ge²p² global foundation
governance, ethics, evidence, policy, practice

Genomic Medicine :: Governance, Ethics, Policy, Practice – A Monthly Digest

September 2023 Number 07

Genomic medicine – spanning pre-clinical basic science through clinical development and translation to daily patient interventions – continues to evolve at an extraordinary pace. Advances in the scientific and technical dimensions of genomic medicine are extensively communicated through the peer-reviewed journal literature and supporting grey literature.

Complementing this technical literature is a growing body of research, analysis and commentary addressing the governance, ethics, regulation, and policy dimensions of genomic medicine. Much of this content is communicated through academic journals and grey literature. This digest intends to capture and curate the most substantive examples of this non-technical content.

Further, we intend this digest to provide a useful summary of key strategic and programmatic announcements from across the genomic medicine ecology as issued by multilateral agencies, INGOs, governments/regulatory bodies, academic and research institutions, consortiums and collaborations, foundations, investors, and commercial organizations.

Given the complexity and velocity of the field, we recognize that this digest will be indicative, not exhaustive. We invite suggestions and ideas on how it can evolve to be more useful.

The digest is a program of the GE2P2 Global Foundation which is solely responsible for its content. Questions and comments should be directed to the Editor or Associate Editor:

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This edition reflects our substantially increased coverage of the genomic medicine landscape and organizes content as below:

Milestones, Strategic Announcements, Research, Actions

In this section, we will present what we assess to be significant developments in governance, ethics and policy in the genomic medicine field and provide additional context via an Editor's Note where indicated. Please help us strengthen this section by alerting us to developments we may not have encountered/included.

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DNA.I. - Early findings and emerging questions on the use of AI in genomics

Report, August 2023
Ada Lovelace Institute, Nuffield Council on Bioethics

This report was authored by Harry Farmer, with substantial input from Andrew Strait and Francine Bennett (Ada Lovelace Institute), and Catherine Joynson and Peter Mills (Nuffield Council on Bioethics).

Executive summary

In recent years, the scientific fields of artificial intelligence (AI) and genomics have experienced increased public attention and investment by public and private institutions. The UK Government, for example, has made explicit plans to become 'the most advanced genomic healthcare system in the world', and lists AI as one of five 'critical technologies' that can make the country a scientific superpower.*1*

Both AI and genomics have already been used to address major scientific challenges, including genomic sequencing to identify novel COVID-19 variants*2* and the use of AI and machine learning to predict the structure of proteins.3 **But both fields have also resulted in controversies over their ethical and societal implications**, and raised a host of difficult issues for those looking to regulate, direct and govern their development and use. In genomics, recent debates about acceptable uses of CRISPR-Cas9 have raised concerns around the ethics of genetic engineering.*4* Similarly, the field of AI has recently experienced an increasingly intense public conversation about the ethical and societal implications of foundation models, powerful AI systems capable of a wide range of general tasks.*5*

AI and genomics are also becoming progressively more intertwined. Many recent advances in genomics have been made possible by the use of AI,*6* and AI research and product teams have increasingly sought to use genomic data to create AI-powered genomics research and products.*7* Economic forecasts have suggested the market for AI and genomics technologies could reach more than £19.5 billion by 2030, up from half a billion in 2021.*8*

The increasing convergence of AI and genomics is set to present policymakers with a new set of practical and theoretical challenges. Considered separately, developments in AI and in genomics already pose **deep questions concerning agency, privacy, quality, bias and power**. Considered in relation to one another, the issues posed by the two technologies become harder to predict, more complex and more numerous.

While there has been much research considering the ethical impacts of AI and genomics as separate technologies, comparatively **little attention has been paid to exploring the broader implications of the two technologies when used together,** and from a structural perspective. For policymakers seeking to navigate and regulate AI and genomics, this is a critical evidence gap.

AI and genomics futures is a joint project between the Ada Lovelace Institute and the Nuffield Council on Bioethics that investigates the ethical and political economy issues arising from the application of AI to genomics – which we refer to throughout this report as **AI-powered genomics.**

This report of our early findings sets out the results of our research, its significance for policymakers, and the specific topics and questions we will focus on.

Our research shows that:

- **AI-powered genomics has seen significant growth** in the past decade, driven principally by advances in machine learning and deep learning, and has developed into a distinctive, specialised field.
- **Private-sector investment in companies working on AI-powered genomics has been substantial** – and has mainly gone to companies working on data collection, drug discovery and precision medicine.
- The most prominent current and emerging themes in research on AI-powered genomics relate to **proteins and drug development, and the prediction of phenotypic traits from genomic data.**

Moreover:

- The specific combination of emerging themes and capabilities identified in AI-powered genomics points to the **increasing viability of two broad techniques within healthcare over the next five to ten years:**
    - **AI-powered genomic health personalisation**: the ability to understand how treatment for the same health condition might vary between different people on the basis of genomic variations, and to tailor and adapt treatments accordingly.
    - **AI-powered genomic health prediction**: the use of genomic data to estimate the probability of different people developing particular health conditions, responding well or badly to particular medicines or treatments, or being affected by lifestyle factors.
- **The potential emergence of these techniques raises profound, urgent ethical, legal and policy questions.**
- While some of these issues are already discussed and accounted for in existing legal, ethical and policy discourse, there are many questions concerning the macro-level impacts of developments in AI-powered genomics that have yet to be adequately explored.
- In particular, there is an urgent, relatively unmet need for sustained thinking and research on the structural, political, and economic implications of AI-powered genomic health prediction, and how its development might be steered and governed in line with public values and priorities.

Professor Dave Archard, Chair of the Nuffield Council on Bioethics, said: "The combination of AI and genomics offers a great deal of opportunity, such as AI-powered genomic health prediction. With the technologies moving at pace, discussion of the ethical, legal and social implications of introducing them into our society must keep up. In the next phase of this work we will be exploring how the development of AI-powered genomic health prediction can be effectively steered and governed in line with public values and priorities, to make the most of its potential."

1 GOV.UK. 'The UK Science and Technology Framework'. Accessed 2 August 2023. https://www.gov.uk/government/publications/uk-science-and-technology-framework/the-uk-science-and-technology-framework.
2 GOV.UK. 'UK Completes over 2 Million SARS-CoV-2 Whole Genome Sequences'. Accessed 2 August 2023. https://www.gov.uk/government/news/uk-completes-over-2-million-sars-cov-2-whole-genome-sequences.
3 'AlphaFold'. Accessed 2 August 2023. https://www.deepmind.com/research/highlighted-research/alphafold.
4 Shinwari, Zabta Khan, Faouzia Tanveer, and Ali Talha Khalil. 'Ethical Issues Regarding CRISPR Mediated Genome Editing'. Current Issues in Molecular Biology, 2018, 103–10. https://doi.org/10.21775/cimb.026.103.
5 Jones, Elliot. 'Explainer: What Is a Foundation Model?' Ada Lovelace Institute, July 2023. https://www.adalovelaceinstitute.org/resource/foundation-models-explainer/.
6 Such as the DeepMind's development of Enformer, an AI tool that has led to improvements in predicting how a gene in a DNA sequence might be expressed: Avsec, Ž., Agarwal, V., Visentin, D. et al. Effective gene expression prediction from sequence by integrating long-range interactions. Nat Methods 18, 1196–1203 (2021). https://doi.org/10.1038/s41592-021-01252-x
7 One example of this is a surge of interest in applying AI techniques to genomic data for drug discovery: Eisenstein, M. Machine learning powers biobank-driven drug discovery. Nat Biotechnol 40, 1303–1305 (2022). https://doi.org/10.1038/s41587-022-01457-1
8 P&S Intelligence. 'AI in Genomics Market Outlook | Revenue Estimation Report, 2022-2030'. Accessed 2 August 2023. https://www.psmarketresearch.com/market-analysis/ai-genomics-market.

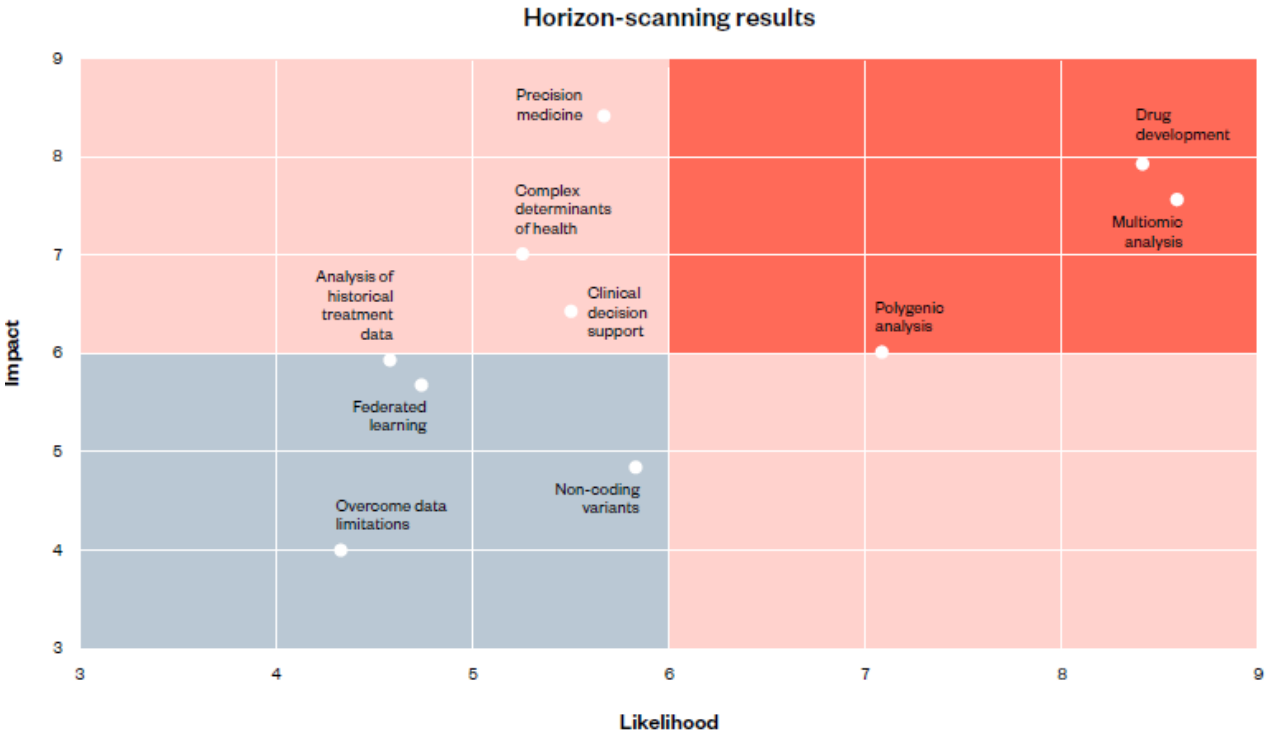

Figure 7: A plot of the results of the horizon-scanning process Those topics deemed most probable are plotted furthest to the right, and those assessed to be most impactful are plotted closest to the top.

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Towards a best practice UK model for ethical standards in genomics healthcare and research

Nuffield Council on Bioethics, UK
27 Jul 2023
The Nuffield Council on Bioethics is today publishing findings from work we have been leading on how to develop a UK best practice approach for ethics in genomics healthcare and research.

