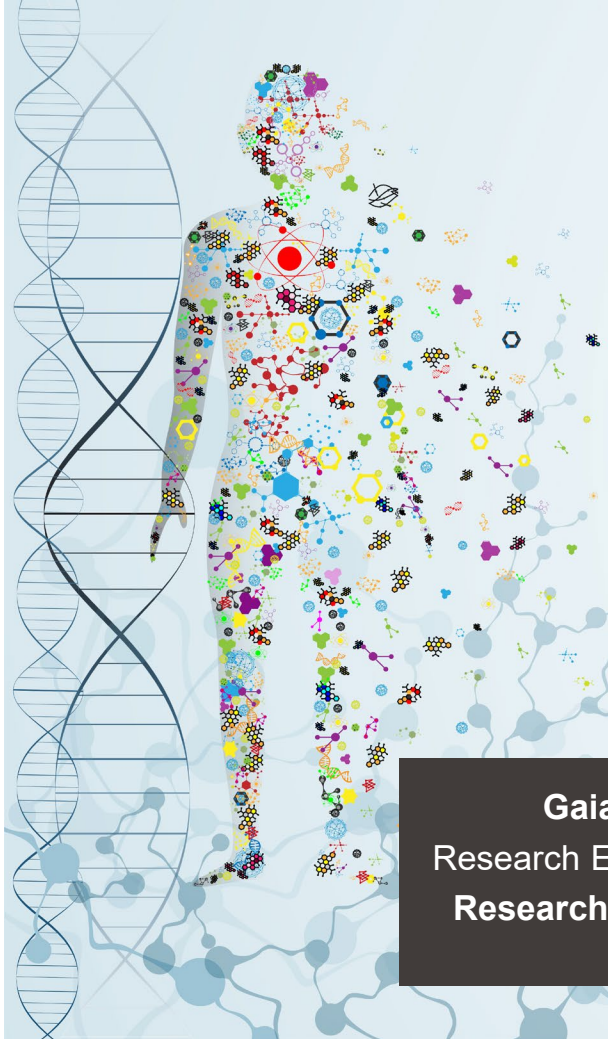


Ethical and Social Issues in Personalized Health

Gaia Barazzetti, PhD
Research Ethics Compliance Officer
Research Office / Ethics Affairs

6 March 2025

NEW TOOLS & RESEARCH STRATEGIES IN PERSONALIZED HEALTH

Gaia Barazzetti

Research Office / Ethics Affairs

- Support/guidance on:
  - ✓**Ethics compliance** of research projects
  - ✓**Ethical authorizations**
- Liaison with EPFL **Human Research Ethics Committee (HREC)**
- **Awareness-raising** initiatives / training

© EPFL – Alain Herzog

What do you think about this video?

https://vimeo.com/128873380

What do you think about this video?

- ✓ How the devices **impact on the quality of life** of the elderly?
- ✓ Are the devices **useful**, **to whom**?
- ✓ **Why** do you think the elderly person ends up with **cheating**?
- ✓ What would you do **if you were the elderly person**?
- ✓ Are the devices **really "personalized"**?
- ✓ …any other thoughts/questions?

OUTLINE

Ethics in research with human participants

Regulatory framework

Consent to research

Return of results

Public engagement

The woman in the photograph

- **Henrietta Lacks**
- **1951**: dies 31 from a cervical cancer, at Johns Hopkins (Baltimore, USA)
- Few months before, samples of cells taken from her cervix and put in culture, without her consent
- **Major breakthrough:** Henrietta's cells prove to be immortal, **1st human cell line "HeLa"**
- Cultured, sold, bought, and shipped by the trillions to labs around the world
- **Henrietta's family not aware** of the extensive use of HeLa cells in research

Gaia Barazzetti

The immortal life of Henrietta Lacks

- **HeLa: key tool in cancer research**
- Polio vaccine, cloning, gene sequencing, in vitro fertilization, drug development (e.g. herpes, leukemia, hemophilia)
- First space missions, first nuclear tests, human longevity…
- No way of knowing how many Henrietta's cells are alive today: 50 million metric tons… they'd wrap 3 times around Earth
- **Standard lab workhorse**, one of the most important discoveries in the life sciences in the last 100 years…

Henrietta, her family & the research community

- **1973: Family learns about** Henrietta's cells use in research totally by chance…
- Blood samples used for genome cartography, family believes they are having blood tests…
- **1980s: The Lacks family public claim for recognition** of Henrietta's posthumous contribution to science… some of them accuse researchers (violation of privacy, lack of transparency)
- **2013: Agreement between NIH and the Lacks**

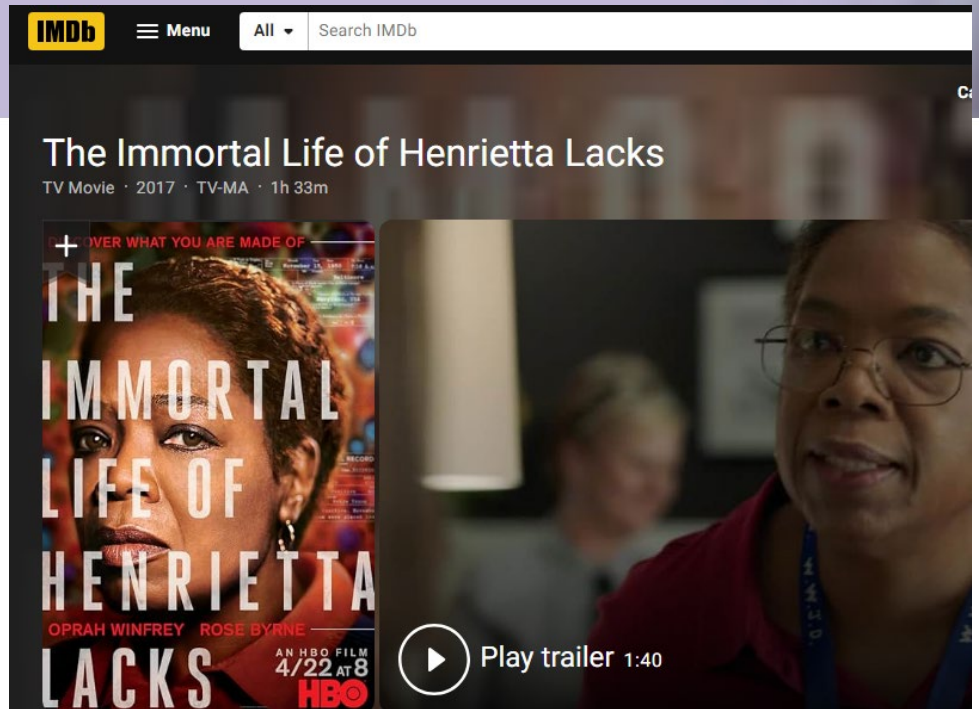
Henrietta Lacks with her husband David.

