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for Genomics & Health
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SIB
Swiss Institute of
Bioinformatics

Universität
Zürich[UZH]

Beaconize this: Federated Data Discovery in Biomedical Genomics

Michael Baudis
Professor of Bioinformatics
University of Zürich
Swiss Institute of Bioinformatics **SIB**
GA4GH Workstream Co-lead *DISCOVERY*
Co-lead ELIXIR Beacon API Development

Republic of Korea
Switzerland 60th anniversary
1963–2023

200+ Genomic Data Initiatives Globally

Clinical/Genomic Medicine

Research

National

Cohorts

How Many Genomes?

RESEARCH

HEALTHCARE

60M individuals
132.5M sequences

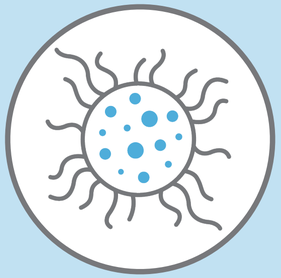
CLINICAL TRIALS

2.7-3M individuals

COHORTS

140M individuals

Global Genomic Data Sharing Can…



Demonstrate patterns in health & disease

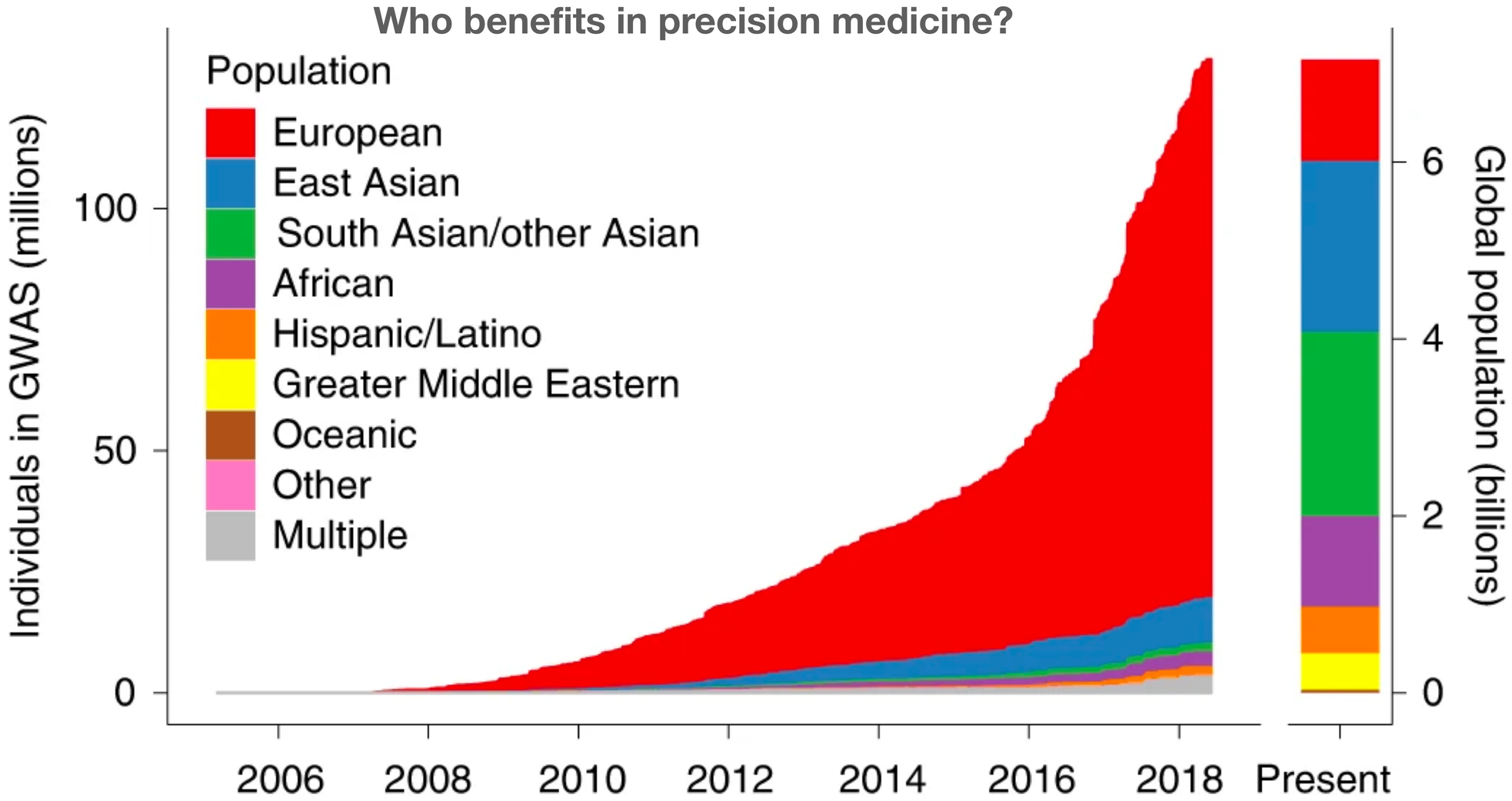
Increase statistical significance of analyses

Lead to “stronger” variant interpretations

Increase accurate diagnosis

Advance precision medicine

Genomic research has long-standing problems with diversity



Slide: Karen-Miga - The Human Pangenome Project @ GA4GH 2023

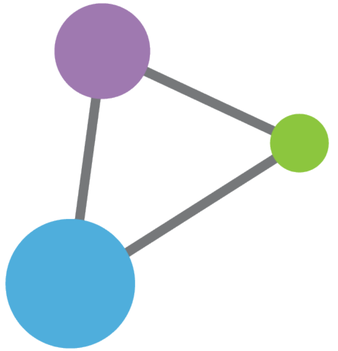
Martin et al 2019

Different Approaches to Data Sharing

Centralized Genomic Knowledge Bases

Data Commons
Trusted, controlled repository of multiple datasets

Hub and Spoke
Common data elements, access, and usage rules



Linkage of distributed and disparate datasets

Different Approaches to Data Sharing

progenetix

European Genome-Phenome Archive

SPHN Swiss Personalized Health Network

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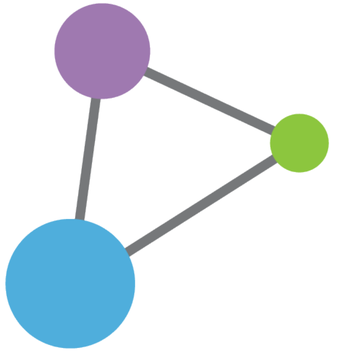

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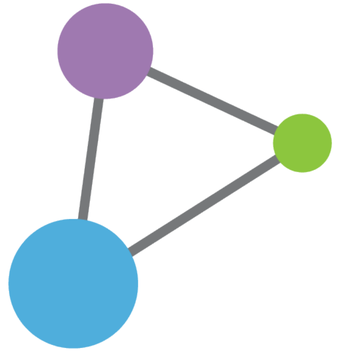

Linkage of distributed and disparate datasets

progenetix.org

Cancer Genomics Reference Resource

- ***open*** resource for oncogenomic profiles
- over **116'000 cancer CNV profiles**
- more than **800 diagnostic types**
- inclusion of reference datasets (e.g. TCGA)
- standardized encodings (e.g. NCIt, ICD-O 3)
- identifier mapping for PMID, GEO, Cellosaurus, TCGA, cBioPortal where appropriate
- core clinical data (TNM, sex, survival ...)
- data mapping services
- recent addition of SNV data for some series

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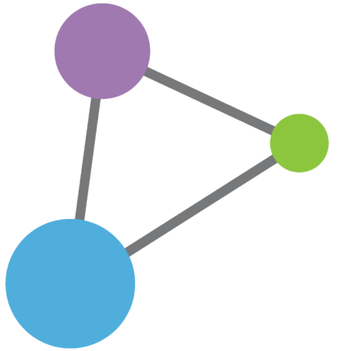