We are pleased to publish:

- **A summary report** which brings together key themes from the workshops which brought together people with experience in clinical genetics, public health, ethics, public engagement, research, policy and regulation, and those with personal experience of genetic conditions. Download the summary report (PDF)
- **A summary of 30 case study submissions** we received to our call for case studies held in summer 2022, illustrating how people in the UK are considering the ethical issues raised by genomics healthcare and research. Download the summary of case studies (PDF)

It is clear that clinicians, researchers, patients and policy makers are encountering a variety of ethical issues in genomics healthcare and research, and that ethical advice and guidance is spread out over many different institutions and locations which can make it hard to navigate.

Our work suggests that a best practice model could help those working in the field of genomics to negotiate these issues more effectively and help to promote a more consistent approach to considering ethical issues. The ultimate aim would be to improve, and make more equitable, the experiences of patients and research participants in studies that use genomic data.

Following today's publications, we are now planning a next-phase of work looking to map out existing resources and guidance on ethical considerations in the use of genomics in healthcare and research. We want to understand what is already available and identify areas where further guidance is needed. If you are someone who has experience in the field of genomics healthcare/research and ethics and would like to suggest resources to include in this developing piece of work, please do get in touch with us on bioethics@nuffieldbioethics.org.

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Ethics in genomics healthcare and research: building connections and sharing best practice

Summary report Published July 2023
Nuffield Council on Bioethics
[Excerpts]

Ethical Issues

…Clinicians, researchers, patients and policy makers are encountering a variety of ethical issues in genomics healthcare and research. These include:

- **Weighing the potential benefits and harms of genomics initiatives**, such as biobanks and research programmes.
- What needs to happen to ensure that patients and participants are able to provide **informed consent** for genomic and genetic testing and screening, and make decisions about this testing in children and people who are not able to give consent themselves.
- Deciding **what findings should be returned to patients** and participants and their families, how to do this and whose responsibility it is.
- Resolving the tension between respecting **data privacy** and facilitating the sharing and use of data for research and diagnosis.
- **Addressing inequalities in how people experience and benefit** from genomics healthcare and research and mitigating the potential for genetic discrimination.
- Understanding and **aligning genomics initiatives with public values**, for example in response to changing societal perceptions of disability and impairment.
- **Managing the expectations** of participants and patients, and generally avoiding hype around genomics.
- Supporting patients and members of the public in the context of **a growing commercial genomic and genetic testing market**.
- Considering the **implications of genomics beyond health**, such as in the fields of education and employment.

Key points

- Clinicians, researchers, patients and policy makers are encountering a variety of ethical issues in genomics healthcare and research.
- The development of a UK best practice approach – or gold standard model – for ethics in genomics healthcare and research could help those working in the field to negotiate ethical issues, promote consistency of approach and, ultimately, create better, more equitable experiences for patients and research participants.
- A best practice approach would need to incorporate different components such as ethical principles, professional guidance, discussion fora, and practical tool kits. The approach should be flexible to allow for interpretation in different contexts and regional variation.
- It is important that any best practice approach is transparent and inclusive, both in how it is produced and developed, and in who has access to it. A joined-up community and high-level buy-in around ethics and genomics will be needed.
- A UK approach to genomics ethics would need to be both sensitive to the international context of

- genomics and specific to UK audiences. It is not appropriate for the UK to aspire to lead the world in ethics. We should approach this task with humility and be open to diverse views.
- A next step would be to create a comprehensive map of existing resources in order to understand what is already available and identify areas where further work is needed.
- Further consideration is needed on the question of whether some elements of a best practice approach should be a requirement, or whether this is a purely advisory initiative.

Next steps

Suggested next steps include:

1. Create a comprehensive map of existing resources in order to understand what is already available and identify areas where further work is needed.
2. Building on this, identify or create an organisation to bring together and disseminate the components of a UK-wide best practice approach to ethics in genomics, with the recommendations of the workshop participants in mind.

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Featured Journal Content

Cell

Aug 17, 2023 Volume 186 Issue 17 p3523-3744 https://www.cell.com/cell/current

Featured Article

An ethical framework for human embryology with embryo models

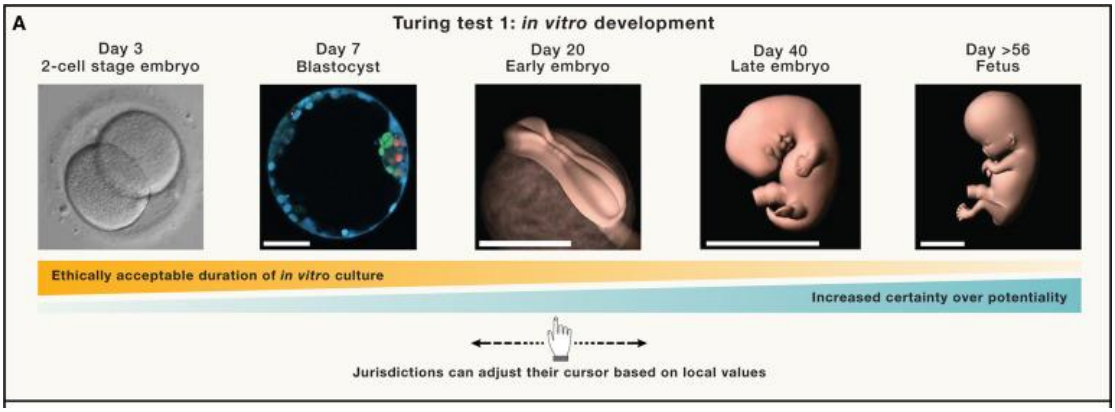
Nicolas C. Rivron, Alfonso Martinez Arias, Martin F. Pera, Naomi Moris, Hafez Ismaili M'hamdi

Open Access

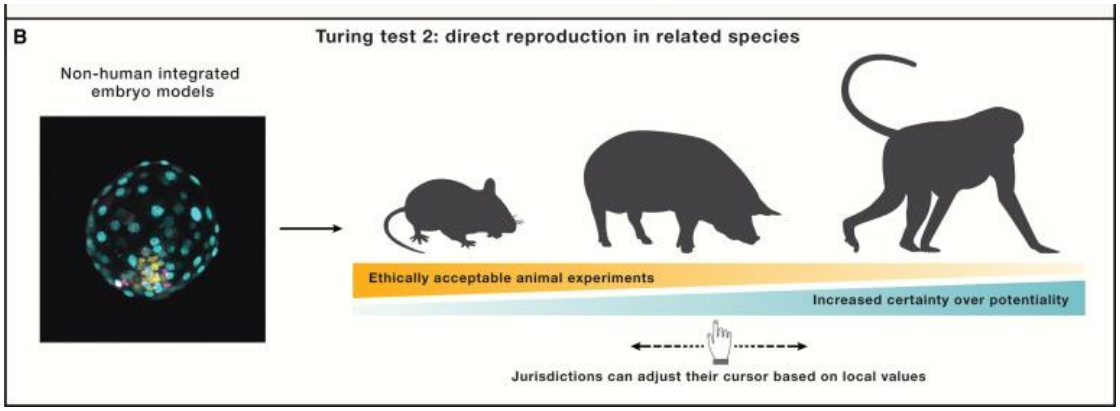
SUMMARY

A human embryo's legal definition and its entitlement to protection vary greatly worldwide. Recently, human pluripotent stem cells have been used to form in vitro models of early embryos that have challenged legal definitions and raised questions regarding their usage. In this light, we propose a refined legal definition of an embryo, suggest ''tipping points'' for when human embryo models could eventually be afforded similar protection to that of embryos, and then revisit basic ethical principles that might help to draft a roadmap for the gradual, justified usage of embryo models in a manner that aims to maximize benefits to society.

> *A human embryo model could be legally considered similar to a human embryo if it has shown a potential to form a fetus. Once it has passed this tipping point, it could become fully entitled as an embryo, regardless of how it formed. Because the Turing test would require the transfer of human embryo models in utero, which is prohibited due to justified ethical concerns, indirect tests can be used. We propose that human embryo models pass the tipping point when two tests are successfully passed.*



(A) A given human embryo model shows the potential to efficiently and faithfully produce the complete embryo in vitro as it normally forms up to a certain stage of development. This time point will be a compromise, based on local values, between a brief enough period of in vitro culture that is ethically acceptable and a sufficiently long period of in vitro culture that allows better evaluation of the model's potential.



(B) An embryo model formed by the same methodology has the potential to produce live and fertile animals in multiple species, particularly those closely related to humans, including pigs and non-human primates. The choice of species should represent a trade-off between their entitlement to protection and a development similar to that of humans. This balance should be evaluated in the context of local values.

- Box 1

Possible applications of basic ethics principles to embryo models

- Human embryo models should not be transferred into a uterus, whether animal or human, because of the risk of developing abnormally, resulting in possible harm to the gestational carrier and resulting fetus (already implemented in the ISSCR guidelines).[14,15]
- Permission from an ethics committee to culture human embryo models throughout developmental stages of increasing worthiness of protection should require a proportional increase in potential benefit.
- Permission from an ethics committee to culture human embryo models for a specified period of time should take into account the quality of the model, justification of the objectives, technical feasibility, and consistency of the practice with local and international values.
- For a specific goal, forming an embryo model that is more complete than necessary might yield equal benefits but cause more concerns. Therefore, if possible, less complete models should be preferred. Consequently, while the use of human integrated embryo models is justified in the early stages of development, alternatives might make their use less justified at later stages.

Box 2

Executive summary

- Scientific research using human embryo models made from stem cells has great potential to advance our understanding of development, infertility, pregnancy loss, birth defects, and the developmental origins of adult diseases.

- As human embryo models become more similar to the human embryo, a refined legal definition of the human embryo is needed to determine the conditions under which the models could be granted similar protection.
- As part of a refined definition, the potentiality of cells to develop into a fetus should take into account both an intrinsic developmental potential and an absolute requirement for support normally provided at least by the extraembryonic cells and the uterine environment.
- We surmise a refined definition of the human embryo as "a group of human cells supported by elements fulfilling extraembryonic and uterine functions that, combined, have the potential to form a fetus."
- Because it is prohibited to evaluate the potential of a human embryo model by transfer to a uterus, we propose that if (1) a given human embryo model is capable of efficiently and faithfully forming the entire embryo up to a given stage of development and (2) the same embryo model has the capacity to form living and fertile animals in multiple species, particularly non-human primates, then that human embryo model has reached a "tipping point" and should be considered similar to a human embryo for ethical and regulatory purposes.
- It is crucial that scientific societies and ethics committees ensure that the in vitro development of human embryo models happens gradually and that the quality and reproducibility of results are assured before researchers are allowed to explore later stages. This quality justifies the research, limits the likelihood of precipitous research in areas of widespread ethical concern without broad consultation, and allows assessment of whether societal benefits can be achieved.
- Because, for a specific goal, a human embryo model that is more complete than necessary might yield equal benefits but raise more concerns, less complete models should be preferred when possible. Consequently, while the use of human integrated embryo models is justified in the early stages of development, alternatives might make their use less justified in later stages.