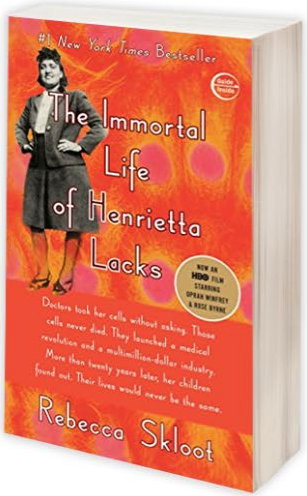
Henrietta Lacks' family gather around a historical marker dedicated to her in Virginia in 2011.

Family matters

Kathy L. Hudson and **Francis S. Collins** discuss how and why the US National Institutes of Health worked with the family of Henrietta Lacks, the unwitting source of the HeLa cell line, to craft an agreement for access to HeLa genome data.

The Immortal Life of Henrietta Lacks named by more than 60 critics as one of the best books of 2010.





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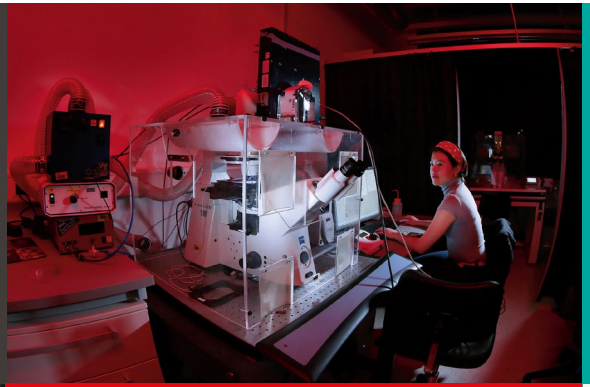
Research with human biologic samples

- **Separate human body parts ≠ Human person**
- **Persons (their interests) may be concerned:**
  - ✓Privacy protection
  - ✓Respect of personal values
  - ✓DNA samples: relatives concerned
- **Multiple uses in research**, by **different users**, **over long periods of time** (e.g., *post-mortem*)

Three fundamental ethical guiding principles for research with humans

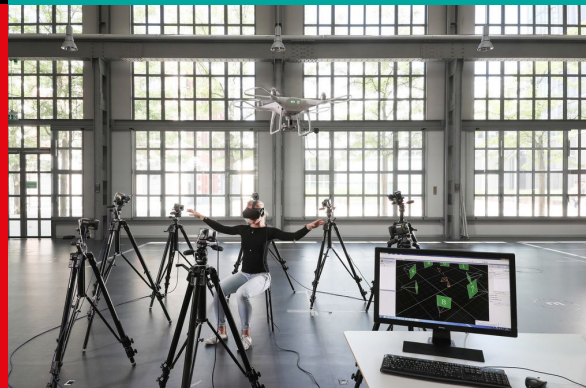
Gaia Barazzetti

Respect for persons



Beneficence

Justice



Respect for persons

- **Respect personal autonomy**
- **Protect** non-autonomous persons

Informed consent:

✓**Obtain consent** of autonomous persons

✓Non-autonomous persons: **obtain consent of legal guardian**

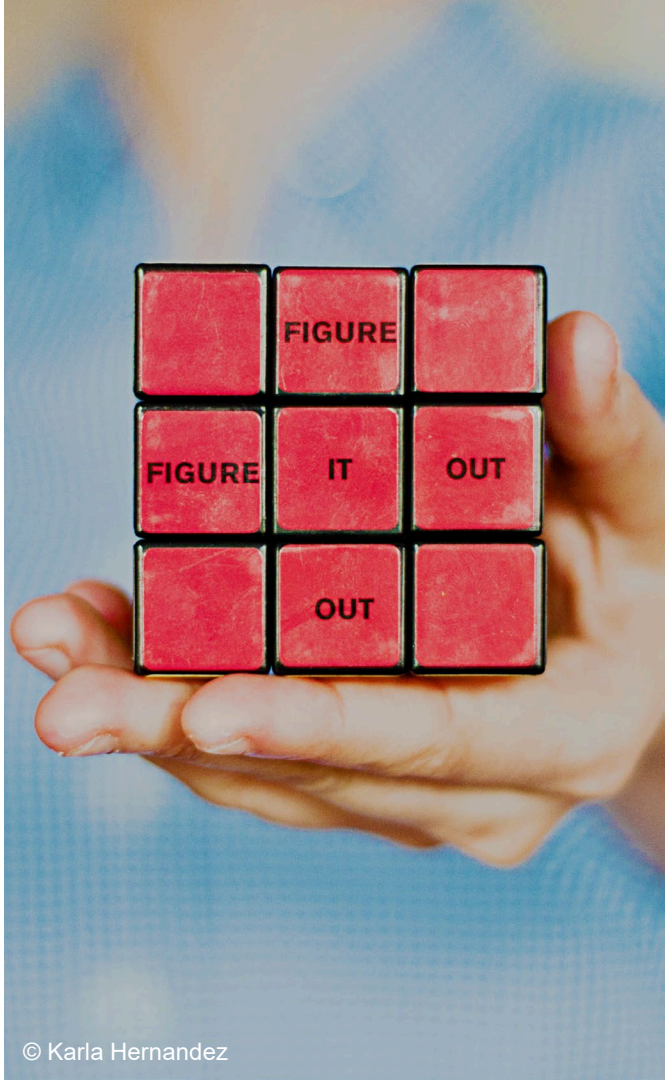
Beneficience

- **Do not harm**
- Maximize potential **advantages** and reduce possible **disadvantages**

Favourable risks/benefits ratio:

✓**Minimize** as much as possible **research risks** (no such thing as “zero risk”)

✓**Maximize** potential **research benefits**



© Karla Hernandez

Justice

- **Fair distribution** of **risks/benefits** of research

Fair research subjects selection:

✓Clarify **inclusion-exclusion criteria**

✓**Non-discrimination**

Research on vulnerable participants

- **Vulnerable persons:**
  - ✓ Persons lacking capacity in the consent procedure
  - ✓ Children, adolescents
  - ✓ Prisoners
  - ✓ Emergency situations
  - ✓ …
- **Vulnerability: limited autonomy**, social **stigmatization**, physical/psychological **sensitivity** to research procedures, people in **poor/low-income/developing countries**, etc.