Linkage of distributed and disparate datasets

The EGA

European Genome-Phenome Archive

Long term secure archive for human biomedical research sensitive data, with focus on reuse of the data for further research (or "*broad and responsible use of genomic data*")

EUROPEAN GENOME-PHENOME ARCHIVE

CRG Centre for Genomic Regulation

EMBL-EBI

Global Alliance for Genomics & Health

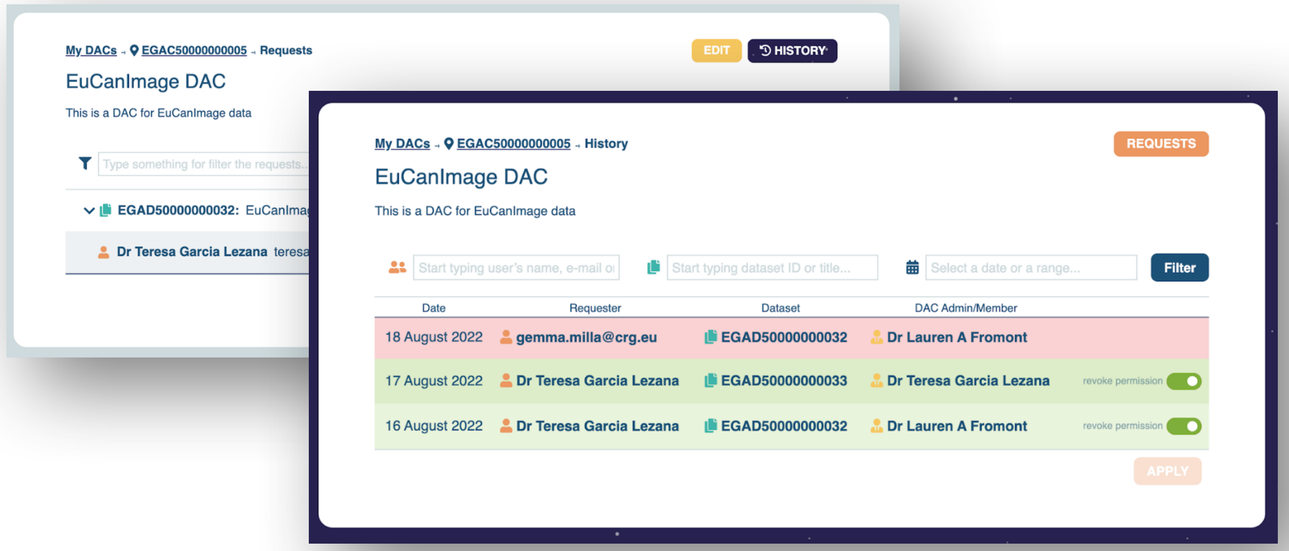
DRIVER PROJECT

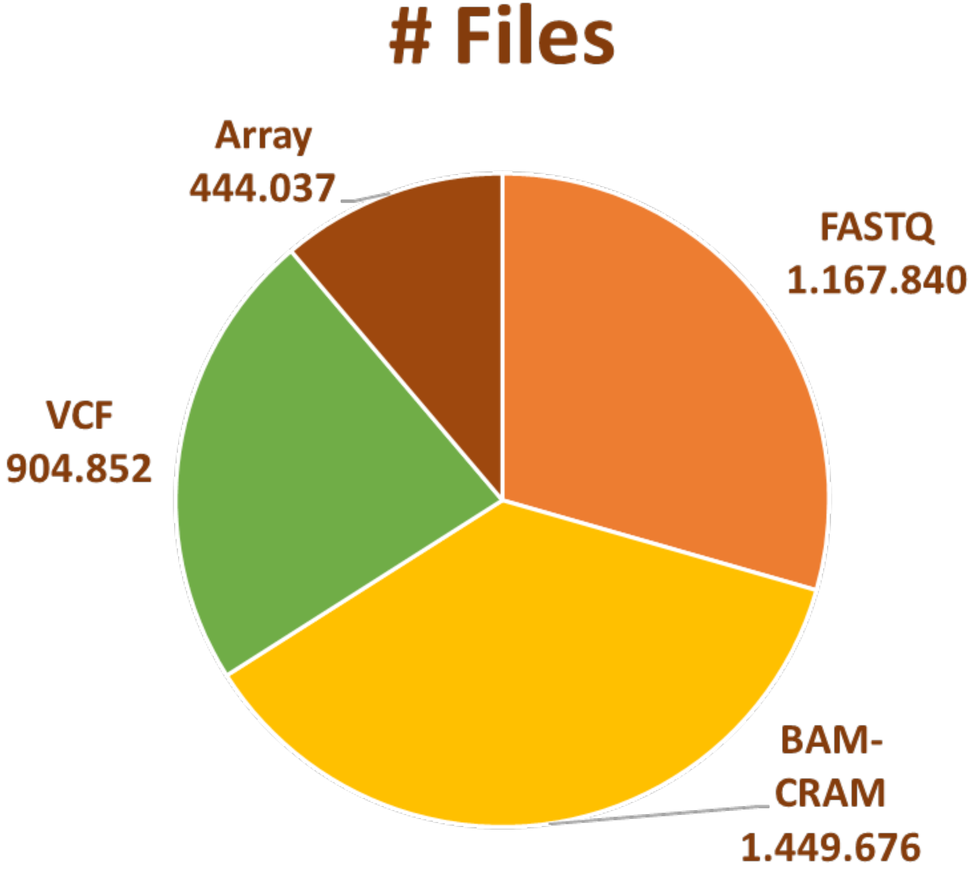
Slide: adapted from Jordi Rambla@ GA4GH 2023

The EGA

European Genome-Phenome Archive

- EGA “owns” nothing; data controllers tell who is authorized to access ***their*** datasets
- EGA admins provide smooth “all or nothing" data sharing process