Conclusions

Definition of the embryo

Advances in forming human embryo models demand a reconsideration of the legal definitions of human embryos. We suggest that this definition should be based on the developmental potential to form a fetus, which incorporates not only the intrinsic capability of cells but also the provision of a supporting environment integral to realizing this potential. We surmise a definition of an embryo in legal terms as a group of human cells supported by elements fulfilling extraembryonic and uterine functions that, combined, have the potential to form a fetus.

Tipping points for embryo models

While no human embryo model is yet suspected of having the potential to form a fetus, it is possible that some models may do so in the future. As long as this potential remains unproven, we suggest using the terms "embryo models," "embryonic models," or "stem-cell-based embryo models." But when these models have passed a defined tipping point, we suggest they should then become fully entitled as embryos, regardless of how they came into being. The definition of a tipping point requires a Turing test that is complicated by the fact that transferring human embryo models into the uterus of any species is prohibited. We propose that human embryo models could be deemed equivalent to embryos when: (1) they have been shown to have the potential to efficiently and faithfully develop in vitro as normally formed up to a moment to be decided upon based on local ethical and regulatory considerations and (2) when equivalent animal embryo models are shown to have the potential to form living and fertile animals in multiple species, including the ones that are the closest to humans (e.g., pigs, monkeys).

Basic ethics principles

We likewise propose a wider discussion based on the application of fundamental ethical principles largely shared in science and medicine that take into account the quality of the model, the justification of the goals, their technical feasibility, and whether public discussions result in a match with local and international values. This discussion would be important to decide (1) what limits to impose on the duration of in vitro

culture of human integrated embryo models, (2) what are the justifications of the scientific and medical aims for using embryo models with different levels of completeness, and (3) the extent to which human embryology using stem cells is a desirable alternative complementary to the classical use of embryos.

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Institution/Organization Announcements *[list in formation]*

We recognize this listing is incomplete, unbalanced and skewed to the Global North…please help us make it more complete, more inclusive, and more useful by recommending additional organizations/institutions/ programs to monitor.

Academy of Medical Sciences [UK] [accessed 30 Aug 2023]
https://acmedsci.ac.uk/
News
[No new digest content identified]

Africa CDC - Institute of Pathogen Genomics [IPG] [accessed 30 Aug 2023]
https://africacdc.org/institutes/ipg/
Africa PGI is an initiative of the Africa CDC Institute for Pathogen Genomics, a continent-wide leadership initiative established in 2019 to support public health pathogen genomics and bioinformatics across Africa.
News & Announcements
[No new digest content identified]

African Society of Human Genetics [accessed 30 Aug 2023]
https://www.afshg.org/
Press Releases
[No new digest content identified]

Paul G. Allen Frontiers Group [accessed 30 Aug 2023]
https://alleninstitute.org/news-press/
News
[No new digest content identified]

ARM [Alliance for Regenerative Medicine] [accessed 30 Aug 2023]
https://alliancerm.org/press-releases/
Selected Press Releases; Events
Cell-Gene Meeting on the Mesa – 2023
October 10-12, 2023, Carlsbad, CA
[Selected session]
Day 1. Tuesday, October 10, 2023 4:00pm – 5:00pm
THE IMPORTANCE OF ETHICS IN GENE AND CELL THERAPY
With the recent technical and commercial success of cell and gene therapies comes select challenges facing the field. Many of these challenges can be categorized as "ethical" issues confronting leaders in the field and other key stakeholders. This panel will explore a broad range of some of the most difficult ethical dilemmas facing the industry.

Chair: Tim Hunt, CEO, Alliance for Regenerative Medicine (ARM)
Speakers:
- Chris Fox, President, Novartis Gene Therapies
- Ben Hurlbut, Ph.D., Associate Professor, School of Life Sciences, Arizona State University
- Janet Lambert, Former CEO, Alliance for Regenerative Medicine (ARM)
- Rob Perez, Operating Partner, General Atlantic; Founder and Chairman, Life Science Cares
- Durhane Wong-Rieger, Ph.D., President and CEO, Canadian Organization for Rare Diseases

BMGF - Gates Foundation [[accessed 30 Aug 2023]
https://www.gatesfoundation.org/ideas/media-center
Press Releases and Statements
[No new digest content identified]

Bill & Melinda Gates Medical Research Institute [accessed 30 Aug 2023]
https://www.gatesmri.org/news
The Bill & Melinda Gates Medical Research Institute is a non-profit biotech organization. Our mission is to develop products to fight malaria, tuberculosis, and diarrheal diseases—three major causes of mortality, poverty, and inequality in developing countries. The world has unprecedented scientific tools at its disposal; now is the time to use them to save the lives of the world's poorest people
News: Articles and Publications
[No new digest content identified]

American College of Medical Genetics and Genomics [accessed 30 Aug 2023]
https://www.acmg.net/
The ACMG is the only nationally recognized interdisciplinary professional membership organization that represents the interests of the entire medical genetics team including clinical geneticists, clinical laboratory geneticists, and genetic counselors.
News & Releases
[No new digest content identified]

American Board of Medical Genetics and Genomics (ABMGG) [accessed 30 Aug 2023]
http://www.abmgg.org/pages/resources_appeal.shtml
The mission of the ABMGG is to serve the public and medical profession by establishing professional certification standards and promoting lifelong learning as well as excellence in medical genetics and genomics.
[No new digest content identified]

American Society for Gene and Cell Therapy [ASGCT] [accessed 30 Aug 2023]
https://asgct.org/
News/Publications
ASGCT Policy Summit
September 18-19, 2023 | Renaissance Washington, DC Downtown Hotel
Program & Agenda
The Policy Summit brings together various policy, industry, and science stakeholders to discuss common challenges in the CGT field and explore innovative solutions.

American Society of Human Genetics (ASHG) [accessed 30 Aug 2023]
http://www.ashg.org/
We work to advance human genetics and genomics in science, health, and society through excellence in research, education, and advocacy.
Press Releases
ASHG Announces 2023-2025 Human Genetics Scholars
August 14, 2023
SHG with generous support from National Human Genome Research Institute (NHGRI), Biogen, GlaxoSmithKline (GSK), Merck & Co, and Roche, is pleased to recognize this year's Scholars. The Human Genetics Scholars Initiative was developed to advance diversity and inclusion in the human genetics research workforce.

ARRIGE [accessed 30 Aug 2023]
https://www.arrige.org/
News
[No new digest content identified]

Broad Institute of MIT and Harvard [accessed 30 Aug 2023]
A collaborative research institute focused on genomics and personalized medicine, undertaking various projects in genomic medicine.
https://www.broadinstitute.org/
Latest News
News 07.20.2023
A look back at the first year of NeuroDev
Researchers are working to characterize the genetic and phenotypic data of people with neurodevelopmental conditions in Kenya and South Africa.

CDC – Office of Genomics and Precision Public Health [accessed 30 Aug 2023]
https://www.cdc.gov/genomics/default.htm
Updates
Training Opportunity in Genomics and Precision Public Health, Atlanta, September 7- 8, 2023
This week, we spotlight our upcoming training event in collaboration with Oak Ridge Institute for Science and Education, Atlanta, September 7-8, 2023. The in-person and online course is targeted toward trainees in public health as an introduction to concepts and approaches of genomics, big data and precision health for improving health care and population health.

Center for Genetics and Society [USA] [accessed 30 Aug 2023]
www.geneticsandsociety.org
…a non-profit public affairs and policy advocacy organization working to encourage responsible uses and effective societal governance of human genetic and reproductive biotechnologies.
Press
[No new digest content identified]

Center for the Ethics of Indigenous Genomic Research [CEIGR] – University of Oklahoma [accessed 30 Aug 2023]

https://www.ou.edu/cas/anthropology/ceigr
[No new digest content identified]

Center for ELSI Resources and Analysis (CERA) [accessed 30 Aug 2023]
https://elsihub.org/about/our-mission
Call for Proposals: The 6th ELSI Congress
The 6th ELSI Congress is now accepting proposals for panels, papers and posters on topics across the expanding range of ELSI research. The 6th ELSI Congress will be held at Columbia University in New York City from June 10-12, 2024. The theme of the conference will be Reimagining the Benefits of Genomic Science.
We welcome all with an interest in the ethical, legal, and social implications (ELSI) of genomic research. Researchers, scholars, practitioners, trainees, policymakers, journalists, and the general public are invited to share and explore the latest ELSI research at ELSIcon2024.
The deadline for submissions is 11:59 PM EST, Friday, December 1, 2023: Submit a Proposal

Francis Crick Institute [accessed 30 Aug 2023]
https://www.crick.ac.uk/news-and-reports
News
Researchers identify stem cells in the thymus for the first time
Type: News 30 August 2023
Researchers at the Francis Crick Institute have identified stem cells in the human thymus for the first time. These cells represent a potential new target to understand immune diseases and cancer and how to boost the immune system.

The Francis Crick Institute and LifeArc partner with five African research institutions to support scientists
Type: News 14 August 2023
The Crick Africa Network (CAN) is set to extend for a further five years, supporting more young African scientists to build their careers in research, thanks to a £7.5 million investment from the self-funded charitable medical research organisation, LifeArc.

FDA Cellular & Gene Therapy Guidances [accessed 30 Aug 2023]
https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/cellular-gene-therapy-guidances
[No new digest content identified]

Genetic Alliance [accessed 30 Aug 2023]
http://www.geneticalliance.org/
News/Press Releases
[No new digest content identified]

The Genomic Medicine Foundation [accessed 30 Aug 2023]
https://www.genomicmedicine.org
The Genomic Medicine Foundation is a non-profit organization providing up to date and evidence-based information on genetics/genomics relevant to clinical medicine and healthcare.
News, Events
The IX International Cardiovascular Genomic Medicine Conference
October 23 - October 24

Surgeon's Quarter Mission Hall Edinburgh, 1 Roxburgh Place
Edinburgh, Scotland EH8 9SU

Global Alliance for Genomics and Health [accessed 30 Aug 2023]
https://www.ga4gh.org/
News, Events
[No new digest content identified]

Genetic Alliance [accessed 30 Aug 2023]
https://geneticalliance.org/about/news
News
[No new digest content identified]

Genomics England [accessed 30 Aug 2023]
https://www.genomicsengland.co.uk/
We partner with the NHS to provide whole genome sequencing diagnostics. We also equip researchers to find the causes of disease and develop new treatments – with patients and participants at the heart of it all.
Latest
6 Jul 2023
Genomics England celebrates its 10-year anniversary

Genetics Society of America (GSA) [accessed 30 Aug 2023]
http://genetics-gsa.org/
Using the tools of genetics and genomics, nearly 6,000 GSA members from more than 50 countries around the world investigate a wide variety of biological questions and applications.
News
[No new digest content identified]

Global Genomic Medicine Consortium [G2MC] [accessed 30 Aug 2023]
https://g2mc.org/
G2MC is an international community formed to advance the implementation of genomic medicine and improve health for all.
[No new digest content identified]

Global Citizens' Assembly on Genome Editing (GCA) [accessed 30 Aug 2023]
https://www.globalca.org/
Latest News
[No new digest content identified]

HHMI - Howard Hughes Medical Institute [to 30 Aug 2023]
https://www.hhmi.org/news
Press Room
[No new digest content identified]

H3Africa [accessed 30 Aug 2023]
https://h3africa.org/
News
[No new digest content identified]

ICH [accessed 30 Aug 2023]
https://www.ich.org/
Public Consultations; Work Products; Working Groups
Discussion Groups
Cell and Gene Therapies Discussion Group (CGTDG)

The Remit of the ICH Cell and Gene Therapies Discussion Group (CGTDG) has been endorsed by the ICH Management Committee in May 2023.