OUTLINE

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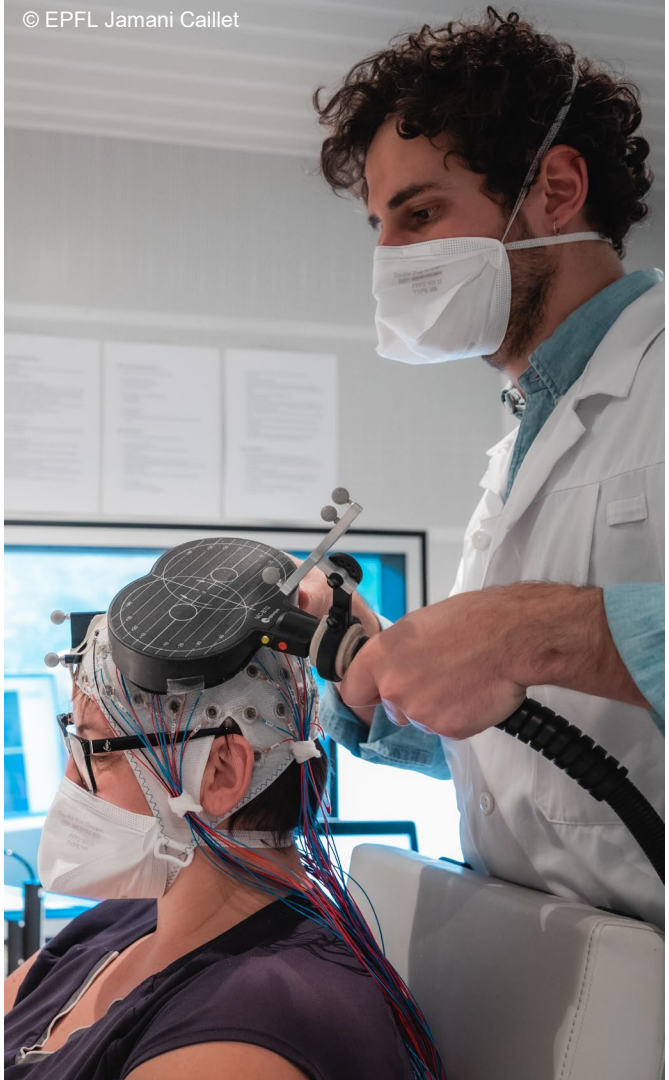
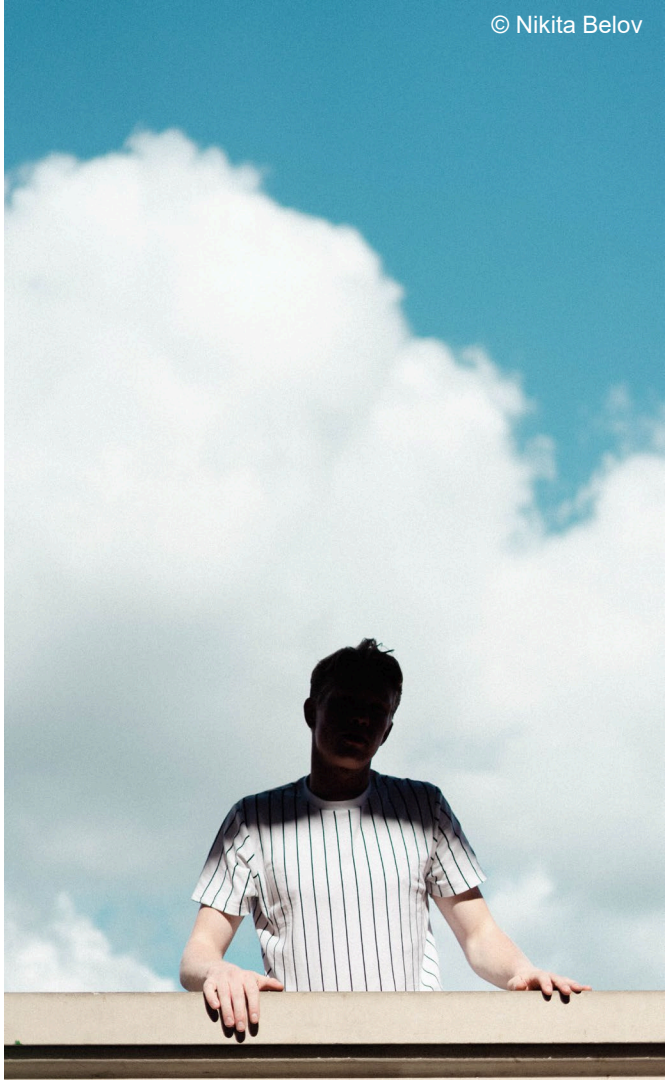
Federal Act on Research Involving Human Beings (Human Research Act – HRA)

- **Aim:** Protection of individual's **dignity, health and privacy**
- **Scope:** Research concerning **human diseases and the structure/function of the human body** (persons, deceased persons, embryos and fetuses, **biological material**, **health-related data**)
- **Health-related data:** information concerning health/disease of an identifiable person, including **genetic data**
- **Authorization of Cantonal ethics commission**



What is “personal” data?

