

# **Genomic Data & Privacy**

## **Risks & opportunities**

**Michael Baudis | UZH BIO392 | October 2021**

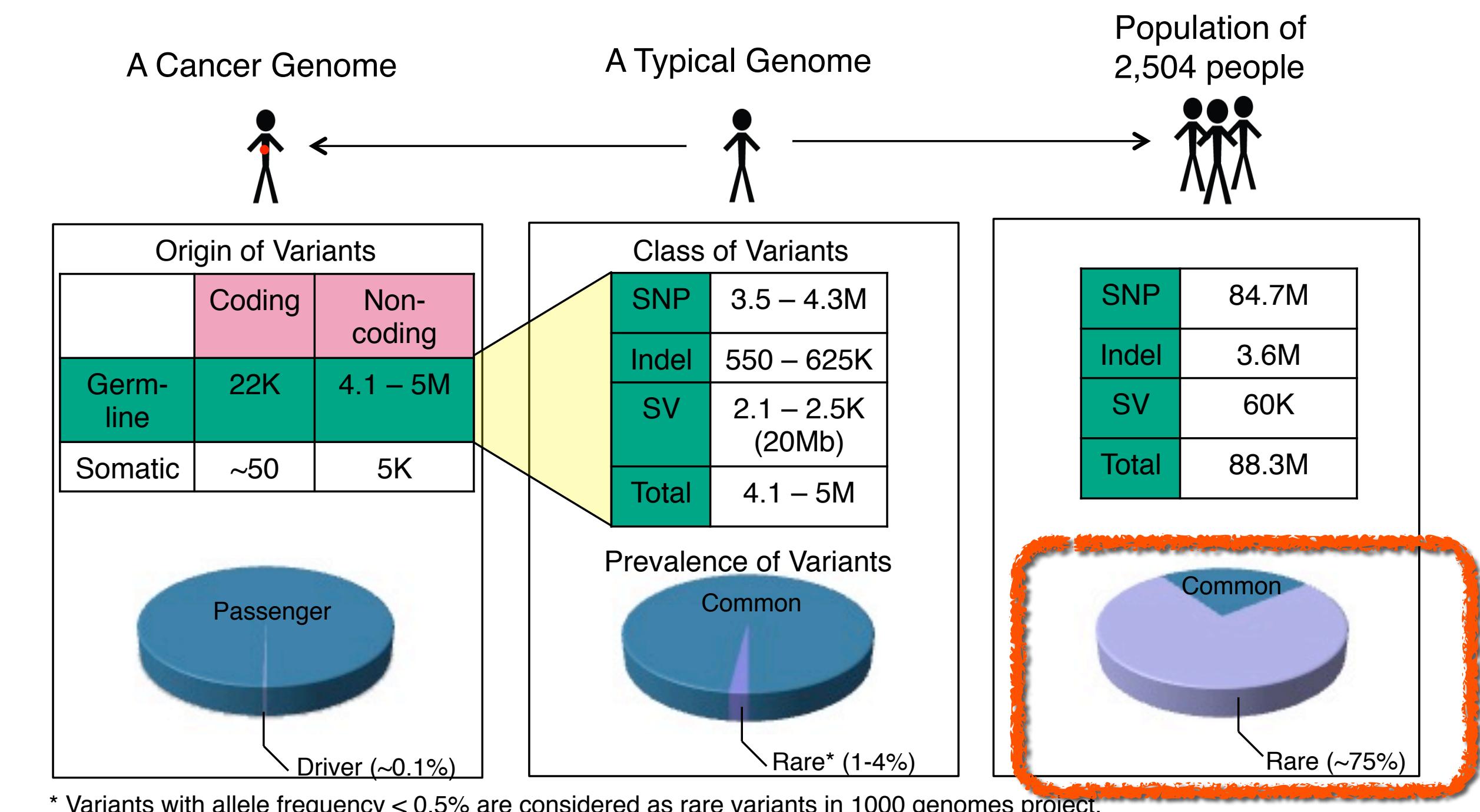
The trouble with human genome variation



# Finding Somatic Mutations In Cancer

## Many Needles in a Large Haystack

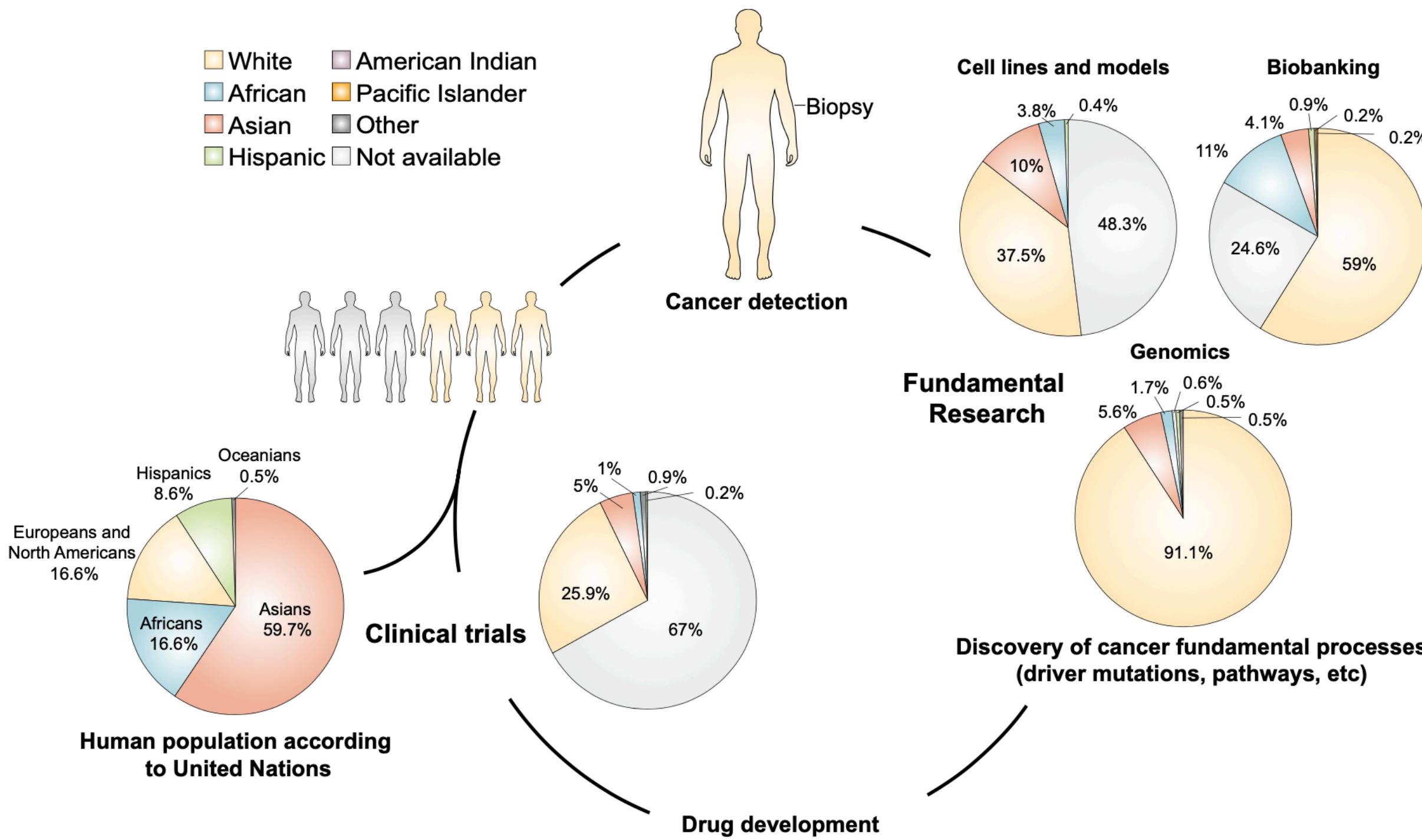
- a typical human genome (~3 billion base pairs) has ~5 million variants
- most of them are "**rare**"; i.e. can only be identified as recurring when sequencing thousands of people
- cancer cells accumulate additional variants, only **few** of which ("**drivers**") are relevant for the disease



The 1000 Genomes Project Consortium, Nature. 2015. 526:68-74  
Khurana E. et al. Nat. Rev. Genet. 2016. 17:93-108

Graphic adapted from Mark Gerstein (GersteinLab.org; @markgerstein)

# Limited Population Diversity in Cancer Studies



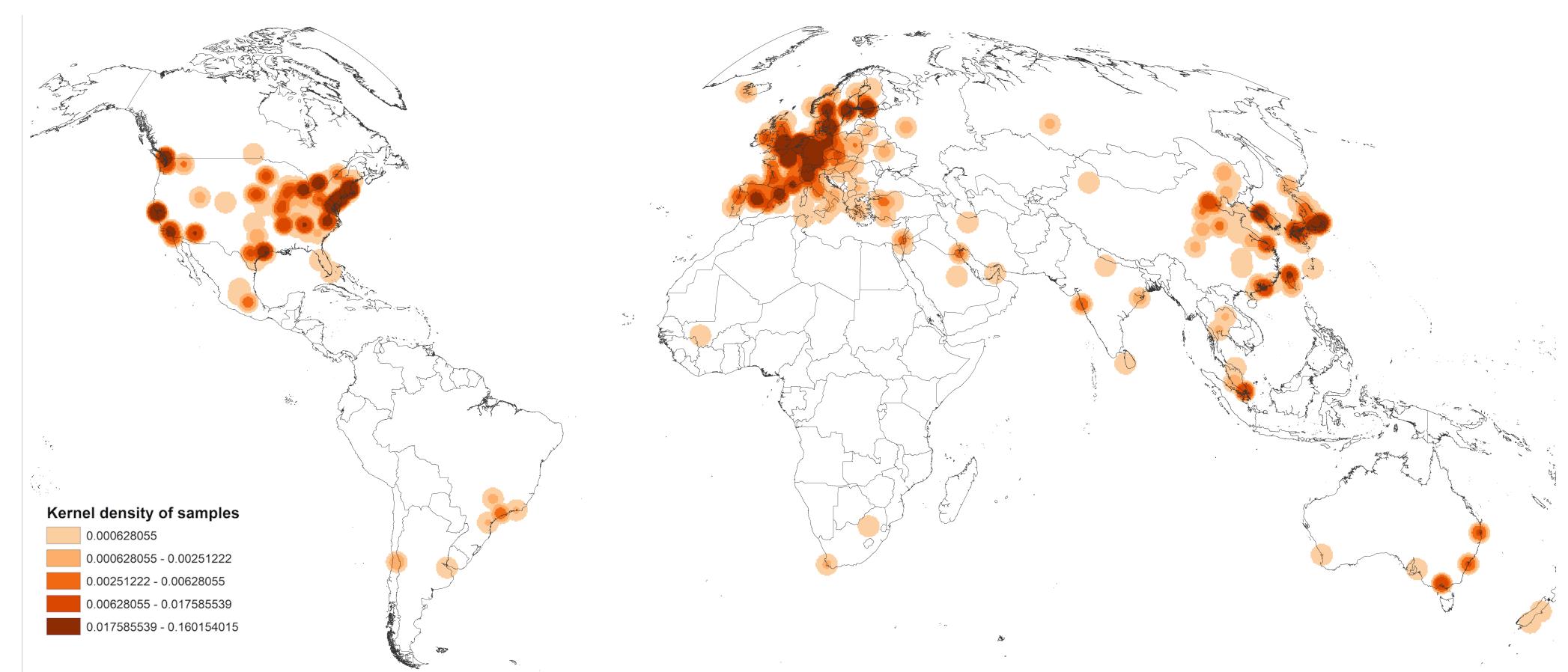
**Figure 1.** Racial/Ethnic disparities in cancer research. Racial/ethnic inclusion was studied in several aspects of oncological research, from cell lines and patient-derived xenografts to biobanking, genomics and clinical trials.

Guerrero S, López-Cortés A, Indacochea A, et al. Analysis of Racial/Ethnic Representation in Select Basic and Applied Cancer Research Studies. *Sci Rep.* 2018;8(1):13978.

## Publication Landscape of Cancer CNV Profiling

Publication statistics for cancer genome screening studies. The graphic shows our assessment of publications reporting whole-genome screening of cancer samples, using molecular detection methods (chromosomal CGH, genomic array technologies, whole exome and genome sequencing).

For the years 1993-2018, we found 3'229 publications reporting 174'530 individual samples in single series from 1 to more than 1000 samples. Y-axis and size of the dots correspond to the sample number; the color codes indicate the technology used.