The CGTDG will serve as a technical discussion forum for issues related to ICH harmonisation efforts in the field of CGT products. The CGTDG will develop a holistic CGT roadmap within the scope of modalities identified below, including prioritisation of areas of most need for harmonisation whereby technical consensus can be achieved with specific recommendations for new guideline development or revisions to existing ICH Guidelines.

PDF: Cell and Gene Therapies Discussion Group Remit
[Excerpt]
Scope of Activities
Given the scientific complexities and diverse array of CGT modalities, it is proposed that the CGTDG focus its initial scope on CGT modalities of relatively high maturity, whereby greater scientific and regulatory expertise have already been achieved. The selection of such modalities can be linked to classes of products that have achieved global marketing authorization or those modalities that are prominent in global clinical development programs. The proposed modalities within scope are:

- Ex-vivo genetically modified chimeric antigen receptor engineered T cell (CAR-T cell), including both autologous and allogeneic;
- In-vivo viral vector-based gene therapy (e.g., AV, AAV, …).

The initial work of the CGTDG will be to drive alignment on high level principles within selected modalities where baseline consensus can be achieved. The CGTDG will:

- Review areas that will benefit from ICH harmonization, and prioritize those areas of most need to enable future ICH work in a staggered approach;
- Assess current ICH Guidelines for their applicability to CGT products, and;
- Make specific recommendations regarding the development of new ICH guidelines for CGT products and/or revisions to existing guidelines as deemed necessary.

CGTDG is not tasked with the development or revisions of specific ICH Guidelines but may act as an advisor group to existing ICH Expert Working Group (EWG) undergoing new or revised guideline development where CGT products are in scope.

Given the diversity of the field and rapidly evolving science, the CGTDG should monitor innovation trends in clinical development and be given reasonable level of flexibility in adapting its work within the broader MC mandate. Significant changes to the overall scope should be presented to the MC for review and endorsement as per standard ICH procedures.

Innovative Genomics Institute
https://innovativegenomics.org/about-us/

The IGI is composed of diverse researchers at the University of California, Berkeley, the University of California, San Francisco, and the University of California, Davis. Together, our scientists have powerful combined expertise. They conduct world-class research, driven by the real possibility of using genome engineering to treat human diseases, end hunger, and respond to climate change.
News
Making Genetic Therapies Affordable and Accessible: IGI's New Recommendations
July 6, 2023 Press Releases
By Hope Henderson
In 2022, IGI's Public Impact Team launched a year-long Affordability Task Force (ATF) project aimed at solving one of the trickiest challenges for genomic medicines: price… "Our focus is on accessibility for low-income individuals living in the United States, and also on accessibility for individuals in low and middle-income countries. This is particularly crucial for sickle cell disease, which is one of our flagship projects," says Kliegman. To learn more about the ATF and read the complete ATF Report with recommendations for how to bring down prices for genomic therapies, click here.

INSERM [to 30 Aug 2023]
https://www.inserm.fr/en/home/
Press Releases
[No new digest content identified]

Institut Pasteur [to 30 Aug 2023]
https://www.pasteur.fr/en/press-area
Press Documents
[No new digest content identified]

NIH [to 30 Aug 2023]
http://www.nih.gov/
News Releases
Parkinson's disease gene variant found in study of some people of African ancestry
August 23, 2023 — NIH-supported, international study underscores importance of research of diverse populations.

Researchers assemble the first complete sequence of a human Y chromosome
August 23, 2023 — New sequence reveals genomic factors in fertility, including sperm production.

Researchers assemble the first complete sequence of a human Y chromosome
August 23, 2023 — New sequence reveals genomic factors in fertility, including sperm production.

NIH National Human Genome Research Institute (NHGRI) [accessed 30 Aug 2023]
https://www.genome.gov/
News
NIH funds new Genomics and Public Service Fellowship Program
Sarah A. Bates, M.S., M.A. June 20, 2023
Program to support emerging genomics leaders in policy, education, communications and scientific program management.

NIH – All of Us Research Program [accessed 30 Aug 2023]
https://allofus.nih.gov/news-events/announcements
An historic effort to collect and study data from one million or more people living in the United States. The goal of the program is better health for all of us. Our mission is to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for all of us. This mission is carried out through three connected focus areas that are supported and made possible by a team that maintains a culture built around the program's core values.
Announcements
All of Us Research Program Updates Data Use Eligibility to Propel Precision Medicine
The National Institutes of Health's All of Us Research Program is now taking applications from international academic, not-for-profit, and health care organizations to access data through its Researcher Workbench. The program began testing its secure, cloud-based data platform three years ago with…
August 3, 2023
Type: Announcements

Applied Genomics and Biological Technologies (AGBT) Precision Health Meeting Workshop: Leveraging the All of Us Researcher Workbench to Advance Precision Health
In this workshop at the AGBT Precision Health Meeting, attendees will learn about the extensive data available on the All of Us Researcher Workbench. They will also complete an example genomic analysis. The workshop will be held on September 7 from 2:45 – 4:15 p.m.
Review the AGBT Precision Health Meeting Agenda
Type: Event

Nuffield Council on Bioethics [to 30 Aug 2023]
https://www.nuffieldbioethics.org/news
News
[See *Perspectives, Milestones* above]

Penn Center for Global Genomics & Health Equity [University of Pennsylvania] [accessed 30 Aug 2023]
https://globalgenomics.med.upenn.edu/index.php
Latest News
[No new digest content identified]

PHG Foundation
https://www.phgfoundation.org
The PHG Foundation is a non-profit think tank and a linked exempt charity of the University of Cambridge. We were originally founded as the Public Health Genomics Unit in 1997, and became the charitable PHG Foundation ten years later.

The Royal Society [accessed 30 Aug 2023]
https://royalsociety.org/
What's New
G20 national science academies call for action on green energy, a holistic approach to global health and connecting science with society and culture
25 August 2023
The Royal Society has today joined with the national science academies of the G20 nations to publish a communique ahead of the G20 summit being held from Sept 9-10 in India.

The communique addresses three key themes around transformative science for sustainable development: clean energy for a greener future; universal and holistic health; and connecting science with society and culture.

Adrian Smith, President of the Royal Society said: "Many of the problems that face us today are shared global problems and we can only effectively tackle those issues through international cooperation. Whether it is ensuring that emerging technologies are developed in just, equitable, safe and sustainable ways, increasing healthy life expectancies around the world or transitioning to clean energy, nations and their governments must act together.

"The communique we have published today offer the governments of the G20 nations ways forward for the application of science to improving lives. We hope it will help guide the discussions at the upcoming summit."

Read the full statement (PDF).

UNESCO–The World Academy of Sciences [accessed 30 Aug 2023]

https://twas.org/

News

24 July 2023

TWAS Annual Report 2022 released

Yearly publication lays out the Academy's progress and key accomplishments

Wellcome Sanger Institute [accessed 30 Aug 2023]

https://www.sanger.ac.uk/

A leading genomics research institute in the United Kingdom, known for its work in sequencing genomes and understanding the role of genetics in health and disease.

News

30 Aug 2023

Peter Campbell honoured with Darwin Medal by the Royal Society

The award, created in memory of Charles Darwin, recognises Dr Campbell's outstanding achievements and dedication to advancing knowledge and understanding of the genomic roots of cancer and how cells evolve over a person's lifetime.

30 Aug 2023

Richard Durbin recognised for his contribution to the biology of genomes

Professor Durbin has been awarded the 39th International Prize for Biology in recognition of his pioneering work to develop and openly share innovative bioinformatics technologies and genomic research data

23 Aug 2023

Diversity of human Y chromosome revealed

Researchers assemble the full Y chromosome across multiple individuals for the first time, revealing unexpected diversity, with clues for its role ...

7 Aug 2023

Building an atlas of gene variants to understand health and disease

Mutational scanning technologies are revolutionising the way we understand human genetic variation. A symposium in July brought together researchers from over 50 countries to explore the possibilities of this incipient genomic method, and how it can benefit clinicians and patients.

WHO - Human genome editing [accessed 30 Aug 2023]

https://www.who.int/teams/health-ethics-governance/emerging-technologies/human-genome-editing
News; Publications
[No new digest content identified; last update on page July 2021]

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Academic Journal Watch

This section aggregates key articles from a baseline of journals that are clearly focused on genomic medicine and supporting disciplines. These journal titles are listed for reference, even if there is no new content for this edition of the digest. This is complemented by weekly monitoring of about 150 journals across disciples and continuing use of google scholar to capture relevant content. Overall, this content is presented by journal source in alphabetical order. If you would like to suggest a journal to be monitored for this section, please contacts the editors as above.

American Journal of Human Genetics
Aug 03, 2023 Volume 110 Issue 8 p1227-1444
https://www.cell.com/ajhg/issue?pii=S0002-9297(22)X0009-8
[No new digest content identified]

Annals of Internal Medicine
August 2023 Volume 176, Issue 8
https://www.acpjournals.org/toc/aim/current
[No new digest content identified]

Biomedical Signal Processing and Control
Volume 86 (B), September 2023, 105263. 11 July 2023
Article
Reviewing methods of deep learning for intelligent healthcare systems in genomics and biomedicine
Imran Zafar, Shakila Anwar, Faheem kanwal, Waqas Yousaf, Fakhar Un Nisa, Tanzeela Kausar, Qurat ul Ain, Ahsanullah Unar, Mohammad Amjad Kamal, Summya Rashid, Khalid Ali Khan, Rohit Sharma
Abstract
The advancements in genomics and biomedical technologies have generated vast amounts of biological and physiological data, which present opportunities for understanding human health. Deep learning (DL) and machine learning (ML) are frontiers and interdisciplinary fields of computer science that consider comprehensive computational models and provide integral roles for disease diagnosis and therapy investigation. DL-based algorithms can discover the intrinsic hierarchies in the training data to show great promise for extracting features and learning patterns from complex datasets and performing various analytical tasks.

This review comprehensively discusses the wide-ranging DL approaches for intelligent healthcare systems (IHS) in genomics and biomedicine. This paper explores advanced concepts in deep learning (DL) and discusses the workflow of utilizing role-based algorithms in genomics and biomedicine to integrate intelligent healthcare systems (IHS). The aim is to overcome biomedical obstacles like patient disease classification, core biomedical processes, and empowering patient-disease integration.

The paper also highlights how DL approaches are well-suited for addressing critical challenges in these domains, offering promising solutions for improved healthcare outcomes. We also provided a concise concept of DL architectures and model optimization in genomics and bioinformatics at the molecular level to deal with biomedicine classification, genomic sequence analysis, protein structure classification, and

prediction. Finally, we discussed DL's current challenges and future perspectives in genomics and biomedicine for future directions.