4,328 Studies released
10,470 Datasets
2,309 Data Access Committees

Slide: adapted from Jordi Rambla@ GA4GH 2023

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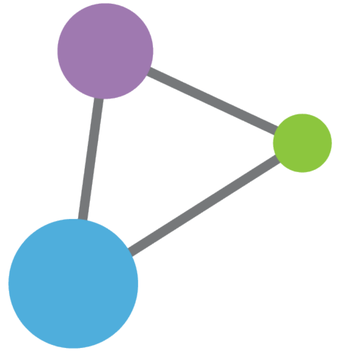
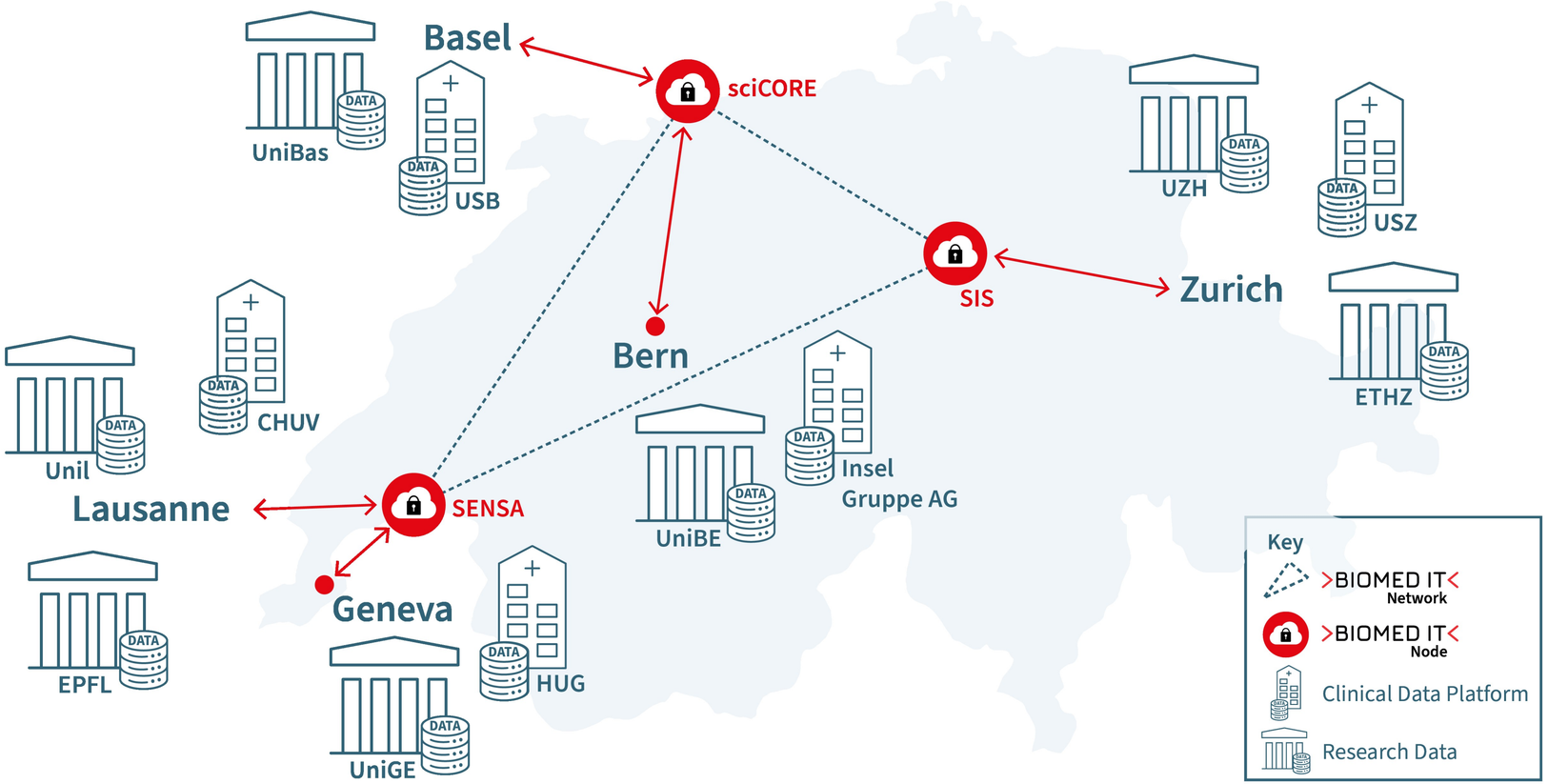


Linkage of distributed and disparate datasets

The Swiss Personalized Health Network



Strategic Focus Area
Personalized Health and Related Technologies

Personalized Health Informatics Group

SPHN Data Coordination Center (DCC)
BioMedIT Network

Different Approaches to Data Sharing

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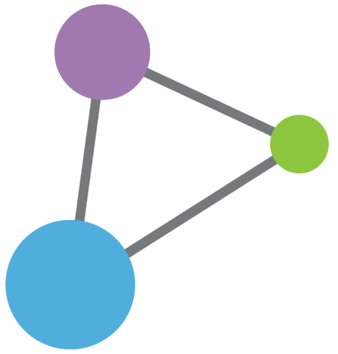

Linkage of distributed and disparate datasets

Federation

A New Paradigm for Data Sharing

FROM

TO

Data Copying

Data Visiting

INFORMATICS

Beacon v2 and Beacon networks: A "lingua federated data discovery n biomedical ger

Jordi Rambla[1,2] | Michael Baudis[3] | Roberto Ariosa[1] | Tim Beck[4] | Lauren A. Fromont[1] | Arcadi Navarro[1,5,6,7] | Rahel Paloots[3] | Manuel Rueda[1] | Gary Saunders[8] | Babita Singh[1] | John D. Spalding[9] | Juha Törnroos[9] | Claudia Vasallo[1] | Colin D. Veal[4] | Anthony J. Brookes[4]

Cell Genomics

CellPress
OPEN ACCESS

Commentary

International federation of genomic medicine databases using GA4GH standards

Adrian Thorogood,[1,2,*] Heidi L. Rehm,[3,4] Peter Goodhand,[5,6] Angela J.H. Page,[4,5] Yann Joly,[2] Michael Baudis,[7] Jordi Rambla,[8,9] Arcadi Navarro,[8,10,11,12] Tommi H. Nyronen,[13,14] Mikael Linden,[13,14] Edward S. Dove,[15] Marc Fiume,[16] Michael Brudno,[17] Melissa S. Cline,[18] and Ewan Birney[19]

Cell Genomics

CellPress
OPEN ACCESS

Perspective

GA4GH: International policies and standards for data sharing across genomic research and healthcare

Heidi L. Rehm,[1,2,47] Angela J.H. Page,[1,3,*] Lindsay Smith,[3,4] Jeremy B. Adams,[3,4] Gil Alterovitz,[5,47] Lawrence J. Babb,[1] Maxmillian P. Barkley,[6] Michael Baudis,[7,8] Michael J.S. Beauvais,[3,9] Tim Beck,[10] Jacques S. Beckmann,[11] Sergi Beltran,[12,13,14] David Bernick,[1] Alexander Bernier,[9] James K. Bonfield,[15] Tiffany F. Boughtwood,[16,17] Guillaume Bourque,[9,18] Sarion R. Bowers,[15] Anthony J. Brookes,[10] Michael Brudno,[18,19,20,21,38] Matthew H. Brush,[22] David Bujold,[9,18,38] Tony Burdett,[23] Orion J. Buske,[24] Moran N. Cabili,[1] Daniel L. Cameron,[25,26] Robert J. Carroll,[27] Esmeralda Casas-Silva,[123] Debyani Chakravarty,[29] Bimal P. Chaudhari,[30,31] Shu Hui Chen,[32] J. Michael Cherry,[33] Justina Chung,[3,4] Melissa Cline,[34] Hayley L. Clissold,[15] Robert M. Cook-Deegan,[35] Mélanie Courtot,[23] Fiona Cunningham,[23] Miro Cupak,[6] Robert M. Davies,[15] Danielle Denisko,[19] Megan J. Doerr,[36] Lena I. Dolman,[19]

(Author list continued on next page)

Cell Genomics

CellPr
OPEN AC

Technology

The GA4GH Variation Representation Specification: A computational framework for variation representation and federated identification

Alex H. Wagner,[1,2,25,*] Lawrence Babb,[3,*] Gil Alterovitz,[4,5] Michael Baudis,[6] Matthew Brush,[7] Daniel L. Cameron,[8] Melissa Cline,[10] Malachi Griffith,[11] Obi L. Griffith,[11] Sarah E. Hunt,[12] David Kreda,[13] Jennifer M. Lee,[14] Stephanie Li,[15] Javier Lopez,[16] Eric Moyer,[17] Tristan Nelson,[18] Ronak Y. Patel,[19] Kevin Riehle,[19] Peter N. Robinson,[20] Shawn Rynearson,[21] Helen Schuilenburg,[12] Kirill Tsukanov,[12] Brian Walsh,[7] Melissa Konopko,[15] Heidi L. Rehm,[3,22] Andrew D. Yates,[12] Robert R. Freimuth,[23] and Reece K. Hart[3,24,*]