# The vision: Federation of data



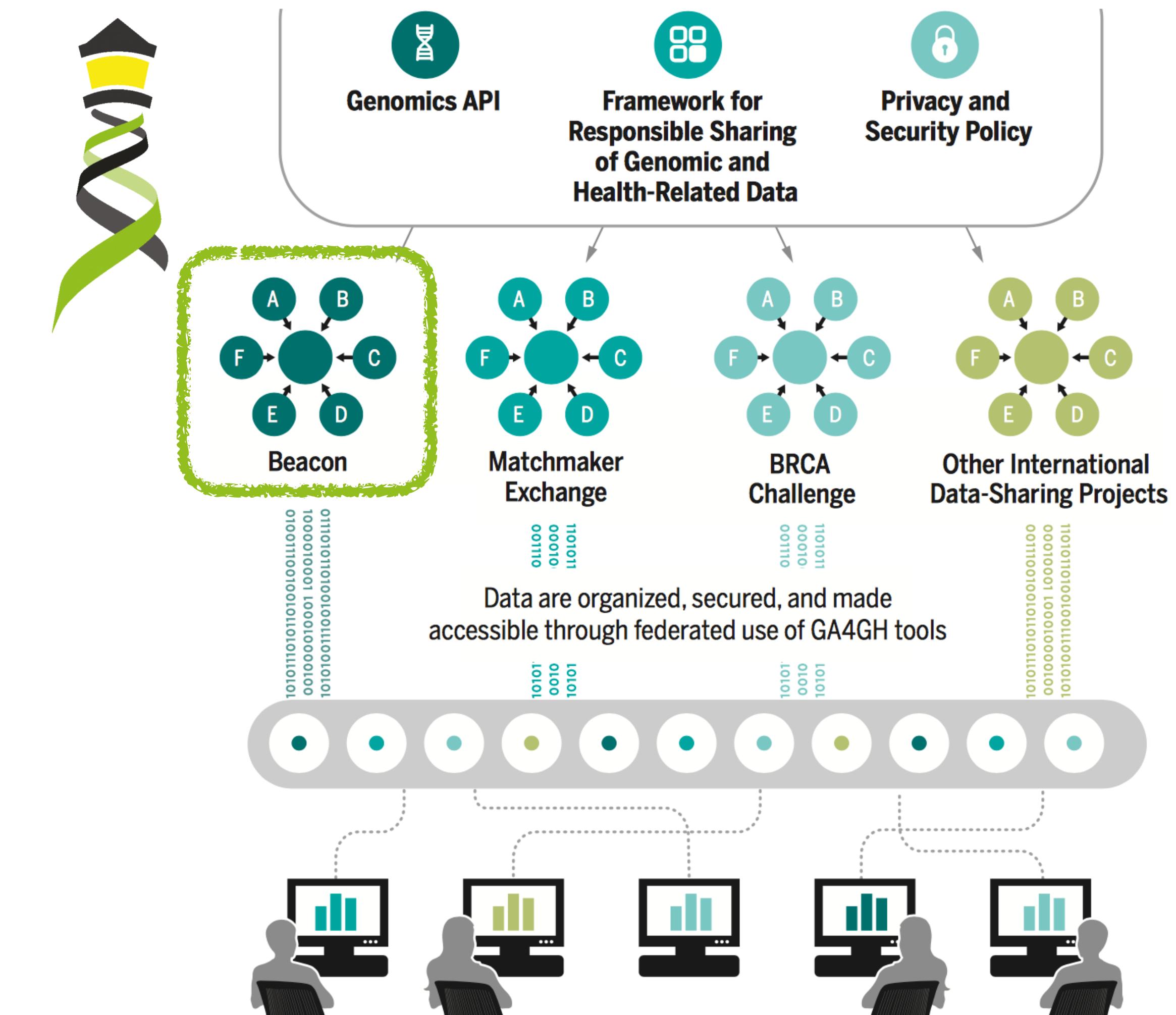


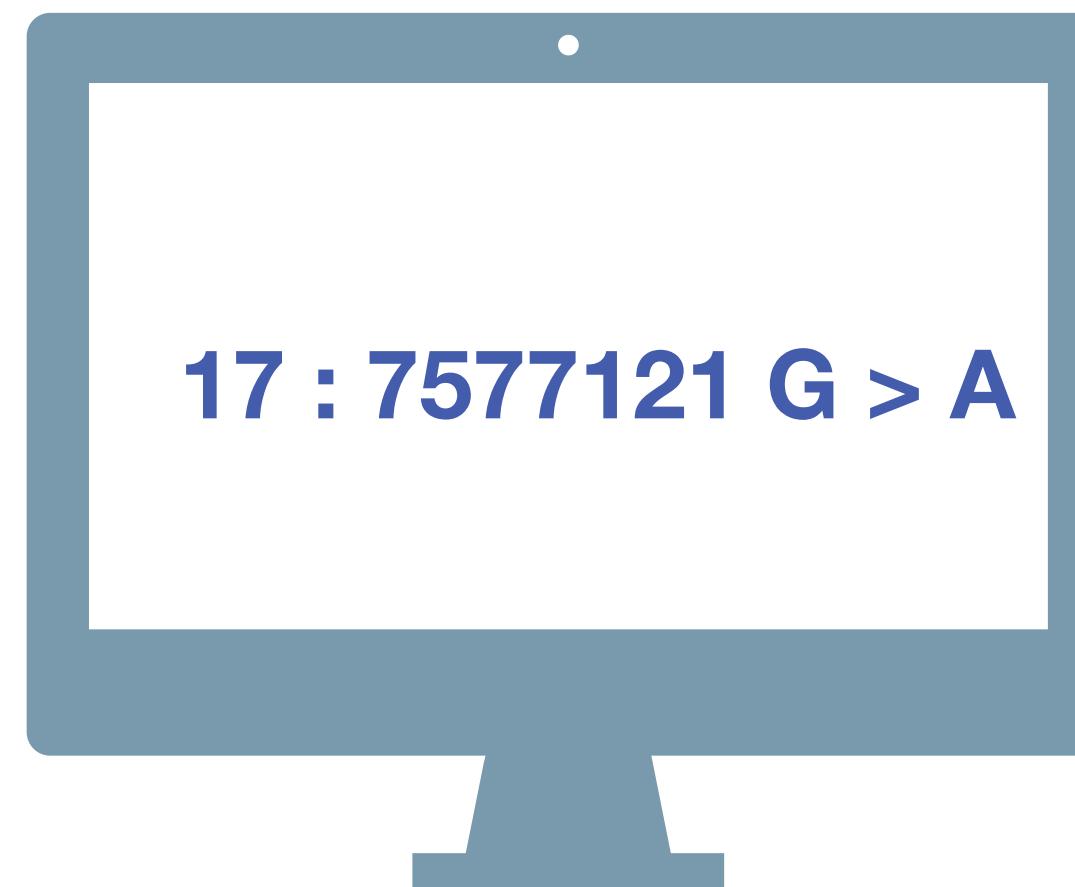
## GENOMICS

# *A federated ecosystem for sharing genomic, clinical data*

Silos of genome data collection are being transformed into seamlessly connected, independent systems

**A federated data ecosystem.** To share genomic data globally, this approach furthers medical research without requiring compatible data sets or compromising patient identity.

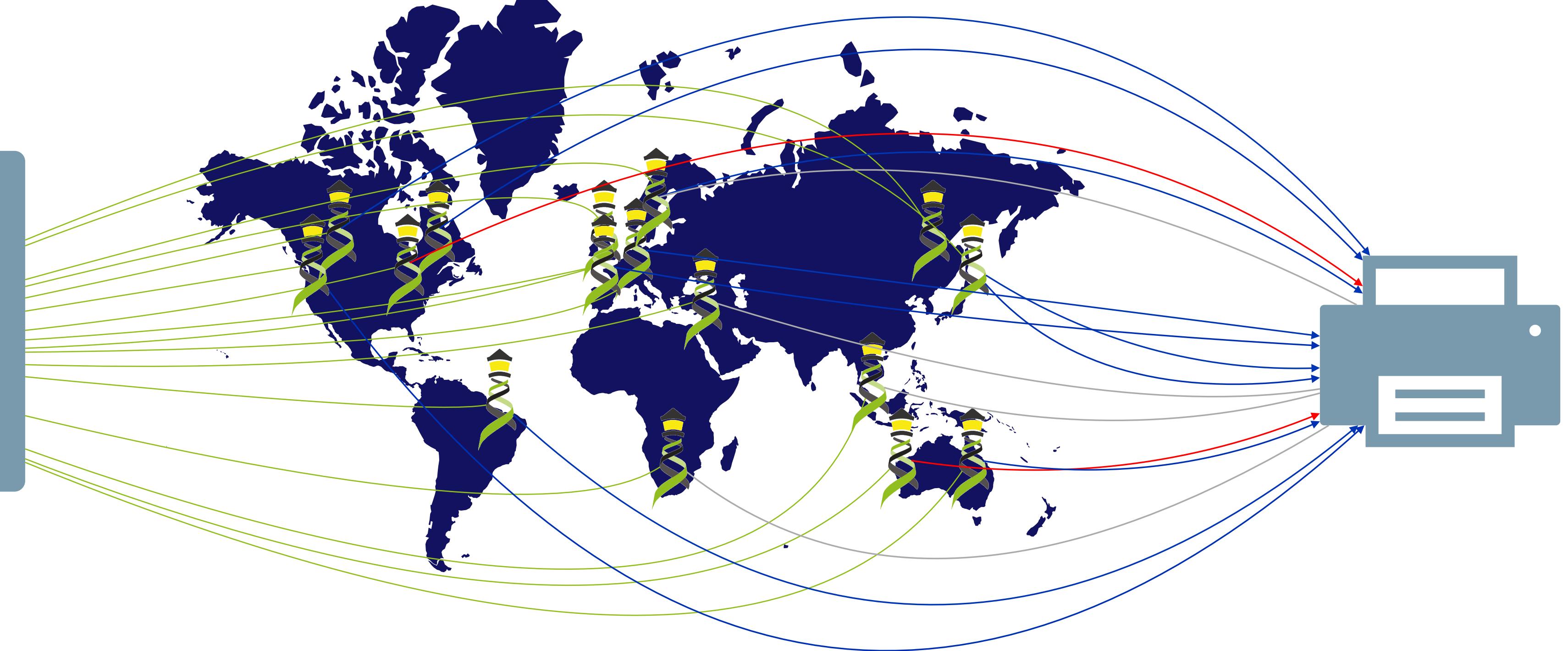
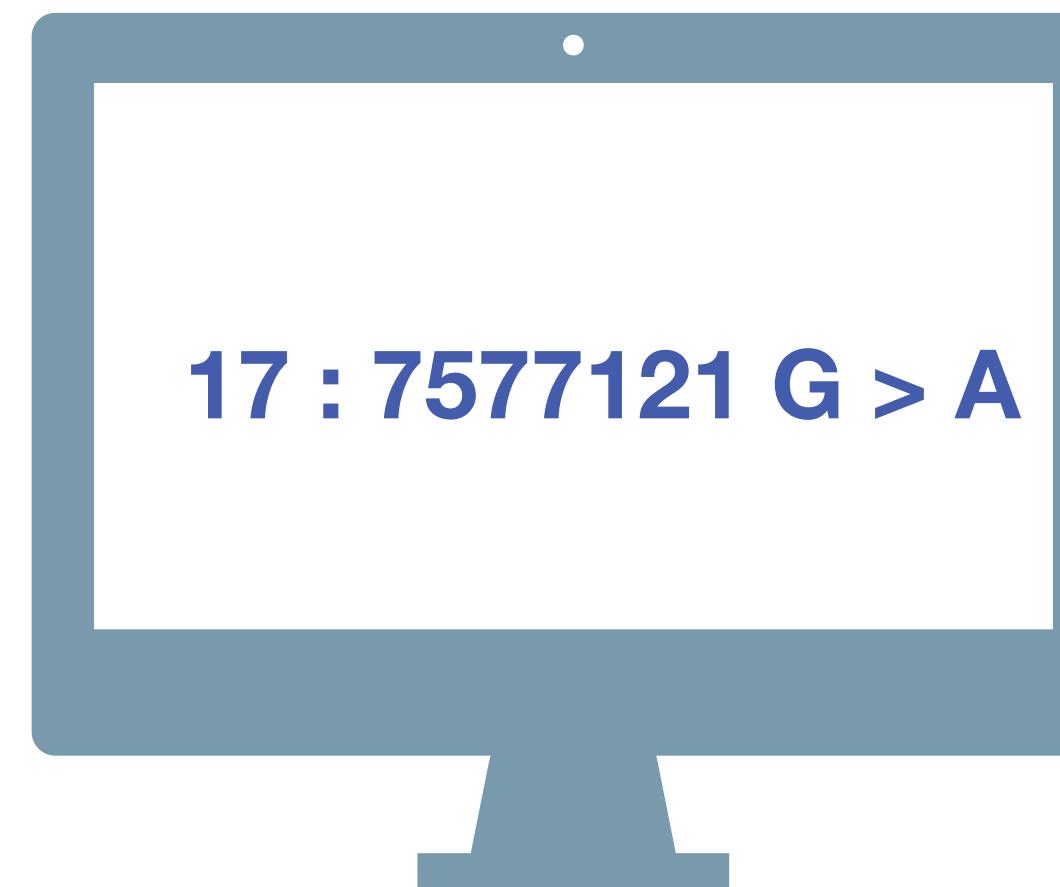




# Beacon

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 Project in 2016

An open web service that tests the willingness of international sites to share genetic data.



Beacon Network

Search Beacons

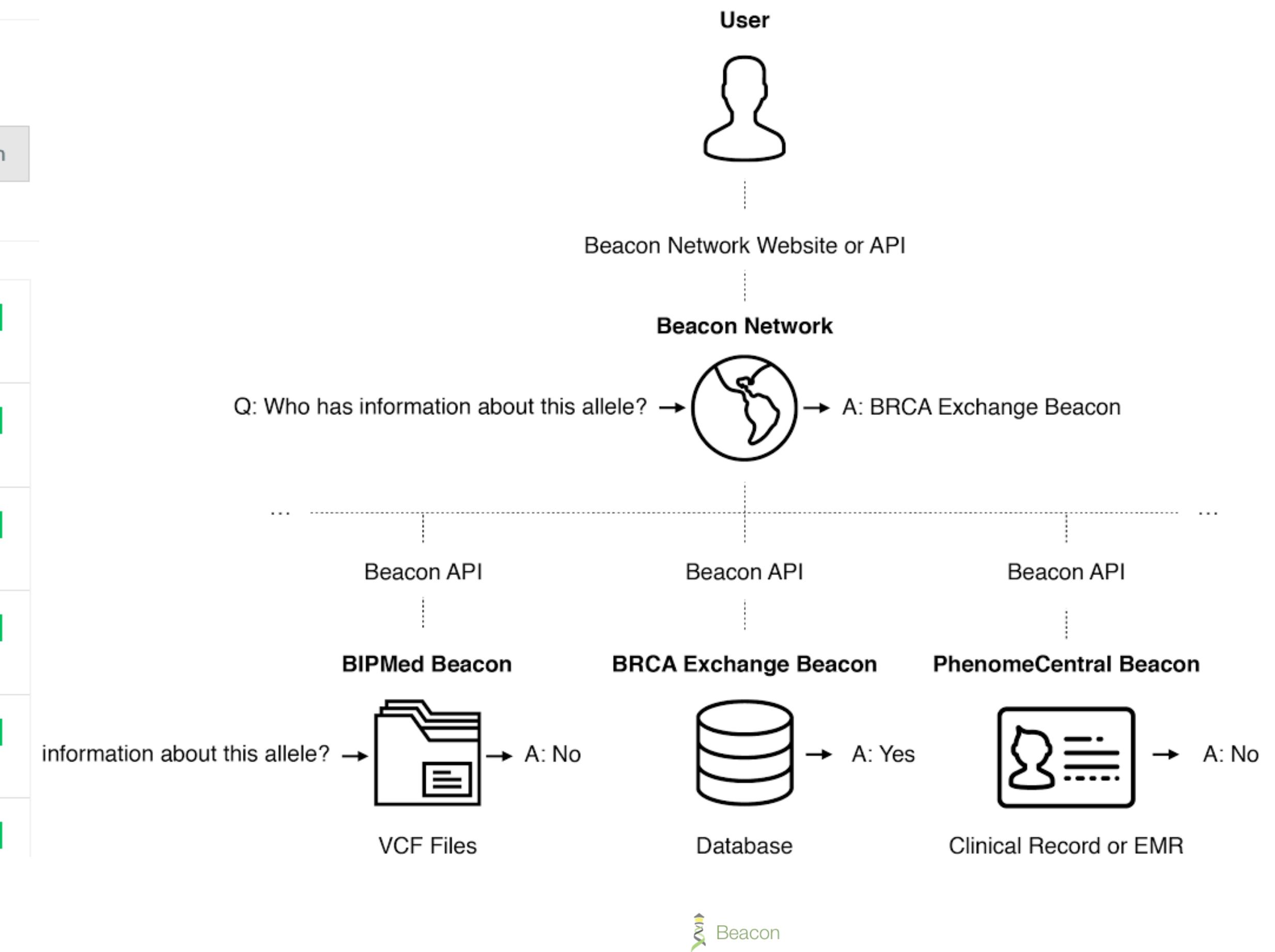
Search all beacons for allele

GRCh37 ▾ 10:118969015 C / CT Search

Response All None  
 Found 16  
 Not Found 27  
 Not Applicable 22

Organization All None  
 AMPLab, UC Berkeley  
 BGI  
 BioReference Laborato...  
 Brazilian Initiative on ...  
 BRCA Exchange  
 Broad Institute  
 Centre for Genomic R...  
 Centro Nacional de A...  
 Curoverse  
 EMBL European Bio...  
 Global Alliance for G...  
 Google  
 Institute for Systems ...  
 Instituto Nacional de ...

