*Friday 8 October, 3:15–4:15pm CET*

## ANTICIPATE

# Negotiating the Boundaries of our Genetic Future

## Abstract

The price of sequencing a human genome has fallen from $2.7 billion to $300 in just 20 years. This dramatic improvement in our ability to read DNA is now setting the stage for an even bigger revolution in our ability to write our genetic futures. Over the next decade gene therapies that can tackle the most intractable inherited diseases and cancers will go mainstream. Within 25 years the ability to enhance human capabilities will come within reach, letting us augment sensory capacities and enabling us to thrive in space. That could pose complex biosecurity challenges and raise profound questions about what it means to be human. Given the immense costs of today's experimental gene therapies, work needs to be done to ensure their benefits are shared equitably.

- What are the opportunities and risks posed by our growing mastery over human genetics?
- Where does the line between healing and augmentation lie and who decides what is allowed?
- Genetic capabilities will appear gradually and surreptitiously. How do we ensure their benefits are shared equitably?

## Participants

*Moderated by:*

**Jane Metcalfe**, Founder, NEO.LIFE; Co-Founder, WIRED magazine, USA

*With:*

**George Church**, Professor of Genetics, Harvard Medical School; Professor, Health Sciences and Technology, Harvard and MIT, USA *(remotely)*

**Katherine Littler**, Co-Lead, Global Health Ethics & Governance Unit, World Health Organization, UK

**Effy Vayena**, Professor of Bioethics, ETHZ; Founder, Health Ethics and Policy Lab, Department of Health Sciences and Technology; Member, GESDA Academic Forum, Greece/Switzerland *(remotely)*

**Ambroise Wonkam**, Professor and Senior Medical Genetics Consultant, Division of Human Genetics, Faculty, Health Sciences, University of Cape Town, Cameroon



## Highlights

Almost two decades have passed since the completion of the Human Genome Project, an international collaboration that resulted in our ability to read the complete genetic blueprint for building a human being. That 13 year-effort, which revealed there are probably about 20,500 human genes, marked the beginning of the genomics era in which researchers created inexpensive home DNA testing kits. This reference genome changed how scientists conduct research and share genetic data, and it has steadily grown in size as the use of genomics in health care and other pursuits becomes routine.

The vast majority of this reference genome, however, is from European DNA: The genomes of more than one million individuals have been sequenced but less than 2% are from Africa or recent African descent, raising questions of inclusion and equity. Moreover, the lack of African genetic material impedes our understanding of basic functions and diseases, because African genomes are the oldest and most diverse. The new Crispr gene-editing tools, discovered in 2012, opened new and questionable frontier uses, showing how science and technology often outpaces our ability to understand their applications.



"What's really interesting about this discussion is how grey it is, how grey the areas are, whether you're talking about the language, which technology we should focus on, or where we're going," said Katherine Littler, whose unit within the UN health agency has been developing guidance for governments on how to make ethical decisions. "There is a plethora of governance mechanisms out there, depending on whether you're talking about somatic or hereditary or germline. It really depends. And I think we're at very differing stages all over the globe in terms of governance and oversight. And we have very different starting points of what we think is acceptable, or where we are starting from." She urged more preparedness along the lines of anticipatory science. "We talk about epidemic preparedness, but we should be talking about preparedness for genome and emerging technologies," said Littler. "And when I define preparedness, I'm not talking about just the science. I'm really talking about the governance, because I think governance really is not the panacea, but it's what will help us address a lot of the challenges."

Gene-editing pioneer George Church, who gained notoriety proposing to use synthetic biology for "de-extinction" – the resurrection of an extinct species, like the woolly mammoths – recently announced the launch of a startup that uses gene-editing technology to fight climate change by preserving endangered animals. He also keeps a list of genes that could be modified to enhance human abilities. He noted that people question the safety of COVID-19 vaccines, even though 16 childhood vaccines exist today that are among the cheapest, safest technologies ever made. "All vaccines could be classified as enhancements or augmentation, relative to our ancestors, who lived in fear of these 17 diseases and ones like it," he said. "Almost all powerful and popular technologies are enhancements, whether they're cars or books or computers, etc. I think what's more significant here is whether they're reversible or not. If you try to reverse, say, the cell[phone], the telephone revolution, that would be politically very difficult to do. So, in a way that's irreversible, at least so far."