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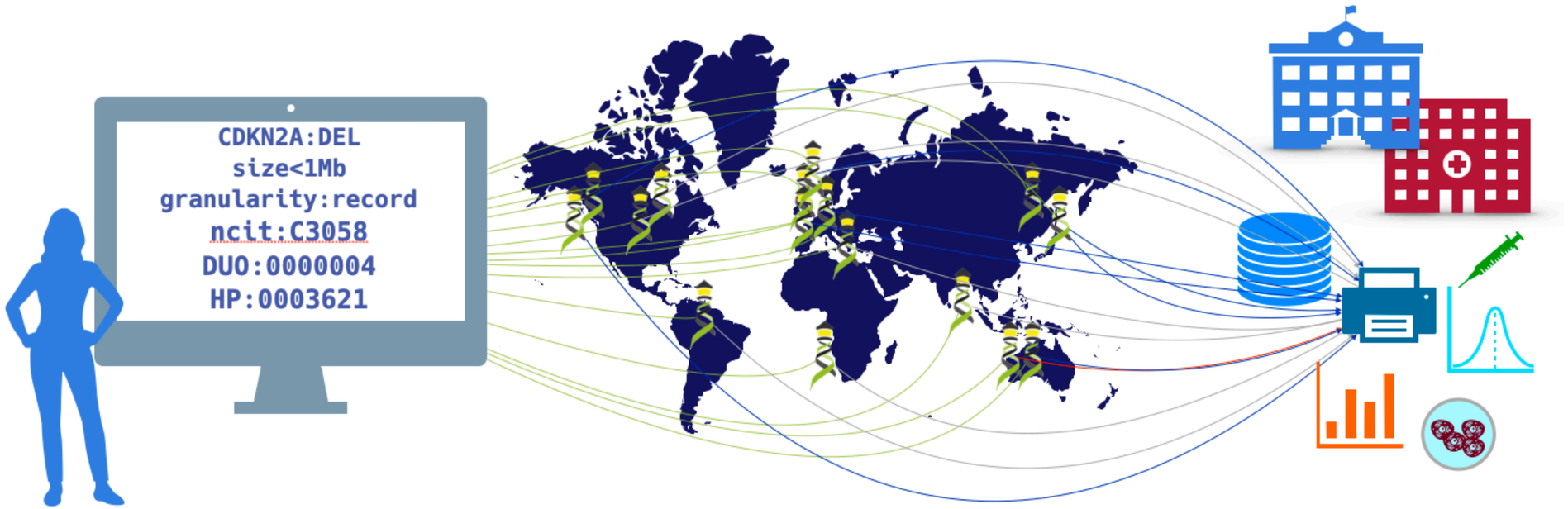
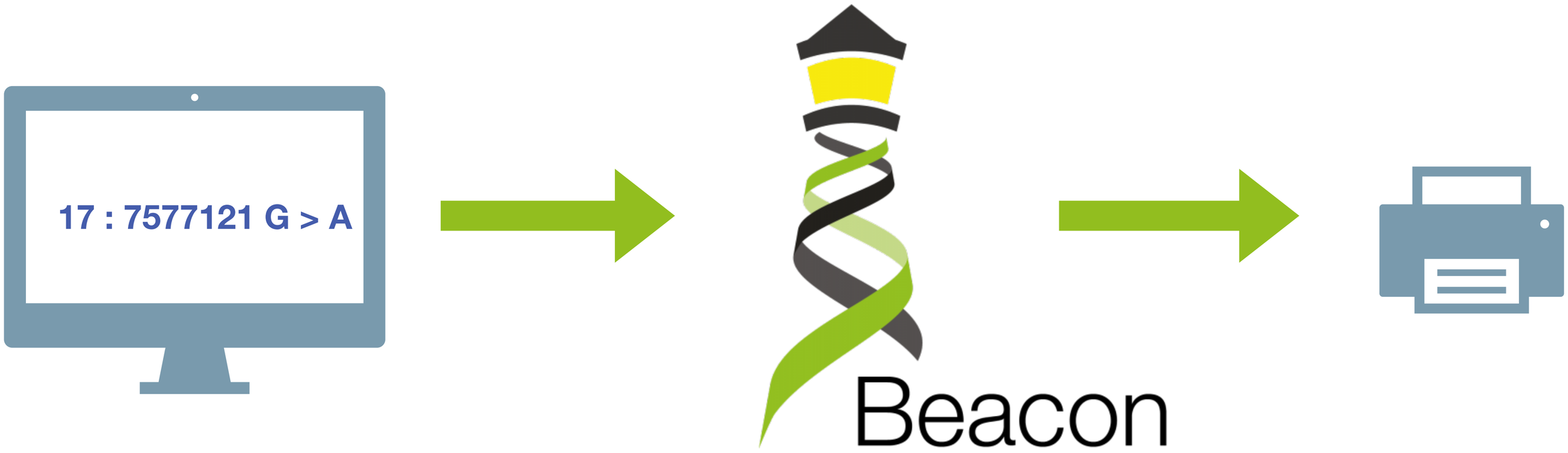


The GA4GH Beacon Protocol

Federating Genomic Discoveries



A ***Beacon*** answers a query for a specific genome variant against individual or aggregate genome collections

YES | **NO** | **\0**

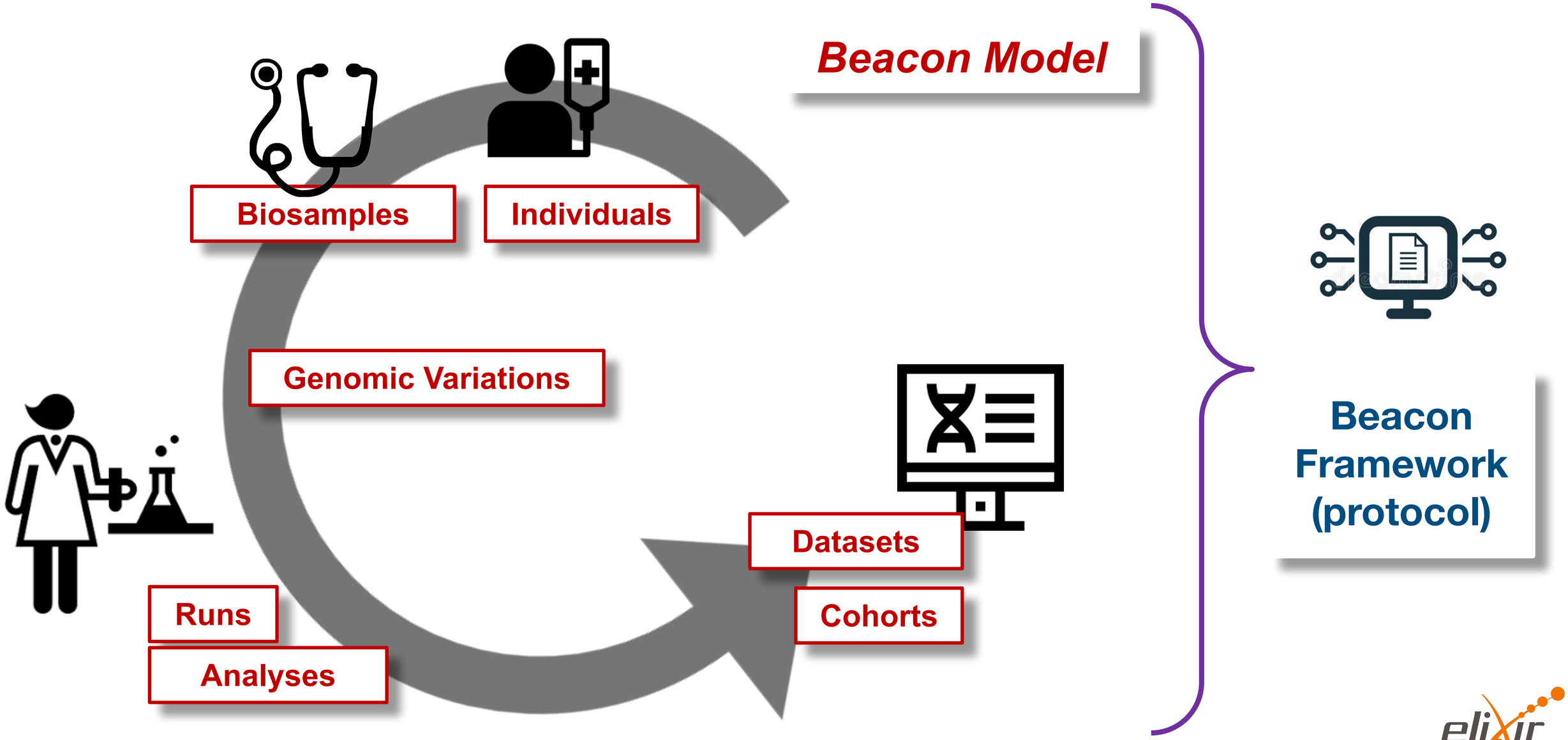
Have you seen this variant? It came up in my patient and we don't know if this is a common SNP or worth following up.