BMC Medical Ethics
http://www.biomedcentral.com/bmcmedethics/content
(Accessed 30 Aug 2023)
[No new digest content identified]

BMC Medicine
http://www.biomedcentral.com/bmcmed/content
(Accessed 30 Aug 2023)
[No new digest content identified]

Cell
Aug 17, 2023 Volume 186 Issue 17 p3523-3744
https://www.cell.com/cell/current
Featured Article
An ethical framework for human embryology with embryo models
Nicolas C. Rivron, Alfonso Martinez Arias, Martin F. Pera, Naomi Moris, Hafez Ismaili M'hamdi
[See *Featured Journal Content* above]

Cell Genomics
Aug 09, 2023 Volume 3 Issue 8
https://www.cell.com/cell-genomics/current
Perspective
Genome annotation: From human genetics to biodiversity genomics
Roderic Guigó
The genomes of the 1.8 million species living on Earth will be sequenced within the next decade. This will have a transformative impact on biology, helping to understand the genetic basis of biological traits. To maximize impact, genes, the regions in the genomes that encode these traits, need to be identified. This task is challenging given the complexity of eukaryotic genomes. Here, Guigó reviews the problem of gene finding and discusses strategies to identify all genes in eukaryotic species.

Resource
Genotyping and population characteristics of the China Kadoorie Biobank
Robin G. Walters, et al. for the China Kadoorie Biobank Collaborative Group
Walters et al. present genetic analyses of >100,000 participants of the China Kadoorie Biobank (CKB), a population-based, prospective cohort of >512,000 from 10 diverse regions of China. They describe how the CKB has contributed to understanding of the genetic basis for many diseases and risk factors and report GWASs of 124 diverse disease outcomes.

Circulation
https://www.ahajournals.org/toc/circ/148/9
Online First
AHA POLICY STATEMENT

Principles for Health Information Collection, Sharing, and Use: A Policy Statement From the American Heart Association

Kayte Spector-Bagdady, JD, MBe, Chair; Antonis A. Armoundas, PhD; Rima Arnaout, MD; Jennifer L. Hall, PhD, FAHA; Brooke Yeager McSwain, MSc, MA; Joshua W. Knowles, MD, PhD, FAHA; W. Nicholson Price II, JD, PhD; Danda B. Rawat, PhD; Barbara Riegel, PhD, RN, FAHA; Tracy Y. Wang, MD, MHS, MSc, FAHA; Kevin Wiley Jr, PhD, MPH; Mina K. Chung, MD, FAHA, Vice Chair; on behalf of the American Heart Association Advocacy Coordinating Committee

ABSTRACT:

The evolution of the electronic health record, combined with advances in data curation and analytic technologies, increasingly enables data sharing and harmonization. Advances in the analysis of health-related and health-proxy information have already accelerated research discoveries and improved patient care. This American Heart Association policy statement discusses how broad data sharing can be an enabling driver of progress by providing data to develop, test, and benchmark innovative methods, scalable insights, and potential new paradigms for data storage and workflow. Along with these advances come concerns about the sensitive nature of some health data, equity considerations about the involvement of historically excluded communities, and the complex intersection of laws attempting to govern behavior.

Data-sharing principles are therefore necessary across a wide swath of entities, including parties who collect health information, funders, researchers, patients, legislatures, commercial companies, and regulatory departments and agencies. This policy statement outlines some of the key equity and legal background relevant to health data sharing and responsible management. It then articulates principles that will guide the American Heart Association's engagement in public policy related to data collection, sharing, and use to continue to inform its work across the research enterprise, as well as specific examples of how these principles might be applied in the policy landscape. The goal of these principles is to improve policy to support the use or reuse of health information in ways that are respectful of patients and research participants, equitable in impact in terms of both risks and potential benefits, and beneficial across broad and demographically diverse communities in the United States.

Clinical Therapeutics

July 2023 Volume 45 Issue 7 p617-684

http://www.clinicaltherapeutics.com/current

[No new digest content identified]

Clinical Trials

Volume 20 Issue 4, August 2023

https://journals.sagepub.com/toc/ctja/20/4

[No new digest content identified]

The CRISPR Journal

Volume 6, Issue 4 / August 2023

https://www.liebertpub.com/toc/crispr/6/4

Editorial Free

CRISPR Milestones for Sustainable Agriculture and Forestry

Rodolphe Barrangou

Pages:303–304 Published Online:14 August 2023

[Excerpt]

Blazing a Trail for CRISPR in Forestry

As illustrated on the cover of this issue, recent studies in the deployment of genome editing in trees are opening new avenues for sustainable forestry. The "First Cut" by Yiping Qi and Gen Li (see page 305)2 covers

two related articles on gene editing in poplar trees—one in this issue from 339 (University of Georgia),[3] another from Jack Wang and my colleagues at NC State, recently published in Science.[4]

Our study showed that multiplex genome editing can yield poplar trees with reduced lignin and altered fiber content to generate healthy trees that hold substantial promise for the pulping industry. Besides providing a proof of concept that wood fibers can be engineered using CRISPR, we showed that the edited trees can be used to generate paper, while providing substantial operational benefits. The resulting industrial pulping process would require less wood, energy, and chemical inputs, while releasing production capacity.

Remarkably, modeling results predicted substantial reduction in the corresponding global warming potential. This opens the door for more sustainable forestry on a global basis, with several commercially relevant species in play, such as pine and eucalyptus, widely used in timber, pulping, and other industries.

That said, the geographical and time scales under which forests are grown are a sobering reminder of the work and challenges that lie ahead, with anticipated commercial deployment of these approaches at scale anticipated in the 2040s. This might be just in time for some of our lofty 2050 sustainability goals. Of course, the scale of the economic and environmental benefits that we collectively stand to gain with more sustainable forestry, at a time when carbon capture is a strategic priority, is tremendous. Encouragingly, as trees can live hundreds and sometimes even thousands of years, such advances may benefit several human generations, so we must diligently and responsibly ensure that we collectively blaze a path for more sustainable forestry.

Current Genetic Medicine Reports
Volume 10, issue 3, September 2022
https://link.springer.com/journal/40142/volumes-and-issues/10-3
[No new digest content identified]

Current Medical Research and Opinion
Volume 39, Issue 8 2023
https://www.tandfonline.com/toc/icmo20/current
[No new digest content identified]

Current Protocols in Human Genetics
https://currentprotocols.onlinelibrary.wiley.com/journal/19348258
[Accessed 30 Aug 2023]
[No new digest content identified]

European Journal of Medical Genetics
Volume 66, Issue 9, September 2023, 104810. 23 July 2023
Review
Ethical challenges in autism genomics: Recommendations for researchers
Heini M. Natri, Carolyn R. Chapman, Síofra Heraty, Patrick Dwyer, Nick Walker, Steven K. Kapp, Heather A. Dron, Julian A. Martinez-Agosto, Lea Mikkola, Mary Doherty
Abstract
Equitable and just genetic research and clinical translation require an examination of the ethical questions pertaining to vulnerable and marginalized communities. Autism research and advocate communities have expressed concerns over current practices of genetics research, urging the field to shift towards paradigms and practices that ensure benefits and avoid harm to research participants and the wider autistic community. Building upon a framework of bioethical principles, we provide the background for the concerns and present recommendations for ethically sustainable and justice-oriented genetic and genomic autism research. With

the primary goal of enhancing the health, well-being, and autonomy of autistic persons, we make recommendations to guide priority setting, responsible research conduct, and informed consent practices. Further, we discuss the ethical challenges particularly pertaining to research involving highly vulnerable individuals and groups, such as those with impaired cognitive or communication ability. Finally, we consider the clinical translation of autism genetics studies, including the use of genetic testing. These guidelines, developed by an interdisciplinary working group comprising autistic and non-autistic individuals, will aid in leveraging the potential of genetics research to enhance the quality of life of autistic individuals and are widely applicable across stigmatized traits and vulnerable communities.

Genetics in Medicines
Volume 25, Issue 7 July 2023
https://www.sciencedirect.com/journal/genetics-in-medicine/vol/25/issue/7
Editorial
The value of intersectionality for genomic research on human behavior
Lucas J. Matthews, Daphne O. Martschenko, Maya Sabatello
Article 100860
Introduction

Since conception, research into the genetics of human behavior has generated controversy. Too often, behavioral genetics has been used to justify racism, classism, sexism, and ableism and to reinforce existing sociopolitical disparities in wealth, health, and education. Whether to conduct such research, how its scope ought to be affected by sociopolitical concerns, and what its implications are for individuals, communities, and society at large, have all captivated scholarly attention. Central to these debates are worries that emphasis on the genetic underpinnings of behavior will distract from important environmental or structural factors (eg, systemic inequities) that play crucial roles in human behavioral development.

Today, major technological advancements in human genetics raise new and critical questions about how to interpret findings from genome-wide association studies (GWASs) of human behavior and its associated risks and benefits. This research holds the potential to enhance the understanding of common and complex health conditions and improve clinical care, especially once the current disparities in genomic cohorts are addressed. However, growing efforts to apply behavioral genomic information to nonclinical settings (eg, education) also threaten to reinforce and exacerbate stigma and discrimination while compromising privacy, justice, and equity.

Investigating the promises and perils of genomic research on human behavior is of growing interest to the scientific research community and society more broadly. With few exceptions, however, studies have largely focused on single-factor analyses, such as race, (dis)ability, gender, and class (separately), to understand the ethical, social, and practical implications of this research. Although informative, such research treats each factor as comprising a homogeneous community; it overlooks the fact that the complexity of individuals and communities would benefit from multiaxis analyses. Identifying strategies for addressing social and ethical concerns about this nascent area of genomic research is crucial, but it requires intersectional approaches that consider the multiaxis dimensions of discrimination, oppression, and privilege. In this commentary, we use genomic prediction of education-related traits and outcomes to illustrate the importance of intersectional analyses to human genetics, particularly behavioral genomics.
Section snippets
Major Transitions: From Twin Studies to Genomics

By way of identifying associations, genomic research aims to elucidate potentially causal relationships between genotype (eg, genes or genetic variation) and phenotype (i.e., traits or outcomes of scientific interest). To that end, human behavioral genomic research seeks to identify associations between genetic variation and behavioral phenotypes, such as IQ and schizophrenia. GWASs are the primary method for identifying such associations. In addition, GWASs have significantly enhanced the…
Genomic Research on Human Behavior and Intersectionality

Intersectionality focuses on understanding and analyzing the many interlocking complexities in our world and in human experiences. Originally developed by women of color during the American Civil Rights and Black Power movements of the 1960s and 1970s, intersectionality highlights the many different social constructions that conjoin to produce discrimination and privilege. Accordingly, intersectionality rejects dichotomies such as "Black-White," "Rich-Poor," or "Able-Disabled," arguing that…

Considerations for Genomic and Ethical, Legal and Social Implications (ELSI) Researchers

An intersectional approach can elucidate the ways in which polygenic prediction of educational outcomes and other socially relevant phenotypes might interact with existing forms of oppression, stigma, and discrimination. Genomic researchers who investigate social and behavioral phenotypes and scholars interested in the ethics of such research ought to build upon existing intersectional scholarship to develop a more thorough understanding of the downstream implications of genomic data…

Genome Medicine
https://genomemedicine.biomedcentral.com/articles
[Accessed 30 Aug 2023]
[No new digest content identified]

Human Gene Therapy
Volume 34, Issue 15-16 / August 2023
https://www.liebertpub.com/toc/hum/34/15-16
[No new digest content identified]

International Journal of Law and Policy
Volume: 1 Issue: 5, 12 July 2023
Article
Analyzing the Legal Labyrinth: Current Trends in Genetic Research and Their Legal Perspectives
Ollanazarova Mamura Muzaffarovna
Abstract
Genetic research has experienced rapid advancements in recent years, giving rise to a host of legal challenges at the intersection of intellectual property rights, data privacy, and ethical concerns. This article aims to analyze a key legal issue related to genetic research and propose potential solutions. We conducted a literature review, comparative analysis, and policy evaluation to identify the shortcomings of existing legal frameworks and highlight best practices from different jurisdictions. Our findings indicate that current legal frameworks may not adequately address the challenges posed by genetic research. We propose potential solutions, such as developing a comprehensive legal framework for genetic research, encouraging international collaboration and harmonization of laws and regulations, and implementing strong oversight mechanisms. By addressing these legal challenges and implementing the proposed solutions, policymakers and stakeholders can create a stable and predictable environment for genetic research that maximizes its benefits while minimizing potential harms and inequities.