- **Personal data:** all information relating to an **identified or identifiable natural person** (e.g., name, address/ZIP code, e-mail, IP address, body characteristics, usage of social networks)
- **Sensitive data:** data relating to **religious**, **philosophical**, **political** or **trade union-related views or activities**, data relating to **health**, the **private sphere** or affiliation to **ethnicity**, **genetic** data, **biometric** data that uniquely identifies a natural person, data relating to **administrative** and **criminal** proceedings or sanctions, data relating to **social assistance measures**



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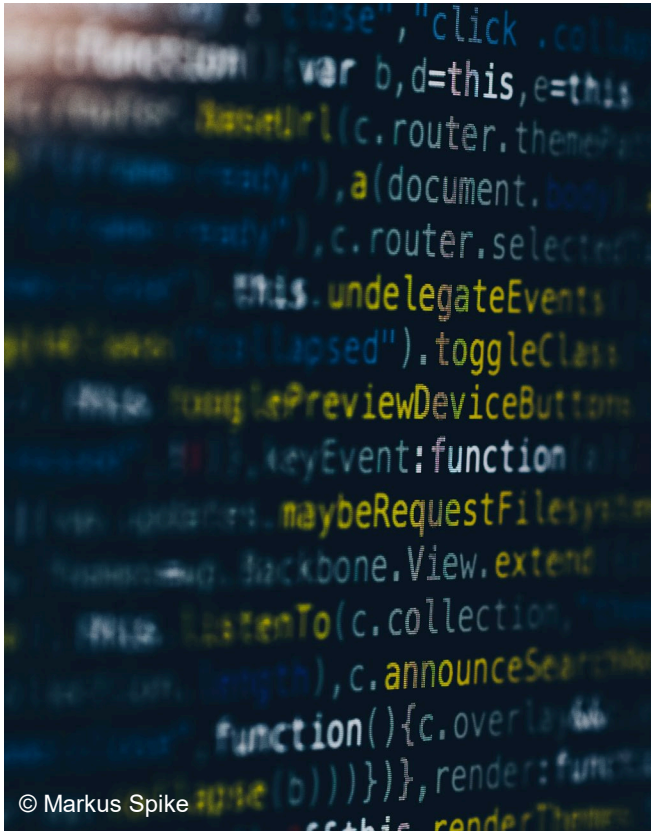
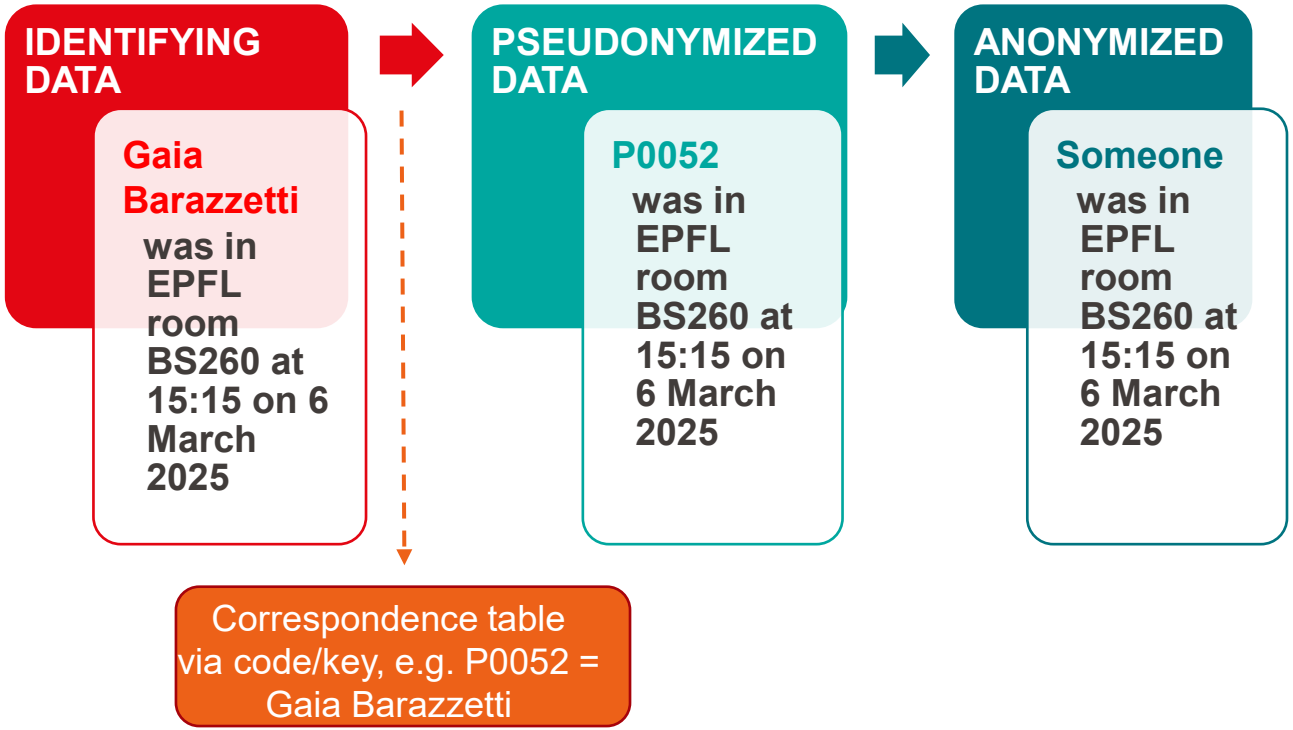
Federal Act on Data Protection (FADP)



- **Aim: protection** of the **personality** and **fundamental rights** of individuals whose data is being processed
- **Scope:** applies to **personal data processing** (collection, storage, use, disclosure, archiving, destruction)
- As of September 1st, 2023: **revised** to be more in line with the **EU-GDPR** (General Data Protection Regulation)

Anonymized vs. Pseudonymized (or Coded) Data



Limitations in anonymizing genetic data

https://www.ncbi.nlm.nih.gov/pubmed/23329047

Identifying Personal Genomes by Surname Inference

Melissa Gymrek,[1,2,3,4] Amy L. McGuire,[5] David Golan,[6] Eran Halperin,[7,8,9] Yaniv Erlich[1]*

Sharing sequencing data sets without identifiers has become a common practice in genomics. Here, we report that surnames can be recovered from personal genomes by profiling short tandem repeats on the Y chromosome (Y-STRs) and querying recreational genetic genealogy databases. We show that a combination of a surname with other types of metadata, such as age and state, can be used to triangulate the identity of the target. A key feature of this technique is that it entirely relies on free, publicly accessible Internet resources. We quantitatively analyze the probability of identification for U.S. males. We further demonstrate the feasibility of this technique by tracing back with high probability the identities of multiple participants in public sequencing projects.