A Beacon network federates *genome variant queries* across databases that support the ***Beacon API***

Here: The variant has been found in **few** resources, and those are from **disease** specific **collections**.

Beacon v2

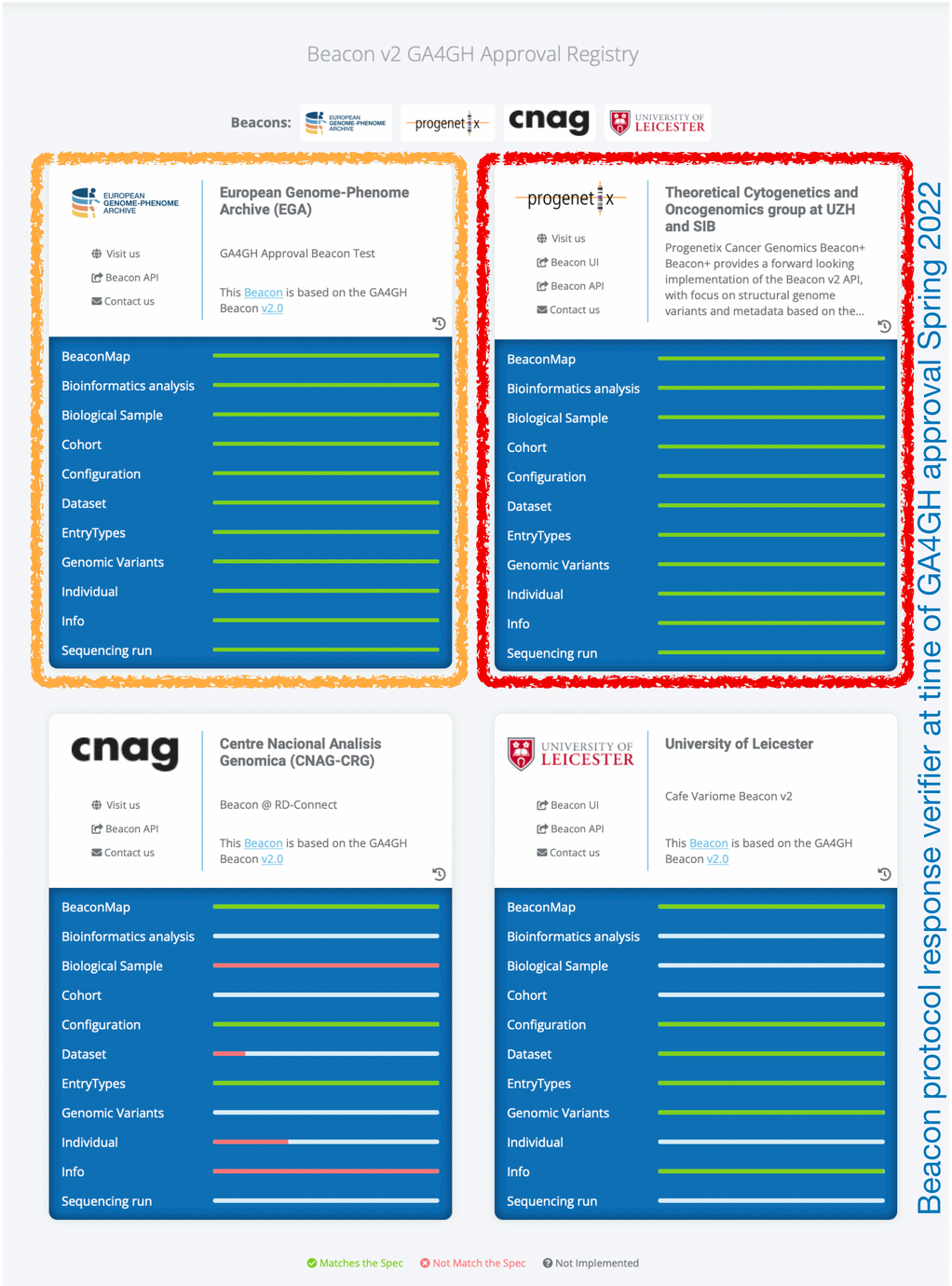
docs.genomebeacons.org



Progenetix & Beacon

Implementation driven standards development

- Progenetix Beacon+ has served as implementation driver since 2016
- prototyping of advanced Beacon features such as
  - ➡ structural variant queries
  - ➡ data handovers
  - ➡ Phenopackets integration



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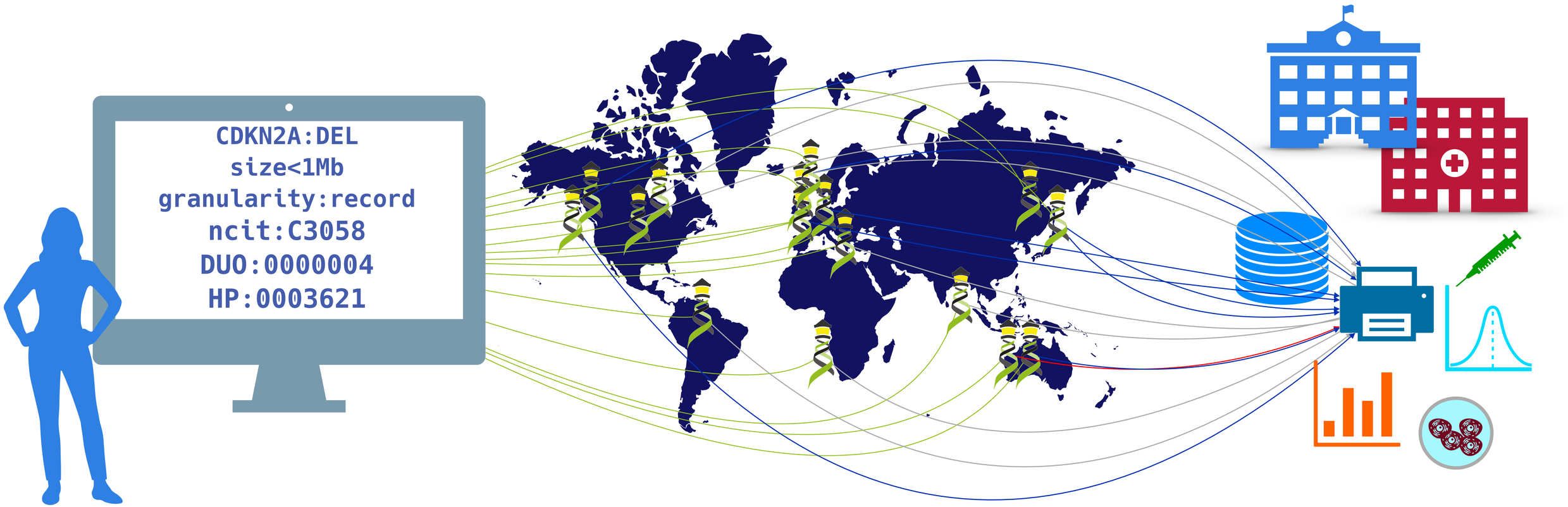
progenetix

elixir



Can you provide data about focal deletions in CDKN2A in Glioblastomas from juvenile patients with unrestricted access?