JAMA
August 22/29, 2023, Vol 330, No. 8, Pages 677-778
Viewpoint
Fair Allocation of Scarce CAR T-Cell Therapies for Relapsed/Refractory Multiple Myeloma
Benjamin A. Derman, MD; William F. Parker, MD, PhD
free access
JAMA. 2023;330(8):687-688. doi:10.1001/jama.2023.11846

This Viewpoint discusses the unfairness of current CAR T-cell therapy allocation practices and offers alternative methods to more fairly allocate therapy.

"…Although the total supply of CAR T cells is difficult to quantify, it is undoubtedly insufficient for the more than 170 000 individuals in the US with multiple myeloma. A 2023 study of centers offering CAR T-cell therapy for multiple myeloma found that for every allocated slot per month per center, there were 20 patients on the waitlist; patients were waiting a median of 6 months prior to leukapheresis.[3] Despite ongoing efforts to increase supply through expanding manufacturing capabilities, this severe shortage will likely increase as CAR T-cell therapy demonstrates superior efficacy over alternatives earlier in the course of multiple myeloma.[1,2] Even if new therapies such as off-the-shelf bispecific antibodies reduce demand, there will not be enough CAR T-cell therapy slots for all eligible patients…

Journal of Medical Ethics
http://jme.bmj.com/content/current
Original Research
Rights and duties of genetic counsellors in Germany related to relatives at risk: comparative thoughts on the German Genetic Diagnostics Act
Susanne A Schneider, Uwe H Schneider
Abstract

Genetic testing has familial implications. Counsellors find themselves in (moral) conflict between medical confidentiality (towards the patient) and a potential right or even duty to warn at-risk relatives. Legal regulations vary between countries. English literature about German law is scarce. We reviewed the literature of relevant legal cases, focusing on German law, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. This article aims to familiarize counsellors with their responsibilities, compare the situation between countries and point out legally unresolved areas.

According to the German Genetic Diagnostics Act (Gendiagnostikgesetz) in case of an 'avoidable or treatable' genetic disorder, geneticists ought to confine themselves to the obligated advice to the patient. Whether a breach of the duty of confidentiality can be justified in exceptional cases by 'necessity as justification' for actively informing relatives at risk remains legally unclear. In case of a 'neither avoidable nor treatable' genetic disease, geneticists should also refrain from actively informing relatives as the justifiable state of emergency does not permit to break the duty of confidentiality.

The Journal of Pediatrics
Volume 261, October 2023
https://www.sciencedirect.com/journal/the-journal-of-pediatrics/vol/261/suppl/C
[No new digest content identified]

Journal of Pharmaceutical Policy and Practice
https://joppp.biomedcentral.com/
[Accessed 26 Aug 2023]
[No new digest content identified]

The Lancet
https://www.thelancet.com/journals/lancet/issue/current
Aug 12, 2023 Volume 402 Number 10401 p503-584, e9
Editorial
AI in medicine: creating a safe and equitable future
The Lancet

[Excerpt]

…How then to ensure that AI is a force for good in medicine? The scientific community has a key role in rigorous testing, validation, and monitoring of AI. The UN is assembling a high-level advisory body to build global capacity for trustworthy, safe, and sustainable AI; it is crucial that health and medicine are well represented. An equitable approach will require a diversity of local knowledge. WHO has partnered with the International Digital Health and AI Research Collaborative to boost participation from LMICs in the governance of safe and ethical AI in health through cross-border collaboration and common guidance. But without investment in local infrastructure and research, LMICs will remain reliant on AI developed in the USA and Europe, and costs could be prohibitive without open access alternatives. At present, the pace of technological progress far outstrips the guidance, and the power imbalance between the medical community and technology firms is growing.

Allowing private entities undue influence is dangerous. The UN Secretary General has urged the Security Council to help ensure transparency, accountability, and oversight on AI. Regulators must act to ensure safety, privacy, and ethical practice. The EU's AI Act, for example, will require high risk AI systems to be assessed before approval and subjected to monitoring. Regulation should be a key concern of the first major global summit on AI safety, being held in the UK later this year. Although technology companies should be part of the regulatory conversation, there are already signs of resistance. Amazon, Google, and Epic have objected to proposed US rules to regulate AI in health technologies. The tension between commercial interests and transparency risks compromising patient wellbeing, and marginalised groups will suffer first.

There is still time for us to create the future we want. AI could continue to bring benefits if integrated cautiously. It could change practice for the better as an aid—not a replacement—for doctors. But doctors cannot ignore AI. Medical educators must prepare health-care workers for a digitally augmented future. Policy makers must work with technology firms, health experts, and governments to ensure that equity remains a priority. Above all, the medical community must amplify the urgent call for stringent regulation.

Volume 402, ISSUE 10398, P265, July 22, 2023

Editorial

Genomic newborn screening: current concerns and challenges

The Lancet

60 years ago, the first newborn screening test for phenylketonuria, a rare inherited metabolic disease, was developed. The heel prick test, devised by Robert Guthrie, enabled babies with the condition to be identified soon after birth and begin a diet low in foods containing phenylalanine, thereby preventing them from developing intellectual disability, seizures, and behavioural problems. Since Guthrie's breakthrough, blood-based screening programmes have been expanded to cover more genetic disorders. The number of diseases covered varies: the USA currently screens for 63 disorders, the UK screens for nine, and Australia screens for 27. Yet implementation of newborn screening programmes is highly variable in low and middle-income countries, particularly on the African continent. Such inequity needs to change. The development of genomic sequencing technologies now offers an unprecedented opportunity to expand screening programmes. More than 4000 genes have been associated with recognisable monogenic diseases affecting an estimated 400–700 million people worldwide. In the US, health-care costs and utilisation of services by patients with these rare diseases accounted for an estimated US$768 billion in inpatient costs alone in 2016. Why then do we not screen the whole genome of all newborns, given the wealth of information and potential benefits it could provide?

The question has been the subject of much debate and is soon to be explored further by a UK-based project, the Newborn Genomes Programme, which is currently aiming to sequence the genomes of up to 100 000 newborn babies. Details of the £105 million project remain incomplete. The aim is to provide information to parents on between 200 and 400 rare diseases. The exact figure will be revealed when experts from different specialities can finally agree on whether acceptable treatments are currently available for the individual conditions. Sequencing will be carried out at the time that the current heel prick test is done, and the results will be stored and then reanalysed as needed. Several ongoing research projects—including the US-based Newborn Screening in Genomic Medicine and Public Health programme and the BabySeq Project—

have identified important ethical, technical, and financial dilemmas which all potential stakeholders ought to be aware of.

Firstly, interpreting whole genome data has notable challenges. Some mutations, although known to cause a recognised disease in childhood, might only result in the person developing the disease later in life, or in some cases, not at all. Additionally, sequencing the whole genome of newborn babies will identify possible genetic changes of unknown importance. Where outcomes are uncertain, this will necessitate lengthy, costly follow-up, with accompanying psychological harms. Secondly, using a whole genome approach restricted to only those diseases where there are currently recognisable and affordable treatments available would have no advantage over simply expanding current screening programmes by using targeted gene panels covering the additional diseases. Thirdly, whole-genome sequencing has been shown to have a considerable false negative rate compared with current conventional screening tests employing mass spectrometry and other laboratory investigations. Ethically, obtaining informed consent from parents to take part in such screening programmes, particularly where outcomes are sometimes of uncertain importance, is difficult enough in the short term. For the longer term, parents cannot give consent, nor can they know the wishes of their grown-up child about participating in such a programme.

Keeping large, clearly identifiable data safe is problematic and potentially exploitable; inappropriate sharing of such information with secondary agencies, including insurance and pharmaceutical companies and law enforcement, remains a realistic possibility. Economically, the implications of a newborn screening programme involving whole-genome sequencing are substantial: not only the cost of prolonged follow-up and monitoring of babies with identified mutations and variants but also additional costs that might include genetic testing of the parents. Genomic sequencing could screen for many more conditions than current conventional programmes, but the risk benefit balance remains uncertain. Given such uncertainties, focusing on improving screening by upgrading targeted gene panels might be more sensible in the short term. Whole genome sequencing in the long term deserves thorough examination and universal caution.

Molecular Therapy
Aug 02, 2023 Volume 31 Issue 8 p2299-2552
https://www.cell.com/molecular-therapy-family/molecular-therapy/current
[No new digest content identified

Nature
Volume 620 Issue 7975, 24 August 2023
https://www.nature.com/nature/volumes/620/issues/7975
[No new digest content identified

Nature Biotechnology
Volume 41 Issue 8, August 2023
https://www.nature.com/ng/volumes/55/issues/8
[No new digest content identified

Nature Genetics
Volume 55 Issue 8, August 2023
https://www.nature.com/ng/volumes/55/issues/8
[No new digest content identified

Nature Reviews Genetics

Volume 24 Issue 8, August 2023
https://www.nature.com/nrg/volumes/24/issues/8
Editorial 18 Jul 2023
A focus on single-cell omics
Single-cell omics approaches are providing unprecedented insights into cellular function and dysfunction. This Editorial highlights the remarkable potential of these technologies and their profound impact on our understanding of biology and disease.