BioReference	Hosted by BioReference Laboratories	Found
Catalogue of Somatic Mutations in Cancer	Hosted by Wellcome Trust Sanger Institute	Found
Cell Lines	Hosted by Wellcome Trust Sanger Institute	Found
Conglomerate	Hosted by Global Alliance for Genomics and Health	Found
COSMIC	Hosted by Wellcome Trust Sanger Institute	Found
dbGaP: Combined GRU Catalog and NHLBI Exome Seq...		Found



35+

Organizations

90+

Beacons

200+

Datasets

100K+

Releases  
Individuals

Date	Tag	Title
2016-01-24	v0.4.0	Beacon
2016-05-31	v0.3.0	Beacon



# Genome Beacons Compromise Security?

Querying for thousands of specific SNV occurrences in a genomic data pool can identify individuals in an anonymized genomic data collection

Stanford researchers identify potential security hole in genomic data-sharing network

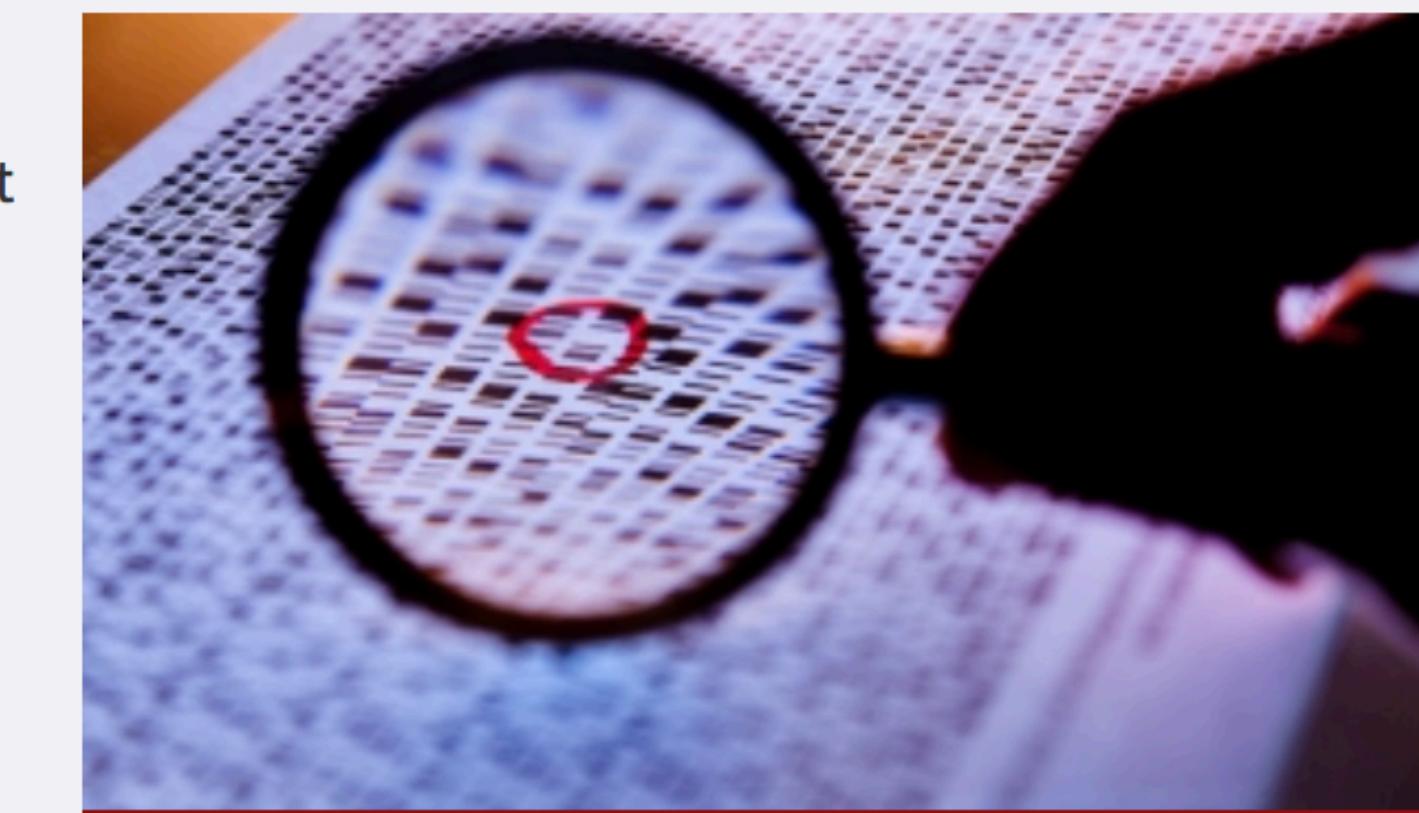
Hackers with access to a person's genome might find out if that genome is in an international network of disease databases.

OCT 29  
2015

Sharing genomic information among researchers is critical to the advance of biomedical research. Yet genomic data contains identifiable information and, in the wrong hands, poses a risk to individual privacy. If someone had access to your genome sequence — either directly from your saliva or other tissues, or from a popular genomic information service — they could check to see if you appear in a database of people with certain medical conditions, such as heart disease, lung cancer or autism.

Work by a pair of researchers at the [Stanford University School of Medicine](#) makes that genomic data more secure. [Suyash Shringarpure](#), PhD, a postdoctoral scholar in genetics, and [Carlos Bustamante](#), PhD, a professor of genetics, have demonstrated a technique for hacking a network of global genomic databases and how to prevent it. They are working with investigators from the Global Alliance for Genomics and Health on implementing preventive measures.

The work, published Oct. 29 in *The American Journal of Human Genetics*, also bears importantly on the larger question of how to analyze mixtures of genomes, such as those from different people at a crime scene.



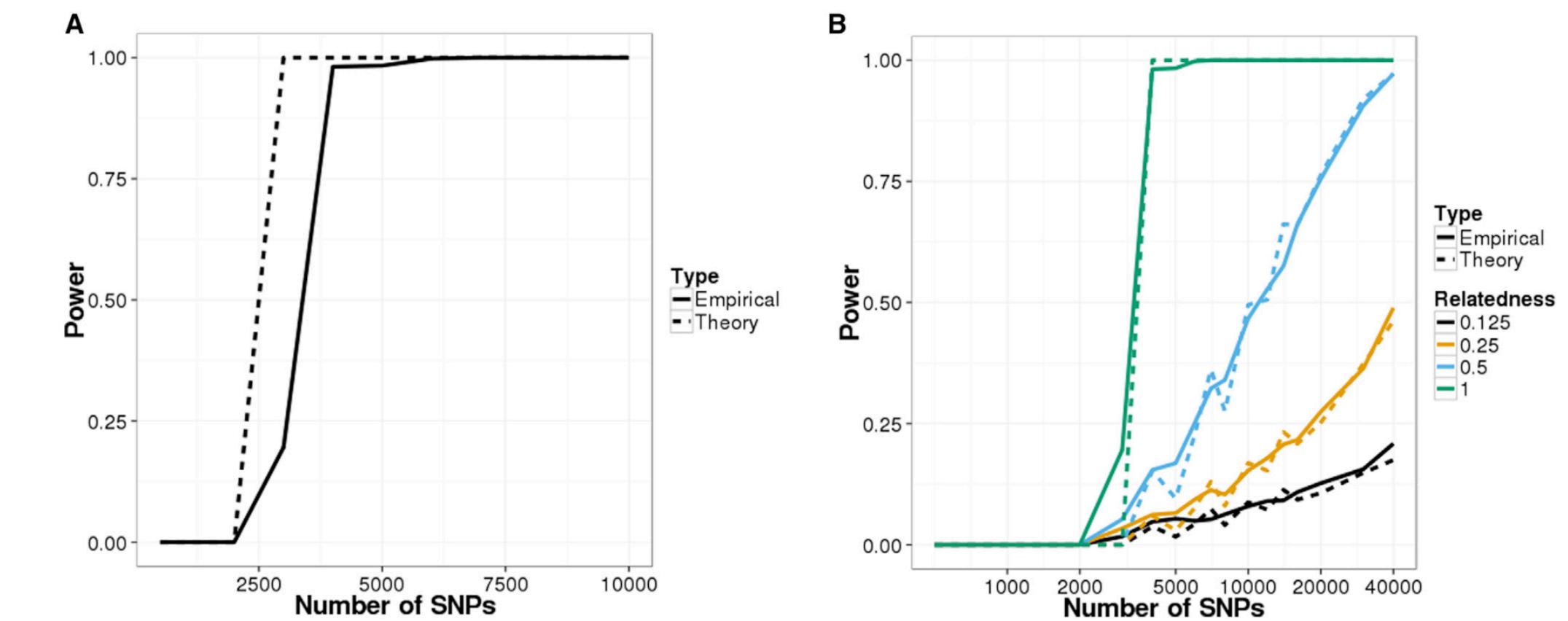
Stanford researchers are working with the Global Alliance for Genomics and Health to make genomic information in the Beacon Project more secure.  
*Science photo/Shutterstock*

# IDENTIFICATION OF INDIVIDUALS FROM MIXED COLLECTIONS USING RARE ALLELES

## Privacy Risks from Genomic Data-Sharing Beacons

Suyash S. Shringarpure<sup>1,\*</sup> and Carlos D. Bustamante<sup>1,\*</sup>

The human genetics community needs robust protocols that enable secure sharing of genomic data from participants in genetic research. Beacons are web servers that answer allele-presence queries—such as “Do you have a genome that has a specific nucleotide (e.g., A) at a specific genomic position (e.g., position 11,272 on chromosome 1)?”—with either “yes” or “no.” Here, we show that individuals in a beacon are susceptible to re-identification even if the only data shared include presence or absence information about alleles in a beacon. Specifically, we propose a likelihood-ratio test of whether a given individual is present in a given genetic beacon. Our test is not dependent on allele frequencies and is the most powerful test for a specified false-positive rate. Through simulations, we showed that in a beacon with 1,000 individuals, re-identification is possible with just 5,000 queries. Relatives can also be identified in the beacon. Re-identification is possible even in the presence of sequencing errors and variant-calling differences. In a beacon constructed with 65 European individuals from the 1000 Genomes Project, we demonstrated that it is possible to detect membership in the beacon with just 250 SNPs. With just 1,000 SNP queries, we were able to detect the presence of an individual genome from the Personal Genome Project in an existing beacon. Our results show that beacons can disclose membership and implied phenotypic information about participants and do not protect privacy *a priori*. We discuss risk mitigation through policies and standards such as not allowing anonymous pings of genetic beacons and requiring minimum beacon sizes.

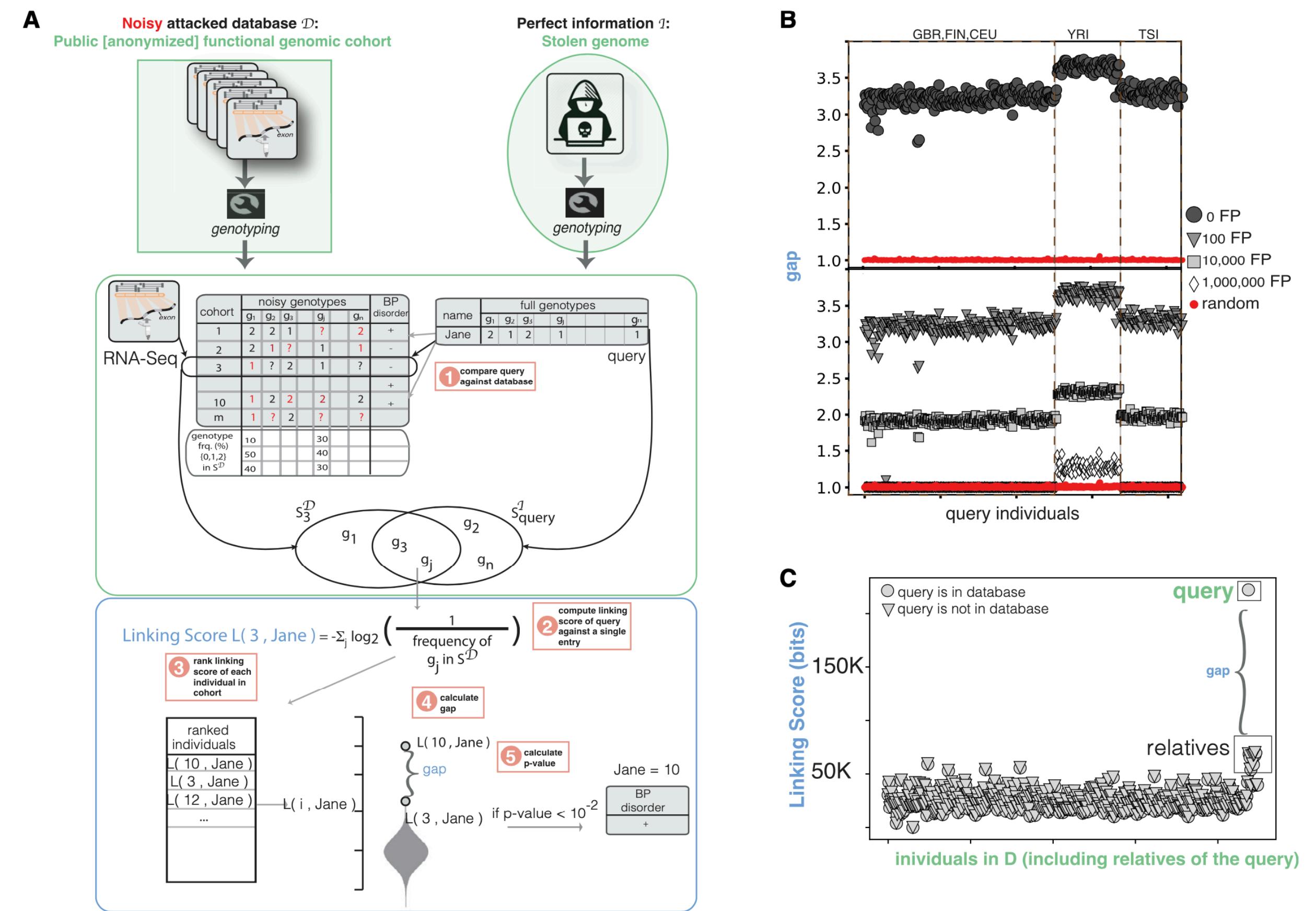


**Figure 1. Power of Re-identification Attacks on Beacons Constructed with Simulated Data**  
Power curves for the likelihood-ratio test (LRT) on (A) a simulated beacon with 1,000 individuals and (B) detecting relatives in the simulated beacon. The false-positive rate was set to 0.05 for all scenarios.

