Data Sharing, GeneMatcher and VariantMatcher

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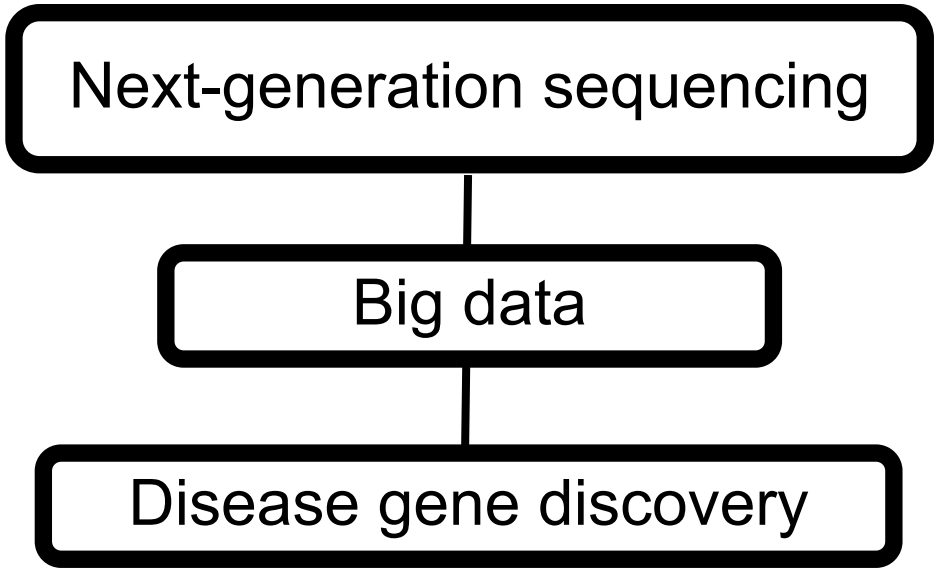
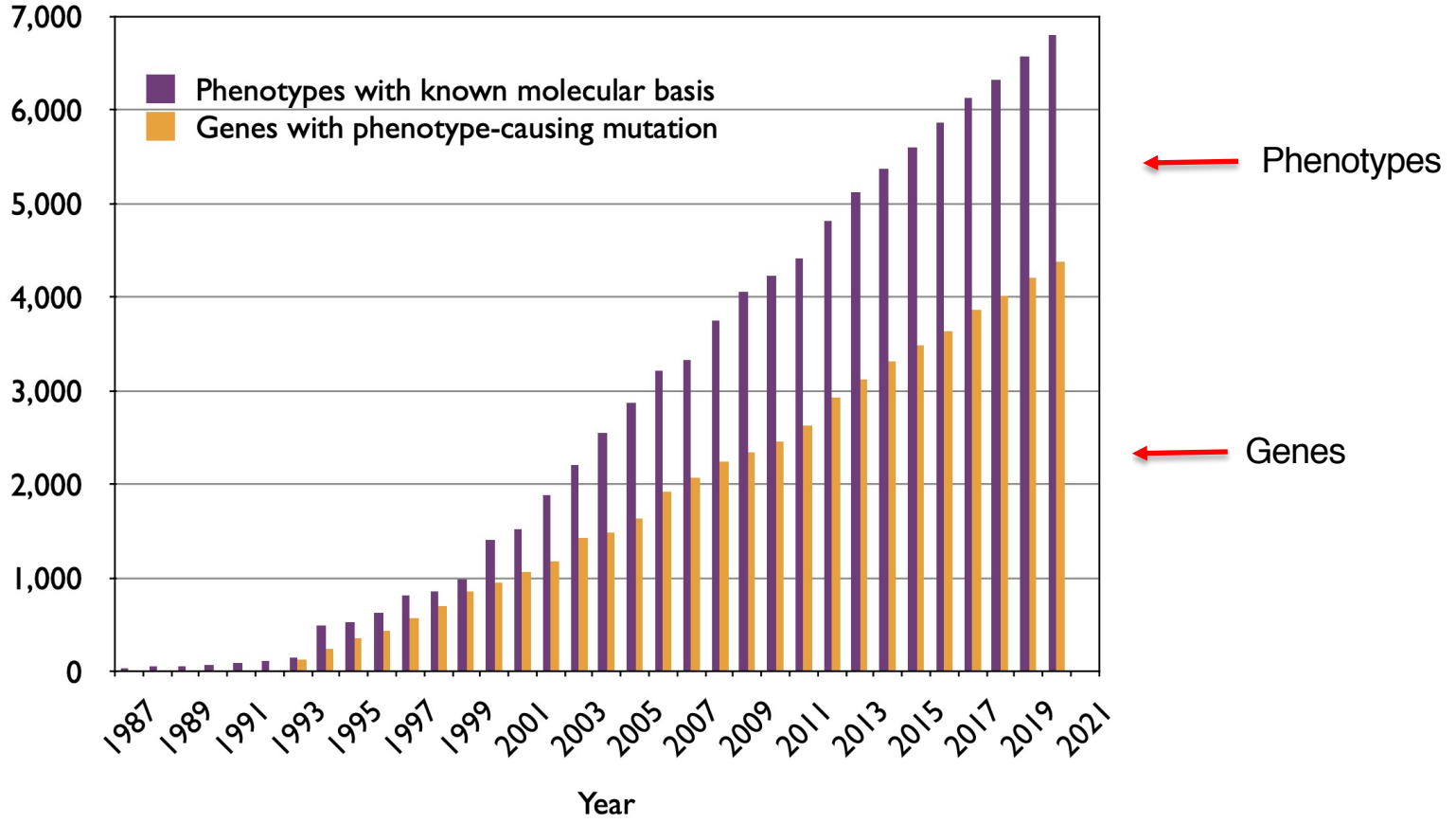
Data Sharing and Disease Gene Discovery