New England Journal of Medicine
August 31, 2023 Vol. 389 No. 9
https://www.nejm.org/toc/nejm/medical-journal
Original Article
CRISPR-Cas9 Editing of the HBG1 and HBG2 Promoters to Treat Sickle Cell Disease
Akshay Sharma, M.B., B.S., et al.
Abstract
Background
Sickle cell disease is caused by a defect in the β-globin subunit of adult hemoglobin. Sickle hemoglobin polymerizes under hypoxic conditions, producing deformed red cells that hemolyze and cause vaso-occlusion that results in progressive organ damage and early death. Elevated fetal hemoglobin levels in red cells protect against complications of sickle cell disease. OTQ923, a clustered regularly interspaced short palindromic repeats (CRISPR)–Cas9–edited CD34+ hematopoietic stem- and progenitor-cell (HSPC) product, has a targeted disruption of the HBG1 and HBG2 (γ-globin) gene promoters that increases fetal hemoglobin expression in red-cell progeny.
Methods
We performed a tiling CRISPR-Cas9 screen of the HBG1 and HBG2 promoters by electroporating CD34+ cells obtained from healthy donors with Cas9 complexed with one of 72 guide RNAs, and we assessed the fraction of fetal hemoglobin–immunostaining erythroblasts (F cells) in erythroid-differentiated progeny. The gRNA resulting in the highest level of F cells (gRNA-68) was selected for clinical development. We enrolled participants with severe sickle cell disease in a multicenter, phase 1–2 clinical study to assess the safety and adverse-effect profile of OTQ923.
Results
In preclinical experiments, CD34+ HSPCs (obtained from healthy donors and persons with sickle cell disease) edited with CRISPR-Cas9 and gRNA-68 had sustained on-target editing with no off-target mutations and produced high levels of fetal hemoglobin after in vitro differentiation or xenotransplantation into immunodeficient mice. In the study, three participants received autologous OTQ923 after myeloablative conditioning and were followed for 6 to 18 months. At the end of the follow-up period, all the participants had engraftment and stable induction of fetal hemoglobin (fetal hemoglobin as a percentage of total hemoglobin, 19.0 to 26.8%), with fetal hemoglobin broadly distributed in red cells (F cells as a percentage of red cells, 69.7 to 87.8%). Manifestations of sickle cell disease decreased during the follow-up period.
Conclusions
CRISPR-Cas9 disruption of the HBG1 and HBG2 gene promoters was an effective strategy for induction of fetal hemoglobin. Infusion of autologous OTQ923 into three participants with severe sickle cell disease resulted in sustained induction of red-cell fetal hemoglobin and clinical improvement in disease severity. (Funded by Novartis Pharmaceuticals; ClinicalTrials.gov number, NCT04443907. opens in new tab.)

Pediatrics
Volume 152, Issue 2 August 2023
https://publications.aap.org/pediatrics/issue/152/2
[No new digest content identified]

Personalized Medicine
2023 20:3, 283-297. 14 July 2023
Systematic Review
Institutionalization of personalized medicine in India: analysis of research trends and government interventions
Ishita Goyal & Madhavi Yennappu
Abstract
The biggest challenges that any country faces are affordability and accessibility of quality healthcare. Technological advancements can address these challenges. One such advancement is personalized medicine (PM). This paper discusses the implementation and institutionalization of PM. Using the sectoral innovation system framework, this work describes government interventions with research trends in PM in India. The Web of Science database was used to analyze research trends. Indian government-funded interventions to institutionalize PM were compiled and analyzed. Results suggest that India's healthcare sector is dynamic. The framework discusses some specifics, including the research network, boundaries and government initiatives to promote PM adoption. Based on the policy gaps, this paper further proposes an integrated policy framework for incorporating PM into India's healthcare system.

Perspectives in Clinical Research
28 July 2023
Review Article
Redefining informed consent form in cell and gene therapy trials
Varsha Dalal, Geeta Jotwani, Munna Lal Yadav
Abstract
Informed consent is a foundation of the ethical conduct of research involving human participants. Based on the ethical principle of respect for persons, the goal of informed consent is to ensure that participants are aware of the risks and potential benefits and make a voluntary decision about participating in clinical trial research. The extraordinary scientific advances happening globally have demonstrated the potential of regenerative therapies in transforming the health of the nation by providing a therapeutic option for diseases that were previously considered incurable. These therapies, which include cells and gene therapy (GT) labeled as Advanced Therapeutic Medicinal Products globally, have complex mechanisms of action. Owing to their highly personalized and intricate nature of these therapies, developing the latter often presents unique challenges above and beyond those encountered for small molecule drugs. We recently looked through some cell and GT clinical trials and realized the lacunae in the informed consent form (ICF) provided by the investigators. Especially in a country like India, where the general understanding and perception of patients is limited regarding clinical trials, it is felt that any lapses in the consent process may jeopardize the informed decision-making and safety of the participants and tarnish the reputation of India globally. The present article highlights the need for appropriate patient and public education on the various aspects of cell and gene therapies and aims to address all the elements of ICF in light of the challenges associated with these innovative therapies.

PharmacoEconomics
Volume 41, issue 8, August 2023
https://link.springer.com/journal/40273/volumes-and-issues/41-8
[New issue; No digest content identified]

PLoS Biology

https://journals.plos.org/plosbiology/
(Accessed 30 Aug 2023)
Essay
Towards a post-pandemic future for global pathogen genome sequencing
Jason T. Ladner, Jason W. Sahl
published 01 Aug 2023 PLOS Biology
https://doi.org/10.1371/journal.pbio.3002225
Abstract
Pathogen genome sequencing has become a routine part of our response to active outbreaks of infectious disease and should be an important part of our preparations for future epidemics. In this Essay, we discuss the innovations that have enabled routine pathogen genome sequencing, as well as how genome sequences can be used to understand and control the spread of infectious disease. We also explore the impact of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic on the field of pathogen genomics and outline the challenges we must address to further improve the utility of pathogen genome sequencing in the future.

PLoS Genetics
https://journals.plos.org/plosgenetics/
(Accessed 30 Aug 2023)
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PLoS One
http://www.plosone.org/
[Accessed 30 Aug 2023]
[No new digest content identified]

PNAS - Proceedings of the National Academy of Sciences of the United States
August 22, 2023 vol. 120 no. 34
https://www.pnas.org/toc/pnas/120/34
Brief Report
Applied Biological Sciences Open access
Focused ultrasound–mediated brain genome editing
Yeh-Hsing Lao, Robin Ji, Joyce K. Zhou, and Kam W. Leong
August 14, 2023
Abstract
Gene editing in the brain has been challenging because of the restricted transport imposed by the blood–brain barrier (BBB). Current approaches mainly rely on local injection to bypass the BBB. However, such administration is highly invasive and not amenable to treating certain delicate regions of the brain. We demonstrate a safe and effective gene editing technique by using focused ultrasound (FUS) to transiently open the BBB for the transport of intravenously delivered CRISPR/Cas9 machinery to the brain.

Public Health Genomics
2023, Vol. 26, No. 1
https://karger.com/phg/issue/26/1
[No new digest content identified]

Public Understanding of Science
https://journals.sagepub.com/home/PUS
Research article
First published online August 28, 2023
The divide so wide: Public perspectives on the role of human genome editing in the US healthcare system
JP Nelson, DC Tomblin, A Barbera, M Smallwood - Public Understanding of Science, 2023
Abstract
We report findings from two open-framed focus groups eliciting informed public opinion about the rapidly developing technology of human genome editing in the context of the US healthcare system. Results reveal that participants take a dim view of the present healthcare system, articulating extensive concerns about the accessibility and affordability of care. They feel that, unless these problems are resolved, they stand little chance of benefiting from any eventual human genome editing treatments. They prioritize improvement in healthcare access well above human genome editing development, and human genome editing regulation and oversight above human genome editing research. These results reveal substantial divergence between public perspectives and expert discourse on human genome editing. The latter attends primarily to the moral permissibility of technical categories of human genome editing research and how to treat human genome editing within existing regulatory and oversight systems rather than broader political-economic and healthcare access concerns. This divergence illustrates the importance of openly framed public engagement around emerging technologies.

Science
Volume 381| Issue 6660| 25 Aug 2023
https://www.science.org/toc/science/current
[No new digest content identified]

Science Translational Medicine
Volume 15| 23 Aug 2023; 16 Aug 2023; 9 Aug 2023
https://www.science.org/toc/stm/current
[No new digest content identified]

Pre-Print Servers

Gates Open Research
https://gatesopenresearch.org/browse/articles
[Accessed 30 Aug 2023]
Selected Research
[No new digest content identified]

medRxiv
https://www.medrxiv.org/content/about-medrxiv
[Accessed 30 Aug 2023]
[Filter: All articles]
Selected Research
Extended genome-wide association study employing the African Genome Resources Panel identifies novel susceptibility loci for Alzheimer's Disease in individuals of African ancestry
Nicholas R. Ray, Brian W. Kunkle, Kara Hamilton-Nelson, Jiji T. Kurup, Farid Rajabli, Mehmet I. Cosacak, Caghan Kizil, Melissa Jean-Francois, Michael L. Cuccaro, Dolly Reyes-Dumeyer, Laura Cantwell, Amanda

Kuzma, Jeffery M. Vance, Sujuan Gao, Hugh C. Hendrie, Olusegun Baiyewu, Adesola Ogunniyi, Rufus O. Akinyemi, Alzheimer's Disease Genetics Consortium, Wan-Ping Lee, Eden R. Martin, Li-San Wang, Gary W. Beecham, William S. Bush, Lindsay A. Farrer, Jonathan L. Haines, Goldie S. Byrd, Gerard D. Schellenberg, Richard P. Mayeux, Margaret A. Pericak-Vance, Christiane Reitz
medRxiv 2023.08.29.23294774; doi: https://doi.org/10.1101/2023.08.29.23294774

Despite a two-fold increased risk, individuals of African ancestry have been significantly underrepresented in Alzheimer's Disease (AD) genomics efforts…Increased sample sizes and sample sets from Africa covering as much African genetic diversity as possible will be critical to identify additional disease-associated loci and improve deconvolution of local genetic ancestry effects.

Critical assessment of variant prioritization methods for rare disease diagnosis within the Rare Genomes Project

Sarah L. Stenton, Melanie O'Leary, Gabrielle Lemire, Grace E. VanNoy, Stephanie DiTroia, Vijay S. Ganesh, Emily Groopman, Emily O'Heir, Brian Mangilog, Ikeoluwa Osei-Owusu, Lynn S. Pais, Jillian Serrano, Moriel Singer-Berk, Ben Weisburd, Michael Wilson, Christina Austin-Tse, Marwa Abdelhakim, Azza Althagafi, Giulia Babbi, Riccardo Bellazzi, Samuele Bovo, Maria Giulia Carta, Rita Casadio, Pieter-Jan Coenen, Federica De Paoli, Matteo Floris, Manavalan Gajapathy, Robert Hoehndorf, Julius O.B. Jacobsen, Thomas Joseph, Akash Kamandula, Panagiotis Katsonis, Cyrielle Kint, Olivier Lichtarge, Ivan Limongelli, Yulan Lu, Paolo Magni, Tarun Karthik Kumar Mamidi, Pier Luigi Martelli, Marta Mulargia, Giovanna Nicora, Keith Nykamp, Vikas Pejaver, Yisu Peng, Thi Hong Cam Pham, Maurizio S. Podda, Aditya Rao, Ettore Rizzo, Vangala G. Saipradeep, Castrense Savojardo, Peter Schols, Yang Shen, Naveen Sivadasan, Damian Smedley, Dorian Soru, Rajgopal Srinivasan, Yuanfei Sun, Uma Sunderam, Wuwei Tan, Naina Tiwari, Xiao Wang, Yaqiong Wang, Amanda Williams, Elizabeth A. Worthey, Rujie Yin, Yuning You, Daniel Zeiberg, Susanna Zucca, Constantina Bakolitsa, Steven E. Brenner, Stephanie M. Fullerton, Predrag Radivojac, Heidi L. Rehm, Anne O'Donnell-Luria
medRxiv 2023.08.02.23293212; doi: https://doi.org/10.1101/2023.08.02.23293212

A major obstacle faced by rare disease families is obtaining a genetic diagnosis. The average "diagnostic odyssey" lasts over five years, and causal variants are identified in under 50%. The Rare Genomes Project (RGP) is a direct-to-participant research study on the utility of genome sequencing (GS) for diagnosis and gene discovery. Families are consented for sharing of sequence and phenotype data with researchers, allowing development of a Critical Assessment of Genome Interpretation (CAGI) community challenge, placing variant prioritization models head-to-head in a real-life clinical diagnostic setting.