- ▶ rare allelic variants can be used to identify an individual (or her relatives) in a genome collection without having access to individual datasets
- ▶ however, such an approach requires previous knowledge about the individual's SNPs

# Information Leakage from Functional Genomics Data

- many research studies contain "functional" genomics data, e.g. from expression analyses
- such (anonymized) data may have lower protection levels than data from dedicated genotyping studies
- with a non-noisy genome of interest, attackers can generate linkage scores to identify the best match to the genomic profile



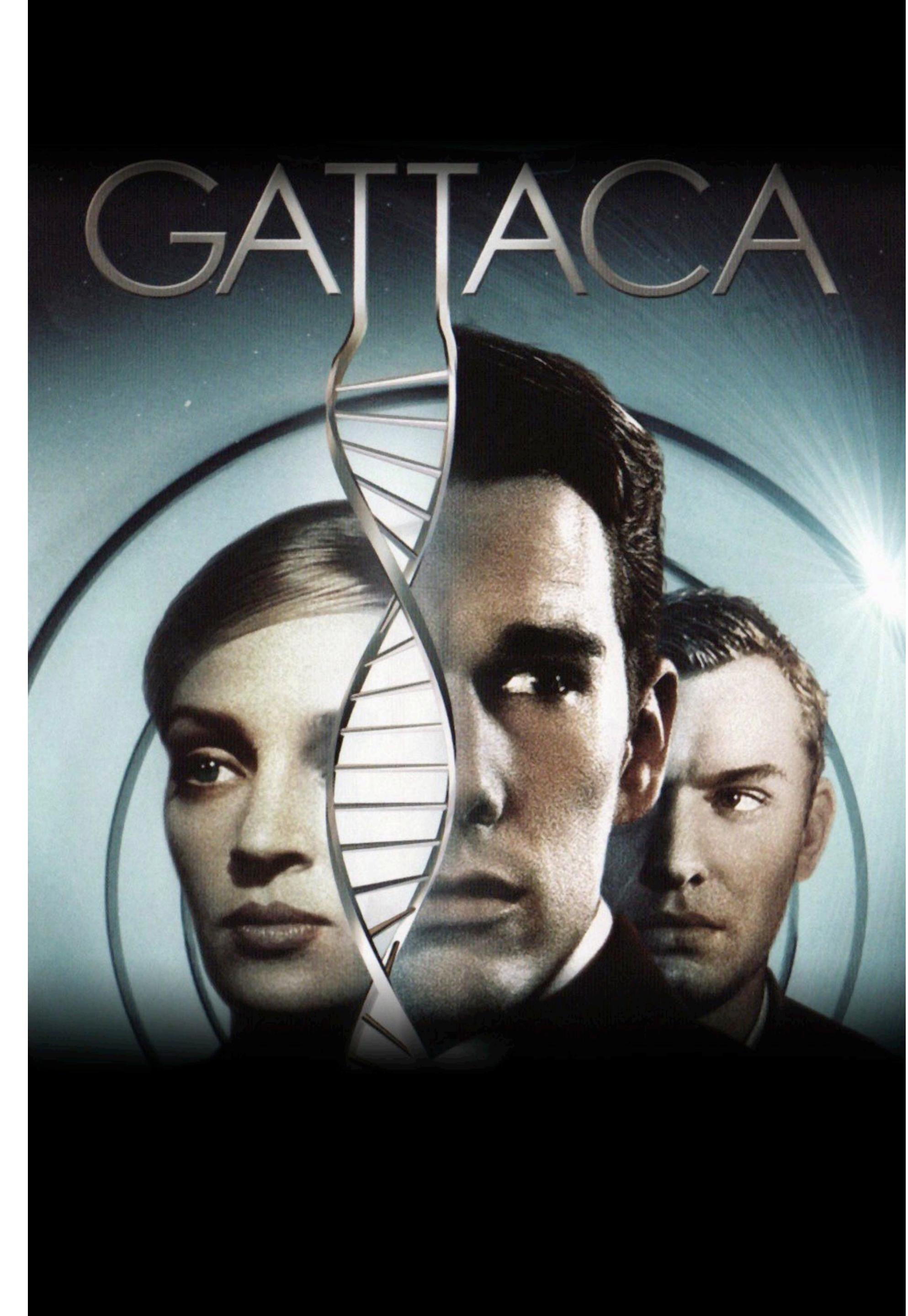
**Figure 1. Functional Genomics Data De-anonymization Scheme with Perfect Genomes**

(A) Anonymized functional genomics data from a cohort of individuals can be seen as a database  $\mathcal{D}$  to be attacked, which contains functional genomics reads and phenotypes for every individual in the cohort. The perfect information  $I$  about an individual can be the genome of an individual. After obtaining genotypes from the functional genomics reads, the attacker scores each individual in the cohort based on the overlapping genotypes between the known individual's genome and the noisy genotypes called from functional genomics. These scores are then ranked and the top-ranked individual in the cohort is selected as the known individual. See also [Figure S1](#).

(B)  $gap$  values for the 1000 Genomes Project individuals in the gEUVADIS RNA-seq cohort. Red circles are the  $gap$  values obtained by linking a random set of genotypes to the RNA-seq panel.  $gap$  values are also shown after adding false-positive genotypes to the genotype set of each individual in the database.

(C) The linking scores for each individual in the functional genomics cohort after the addition of genetically related individuals to the query, with and without the query individual present in the database.

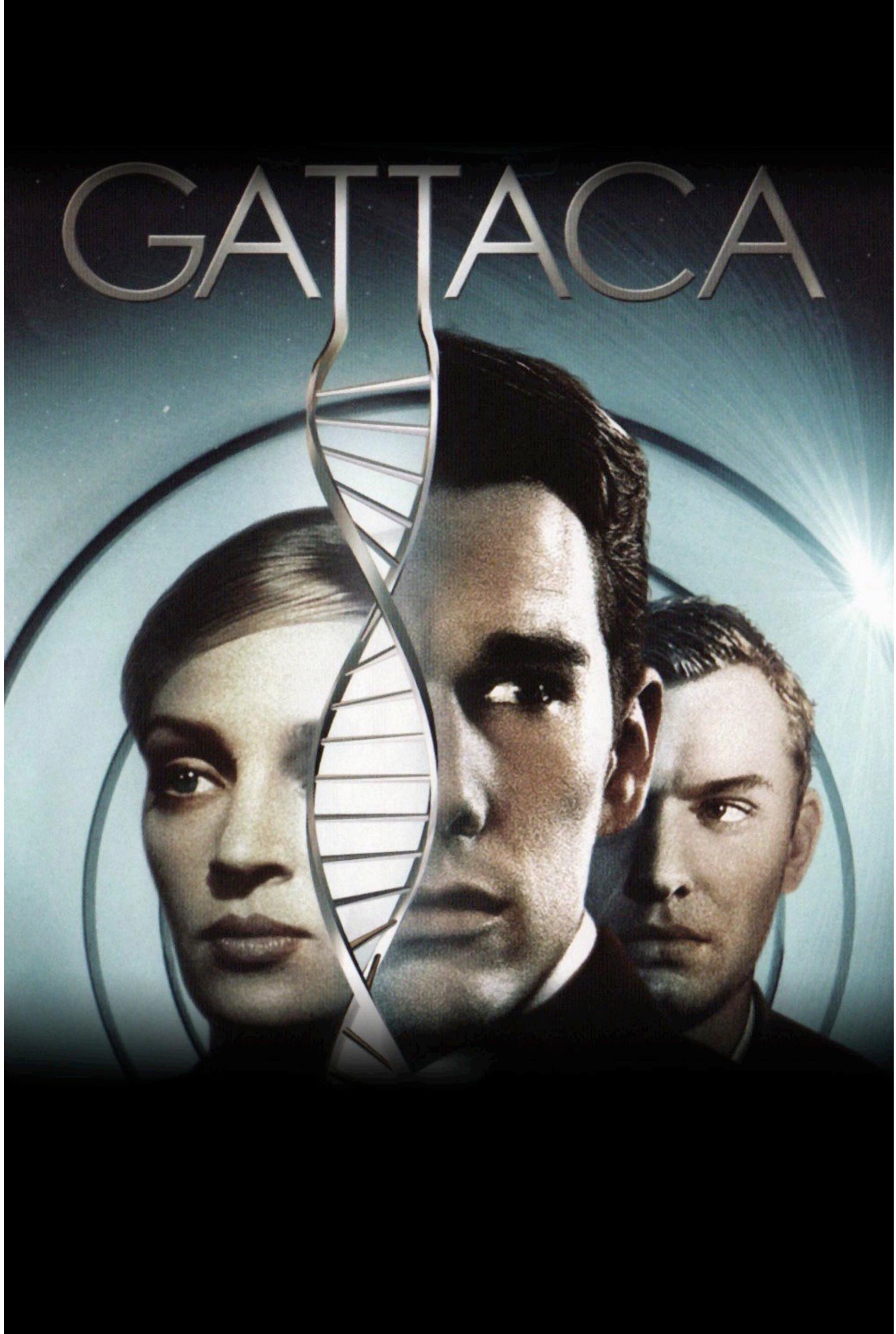
# Genomes & Privacy



# Gattaca (1997)

A genetically inferior man assumes the identity of a superior one in order to pursue his lifelong dream of space travel.

- genetic determinism
  - ▶ main character has been determined to be unsuitable for complex jobs based on genetic analysis
- genetic identification
  - ▶ the use of genetic sampling for personal identification is daily routine





Hi Michael,

Good news! We've discovered new DNA Matches for you.

- Commercial, "Direct to Customer" DNA analyses are provided through independent sites and such affiliated to genealogy services (MyHeritage, Ancestry.com, 23andMe...)
- Genealogy sites identify individuals with matching haplotype blocks & provide a prediction about degree of genetic relation
- Law enforcement agencies (and who else?!) can send individual SNP profiles (e.g. recovered from evidence many years after a crime) using a *Jane Doe* identity, to identify relatives of the suspect - **long range familial search**

# Long-Range Familial Searches

## Daily Journal

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We're donating a portion of every 1-year or 6-month subscription to Tupelo High Band Boosters!  
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New home delivery subscriptions only | Offer ends June 30



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ALL SEC DeVaughn had never been a suspect until genetic genealogy put police on his trail several months ago. Earlier this year, police sent the DNA profile to Parabon, a private genetics company, to compare the suspect's DNA sample to a public genealogy DNA database looking for people with similar DNA profiles who might be kin to the suspect. That eventually led authorities to look at DeVaughn.

Rienzi man charged with 1990 Starkville murder

By William Moore Daily Journal 15 hrs ago Comments

© Copyright 2018 Daily Journal, 1242 S Green St Tupelo, MS



The New York Times

## How a Genealogy Site Led to the Front Door of the Golden State Killer Suspect

Investigators used DNA from crime scenes that had been stored all these years and plugged the genetic profile of the suspected assailant into an online genealogy database. One such service, GEDmatch, said in a statement on Friday that law enforcement officials had used its database to crack the case. Officers found distant relatives of Mr. DeAngelo's and, despite his years of eluding the authorities, traced their DNA to his front door.

The New York Times, April 26, 2018

Attacks Associated With the Golden State Killer



# Rapid re-identification of human samples

...

We developed a rapid, inexpensive, and portable strategy to re-identify human DNA using the MinION. Our strategy requires only ~60 min preparation and 5-30 minutes of MinION sequencing, works with low input DNA, and enables familial searches using Direct-to-Consumer genomic reference datasets. This method can be implemented in a variety of fields:



## Forensics

Identification of abandoned material using DNA fingerprinting is a common practice. The main challenge currently being: time. Our method allows rapid sample preparation at the crime scene (see movie). We envision that the method can be adopted in the field for rapid checks, after a mass disaster, and can be adopted in border control to fight human trafficking.



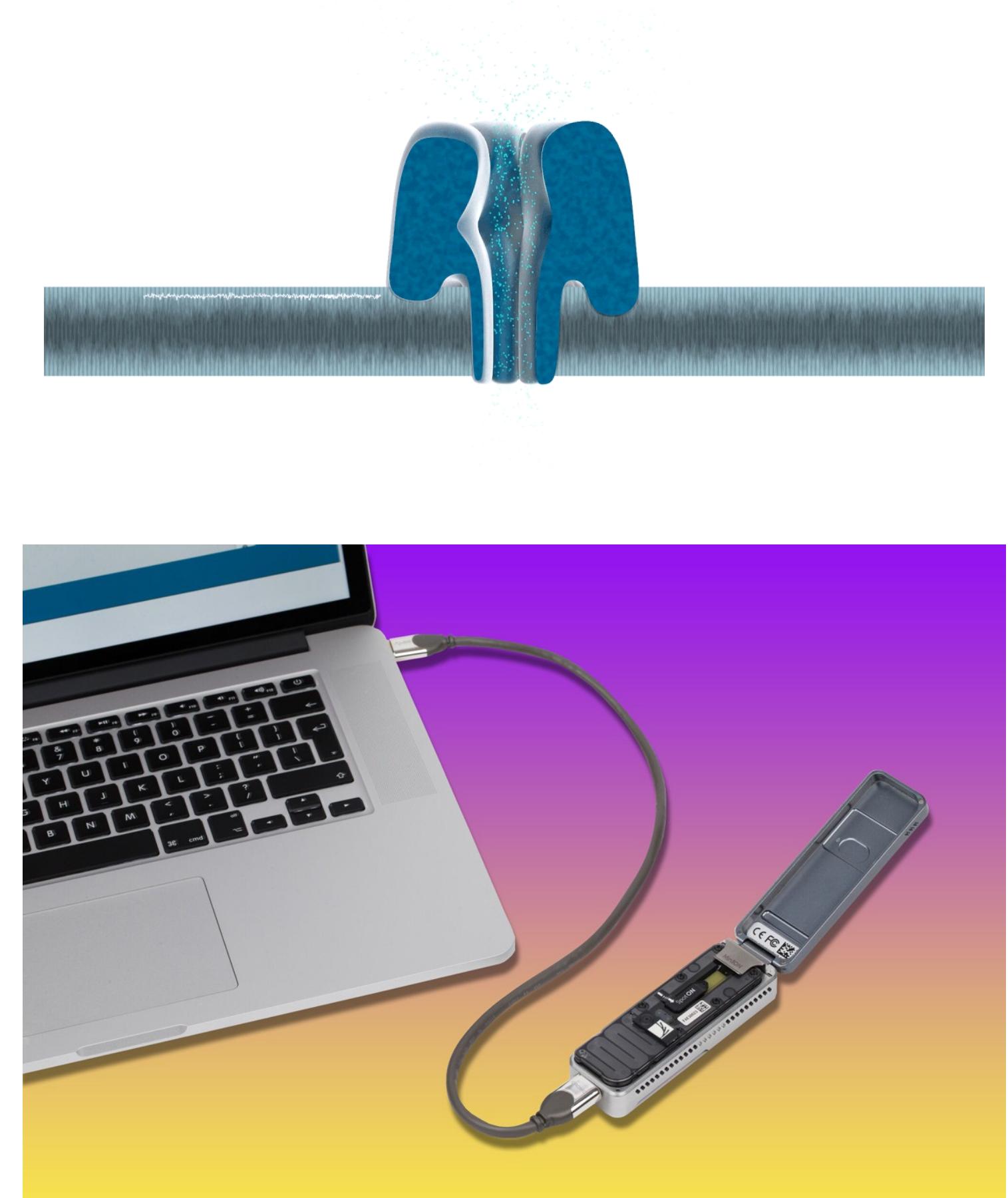
## Clinic

Clinics process many samples, either for analysis or, for example, organ donations. These samples are DNA fingerprinted to prevent sample mix-up mistakes. Our method can be implemented in the clinic for rapid sanity-check of all incoming samples.