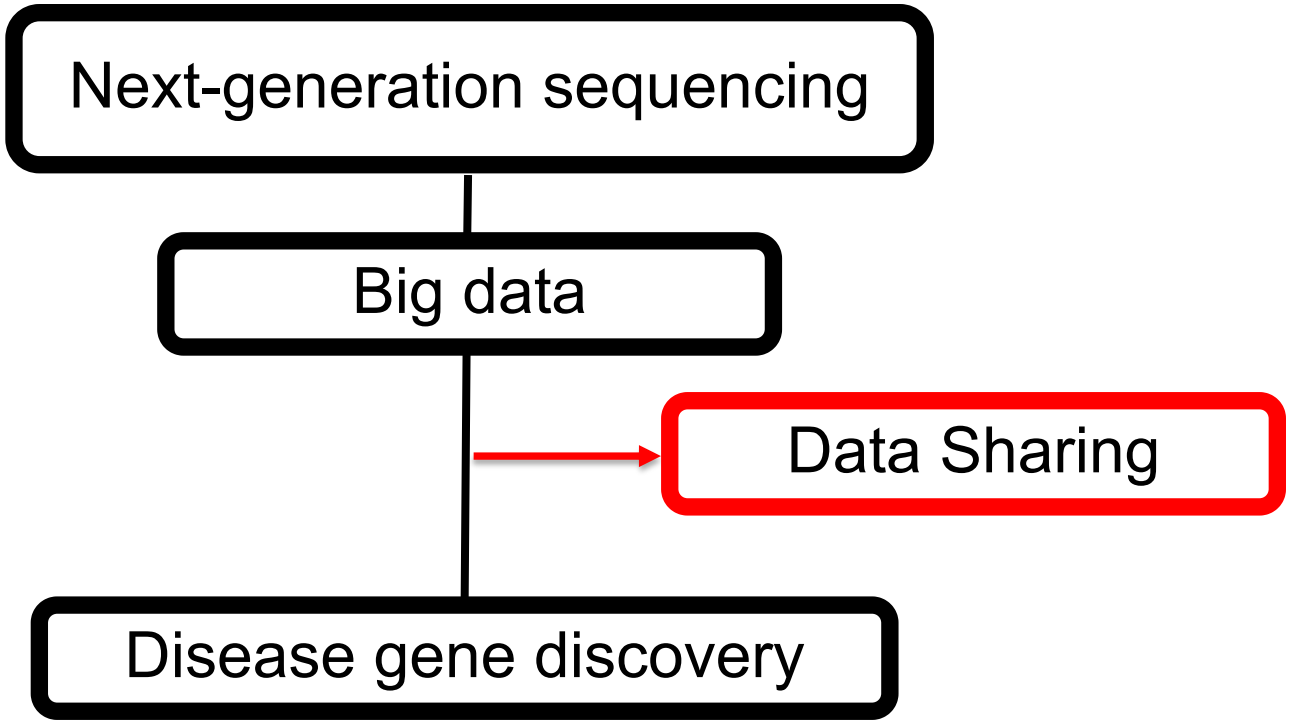
Growth of Gene-Phenotype Relationship



Source: Online *Mendelian Inheritance in Man - 31* December 2020

- The number of genes associated with phenotypes listed in OMIM rose from ~2,500 (12.5%) to ~4,500 (~22%) over the last 11 years.

Data Sharing and Disease Gene Discovery



Data Sharing

- What data to share?
  - ✓ What data is needed for disease gene and variant discoveries?
  - ✓ What data can be shared to ensure patient confidentiality and privacy?
- How to share the data?
- Where to share the data?
- With whom to share data?
- How to ensure that the researchers that generated the data are recognized for their work?
- How to share the data in compliance with the IRB requirements?

Data Sharing Databases

- Restricted, NIH-based databases
  - ✓ dbGaP (The database of Genotypes and Phenotypes)
  - ✓ AnViL (The NHGRI Genomic Data Science Analysis, Visualization and Informatics Lab-space)
  - ✓ CAVATICA (Gabriella Miller Kids First)
- Public, variant-based databases
  - ✓ DECIPHER (copy number variation)
  - ✓ dbSNP
  - ✓ Exome Variant Server
  - ✓ 1000 Genomes Project
  - ✓ ExAC Browser - Harvard Medical School
  - ✓ gnomAD (The Genome Aggregation Database)
  - ✓ ClinVar
  - ✓ HGMD (Human Gene Mutation Database)

What is missing?

- Detailed phenotypic features
- Detailed family history
- Capability to reassess the individual with the variant of interest

How to address some of the problems?

- Share little but share the essential
  - ✓ Gene and/or variant of interest
  - ✓ The name and contact information of the individual responsible for the data
- Ensure simultaneous notification about the match

https://genematcher.org/

GENE MATCHER

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GeneMatcher

GeneMatcher is a freely accessible web site designed to enable connections between clinicians and researchers from around the world who share an interest in the same gene or genes.

GENEMATCHER

Email : Required...

Password : Required...

Log In

Forgotten your password?

Create an account...

