flat nasal bridge, large ears, long philtrum, micrognathia, loose skin, and a triangular face.

◀ 3 to 4 of 12 suggestions ▶

Using AI to help document the phenotype

Piloting New Methods at the Undiagnosed Hackathon

2023: 11 patients → 4 diagnosed

- PhenoTips was founding member

2024: 21 families → 10 diagnosed

- Last year brought 116 clinicians and bioinformaticians together from 28 countries
- Patients nominated by clinicians from UDNI, remained undiagnosed
- Data: Both short and long-read of WGS and RNA-seq, OGM

2025:

Mayo Clinic, USA
September 22-24

undiagnosedhackathon.org



Summary

- Standardized and integrated phenotype-genotype data is critical
- PhenoTips is a Canadian solution to help hospitals and health systems provide genetics services
- New efforts are improving data collection, sharing, and analysis