Beacon *v2* API

The Beacon API v2 represents a simple but powerful **genomics API** for ***federated*** data discovery and retrieval

The Beacon team through the ages

EUROPEAN GENOME-PHENOME ARCHIVE

CRG Centre for Genomic Regulation

Jordi Rambla
Arcadi Navarro
Roberto Ariosa
Manuel Rueda
Lauren Fromont
Mauricio Moldes
Claudia Vasallo
Babita Singh
Sabela de la Torre
Marta Ferri
Fred Haziza

CSC

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Teemu Kataja
Ilkka Lappalainen
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Tim Beck
Colin Veal
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Institut national de la santé et de la recherche médicale

David Salgado

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Centro Nacional de Supercomputación

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JM Fernández

DisGeNET

Laura Furlong
Janet Piñero

elixir

B1MG

Serena Scollen
Gary Saunders
Giselle Kerry
David Lloyd

H3Africa
Human Heredity & Health in Africa

Nicola Mulder
Mamana Mbiyavanga
Ziyaad Parker

EU Can CAN.

David Torrents

AUTISM SPEAKS

Dean Hartley

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Fundación Progreso y Salud
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Javier Pérez
J.L. Fernández
Gema Roldan

CINECA

Thomas Keane
Melanie Courtot
Jonathan Dursi

Heidi Rehm
Ben Hutton

Toshiaki Katayama

GEM Japan

Stephane Dyke

DNASTACK

Marc Fiume
Miro Cupak

BRCA EXCHANGE

Melissa Cline

ENA

EMBL-EBI

Diana Lemos

EUROPEAN JOINT PROGRAMME RARE DISEASES

VICC Variant Interpretation for Cancer Consortium

GA4GH Phenopackets
Peter Robinson
Jules Jacobsen

GA4GH VRS
Alex Wagner
Reece Hart

Beacon PRC
Alex Wagner
Jonathan Dursi
Mamana Mbiyavanga

Alice Mann
Neerjah Skantharajah