Surnames are paternally inherited in most human societies, resulting in their co-segregation with Y-chromosome haplotypes (*1*–*5*). Based on this observation, multiple genetic genealogy companies offer services to reunite distant patrilineal relatives by genotyping a few dozen highly polymorphic short tandem repeats across the Y chromosome (Y-STRs). The association between surnames and haplotypes can be confounded by nonpaternity events, mutations, and adoption of the same surname by multiple founders (*5*). The genetic genealogy community addresses these barriers with massive databases that list the test results of Y-STR haplotypes along with their corresponding surnames. Currently, there are at least eight databases and numerous surname project Web sites that collectively contain hundreds of thousands of surname-haplotype records (table S1).

[1]Whitehead Institute for Biomedical Research, 9 Cambridge Center, Cambridge, MA 02142, USA. [2]Harvard–Massachusetts Institute of Technology (MIT) Division of Health Sciences and Technology, MIT, Cambridge, MA 02139, USA. [3]Program in Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, MA 02142, USA. [4]Department of Molecular Bi-

By combining other pieces of demographic information, such as date and place of birth, they fully exposed the identity of their biological fathers. Lunshof *et al*. (*10*) were the first to speculate that this technique could expose the full identity of participants in sequencing projects. Gitschier (*11*) empirically approached this hypothesis by testing 30 Y-STR haplotypes of CEU participants in these databases and reported that potential surnames can be detected. [CEU participants are multigenerational families of northern and western European ancestry in Utah who had originally had their samples collected by CEPH (Centre d'Etude du Polymorphisme Humain) and were later reconsented to participate in the HapMap project.] However, these surnames could match thousands of individuals, and the study did not pursue full re-identification at a single-person resolution.

Our goal was to quantitatively approach the question of how readily surname inference might be possible in a more general population, apply this approach to personal genome data sets, and demonstrate end-to-end identification of individuals with only public information. We show that full identities of personal genomes can be exposed via surname inference from recreational genetic genealogy databases followed by Internet searches. In all cases in which individuals were

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DeepMind faces legal action over NHS data use

1 October 2021

The records collected by DeepMind went back over the past five years and many were surprised when they learned the use of them

A legal case has been launched on behalf of more than a million people whose confidential medical records were obtained by Google.

Source BBC: LINK to article

UK court tosses class-action style health data misuse claim against Google DeepMind

Natasha Lomas

@riptari / 7:13 am PDT • May 19, 2023

Image Credits: Jonathan Brady/PA / Getty Images

Source TechCrunch: LINK to article

Informed consent: practical issues

- **What information** should be given?
  - Any information necessary to make your choice, including use/dissemination of data collected
- **How** to give it?
  - Information sheet & consent form, plain/understandable language
- Take into account implications for **all subjects concerned**
  - E.g. research in epidemiology, genetics, etc.
- Is consent **really informed**?
  - Understanding of information by the research subject…

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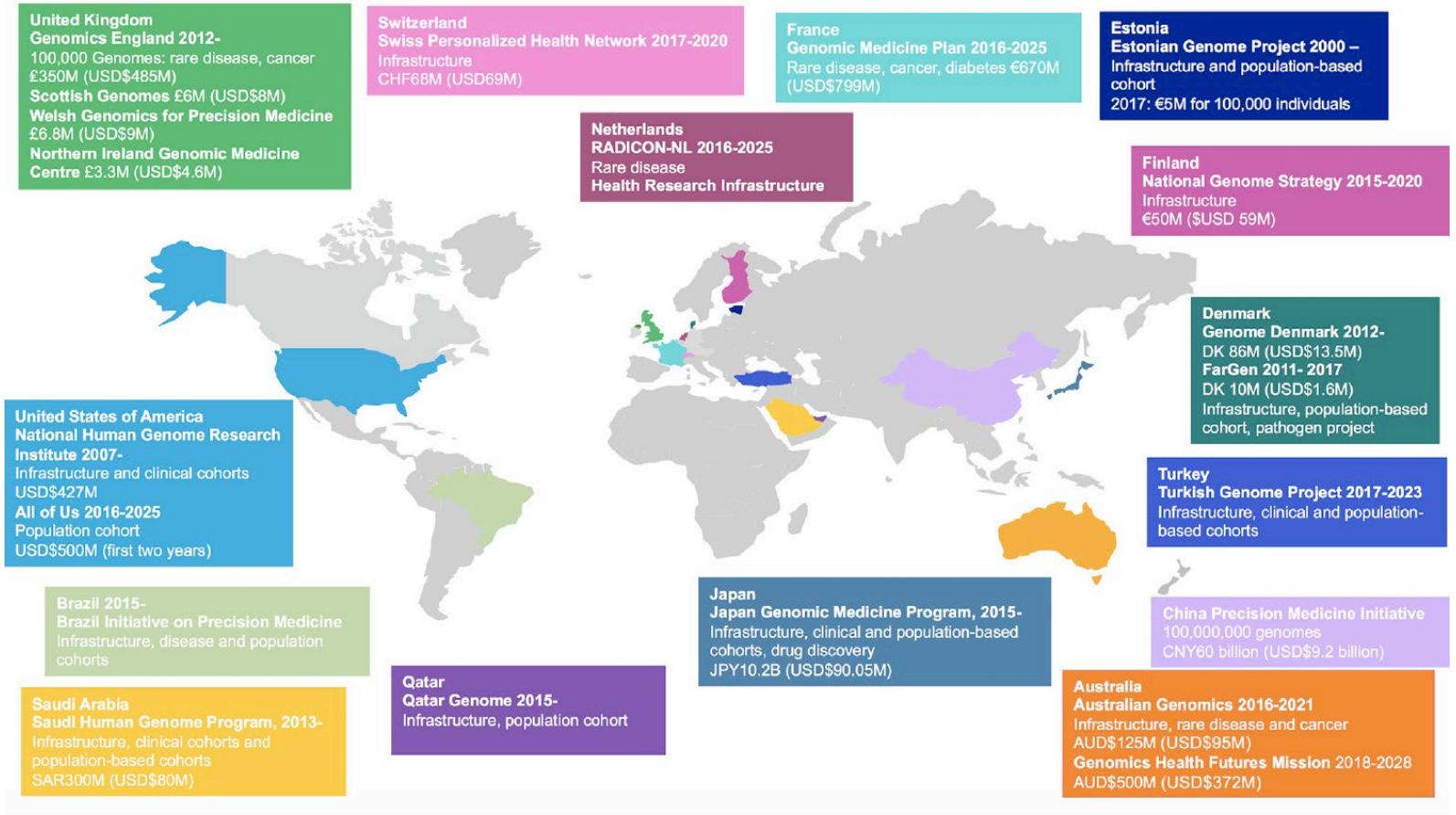
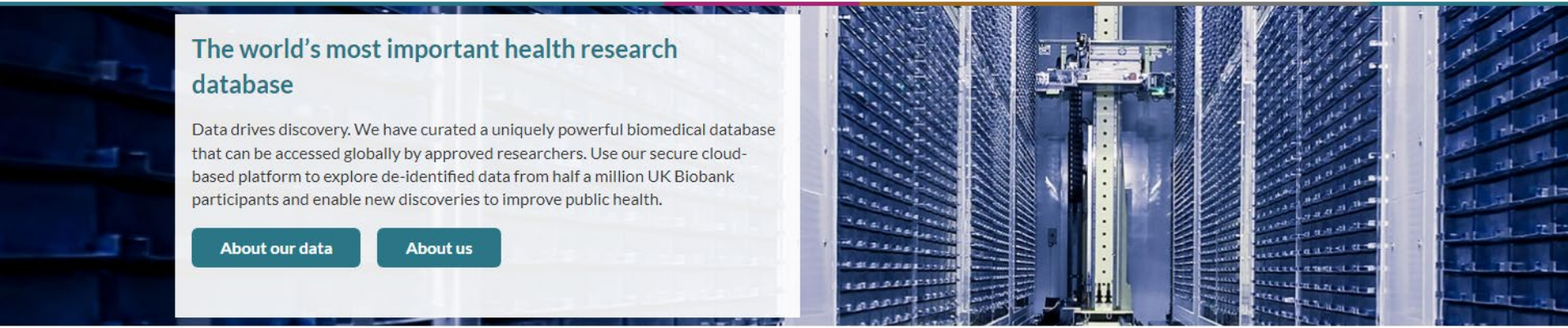
National genomic medicine initiatives worldwide



