Genomic Data & Privacy
Risks & opportunities
Genomic Data & Privacy

Risks & opportunities

• Why do we need a lot of data for understanding genomic variation in health and disease?

• Data sharing protocols ...
  ‣ GA4GH Beacon

• Breaking data privacy
  ‣ Different types of (genomic) privacy attacks
  ‣ Beacon attacks and mitigation
  ‣ DTC and Long-range familial attacks

• Regulation of genome data production & access in Switzerland

• Some strategies for enabling genomic data sharing & re-use
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

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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 biomedi- cal 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 international collaboration of 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, interven- tions, 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,
Genome screening at the core of “Personalised Health”

• **Genome analyses** (including transcriptome, metagenomics) are core technologies for Personalised Health™ applications

• The unexpectedly large amount of **sequence variants** in human genomes - germline and somatic/cancer - requires huge analysis efforts and creation of **reference repositories**

• **Standardized data formats** and **exchange protocols** are needed to connect these resources throughout the world, for reciprocal, international **data sharing** and **biocuration** efforts

• Our work @ UZH:
  - **cancer** genome repositories
  - biocuration
  - protocols & formats

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**Global Alliance for Genomics & Health**
The trouble with human genome variation
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.

### Human Genetic Variation

| Class of Variants | Prevalence of Variants |
|-------------------|------------------------|
| SNP               | 3.5 – 4.3M             |
| Indel             | 550 – 625K             |
| SV                | 2.1 – 2.5K (20Mb)      |
| Total             | 4.1 – 5M               |

#### Origin of Variants

| Germ-line | Coding | Non-coding |
|-----------|--------|------------|
| Somatic   | ~50    | 5K         |

#### Prevalence of Variants

- **Common (~75%)**
- **Rare (~25%)**

*Variants with allele frequency < 0.5% are considered as rare variants in 1000 genomes project.*

Graphic adapted from Mark Gerstein (GersteinLab.org; @markgerstein)
Quantifying Somatic Mutations In Cancer

Pan-Cancer Analysis of Whole Genomes (PCAWG) data show widespread mutations in non-coding regions of cancer genomes (Khurana et al., Nat. Rev. Genet. (2016)).

On average ~19% of a cancer genome are in an imbalanced state (more/less than 2 alleles); Original data based on 43654 cancer genomes from progenetix.org
Limited Population Diversity in Cancer Studies

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.

**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.
The vision: Federation of data
30,000 patients will have their genome sequenced for rare-disease diagnosis

70,000 genomes (patients + relatives) will be sequenced to help rare disease diagnoses

23,000 cancer patients will have their genome sequenced

50,000 genomes will be sequenced for cancer diagnosis

36,223,000 rare disease patients will have their genome sequenced

83,000,000 genomes will be sequenced for rare disease diagnosis

123,768,000 cancer patients will have their genome sequenced

248,000,000 genomes will be sequenced for cancer diagnosis

*Projected figures, based on current data and known status of genomics initiatives worldwide.

Source: From Op-ed on BioRxiv

Slide provided by Heidi Rehm
GA4GH to solve accessibility...
The Global Alliance for Genomics and Health
Making genomic data accessible for research and health

- January 2013 - 50 participants from eight countries
- June 2013 - White Paper, over next year signed by 70 “founding” member institutions (e.g. SIB, UZH)
- March 2014 - Working group meeting in Hinxton & 1st plenary in London
- October 2014 - Plenary meeting, San Diego; interaction with ASHG meeting
- June 2015 - 3rd Plenary meeting, Leiden
- September 2015 - GA4GH at ASHG, Baltimore
- October 2015 - DWG / New York Genome Centre
- April 2016 - Global Workshop @ ICHG 2016, Kyoto
- October 2016 - 4th Plenary Meeting, Vancouver
- May 2017 - Strategy retreat, Hinxton
- October 2017 - 5th plenary, Orlando
- May 2018 - Vancouver
- October 2018 - 6th plenary, Basel
- May 2019 - GA4GH Connect, Hinxton
- October 2019 - 7th Plenary, Boston
- October 2020 - Virtual Plenary ...
Enabling genomic data sharing for the benefit of human health

The Global Alliance for Genomics and Health (GA4GH) is a policy-framing and technical standards-setting organization, seeking to enable responsible genomic data sharing within a human rights framework.
GA4GH API promotes sharing

A federated ecosystem for sharing genomic, clinical data

Silos of genome data collection are being transformed into seamlessly connected, independent systems.
A federated ecosystem for sharing genomic, clinical data

Silos of genome data collection are being transformed into seamlessly connected, independent systems.
Global Alliance “Beacon” - Jim Ostell, NCBI, March 7, 2014

Introduction

... I proposed a challenge application for all those wishing to seriously engage in international data sharing for human genomics. ...

1. Provide a public web service
2. Which accepts a query of the form “Do you have any genomes with an “A” at position 100,735 on chromosome 3?”
3. And responds with one of “Yes” or “No” ...

“Beacon” because ... people have been scanning the universe of human research for signs of willing participants in far reaching data sharing, but ... it has remained a dark and quiet place. The hope of this challenge is to 1) trigger the issues blocking groups ... in way that isn’t masked by the ... complexities of the science, fully functional interfaces, and real issues of privacy, and to 2) in short order ... see real beacons of measurable signal ... from at least some sites ... Once your “GABeacon” is shining, you can start to take the next steps to add functionality to it, and finding the other groups ...