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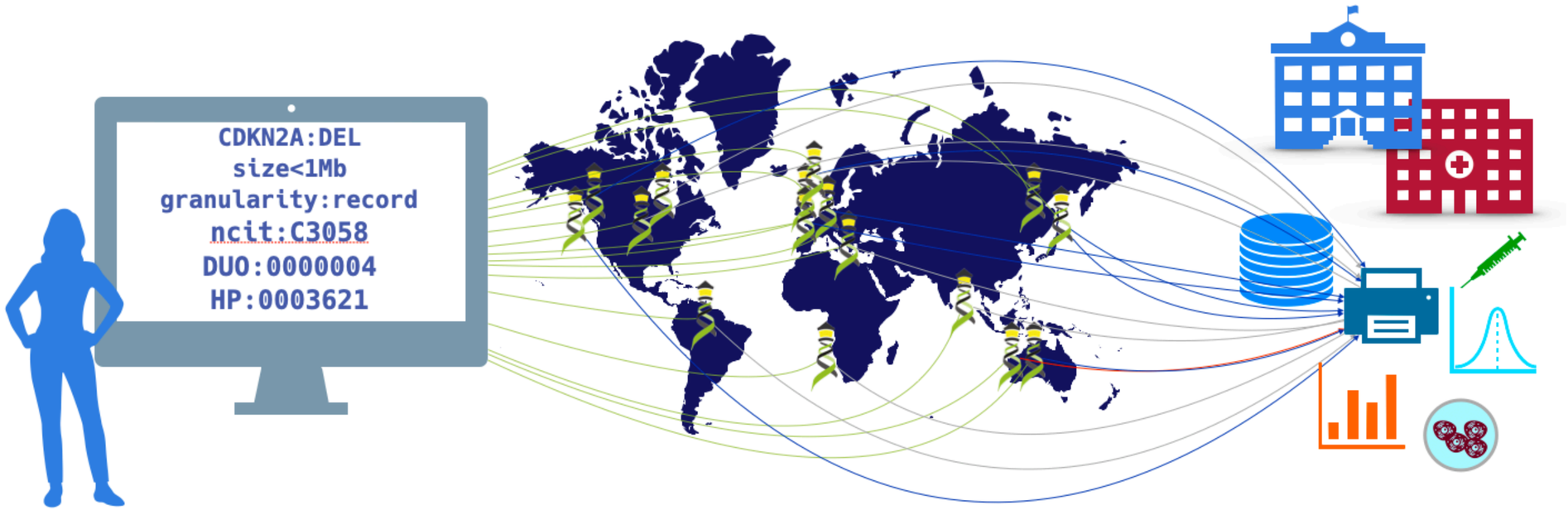
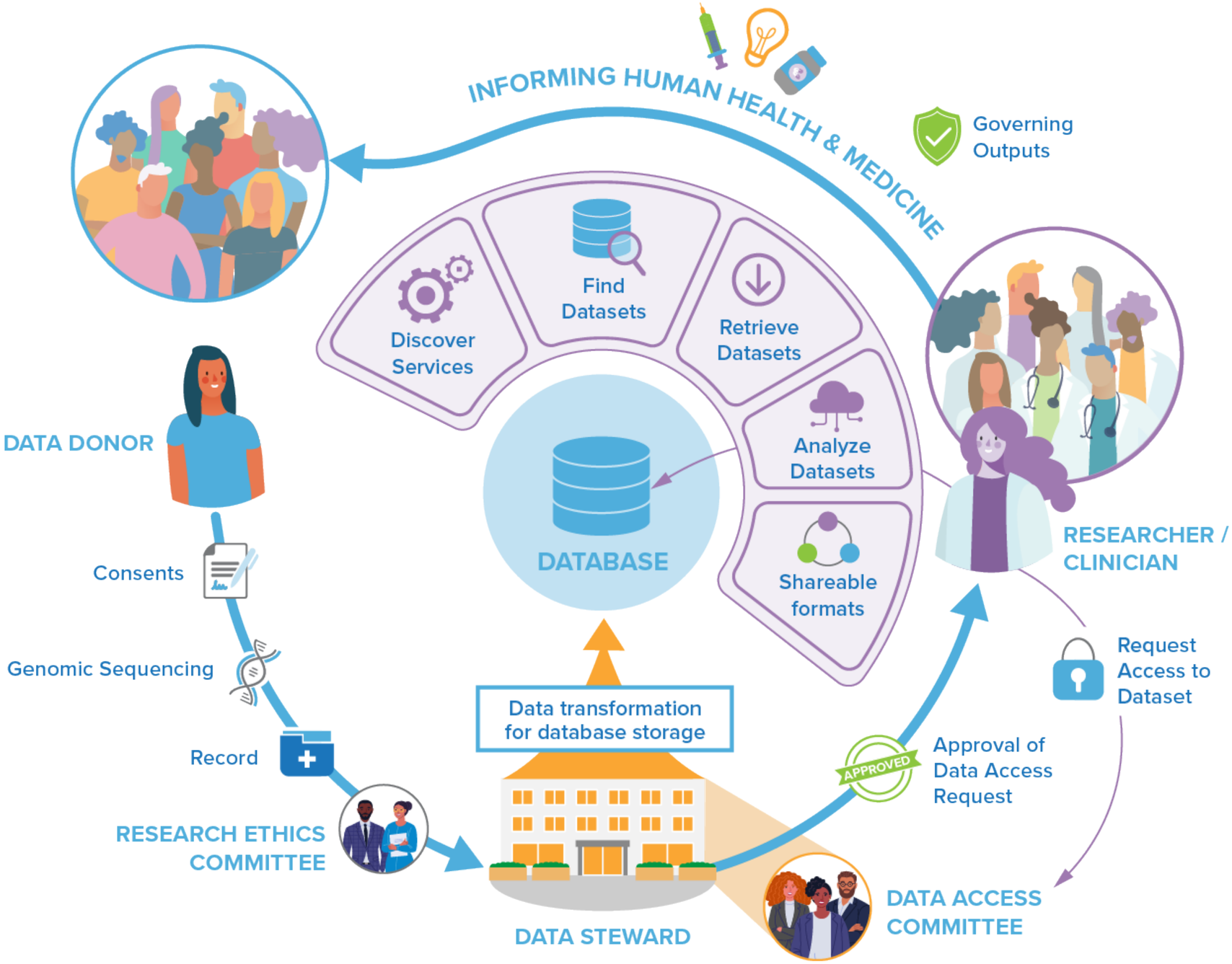
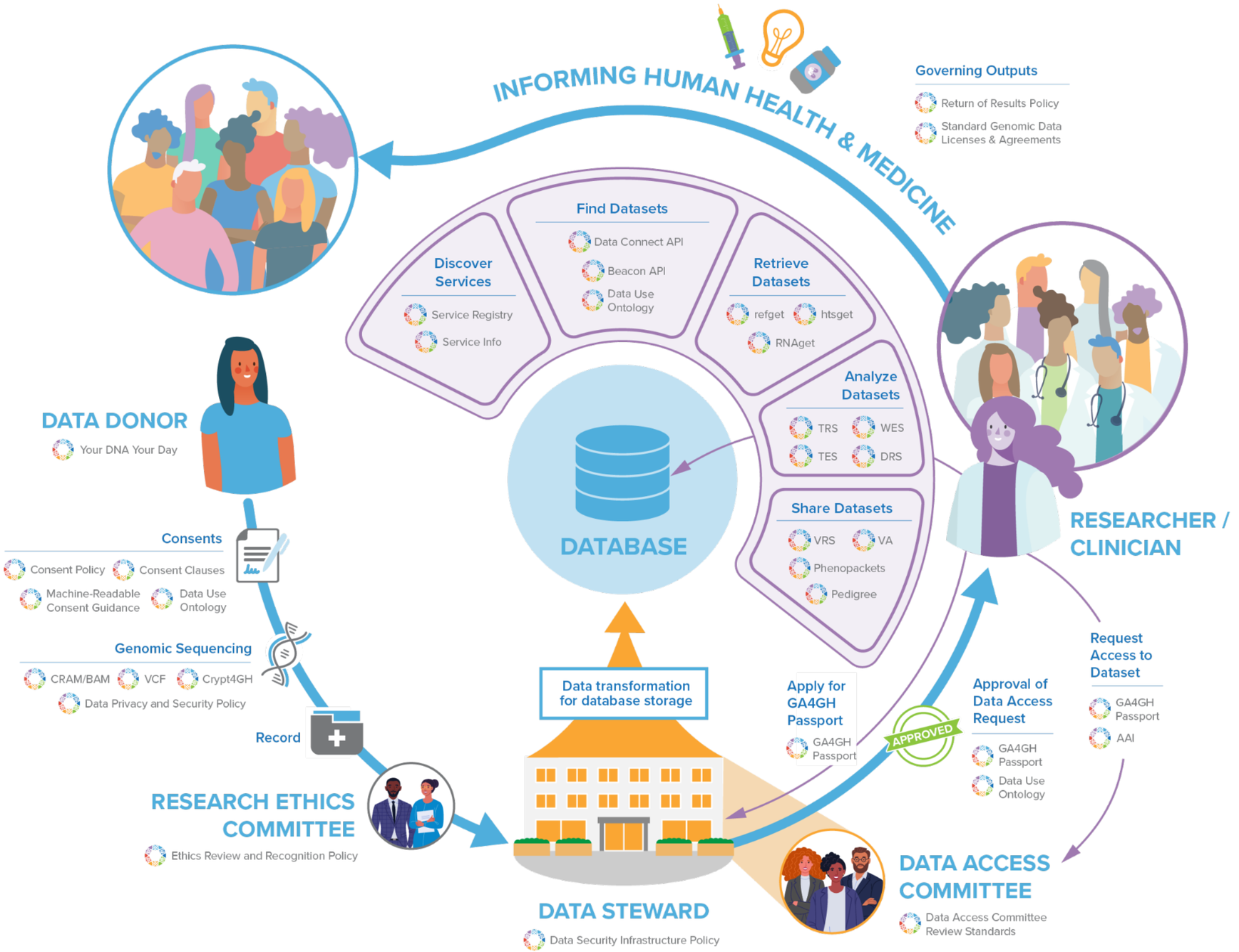


The GA4GH Beacon Protocol

... is only one part of the GA4GH ecosystem

GA4GH ecosystem and outputs


INFORMING HUMAN HEALTH & MEDICINE
Governing Outputs
Discover Services
Find Datasets
Retrieve Datasets
Analyze Datasets
Shareable formats
DATABASE
DATA DONOR
Consents
Genomic Sequencing
Record
RESEARCH ETHICS COMMITTEE
Data transformation for database storage
DATA STEWARD
APPROVED
Approval of Data Access Request
Request Access to Dataset
RESEARCHER / CLINICIAN
DATA ACCESS COMMITTEE


INFORMING HUMAN HEALTH & MEDICINE
Governing Outputs
Return of Results Policy
Standard Genomic Data Licenses & Agreements
Find Datasets
Data Connect API
Beacon API
Data Use Ontology
Discover Services
Service Registry
Service Info
Retrieve Datasets
refget
htsget
RNAget
Analyze Datasets
TRS
WES
TES
DRS
Share Datasets
VRS
VA
Phenopackets
Pedigree
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Apply for GA4GH Passport
GA4GH Passport
APPROVED
Approval of Data Access Request
GA4GH Passport
Data Use Ontology
Request Access to Dataset
GA4GH Passport
AAI
RESEARCH ETHICS COMMITTEE
Ethics Review and Recognition Policy
DATA STEWARD
Data Security Infrastructure Policy
DATA ACCESS COMMITTEE
Data Access Committee Review Standards

Global Collaborations

Global Alliance for Genomics & Health

International HundredK+ Cohorts Consortium

Global Genomic Medicine Consortium

Beyond One Million Genomes Project

WORLD ECONOMIC FORUM

THE MEDICAL GENOME INITIATIVE

World Health Organization Science Council

Human Pangenome Project (HPP) / Human Pangenome Reference Consortium (HPRC)