## Cell line identification

Cross contamination of cell lines in science is a major problem. It results in unrepeatable data, and clinical trials based on inaccurate findings. This problem costs billions of dollars per year. We envision labs can adopt our identification method to ensure the purity of the cell line, and detect contamination.



**The MinION** (Oxford Nanopore)

Source: Sophie Zaaijer

<https://medium.com/neodotlife/nanopore-6443c81d76d3>

# DEMOCRATIZING DNA FINGERPRINTING

Sophie Zaaijer, Assaf Gordon, Robert Piccone, Daniel Speyer, Yaniv Erlich, 2016  
[ddf.teamerlich.org](http://ddf.teamerlich.org)



DNA sequencing for identification/fingerprinting soon “commodity” technology (in contrast with technological/data challenges in “precision medicine”)

MinION by Oxford Nanopore Technologies



The MinION is the smallest DNA sequencer currently around. It's the size of a Mars bar, and can be simply plugged into a laptop with a USB3.0 port.

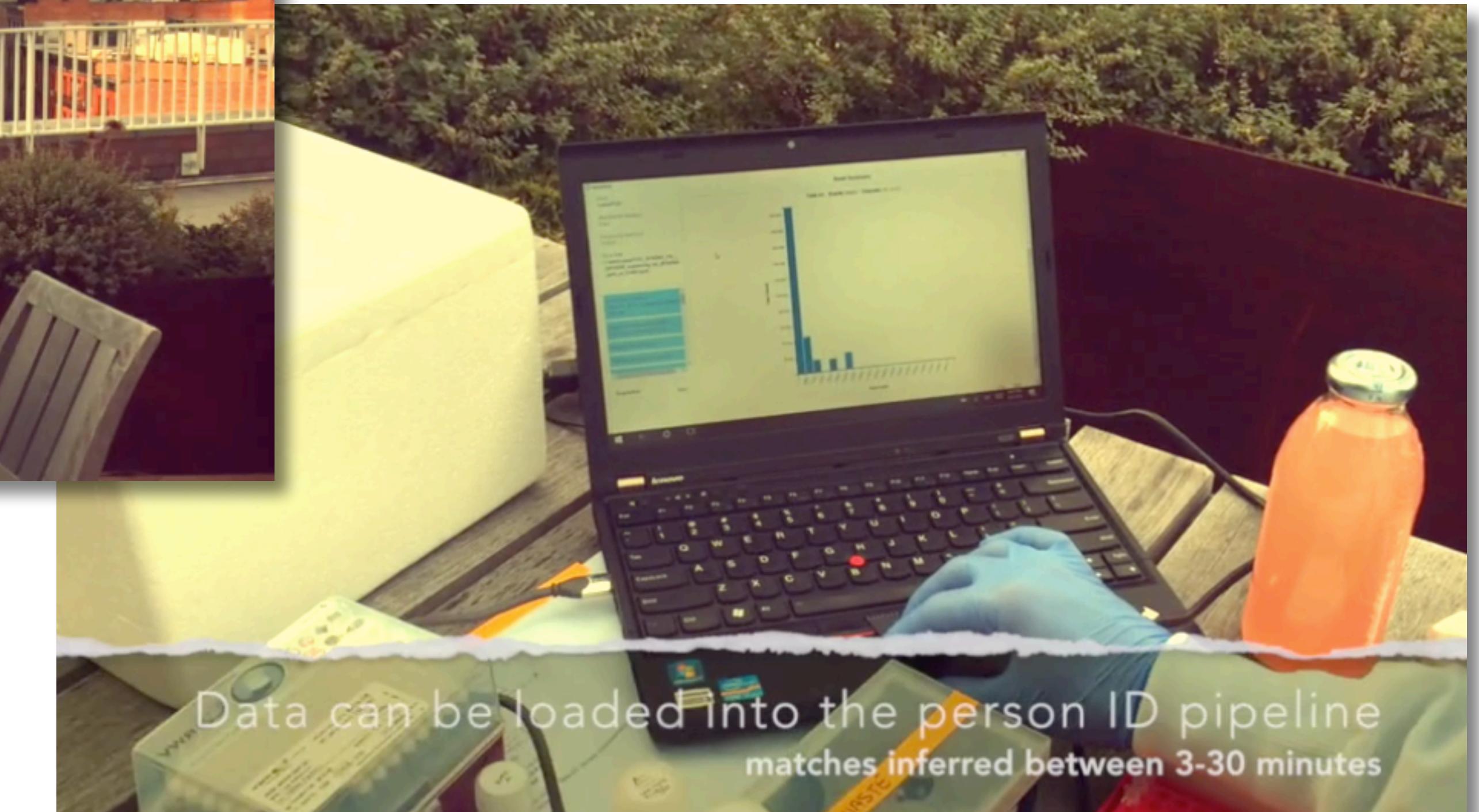
For more information about the MinION please click:  
[Oxford Nanopore Technologies](#)

Bento Lab



The Bento lab is a miniature lab with a centrifuge, thermocycler and a electrophoresis compartment.

For more information about the Bento-lab please click:  
[Bento Lab](#)



Data can be loaded into the person ID pipeline  
matches inferred between 3-30 minutes

# Rapid DNA

## Legalizing DNA Tests for DNA Indexing

Congress / Bills / H.R. 510 (115th) / Summary

### H.R. 510 (115<sup>th</sup>): Rapid DNA Act of 2017

Overview   **Summary**   Details   Text   Study Guide

GovTrack's Summary

[Library of Congress](#)

Rapid DNA is a new technique that can analyze DNA samples in about 90 minutes, instead of days or even weeks as it took previously. A bill that passed the Senate and House last week would expand the use of this technology.

#### What the bill does

The Rapid DNA Act establishes a system for Rapid DNA's nationwide coordination among law enforcement departments, by connecting it to the FBI's Combined DNA Index System.

Labelled [S. 139](#) in the Senate and [H.R. 510](#) in the House, the legislation was introduced by Sen. Orrin Hatch (R-UT) and Rep. James Sensenbrenner (R-WI5).

Former FBI Director James Comey cited a real-life example of how the technology could be used effectively. “[It will] allow us, in booking stations around the country, if someone’s arrested, to know instantly—or near instantly—whether that person is the rapist who’s been on the loose in a particular community before they’re released on bail and get away or to clear somebody, to show that they’re not the person,” Comey [said in testimony](#).

Rapid DNA was used for the [first time ever in a criminal investigation in 2013](#), to nab burglars who stole more than \$30,000 worth of items from an Air Force Member’s Florida home while they were serving in Afghanistan. Presumably more such cases would be solved and quickly with expanded use of rapid DNA.

#### What supporters say

Supporters say it will save both time and taxpayer dollars by speeding up the DNA analysis process in a manner that’s no less effective, reducing the backlog of samples waiting to be tested.

“It will enable officers to take advantage of exciting new developments in DNA technology to more quickly solve crimes and exonerate innocent suspects,” Senate lead sponsor Hatch [said in a press release](#). “Under this legislation, rather than having to all send DNA samples to crime labs and wait weeks for results, trained officers will be able to process many samples in less than two hours.”

#### What opponents say

GovTrack Insider could not locate any members of Congress who expressed public opposition to the legislation, but some members of the public are concerned. The *New Republic* called the rise of rapid DNA [“troubling,”](#) citing the potential for privacy violations and misuses by immigration authorities. They also noted that the FBI already has DNA samples from more than 3.5 percent of Americans, a number likely to grow thanks to a 2015 Supreme Court decision allowing DNA samples to be taken without a warrant.

The Electronic Frontier Foundation expressed doubts about the accuracy of Rapid DNA. “Rapid DNA has only been tested on single-source samples—like a swab taken directly from a person’s inner cheek,” the EFF [writes](#). “And yet, Rapid DNA manufacturers are trying to convince law enforcement agencies to buy these machines to get through their backlog of rape kits and for low-level property crimes—situations where there’s a very good chance the DNA came from multiple people—some of whom may have had no connection to the crime at all.”

#### Votes and odds of passage

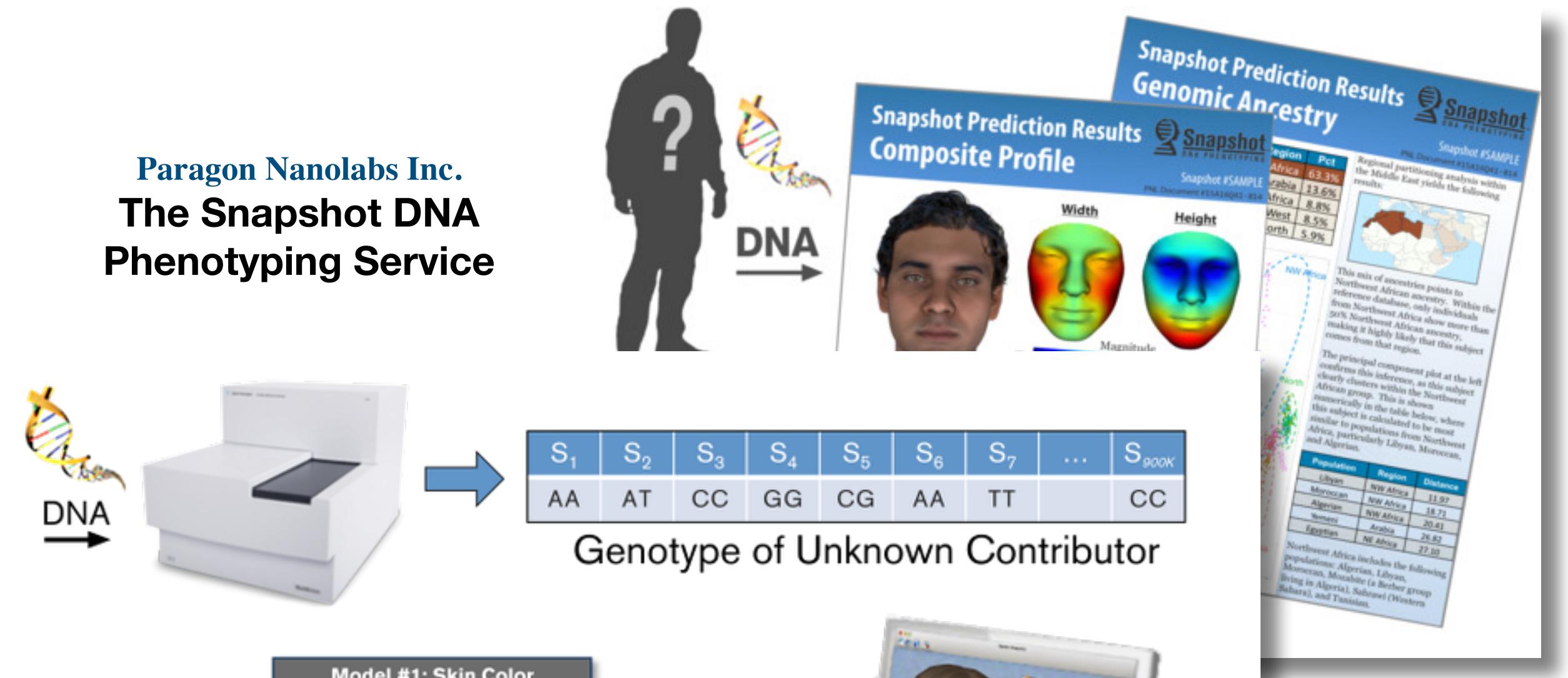
The legislation attracted a bipartisan mix of [12 Senate cosponsors](#), seven Republicans and five Democrats, and [24 House cosponsors](#), 17 Republicans and seven Democrats. It passed both the House and Senate on May 16, by a unanimous consent voice vote in both chambers, meaning no record of individual votes was recorded. It now goes to President Trump’s desk, where he appears likely to sign it.

<https://www.govtrack.us/congress/bills/115/hr510/summary>

# Phenotyping from DNA

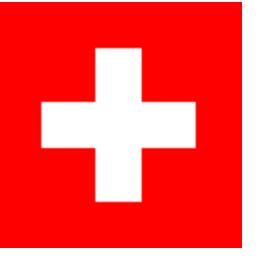
## From DNA to "Wanted" Posters?

- association of genomic variants with phenotypic data collection
- while hair, eye color are easy targets not useful for relevant phenotypic features especially if large environmental component
- huge biases based on input/collection data
- Belgium and Germany do not allow forensic DNA phenotyping
- Switzerland: Bundesrat decision on 2020-12-04 to allow phenotyping for law enforcement purposes



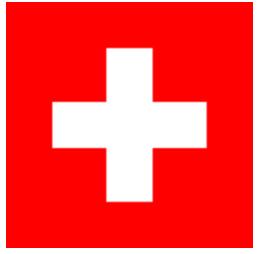
"When the New York Times ran an informal test of the Paragon system with one of its reporters, it failed badly." (ACLU.org)

# Federal Act on the Use of DNA Profiles in Criminal Proceedings and for Identifying Unidentified or Missing Persons, DNA Profiles Act



## An Area in Transition...

- Currently: «Genetic Fingerprint»
- Future: Will it be allowed to take a deeper look and how far can genetic data be used to determine the characteristics of an unknown perpetrator (colour of hair and eyes, height, ethnicity, etc.)
- Switzerland: Bundesrat decision on 2020-12-04 to allow phenotyping for law enforcement purposes



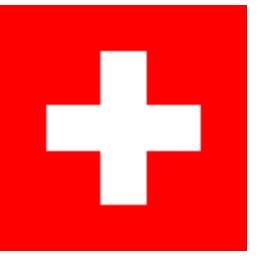
## Federal Act on Human Genetic Testing

- Currently limited to
  - ▶ a. in the medical context;
  - ▶ b. in the context of employment;
  - ▶ c. in the context of insurance;
  - ▶ d. in the context of liability.
- Therefore: Direct to Consumer Tests (DCT) **not** allowed in Switzerland
- But: Changes in the newer future are to be expected... e.g. DTC will be possible in limited ways.