Baylor-Hopkins Center for Mendelian Genomics

VariantMatcher

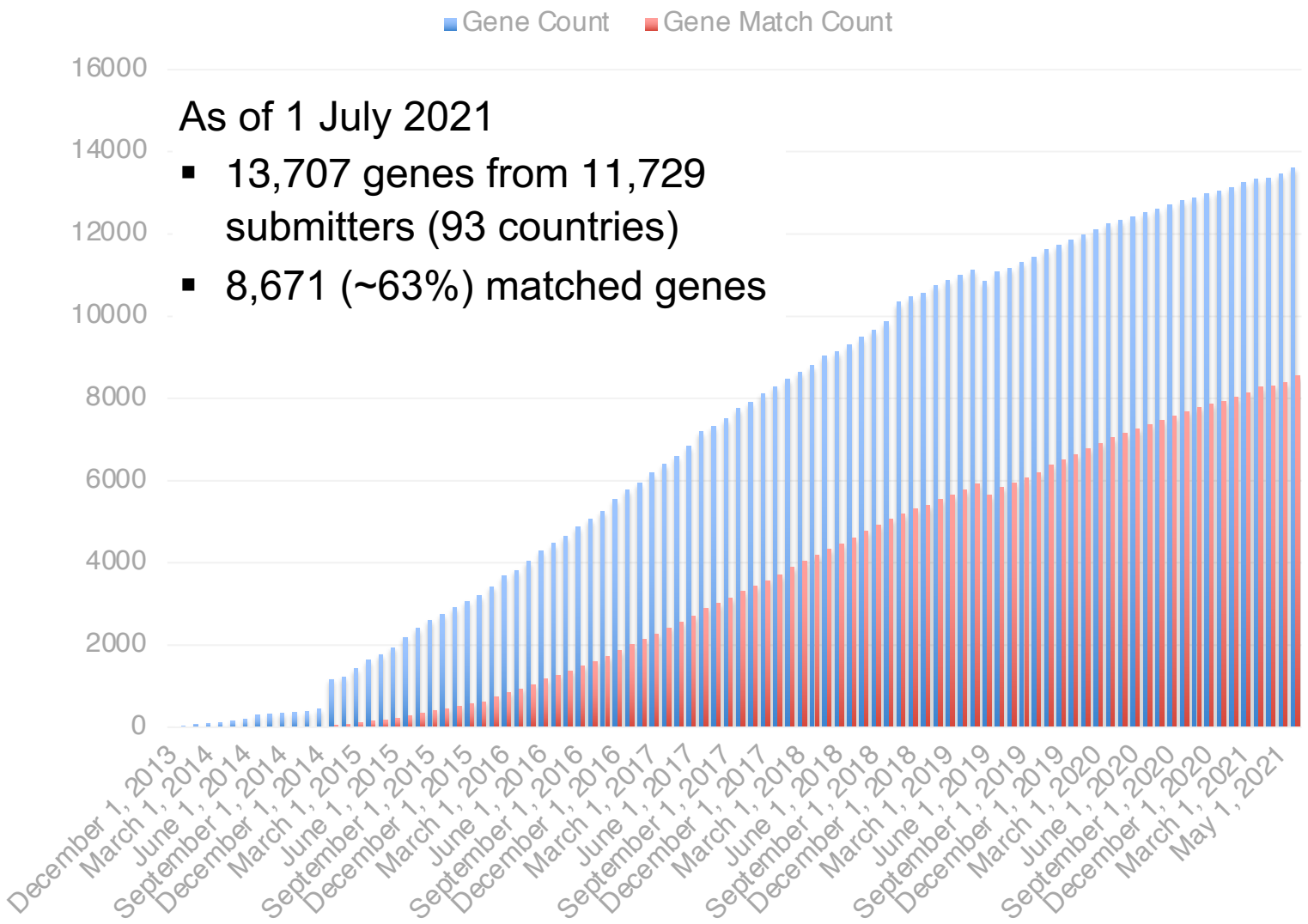
Centers for Mendelian Genomics AGTC

GeneMatcher

- To enable connections between patients, their families, clinicians and researchers from around the world who share an interest in the same gene or genes
- De-identified data
- Automated matching
- Submitters choose to follow up at their discretion
- Also matching on phenotypic features, genomic location and OMIM disease number