https://doi.org/10.1016/j.ajhg.2018.11.014

Researcher log in | Participant log in | Contact us

Enable your research | Explore your participation | Learn more about UK Biobank



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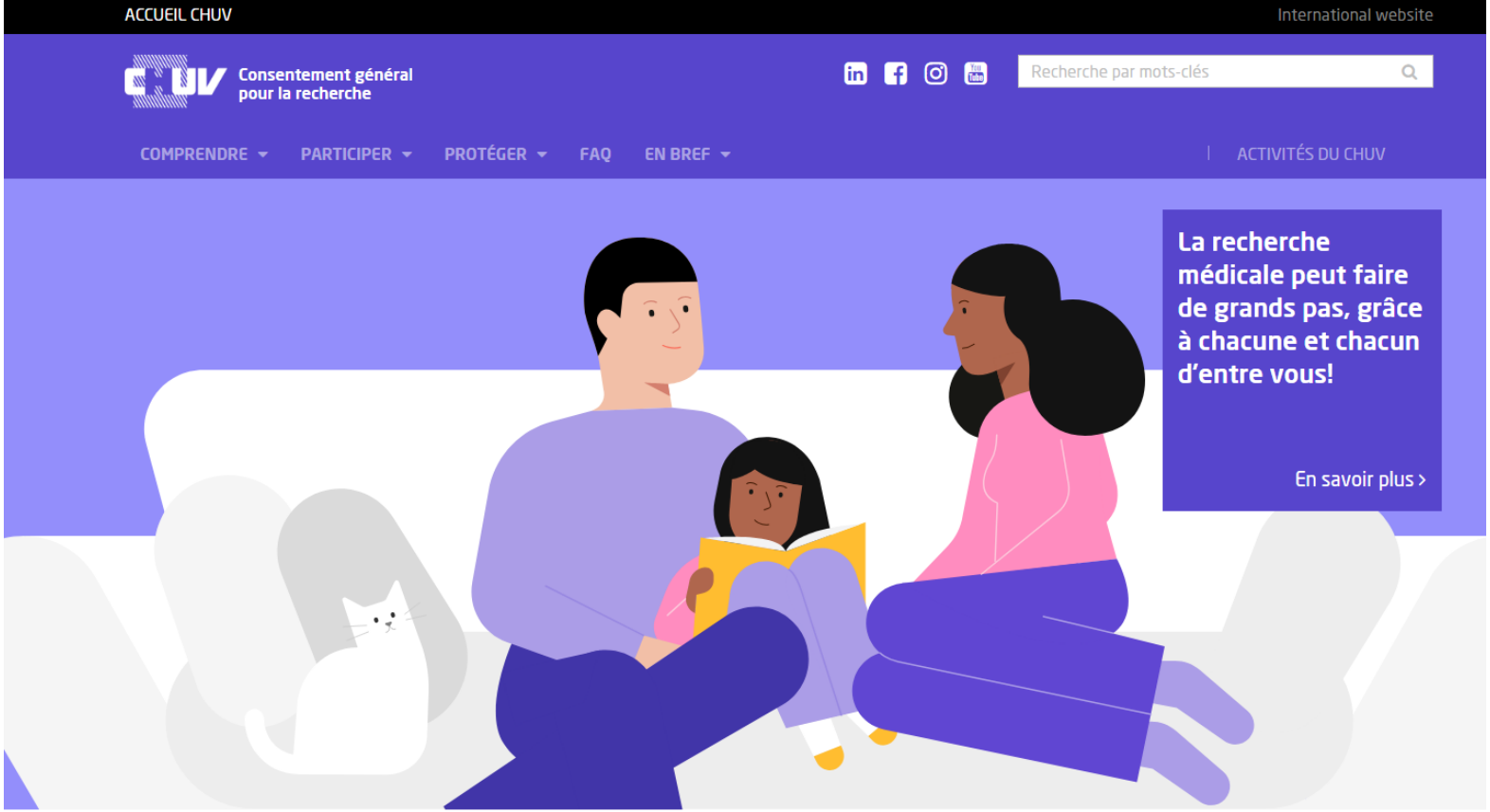
Problems in applying consent