# HGTA : Federal Act on Human Genetic Testing

HGTA new (probably 2021)	medical field	outside the medical field	
Investigated characteristics	medical relevant	especially protective values characteristics	other characteristics
General Requirements	Non-discrimination, information and consent, right to information, right not to know, avoidance of surplus information, protection of samples and genetic data, Circulation concerning public advertising, state of science and technology, penal provisions		
Initiation	Physician	Health professional (controlled taking of samples)	Consumer (DTC)
Persons concerned	Persons with <b>and</b> without capacity of judgement, pregnant woman (PND)	ONLY persons with Capacity of judgement	ONLY persons with Capacity of judgement
Communication of surplus information	as a rule according to decision of the person concerned	Not allowed	Not allowed
Laboratory	subject to authorization (cyto and molecular genetic studies)	subject to authorization (cyto and molecular genetic studies)	not subject to authorisation
Employers and Insurance institutions	Studies and Recovery of Results / Data only in regulated exceptional cases	Prohibition to carry out investigations and the Recovery of Results / Data	Prohibition to carry out investigations and the Recovery of Results / Data

# Data Ownership



- Within Switzerland, there is no coherent approach on ownership of data as such (but academic discussion is ongoing, if that is needed).
- Restrictions of usage and disclosure of data other than personal data mainly stem from contractual relationships.
- In the field of research this leads mostly to a data ownership by the research institution.

Of course the restrictions of the different acts that are in the field need to be respected (procuring data lawfully, consent for further use, etc.)

# **Is Genomic Data Special?**

# Health Related Data & Privacy

## Considerations when evaluating risks of data sharing

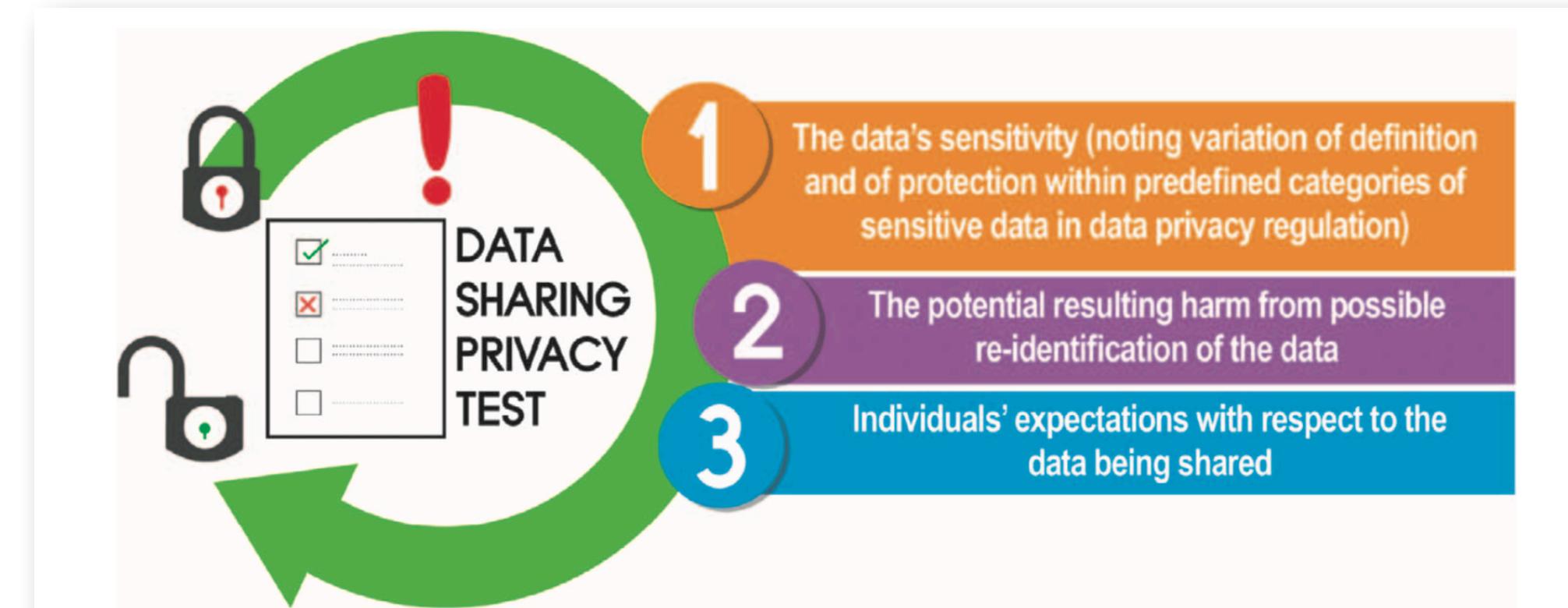
- Is the genetic condition outwardly visible?
- How severe is it? (serious disease, penetrance, age of onset)
- Is it associated with what could be considered to be stigmatizing health information (e.g., associated with mental health, reproductive care, disability)?
- Is it familial (i.e., potential carrier status/reproductive implications for family/relatives)?
- Does it provide information about the likely geographical location of individuals?
- Does it provide information about ethnicity that may be considered potentially stigmatizing information?

## Sharing health-related data: a privacy test?

Stephanie OM Dyke<sup>1</sup>, Edward S Dove<sup>2</sup> and Bartha M Knoppers<sup>1</sup>

Greater sharing of potentially sensitive data raises important ethical, legal and social issues (ELSI), which risk hindering and even preventing useful data sharing if not properly addressed. One such important issue is respecting the privacy-related interests of individuals whose data are used in genomic research and clinical care. As part of the Global Alliance for Genomics and Health (GA4GH), we examined the ELSI status of health-related data that are typically considered 'sensitive' in international policy and data protection laws. We propose that 'tiered protection' of such data could be implemented in contexts such as that of the GA4GH Beacon Project to facilitate responsible data sharing. To this end, we discuss a Data Sharing Privacy Test developed to distinguish degrees of sensitivity within categories of data recognised as 'sensitive'. Based on this, we propose guidance for determining the level of protection when sharing genomic and health-related data for the Beacon Project and in other international data sharing initiatives.

*npj Genomic Medicine* (2016) **1**, 16024; doi:10.1038/npjgenmed.2016.24; published online 17 August 2016



**Figure 1.** The three steps of a Data Sharing Privacy Test to distinguish degrees of data sensitivity within categories of data recognised as 'sensitive'.

# Typical Data Scopes in Genomics (Research) Collections

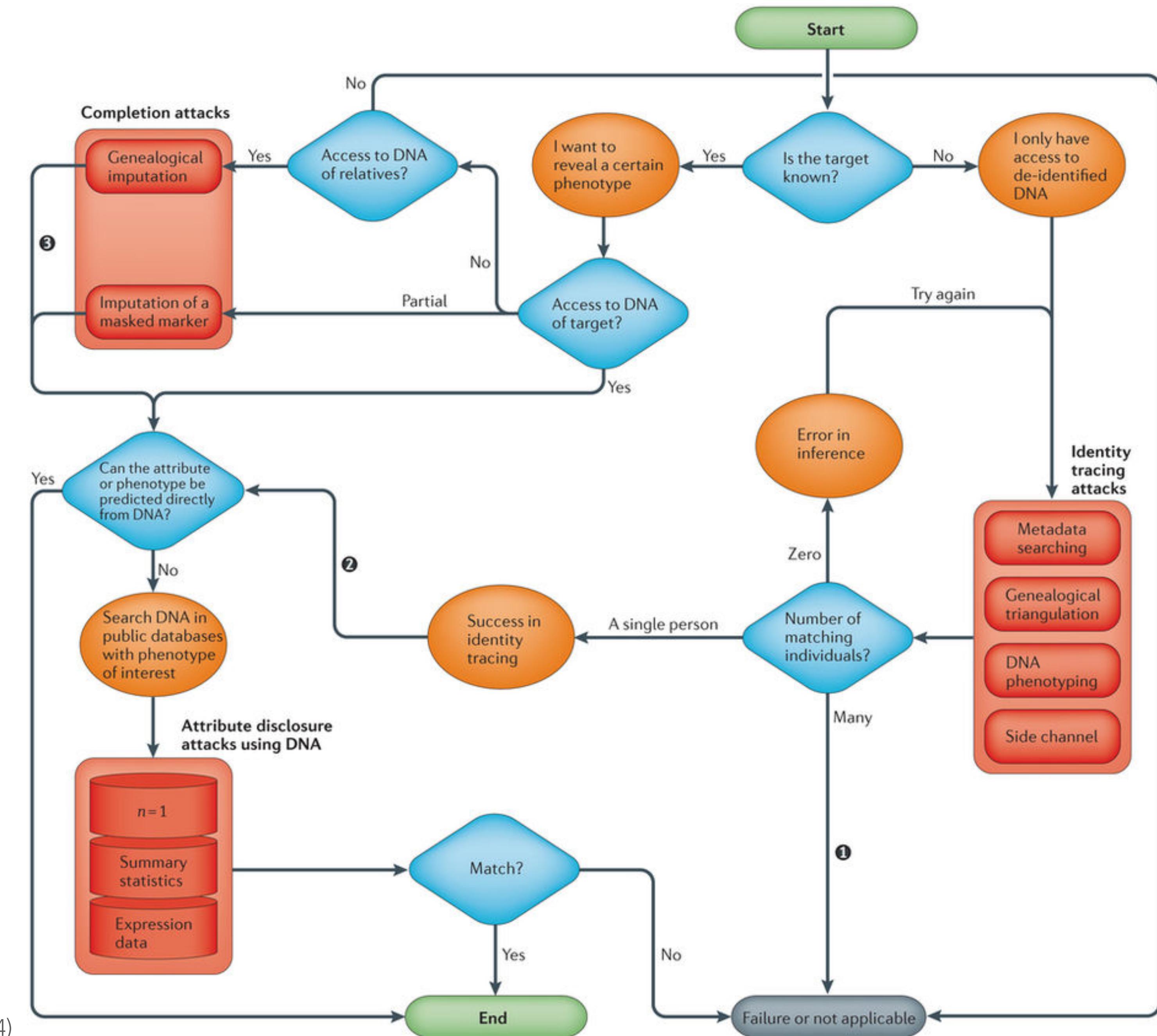
## Biomedical and procedural "Meta"data types

- Diagnostic classification
  - mapping text-based cancer diagnoses to standard classification systems
- Provenance data
  - store identifier-based pointers
  - geographic attribution (individual, biosample, experiment)
- Clinical information
  - **core set** of typical cancer study values:
    - ➡ stage, grade, followup time, survival status, genomic sex, age at diagnosis
  - balance between annotation effort and expected usability

# Routes for breaching and protecting genetic privacy

The map contrasts different scenarios, such as identifying de-identified genetic data sets, revealing an attribute from genetic data and unmasking of data. It also shows the interdependencies between the techniques and suggests potential routes to exploit further information after the completion of one attack. There are several simplifying assumptions (black circles).

In certain scenarios (such as insurance decisions), uncertainty about the target's identity within a small group of people could still be considered a success (assumption 1). For certain privacy harms (such as surveillance), identity tracing can be considered a success and the end point of the process (assumption 2). The complete DNA sequence is not always necessary (assumption 3).



**Generalkonsent**

**BENEFIT**

**BLOCKCHAIN**

**HEALTH**

**PRIVACY**

**CONSENT**

**SECURITY**

**ACCESS**

**Right to Research**

**HACKERS**

**LAWS**

**Genetic  
Information  
Nondiscrimination  
Act**

**Health  
Insurance  
Portability and  
Accountability  
Act**

**SAFETY**

**CRYPTOGRAPHY**

**Way forward...**

# The vision: Federation of data



# ELIXIR - Making Beacons Biomedical



- Authentication to enable non-aggregate, patient derived datasets
  - ELIXIR AAI with compatibility to other providers (OAuth...)
  - Scoping queries through "biodata" parameters
  - Extending the queries towards clinically ubiquitous variant formats
    - cytogenetic annotations, named variants, variant effects
- Beacons as part of local, secure environments
  - local EGA ...
- Beacon queries as entry for **data delivery**
  - handover to stream and download using htsget, VCF, EHRs
- Interacting with EHR standards
  - FHIR translations for queries and handover ...

# Modernizing Patient Consent

forward looking, transparent and technically feasible regulations for enabling access to research material and data while empowering **patients**

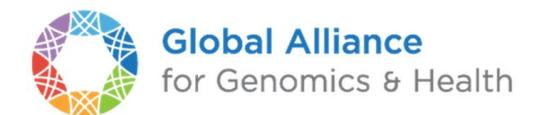
## Generalkonsent: Eine einheitliche Vorlage soll schweizweite Forschung erleichtern

Art des Forschungsmaterials	Biologisches Material und genetische Daten	Nicht-genetische Daten
Personenbezug		
Unverschlüsselt (identifizierend)	Information + Einwilligung in jedes einzelne Forschungsprojekt	Information über Weiterverwendung für zukünftige noch unbestimmte Forschungsprojekte + Generalkonsent für Forschungszwecke
Verschlüsselt	Information über Weiterverwendung für zukünftige noch unbestimmte Forschungsprojekte + Generalkonsent für Forschungszwecke	Information über Weiterverwendung für zukünftige noch unbestimmte Forschungsprojekte + Generalkonsent für Forschungszwecke + über Möglichkeit Weiterverwendung abzulehnen > Widerspruchsrecht
Anonymisiert	<b>Genetische Daten:</b> Information über Weiterverwendung für zukünftige noch unbestimmte Forschungszwecke + über Möglichkeit Weiterverwendung abzulehnen > Widerspruchsrecht <b>Proben:</b> Information zur Anonymisierung > Widerspruchsrecht	Ausserhalb des Geltungsbereichs des HFG



## Consent Codes: Upholding Standard Data Use Conditions

Stephanie O. M. Dyke<sup>1\*</sup>, Anthony A. Philippakis<sup>2</sup>, Jordi Rambla De Argila<sup>3,4</sup>, Dina N. Paltoo<sup>5</sup>, Erin S. Luetkemeier<sup>5</sup>, Bartha M. Knoppers<sup>1</sup>, Anthony J. Brookes<sup>6</sup>, J. Dylan Spalding<sup>7</sup>, Mark Thompson<sup>8</sup>, Marco Roos<sup>8</sup>, Kym M. Boycott<sup>9</sup>, Michael Brudno<sup>10,11</sup>, Matthew Hurles<sup>12</sup>, Heidi L. Rehm<sup>2,13</sup>, Andreas Matern<sup>14</sup>, Marc Fiume<sup>15</sup>, Stephen T. Sherry<sup>16</sup>