Utility

Some have argued that this simple example is not “useful” so nobody would build it. Of course it is not the first priority for this application to be scientifically useful. ...intended to provide a low bar for the first step of real ... engagement. ... there is some utility in ...locating a rare allele in your data, ... not zero.

A number of more useful first versions have been suggested.

1. Provide frequencies of all alleles at that point
2. Ask for all alleles seen in a gene region (and more elaborate versions of this)
3. Other more complicated queries

Implementation

1. Specifying the chromosome ... The interface needs to specify the accession.version of a chromosome, or build number...
2. Return values ... right to refuse to answer without it being an error ... DOS attack ... or because ...especially sensitive...
3. Real time response ... Some sites suggest that it would be necessary to have a “phone home” response ...

"I would personally recommend all those be held for version 2, when the beacon becomes a service."  
Jim Ostell, 2014
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.
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.

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.
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 D to be attacked, which contains functional genomics reads and phenotypes for every individual in the cohort. The perfect information 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 gEU/ADIS 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.
"Sanitize"...

- "functional" genomics data can be sanitized by removing features which are not relevant for the specific use cases.

- An example could be the randomization of variant alleles in datasets where variant call specificity is of minor concern.
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

With information from https://www.imdb.com/title/tt0119177/
• 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
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 unreproducible 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

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

H.R. 510 (115th): 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. 135 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-WI).

Former FBI Director James Comey cited a real-life example of how the technology could be used effectively. “If 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 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 Parabon 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 Person, 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
Genomic Data & Privacy Protection - The Swiss View

Relevant areas

• Medical treatment (Federal Act on Human Genetic Testing, HGTA)
• Human Research (Human Research Act, HRA)
• Tests other than for medical purposes (*new* in the HGTA from 2021 on)
• Law enforcement (Federal Act on the Use of DNA Profiles in Criminal Proceedings and for Identifying Unidentified or Missing Person, DNA Profiles Act)
• Data protection (Data Protection Act, DPA)
• ...

Content provided by Julian Mausbach | Oberassistent für Strafrecht und Strafprozessrecht
Law's View on Modern Medicine

- How do we handle the growing overlap area?
  - unclear; current legislative movement: HRA will relate more to HGTA in the future

HGTA: Federal Act on Human Genetic Testing
HRA: Human Research Act

Content provided by Julian Mausbach | Oberassistent für Strafrecht und Strafprozessrecht
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 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 and 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 |
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?
Art. 5 Definitions

The following definitions apply in this Act:

a. **personal data**: all information relating to an identified or identifiable natural person;

b. **data subject**: natural person whose personal data is processed;

c. **sensitive personal data**:
   1. data on religious, ideological, political or trade union-related views or activities,
   2. data on health, the intimate sphere or the racial or ethnic origin,
   3. genetic data,
   4. biometric data which unequivocally identifies a natural person,

Therewith **Genetic Data is always sensitive data**, and especially Art. 6 Principles of data processing and **High-risk profiling**: profiling which involves a high risk to the personality or fundamental rights of the data subject, as it creates a pairing between data that enables an assessment of essential aspects of the personality of a natural person, needs to be considered deeper.
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?
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).

Yaniv Erlich & Arvind Narayan. Nature Reviews Genetics 15, 409–421 (2014)
Way forward...
The vision: Federation of data
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 ...
SAFETY
PRIVACY
SECURITY
ACCESS
BENEFIT
CONSENT
CRYPTOGRAPHY
HACKERS
HEALTH
LAWS
SAFETY
LAW
Right to Research
Health
Insurance
Portability and Accountability Act
Genetic Information Nondiscrimination Act
Modernizing Patient Consent

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

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**Consent Codes: Upholding Standard Data Use Conditions**

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

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| Consent Code | Name | Abbreviation | Description |
|--------------|------|--------------|-------------|
| no restrictions | NRES | No restrictions on data use. |
| general research use and clinical care | GRU(CC) | For health/medical/biomedical purposes and other 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. |
| 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). |
| Requirements | | | |
| not-for-profit use only | NP | 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 agrees to return derived/enriched data to the database/resource. |
| ethics approval required | BB | Requestor must provide documentation of local BB/REC approval. |
| geographical restrictions | GIS-[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. |

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

Blasimme, A., Vayena, E. & Hafen, E. Democratizing Health Research Through Data Cooperatives. *Philos. Technol.* 31, 473–479 (2018). https://doi.org/10.1007/s13347-018-0320-8
The BioMedIT network

BioMedIT provides researchers with access to a secure and protected computing environment for analysis of sensitive data without compromising data privacy.
GA4GH Passports

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

www.ga4gh.org/ga4gh-passports/
Empowering Beacon use through Access Levels

Integrating permissions and discovery

Do you have allele: T at position: 166226587 on: chromosome 2?

Beacon Metadata Profiles

https://www.youtube.com/watch?v=LyfmvAs7LtQ&feature=youtu.be
Have you seen deletions in this region on chromosome 9 in Glioblastomas from a juvenile patient, in a dataset with unrestricted access?

The Beacon API v2 proposal opens the way for the design of a simple but powerful "genomics API".
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
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!
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
• I'll be back on Zoom at 15:00 for Q&A
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