- Screening & matching genomes generates **research questions** that **cannot be anticipated at the time of collection**
- Individuals are asked to participate in **open-ended datasets/biobanks** that can be used for many protocols, on many different medical conditions
- Datasets/biobanks **linked/added over time**, **accessible by different users**



Consentement général pour la recherche - Accueil - CHUV

Consentement général pour la recherche

Besoin d'aide

Consentement général

Contacts

Unité consentement à la recherche
Boîte aux lettres N° 47

Broad Consent

- ✓**Relevant information** provided (general goals of research, data storage/protection, data sharing) to make an **autonomous choice**
- ✓**Safeguards** in place to protect participants' interests
  - Protocol review/authorization by **research ethics committees**
  - **right to withdraw consent** at any time
- ✓**Consent reaffirmed in case of change of biobank initial purpose**

CHRIS

CHRIS (Cooperative Health Research in South Tyrol) is the name of the population study promoted by the Institute of Biomedicine of Eurac Research and the South Tyrolean Health Authority.

The study

CHRIS is an epidemiological study started in 2011. It takes the form of a long-term health study in South Tyrol and aims to understand the occurrence and development of chronic diseases associated with ageing that are widespread in the population. Examples of such diseases are diabetes, cardiovascular disorders and Parkinson's disease. Through the CHRIS study, researchers have the opportunity to analyze the role of genetic and environmental factors (and their interaction) in determining or contributing to neurological, cardiovascular and metabolic diseases.

CHRIS - Eurac Research

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Dynamic consent

Participants enabled to:

- **Express preferences** about the use of their samples & data through an **IT interactive interface**
- **Track/audit choices** & **change preferences over time**
- **Be informed about progress/outcomes of research**

OUTLINE

Ethics in research with human participants

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Return of results

Public engagement

29.11.2021

INSTITUTE

Contact
info@geenidoonor.ee

Estonian Biobank

The Estonian Biobank has established a population-based biobank of Estonia with a current cohort size of **more than 200,000 individuals** (genotyped with genome-wide arrays), reflecting the age, sex and geographical distribution of the adult Estonian population. Considering the fact that **about 20% of Estonia's adult population** has joined the programme, it is indeed a database that is very important for the development of medical science both domestically and internationally. Researchers from the Estonian Genome Center at the University of Tartu alone have published over 830 research papers in peer-reviewed journals based on data from the Estonian biobank.

Estonian Biobank

ARTICLE

Check for updates

Lessons learned during the process of reporting individual genomic results to participants of a population-based biobank

Liis Leitsalu[1]✉, Anu Reigo[1], Marili Palover[1], Tiit Nikopensius[1], Kristi Läll[1], Kristi Krebs[1], Sulev Reisberg[2,3], Reedik Mägi[1], Mart Kals[1,4], Helene Alavere[1], Margit Nõukas[1], Anneli Kolk[5], Ivi Normet[6], Mari-Liis Tammesoo[1], Ene Käärik[7], Mairo Puusepp[1], Kristjan Metsalu[1], Annely Allik[1,8], Lili Milani[1], Krista Fischer[1,7], Neeme Tõnisson[1,9,11] and Andres Metspalu[1,10,11]

The return of individual genomic results (ROR) to research participants is still in its early phase, and insight on how individuals respond to ROR is scarce. Studies contributing to the evidence base for best practices are crucial before these can be established. Here, we describe a ROR procedure conducted at a population-based biobank, followed by surveying the responses of almost 3000 participants to a range of results, and discuss lessons learned from the process, with the aim of facilitating large-scale expansion. Overall, participants perceived the information that they received with counseling as valuable, even when the reporting of high risks initially caused worry. The face-to-face delivery of results limited the number of participants who received results. Although the participants highly valued this type of communication, additional means of communication need to be considered to improve the feasibility of large-scale ROR. The feedback collected sheds light on the value judgements of the participants and on potential responses to the receipt of genetic risk information. Biobanks in other countries are planning or conducting similar projects, and the sharing of lessons learned may provide valuable insight and aid such endeavors.

European Journal of Human Genetics (2023) 31:1048–1056; https://doi.org/10.1038/s41431-022-01196-6

Return of results

Right to know / Right not to know

EU Convention on Human Rights and Biomedicine

Oviedo 1997

https://www.coe.int/en/web/conventions/full-list/-/conventions/rms/090000168007cf98

Chapter III – Private life and right to information

Article 10 – Private life and right to information

1 Everyone has the right to respect for private life in relation to information about his or her health.

2 Everyone is entitled to know any information collected about his or her health. However, the wishes of individuals not to be so informed shall be observed.

Incidental findings

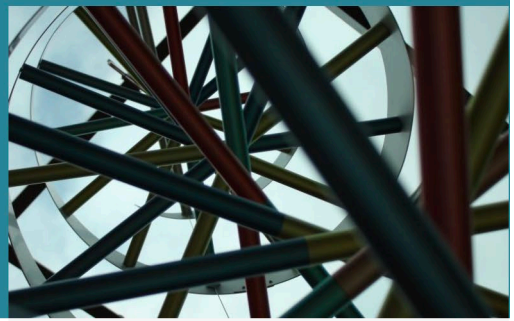
Research results
outside the original purpose of research,
that can have **implications**
for participant's
health/quality of life

Iceland: deCode Genetics & BRCA1/2

https://pulitzercenter.org/reporting/right-not-know-when-ignorance-bliss-deadly

PROJECT

Iceland: Ethical Challenges of Genetic Testing



Donate Now

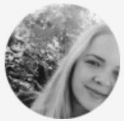
Having BRCA gene mutations can bring the odds of developing breast cancer up to 80 percent. However, that risk can be brought down to almost none with preventative surgeries.

One in every 500 women in the U.S. carries a BRCA1 or BRCA2 mutations. Figuring out who they are would be very complicated and even if it could be done, should it?

This is a question for Iceland, a country that is at the forefront of genetic research. The biopharmaceutical company deCode Genetics has discovered that 0.7 percent of the nation likely carries the BRCA2 mutation. The company knows who these people are and wants to warn them, but it can't. The individuals have the right not

Genetic scientists in Iceland want to warn 2,400 people who are more likely than others to develop breast cancer, but they can't. The individuals have the right not to know.