Consent Codes		
Name	Abbreviation	Description
<b>Primary Categories (I<sup>IV</sup>)</b>		
no restrictions	NRES	No restrictions on data use.
general research use and clinical care	GRU(CC)	For health/medical/biomedical purposes and other biological research, including the study of population origins or ancestry.
health/medical/biomedical research and clinical care	HMB(CC)	Use of the data is limited to health/medical/biomedical purposes, does not include the study of population origins or ancestry.
disease-specific research and clinical care	DS-[XX](CC)	Use of the data must be related to [disease].
population origins/ancestry research	POA	Use of the data is limited to the study of population origins or ancestry.
<b>Secondary Categories (II<sup>IV</sup>)</b> (can be one or more extra conditions, in addition to I <sup>IV</sup> category)		
other research-specific restrictions	RS-[XX]	Use of the data is limited to studies of [research type] (e.g., pediatric research).
research use only	RUO	Use of data is limited to research purposes (e.g., does not include its use in clinical care).
no “general methods” research	NMDS	Use of the data includes methods development research (e.g., development of software or algorithms) ONLY within the bounds of other data use limitations.
genetic studies only	GSO	Use of the data is limited to genetic studies only (i.e., no research using only the phenotype data).
<b>Requirements</b>		
not-for-profit use only	NPU	Use of the data is limited to not-for-profit organizations.
publication required	PUB	Requestor agrees to make results of studies using the data available to the larger scientific community.
collaboration required	COL-[XX]	Requestor must agree to collaboration with the primary study investigator(s).
return data to database/resource	RTN	Requestor must return derived/enriched data to the database/resource.
ethics approval required	IRB	Requestor must provide documentation of local IRB/REC approval.
geographical restrictions	GS-[XX]	Use of the data is limited to within [geographic region].
publication moratorium/embargo	MOR-[XX]	Requestor agrees not to publish results of studies until [date].
time limits on use	TS-[XX]	Use of data is approved for [x months].
user-specific restrictions	US	Use of data is limited to use by approved users.
project-specific restrictions	PS	Use of data is limited to use within an approved project.
institution-specific restrictions	IS	Use of data is limited to use within an approved institution.

SOM Dyke, et al. Consent Codes: Upholding Standard Data Use Conditions. *PLoS Genetics* 12(1): e1005772.  
<http://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1005772>

Contact: Dr. Stephanie Dyke (stephanie.dyke@mcgill.ca)

Switzerland: Definition of a unified "Generalkonsent", to provide a single framework to manage permissions for access to patient derived material and related data

# Empowering Beacon use through Access Levels

## Integrating permissions and discovery



Beacon Metadata Profiles

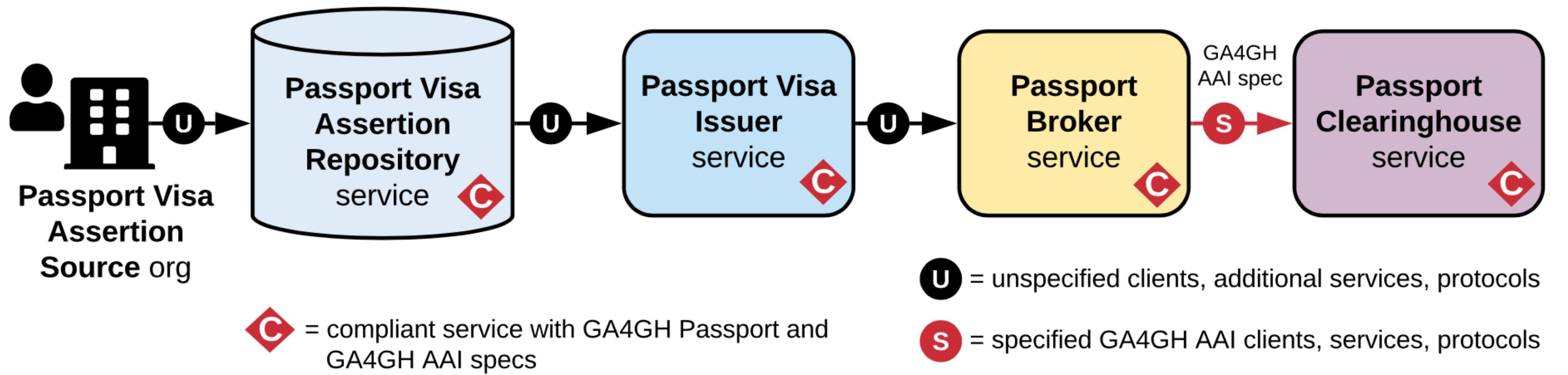


# GA4GH Passports



Global Alliance  
for Genomics & Health

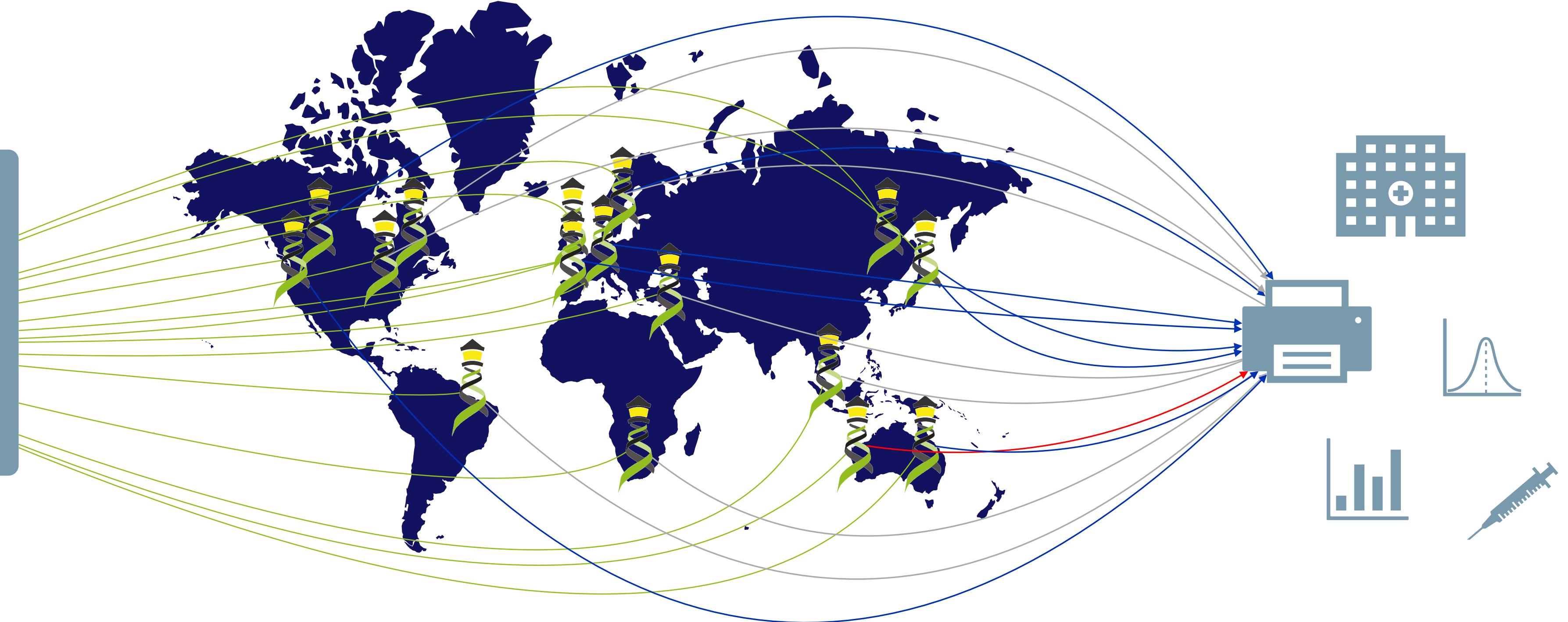
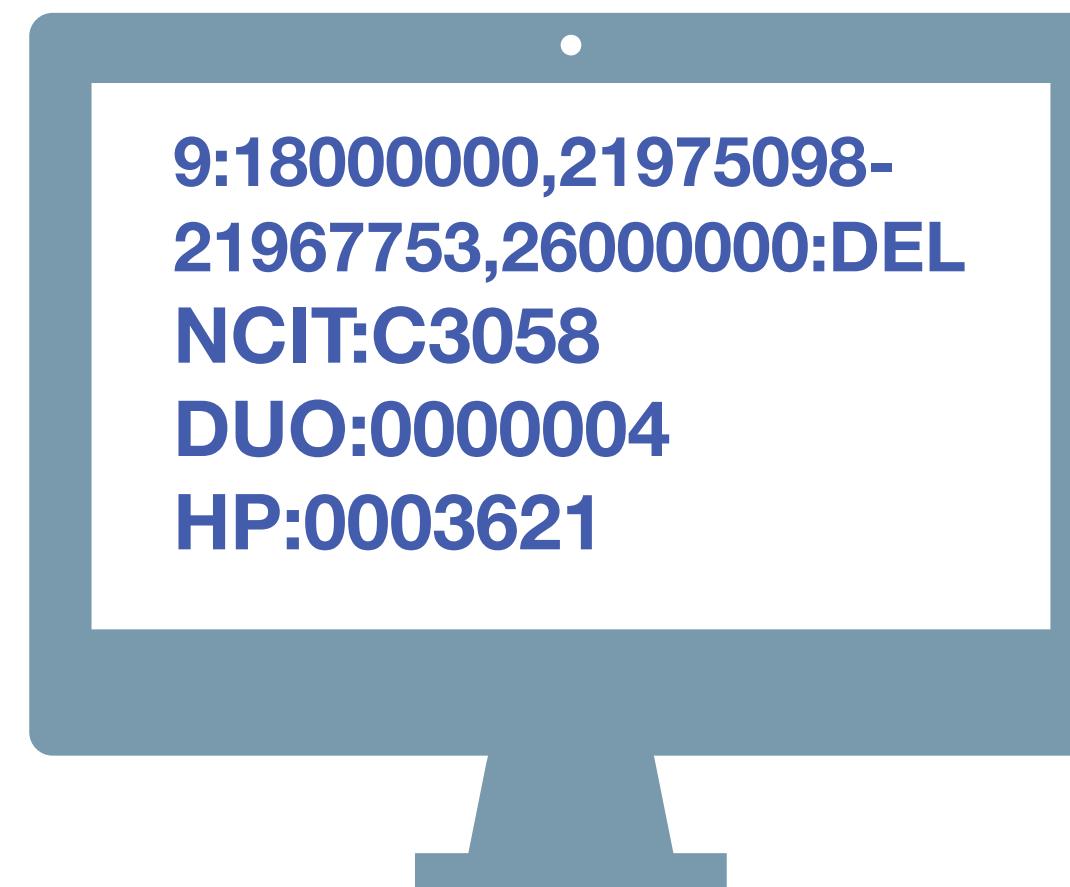
## Communicating a user's data access authorizations



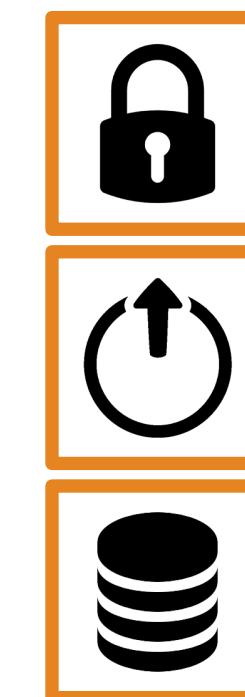
- format to communicate a user's data access authorizations based on either their role (e.g. researcher), affiliation, or access status
- works together with the GA4GH Authentication and Authorization Infrastructure (AAI) OpenID Connect Profile to streamline researchers' data access over federated data access protocols
- both standards approved in Dec 2019 with early implementation by Google Cloud services and ELIXIR

Google Cloud

elixir



Have you seen deletions in this region on chromosome 9 in Glioblastomas from a juvenile patient, in a dataset with unrestricted access?



## Beacon v2 API

The Beacon API v2 proposal opens the way for the design of a simple but powerful "genomics API".

# Improving Data Privacy but Empowering Beneficial Use

## Intersecting Areas of Development

- Make genomic (and functional) data "obfuscated" for malicious use
  - ▶ e.g. spiking / randomization of variants in "not-disease" loci
- access protection with defined user access using standardized protocols for users' roles and permissions, in contrast to individual per user, per dataset access requests over data access committees (DACs)
  - ▶ digital "differential" consent using e.g. data use ontologies
- intentional and unintentional (!) data providers have to be protected from abuse by legal regulations - though thin line regarding "overzealous" use by law enforcement
- alternative solution for active consent
  - ▶ encrypted wide-area networking solutions with managed access control (e.g. SPHN's BiomedIT) and limited access to anonymized data (e.g. using the Beacon protocol with "handover" scenarios)
  - ▶ (genomic) data ownership by the individual "data donors, together with strong privacy protection by law

# Genomic Data & Privacy - Key Areas

- **Re-identification**

- ▶ identification of an individual based on sets of genomic variants they (or close relatives) carry - so one needs some genome data first
- ▶ information to be gained is circumstantial (e.g. their genome is in a particular disease related dataset)
- ▶ currently only risk with some practical use (e.g. **long-range familial attacks**)

- **Genotype-to-Phenotype (G2P) attacks**

- ▶ determination of some disease risk or phenotypic features from a genome itself
- ▶ needs access to genome data which is illegal in many jurisdictions (but technically more & more feasible)
- ▶ real-world use cases are limited but abuse through wrong perception of utility

- **Genomic Determinism**

- ▶ assignment of individual abilities and personal development trajectories from genomic profiling
- ▶ topic of (some good, most bad) SciFi
- ▶ but: **Wehret den Anfängen!**