Growth in number of genes and genes matched in GeneMatcher

https://genematcher.org/



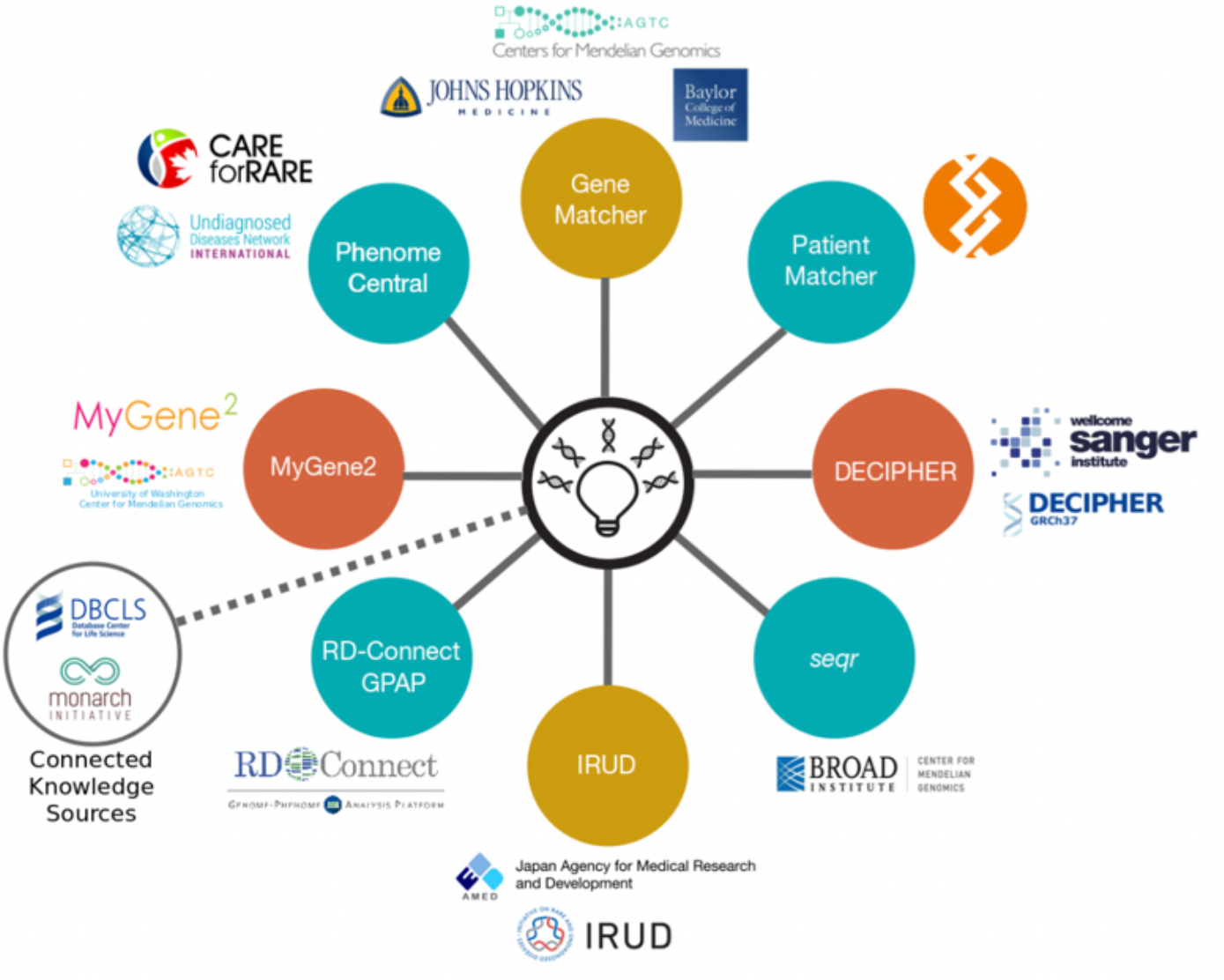
Who are the GeneMatcher users?

- 7,980 users describe themselves as researchers
- 5,220 as health care providers
- 635 as patients
- Of the 13,707 genes in GeneMatcher, 323 were submitted by model organism researchers
  - ✓ 202 were from mouse
  - ✓ 55 from zebrafish
  - ✓ 38 from fruit fly
  - ✓ 14 from yeast
  - ✓ 14 were related to other non-human organisms

How has GeneMatcher contributed to disease gene discovery?

- GeneMatcher is cited in > 484 publications
- As of June 12th 2020, GeneMatcher was acknowledged in 325 publications and 302 genes were described in 249 publications
  - ✓ 157 were related to an autosomal dominant phenotype
  - ✓ 105 were related to an autosomal recessive phenotype
  - ✓ 24 were related to an autosomal dominant and autosomal recessive phenotype
  - ✓ 6 were related to a X-linked recessive or dominant phenotype
- 221 of these genes (~73%) were on GeneMatcher for more than a year before publication
- 231 genes (76.5%) are currently associated to a phenotype in OMIM
- 73 (~32%) had an OMIM phenotype before the gene was posted to GeneMatcher
- Among the genes entered >5 times in GeneMatcher and that had an OMIM phenotype as of 1 June 2020 (1,012), 445 genes were associated with an OMIM phenotype after being deposited in GeneMatcher

GeneMatcher and Matchmaker Exchange



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