AUTHOR



ANNA MARSIBIL CLAUSEN

Student Fellow

Anna Marsibil Clausen is an Icelandic writer and reporter, currently studying at the University of California, Berkeley, Graduate School of Journalism. She reports on the intersection between society...

Iceland: deCode Genetics & BRCA1/2

"If someone goes missing in the highlands we send search parties of a few hundred to look for them," he says. "We do this without asking their permission. We are infringing on their right to be left alone just as much as if we try to save the lives of people with these mutations."

Kári Stefánsson deCode's CEO

"If I would have known, I'm not sure I would have had my two younger children," she says. "I don't want to spread this on. I feel guilty, as a mother."

Erna, 47 years, breast cancer survivor, diagnosed with BRCA2

"To be alive is deadly, and if you are always thinking 'what if,' then you are stuck in a cycle of angst," she says. "As someone who suffers from anxiety I try to shut these thoughts out, but of course they appear."

Íris, 31 years, waited almost a decade to go in for a BRCA1 diagnosis

"I don't like to talk about the right not to know," she says. "This is the right to know when it's right for you."

Vigdís Stefánsdóttir, genetic counsellor, Iceland National University Hospital

Return of results

- Ongoing discussion on criteria:
  - ✓ **Clinically actionable**
  - ✓ **Carrier status**: parental decisions
  - ✓ **Non clinically actionable** but risk of serious health condition (late onset disease)
  - ✓ **Personal value**: genetic relatives, socio-economic conditions, etc.
- Implications for **consent** and **public health**

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Public engagement

Public engagement

"…a group of procedures designed to **consult**, **involve**, and **inform** the public to allow those affected by a decision to have an **input** into that decision"

Smith, L. G. 1983. Impact assessment and sustainable resource management. Harlow, UK: Longman

Rowe, G. and Frewer, L.J. 2000. Public participation methods: a framework for evaluation. *Science Technology & Human Values* 25(1): 3-29

Gaia Barazzetti

Public engagement in Pensonalized Health

- Potential impact on **common good** and **individual rights**
- **Controversial issues**
- **Public trust**
- Social **acceptability** and **desirability**
- **Research participants/patients/publics** as **partners**

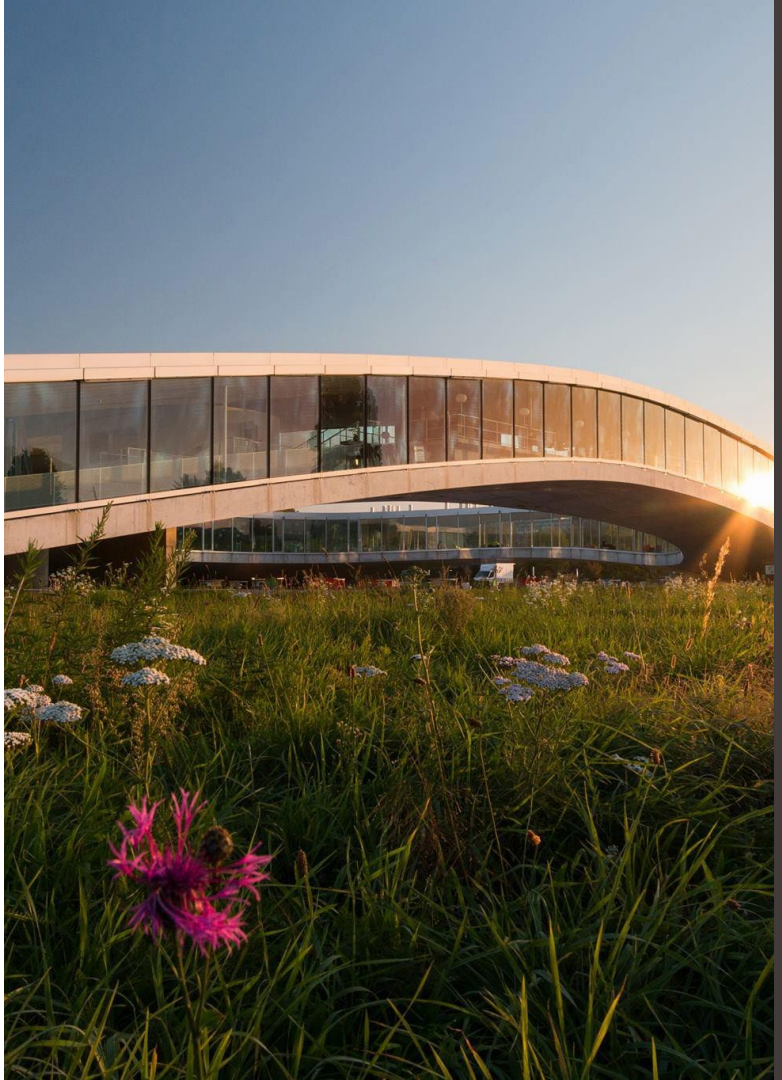
SANTÉ PERSONNALISÉE & SOCIÉTÉ

La santé personnalisée

La santé ou médecine personnalisée est constituée de trois avancées fulgurantes: l'accélération du décryptage génomique, le captage et le stockage de quantités croissantes de données individuelles et la capacité d'analyser et de comparer les gigantesques quantités de données ainsi recueillies. Son but est de délivrer des diagnostics et des traitements médicaux « sur mesure ». Elle ouvre aussi la porte à une évaluation beaucoup plus précise des risques de développer des maladies, longtemps avant qu'elles ne se déclarent. Cette nouvelle approche fait bien sûr progresser la médecine, en offrant des possibilités de prévention et de soins plus efficaces, plus ciblés et grevés de moins d'effets secondaires. Mais elle modifie aussi en profondeur ce que l'on entend par médecine, santé et solidarité. Quant au débat actuel autour de la santé personnalisée, il se réduit encore trop souvent à des discussions entre spécialistes.

ECOS: Espace de convergence des savoirs sur la santé personnalisée

https://www.youtube.com/watch?v=eA3RD5KNuHc



Thank you !

Questions to:
gaia.barazzetti@epfl.ch