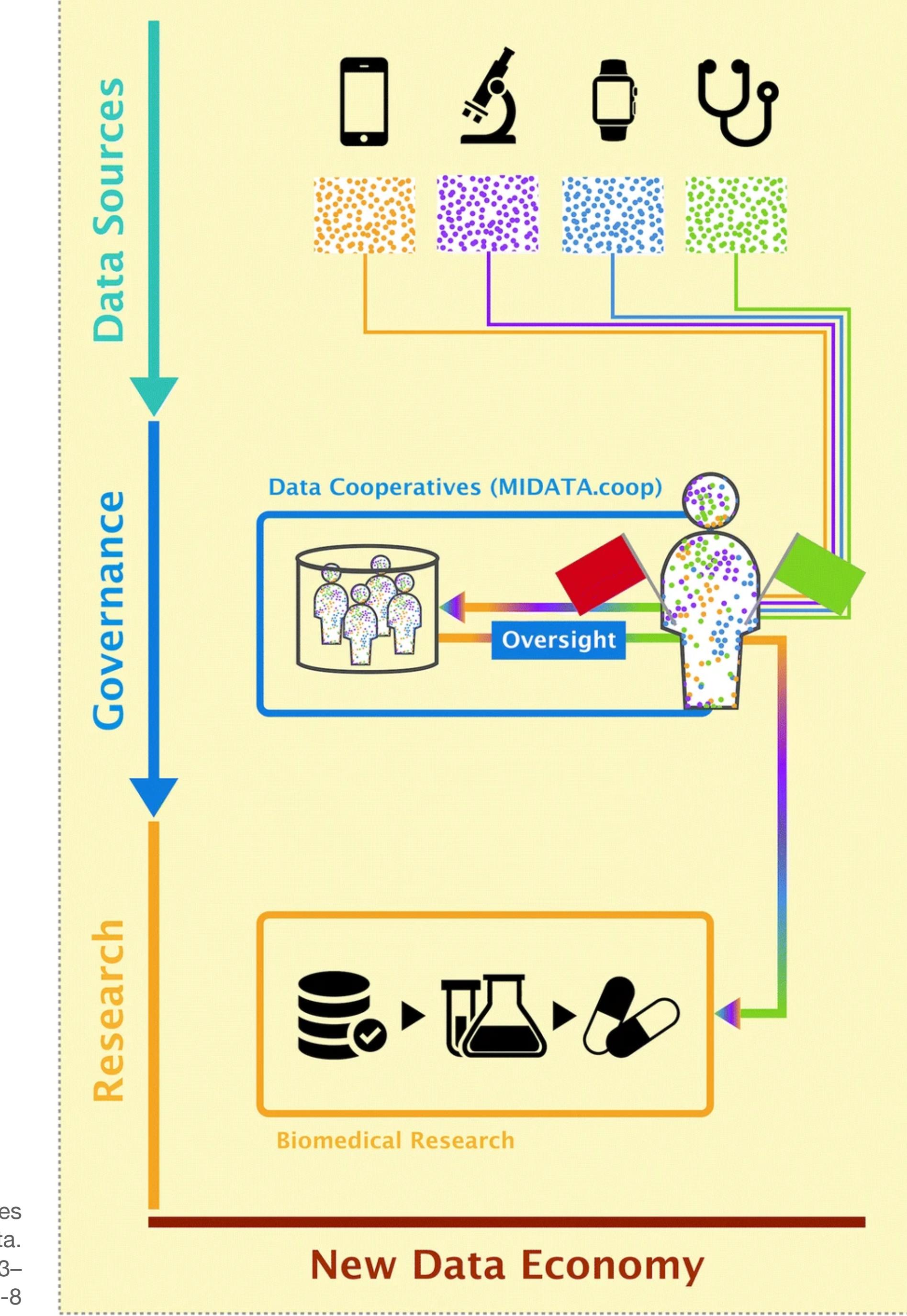
# Genomic Data & Privacy - Some Take-Home Messages

- Many clinical and research applications in genomics **need vast numbers of genomes** to evaluate e.g. genotype-phenotype relationships
- Such data cannot simply be provided by a few reference data curation resources - and those again rely on multitudes of original data resources > **federated data access + data curation**
- Genomic data is considered to potentially expose unwilling individuals through **re-identification**/de-anonymization but also through direct information (genotype -> phenotype/disease)
- Legislative bodies and law enforcement have varying and *curious* approaches to "genomic privacy", with a mix of de-legalizing genomic data generation (e.g. in Switzerland) or strictly limiting its use while also using "eminent domain" to co-opt such data for criminal persecution in a possibly extending set of use cases

# Power to the People?!

## Individuals as Owners & Managers of their Data

- (genomic) data ownership by the individual "data donors"
- supported by technological frameworks for data management and arbitration
- one vision here are "data cooperatives"
- need strong support from policy makers and financial sustainability support



# Share YOUR Genome data?

- The Beacon concept - balanced approach for accessing genome variant data from internationally distributed resources
- However: Genome data has the inherent “risk” of being identified and linked to a person

**Solutions from Technology or Society? Discourse!**

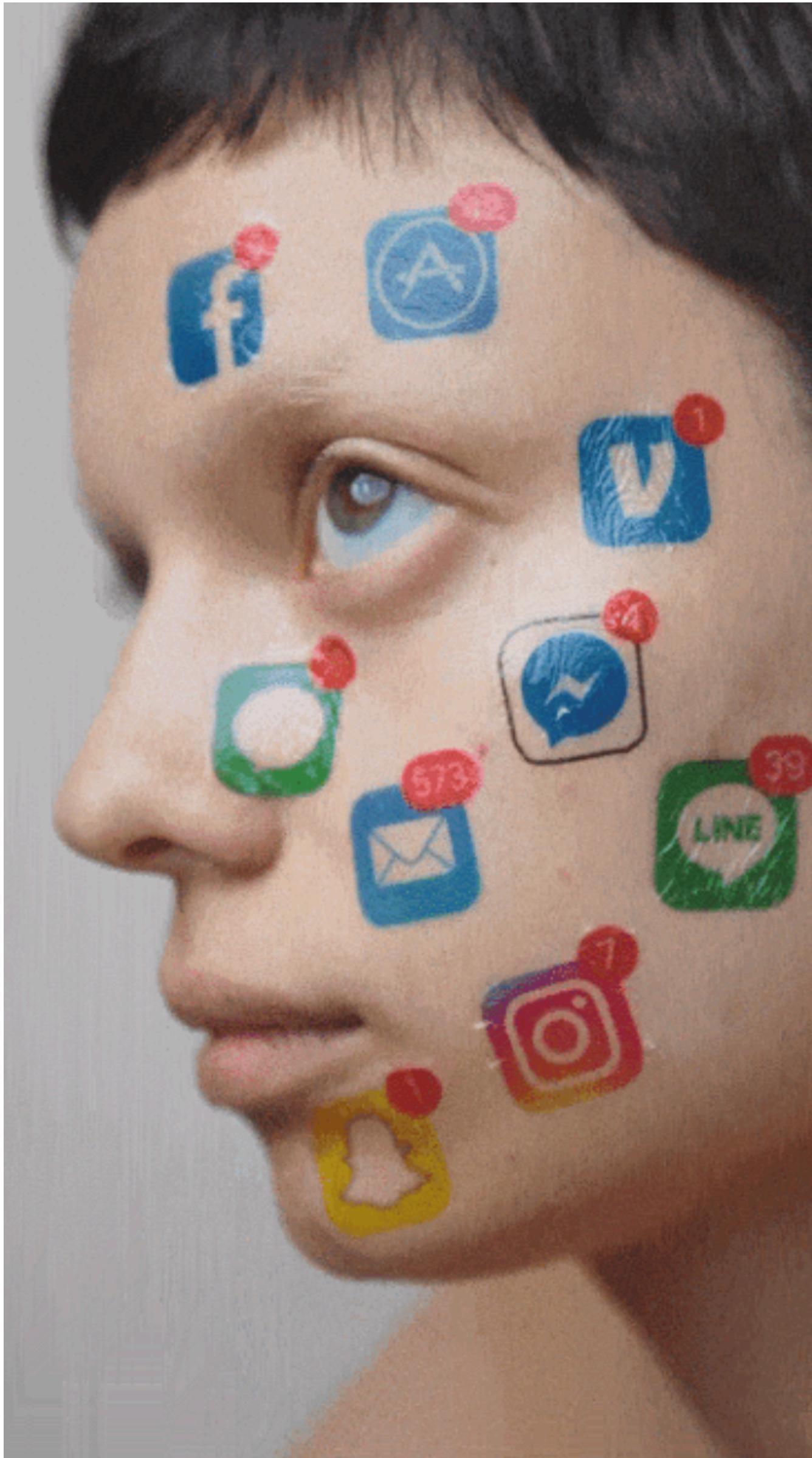
Welcome to openSNP

The screenshot shows the openSNP website homepage. At the top, there is a banner for "MyHeritage DNA" with a "Valentine's Day DNA SALE" offer. The banner includes a "Upload Your Genotyping File" button and a "For Genotyping Users" section. The main navigation menu includes Home, Family tree, Discoveries, DNA (which is highlighted in orange), and Research. Below the banner, there is a large image of a DNA microarray. A sidebar on the right contains text about openSNP's mission to let customers publish their test results and find others with similar genetic backgrounds.

The screenshot shows the 23andMe website homepage. It features a large image of a DNA test kit with the text "Welcome to you". Below the image, there is a "saliva collection kit" and a "phenotype" section. To the right, there is a call-to-action button "Find out what your DNA says about you and your family." Below this, there is a list of features:

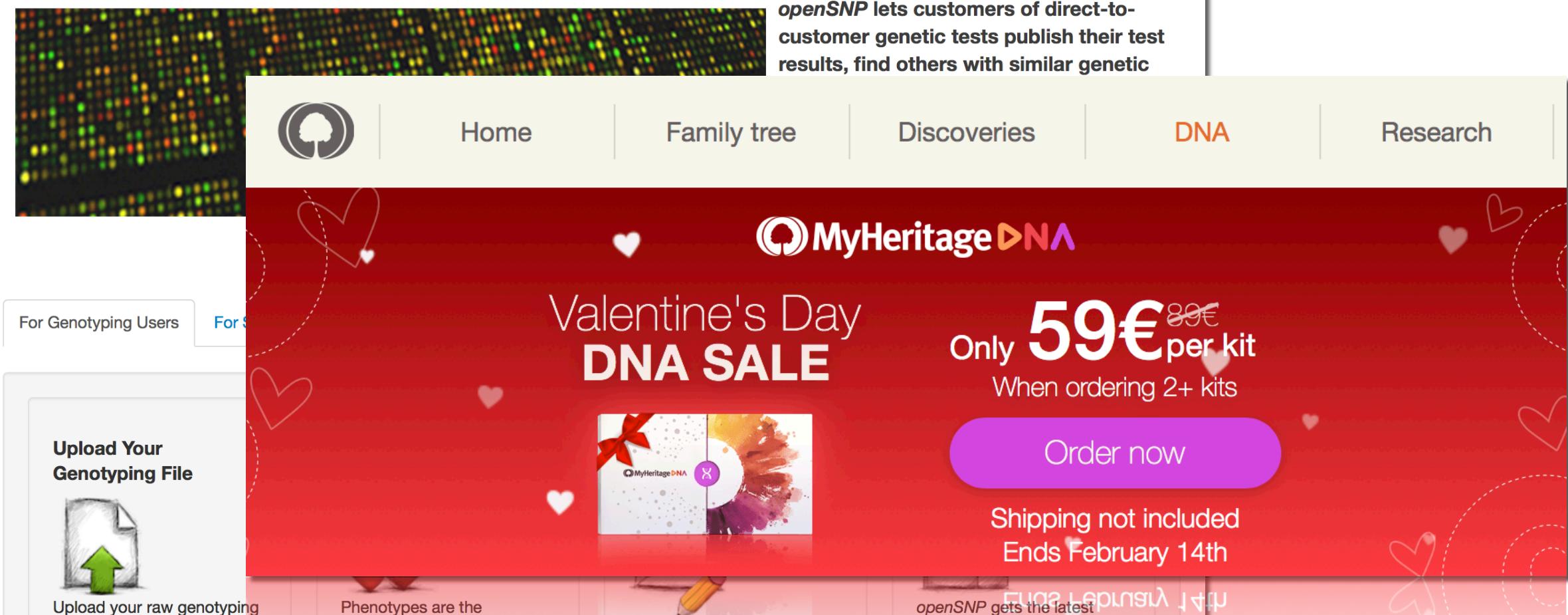
- See how your DNA breaks out across 31 populations worldwide
- Discover DNA relatives from around the world

At the bottom, there are links for "SUBSCRIBE" and "SIGN IN".



John Yuyi, NYT 2018-02-09

# Welcome to *openSNP*



# The Right to Scientific Knowledge

In 1948, the General assembly of the United nations adopted the Universal Declaration of Human Rights (UDHr) to guarantee the rights of every individual in the world. Included were twin rights “to share in scientific advancement and its benefits” and “to the protection of the moral and material interests resulting from any scientific...production of which [a person] is the author” (art. 27, United nations 1948).

from Knoppers et al, 2014

## A human rights approach to an international code of conduct for genomic and clinical data sharing

Bartha M. Knoppers · Jennifer R. Harris · Isabelle Budin-Ljøsne · Edward S. Dove

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**Abstract** Fostering data sharing is a scientific and ethical imperative. Health gains can be achieved more comprehensively and quickly by combining large, information-rich datasets from across conventionally siloed disciplines and geographic areas. While collaboration for data sharing is increasingly embraced by policymakers and the international biomedical community, we lack a common ethical and legal framework to connect regulators, funders, consortia, and research projects so as to facilitate genomic and clinical data linkage, global science collaboration, and responsible research conduct. Governance tools can be used to responsibly steer the sharing of data for proper stewardship of research discovery, genomics research resources, and their clinical applications. In this article, we propose that an international code of conduct be designed to enable global genomic and clinical data sharing for biomedical research. To give this proposed code universal application and accountability, however, we propose to position it within a human rights framework. This proposition is not without precedent: international treaties have long recognized that everyone has a right to the benefits of scientific

progress and its applications, and a right to the protection of the moral and material interests resulting from scientific productions. It is time to apply these twin rights to internationally collaborative genomic and clinical data sharing.

### Introduction

In 1948, the General Assembly of the United Nations adopted the *Universal Declaration of Human Rights* (UDHR) to guarantee the rights of every individual in the world. Included were twin rights “to share in scientific advancement and its benefits” and “to the protection of the moral and material interests resulting from any scientific...production of which [a person] is the author” (Art. 27, United Nations 1948). In the 21st century, where are we in realizing the sharing of scientific advancement and its benefits, and the importance of protecting a scientific producer’s moral and material interests? In this article, we argue that these little-developed twin rights, what we call the right “to benefit from” and “to be recognized for”, have direct application to internationally collaborative genomic and clinical data sharing, and can be activated through an international code of conduct.

Sharing genomic and clinical data is critical to achieve precision medicine (National Research Council 2011), that is, more accurate disease classification based on molecular profiles to enable tailored effective treatments, interventions, and models for prevention. Better communication flow across borders and research teams, encompassing data from clinical and population research, enables researchers to connect the diverse types of datasets and expertise needed to elucidate the genomic basis and complexities of disease etiology. Such data integration can make it possible to reveal the genetic basis of cancer, inherited diseases,

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# Exercises

## Read, Think, Opinionate ...

- The course material contains a number of articles (scientific, news) about topics touched upon in the course.
- Please use the time after the course to pick some you find interesting! Files are available through the course page:
  - ▶ "Longe-range familial attacks" has both news and scientific write-ups (Ehrlich et al. 2018)
  - ▶ the Beacon protocol has article but also online resources at <http://beacon-project.io>
  - ▶ ga4gh.org has links to many related topics