INTERNATIONAL COMMON DISEASE ALLIANCE | Maps to Mechanisms to Medicine

Public Health Alliance for Genomic Epidemiology

CRDSA Clinical Research Data Sharing Alliance

ICODA International COVID-19 Data Alliance

elixir

HUMAN GENOME ORGANISATION HUGO

THE HUMAN VARIOME PROJECT

HGVS HUMAN GENOME VARIATION SOCIETY

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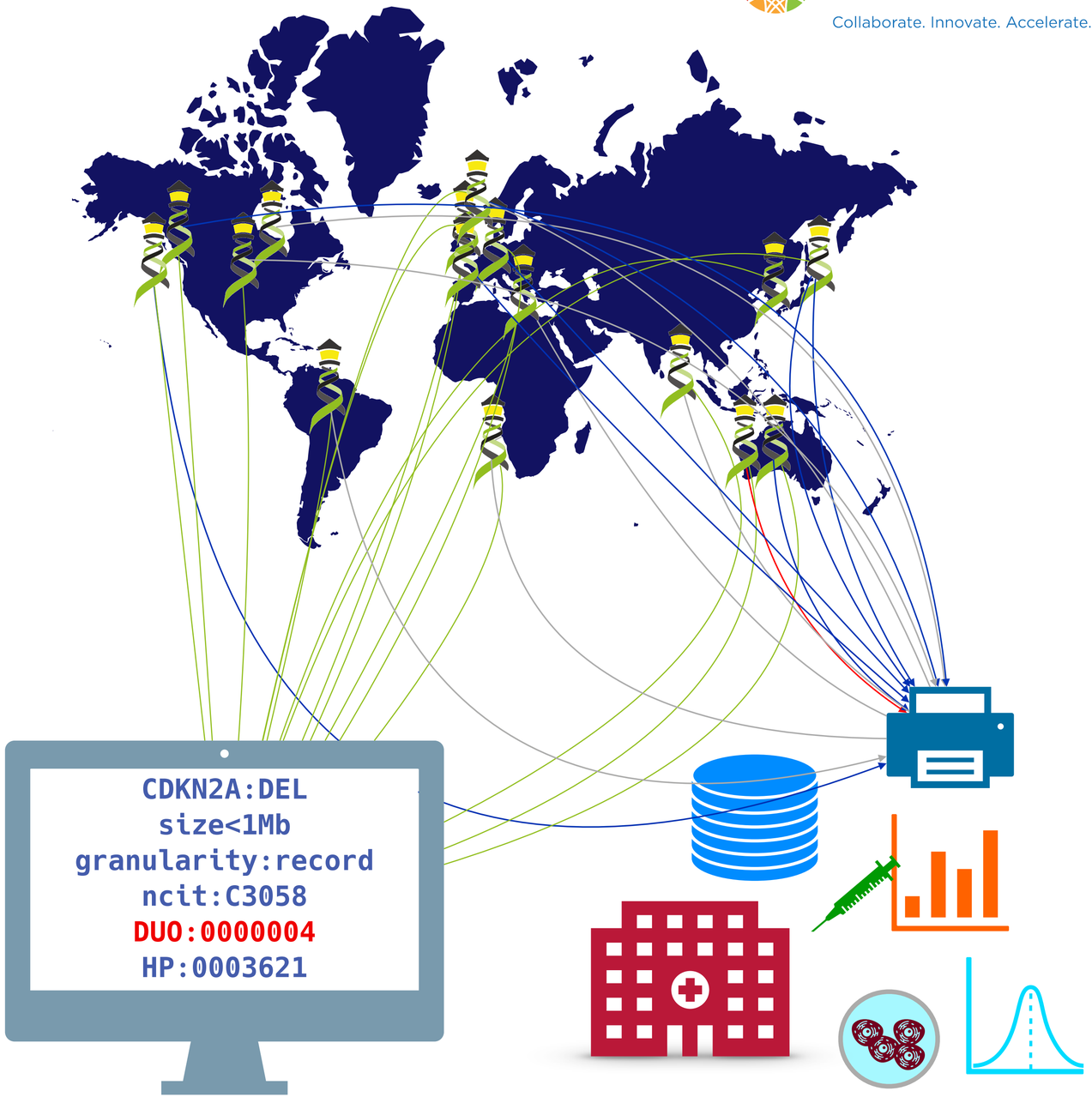
What Can You Do?

- implement procedures and standards supporting **data discovery** (FAIR principles) and federation approaches
- forward looking consent and data protection models adhering to **ORD** principles ("*as secure as necessary, as open as possible*")
- **support** and/or get involved with international **data standards** efforts and projects

➡ **Collaborate!**



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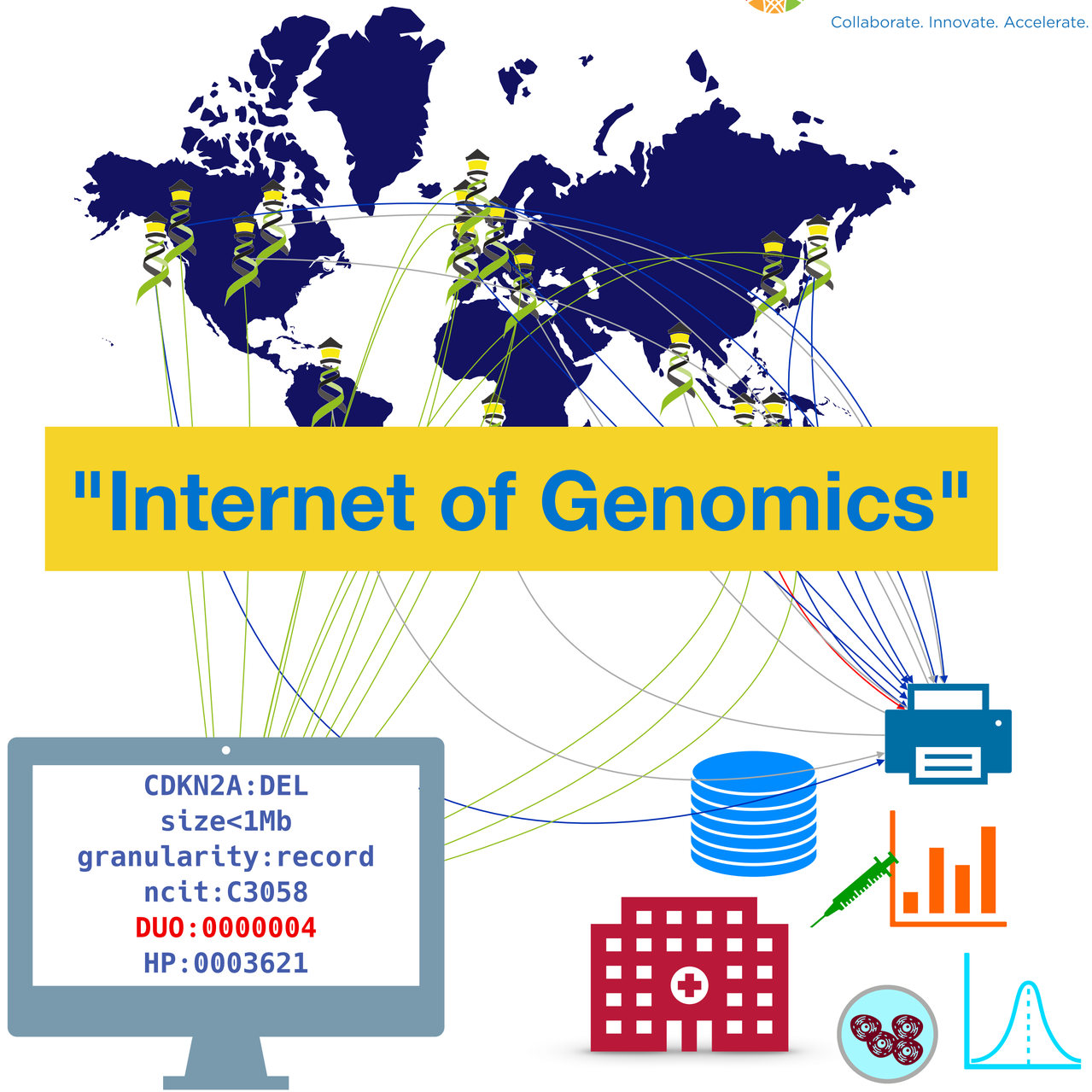

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