Unique Capabilities of Genome Sequencing for Rare Disease Diagnosis

Monica H Wojcik, Gabrielle Lemire, Maha S Zaki, Mariel Wissman, Wathone Win, Sue White, Ben Weisburd, Leigh B Waddell, Jeffrey M Verboon, Grace E. VanNoy, Ana Töpf, Tiong Yang Tan, Volker Straub, Sarah L Stenton, Hana Snow, Moriel Singer-Berk, Josh Silver, Shirlee Shril, Eleanor G Seaby, Ronen Schneider, Vijay G Sankaran, Alba Sanchis-Juan, Kathryn A Russell, Karit Reinson, Gianina Ravenscroft, Eric A Pierce, Emily M Place, Sander Pajusalu, Lynn Pais, Katrin Õunap, Ikeoluwa Osei-Owusu, Volkan Okur, Kaisa Teele Oja, Melanie O'Leary, Emily O'Heir, Chantal Morel, Rhett G Marchant, Brian E Mangilog, Jill A Madden, Daniel MacArthur, Alysia Lovgren, Jordan P Lerner-Ellis, Jasmine Lin, Nigel Laing, Friedhelm Hildebrandt, Emily Groopman, Julia Goodrich, Joseph G Gleeson, Roula Ghaoui, Casie A Genetti, Hanna T Gazda, Vijay S. Ganesh, Mythily Ganapathy, Lyndon Gallacher, Jack Fu, Emily Evangelista, Eleina England, Sandra Donkervoort, Stephanie DiTroia, Sandra T Cooper, Wendy K Chung, John Christodoulou, Katherine R Chao, Liam D Cato, Kinga M Bujakowska, Samantha J Bryen, Harrison Brand, Carsten Bonnemann, Alan H Beggs, Samantha M Baxter, Pankaj B Agrawal, Michael Talkowski, Chrissy Austin-Tse, Heidi L Rehm, Anne O'Donnell-Luria
medRxiv 2023.08.08.23293829; doi: https://doi.org/10.1101/2023.08.08.23293829

Causal variants underlying rare disorders may remain elusive even after expansive gene panels or exome sequencing (ES). Clinicians and researchers may then turn to genome sequencing (GS), though the added value of this technique and its optimal use remain poorly defined. We therefore investigated the advantages of GS within a phenotypically diverse cohort.

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Review

Gene Editing: The Regulatory Perspective

Sarfaraz K. Niazi

Abstract

Gene or genome editing (GE) revises, removes, or replaces a mutated gene at the DNA level; it is a tool. Gene therapy (GT) offsets mutations by introducing a "normal" version of the gene into the body while the diseased gene remains in the genome; it is a medicine. So far, no GE product has been approved, as opposed to 22 GT products that cost up to millions of dollars per dose. The FDA has recently added a guideline specific to gene editing that should be understood to enable faster development of GE products; at the same time, the FDA also needs to bring more clarification and make several amendments to this guideline to make it more rational.

Research Square

https://www.researchsquare.com/

Ethical considerations for Biobanking and Use of Genomics Data in Africa: A narrative review

Research Article

Posted 26 July 2023

Mary Amoakoh-Coleman, Dorice Vieira, James Abugri

Abstract

Background

Biobanking and genomic research requires collection and storage of human tissue from study participants. From participants' perspectives within the African context, this can be associated with fears and misgivings due to a myriad of factors including myths and mistrust of researchers. From the researchers angle ethical dilemmas may arise especially with consenting and sample reuse during storage. The aim of this paper was to explore these ethical considerations in the establishment and conduct of biobanking and biogenomic studies in Africa.

Methods

We conducted a narrative synthesis following a comprehensive search of nine (9) databases and grey literature. Ethical issues studied related to community knowledge and understanding of biobanking and genomic research, regulation, and governance of same by research ethics committees, enrolment of participants, types of informed consents, data collection, storage, usage and sharing as well as material transfer, returning results and benefit sharing.

Results

Of 2,663 title and abstracts screened, 94 full texts were retrieved and reviewed for eligibility. We included 12 studies (7 qualitative; 4 quantitative and one mixed methods). More education of study participants is needed, as well as appropriate community engagement processes that allow community confidence in enrolment into such studies. Competence of review and ethics committees (RECs) should be enhanced to adequately review and govern biobanking and genomic research in Africa. Biospecimen collection and storage is given in trust and participants expect confidentiality of data and results generated. Most participants are comfortable with broad consent due to trust in researchers, though a few would like to be contacted for reconsenting in future studies, and this would depend on whether the new research is for good cause. Sharing data with external partners is welcome in some contexts but some research participants did not trust foreign researchers.

Conclusion

With these varying ethical considerations, we recommend that stakeholders, including research ethics committees, work together to adapt and use clearly defined ethical frameworks, guidelines, and policy documents to harmonize the establishment and running of biobanking and genomic research in Africa.

Wellcome Open Research
https://wellcomeopenresearch.org/browse/articles
[Accessed 30 Aug 2023]
Selected Research
Study Protocol/Open Access
Ethical issues of involving people with intellectual disabilities in genomic research: a scoping review protocol [version 1; peer review: awaiting peer review]
Dorothy Chepkirui, Patricia Kipkemoi, Mary Bitta, Eli Harris, Rosemary Musesengwa, Dorcas Kamuya
Abstract
Background: Psychiatric genomic research is a growing field of research in Africa that is looking at epigenetics of psychiatric disorders; within which a specific focus is neurodevelopmental disorders including intellectual disability (ID). Conducting this type of research is important to identify etiologies and possible interventions or areas for further research. However, genomic research generally, and psychiatric genomic research, faces many social, ethical, cultural, and legal issues; research involving people with ID is particularly challenging. All research stakeholders - researchers, research review bodies, regulators, patient groups - generally agree that involving people with ID require several considerations, including extra protection. It is also recognized that not involving people with ID in research that is relevant to them means that opportunities to learn on specific issues including lived experiences are missed. In this scoping review, we aim to describe the range of ethical and social-cultural issues concerning involvement of people with intellectual disability in genomic research from existing literature.
Methods: This scoping review will be conducted based on the Joanna Briggs Institute guidance for scoping review and reported using the PRISMA-ScR guidelines. Iterative review stages will include systematic search of six databases (Embase, Ovid Global Health, PubMed, Scopus, PsycInfo and Web of Science core collection), screening, charting and synthesis of the data. Forward and backward citation screening will also be done for the articles included in the final review. We will include peer reviewed journal articles, guidance documents and reports. Screening and selection of studies based on the eligibility criteria will be done independently by three reviewers; conflicts will be resolved through discussion with a third reviewer and other experts.
Results: The results will be included in the scoping review publication.
Conclusions: This scoping review will identify key areas of ethical tensions and possible solutions and inform opportunities for empirical ethics studies.

Book Chapters

Regulation of Clinical Research for Cellular and Gene Therapy Products in India
Chapter
Varsha Dalal, Hem Lata, Gitika Kharkwal & Geeta Jotwani
Advances in Experimental Medicine and Biology, vol 1430, pp 135–154. Springer, Cham. 02 August 2023
Abstract
The understanding of disease biology and advances in cellular and molecular biology platforms have ushered in a new era of cell and gene based therapeutic products. The US-FDA refers to this category of products as Cellular and Gene Therapy Products (CGTPs), while the European Medicines Agency, Europe, refers to them as Advanced Therapy Medicinal Products (ATMPs). The research and development (R&D) and final commercialization of these products have thus picked up pace, especially in the last decade. This emerging scenario necessitates framing regulations and guidelines that take into consideration the unique biological nature of these products. Regulators and government agencies of different countries across the globe have

come up with regulations and guidance documents to guide, monitor, and regulate the research and development in this field. India, given its powerful resources of skilled scientific manpower and infrastructure, is also contributing to development of these innovative therapeutic products. Keeping in line with the international counterparts, the Indian regulators and government agencies have developed regulations and guidelines for stakeholders. This chapter summarizes the regulatory landscape for research and development of CGTP in India. It provides an overview of the government agencies and committees overseeing this field and their roles that a stakeholder working in this field needs to have knowledge of. Furthermore, the chapter outlines the salient features of rules, regulations, and guidelines relevant to CGTP, the approval process, the current approved products in Indian market, and finally, the challenges and way forward for CGTP in India.

Canadian Regulatory Framework and Regulatory Requirements for Cell and Gene Therapy Products

Chapter

Jian Wang, Emily Griffiths, Omar Tounekti, Martin Nemec, Eric Deneault, Jessie R. Lavoie & Anthony Ridgway

Regulatory Aspects of Gene Therapy and Cell Therapy Products pp 91–116, Springer Cham. 02 August 2023

Abstract

Health Canada regulates gene therapy products and many cell therapy products as biological drugs under the Canadian Food and Drugs Act and its attendant regulations. Cellular products that meet certain criteria, including minimal manipulation and homologous use, may be subjected to a standards-based approach under the Safety of Human Cells, Tissues and Organs for Transplantation Regulations. The manufacture and clinical testing of cell and gene therapy products (CGTP) presents many challenges beyond those for protein biologics. Cells cannot be subjected to pathogen removal or inactivation procedures and must frequently be administered shortly after final formulation. Viral vector design and manufacturing control are critically important to overall product quality and linked to safety and efficacy in patients through concerns such as replication competence, vector integration, and vector shedding. In addition, for many CGTP, the value of nonclinical studies is largely limited to providing proof of concept, and the first meaningful data relating to appropriate dosing, safety parameters, and validity of surrogate or true determinants of efficacy must come from carefully designed clinical trials in patients. Addressing these numerous challenges requires application of various risk mitigation strategies and meeting regulatory expectations specifically adapted to the product types. Regulatory cooperation and harmonization at an international level are essential for progress in the development and commercialization of these products. However, particularly in the area of cell therapy, new regulatory paradigms may be needed to harness the benefits of clinical progress in situations where the resources and motivation to pursue a typical drug product approval pathway may be lacking. This chapter is dedicated to providing an overview of Health Canada regulatory oversight of CGTP.

United States Food and Drug Administration Regulation of Human Cells, Tissues, and Gene Therapies

Chapter

Sandhya Sanduja, Liz Lessey-Morillon, Rondine Allen, Xiaofei Wang, Gavin Imperato & Judith Arcidiacono

Regulatory Aspects of Gene Therapy and Cell Therapy Products pp 71–89, Springer Cham. 02 August 2023

Abstract

Research and development of gene therapies and cell- or tissue-based therapies has experienced exponential growth in recent decades and the potential for these products to treat diverse, often rare, clinical indications is promising. The Office of Therapeutic Products (OTP) in the Center for Biologics Evaluation and Research (CBER) at the United States Food and Drug Administration (US FDA) is responsible for the regulation of these products, among others, throughout the entire product lifecycle. This chapter provides an overview of the science- and data-driven approach to US FDA regulatory oversight of cell and gene therapy (CGT) products to ensure their safety and efficacy.

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