A more urgent message can be found in the history of smallpox eradication, according to Church. "We did not wait for smallpox vaccination for full understanding of all the genes or even understanding of virology or immunology. We started vaccinating before we could see a virus, before we even knew there were viruses, and before we knew anything about immunology," he said. "So, I'm not recommending that we act on ignorance. I am just saying that occasionally we can reach consensus without full understanding. And in terms of reversibility, I think that editing is definitely reversible. I'm not advocating editing our genomes so much as editing, changing our genetics. It could be messenger RNA, which is perceived as being temporary." RNA is a molecule that is essential in various biological roles in regulating the expression of genes, but does not change the DNA itself.

A more cautionary approach would be preferable, said Ambroise Wonkam, a medical genetics professor whose research focuses on sickle cell disease, genetics of hearing loss and ethical and educational issues involving human genetics in Africa. He recently launched the Three Million African Genomes (3MAG) project to build capacity on the African continent in genomics research and its applications and governance. It is based on an estimate that capturing the full scope of Africa's genetic variation would require sequencing three million people across Africa to cover ethnolinguistic, regional, and

other groups. It also would have benefits worldwide, he said, much like research on Ebola outbreaks helped with the COVID-19 pandemic.

Because of the data gaps, Wonkam said, he was "not sure we are genetically literate enough" to undertake gene editing and, similarly, "not sure we have addressed the question of equity in the level of gene editing". Rather than focus first on applying gene editing to HIV, as a Chinese scientist claimed to have done in 2018 by creating the first human genetically edited babies with the Crispr technology, he said, there are 300,000 children a year that are born with sickle cell disease. "And 80% of those kids are born in Africa. That makes it our priority, right?" he said. However, Church said, "the right question is how many people are affected" and factors such as cost since genetic drugs for rare diseases "are very expensive, while vaccines are very cheap", including those based on RNA.

Africa only has 20 medical geneticists to serve 15 million people, Wonkam said, pointing to a need for more education and genetic literacy. "We have about 20,000 genes in our genome now. If we all look in the OMIM database that we use as medical geneticists, only 25% of the genes that we know are associated with disease conditions," he said. "We have no idea how the 75% are different. Are we genetically literate enough? The answer is no."

George Church and Jane Metcalfe

Wonkam urged people to use a concept from the Akan tribe or language group in Ghana called the power of Sankofa, which translates as "it is not taboo to fetch what is at risk of being left behind" and is symbolized by a bird turning to put an egg on its back. "And actually, Sankofa speaks about the past, but the egg is to fertilize the future," he said. "I believe that we have to go into the past of our genome to understand how actually our genome combats infection by selection, instead of trying to create a new way through editing."

Effy Vayena, a professor of bioethics and founder of a lab focused on ethical and policy challenges in personal medicine and digital health, said she agreed immunization can be considered as an enhancement, but that it is irrelevant to distinguish between a disease treatment and an enhancement.

"That might be a controversial statement, but I would invite us to think a little bit about it in the following way: If we are trying to draw the line between the two, we're probably thinking of health as a sense of physical health, perhaps even mental health. But we're not thinking of well-being. And if we think of well-being and what we can do to improve that, I think the boundary between treating a disease and enhancing is – it gets very messy."

A more fundamental question, Vayena said, is "which version of progress" to follow: for science or for society? "We're constantly trying to improve the human condition with all means we have. We want to reduce human suffering, we want to improve well-being, but we revise constantly the ways in which we do that and its meaning. The question again is how do we do that in a manner that allows all voices to be heard?" Vayena asked. "I really welcome the initiative of GESDA. I think it's an opportunity to lead us to this global dialogue we need. But again, it's about deliberating about our disagreements here, and our opinions, not simply stating them."

Jane Metcalfe, a serial entrepreneur, and publisher who focuses on what she calls the "neobiological revolution", said she agreed. "There's an enormous role for GESDA to play here, if for no other reason than to just bring the various parties together in one room, create a common language and a sort of baseline of knowledge, and then frame the questions and the issues. It is astonishing to me that this many years after the development of Crispr, that's still not really happened," said Metcalfe. "We really are missing all of the stakeholders, including private industry, to come together and have these conversations. So definitely a work to do on GESDA's to-do list."



## Takeaway Messages

**The new Crispr gene-editing tool opened new and questionable frontier uses, showing how science and technology often outpaces our ability to understand their applications.**

**The genomes of more than one million individuals have been sequenced but less than 2% are from Africa or recent African descent, raising questions of inclusion and equity. Moreover, the lack of African genetic material might impede our full understanding of basic functions**

**There is a differing opinion about when and if a technology (such as gene-editing tools) is ready to be integrated with the public and how that process should be carried out, also in terms of communication.**

**We did not wait for full understanding of all the genes or virology or immunology before vaccinating for smallpox. Similarly, some of the technical hurdles in gene-editing technology lie in the fact that it's impossible to wait as long as necessary to really know if something will be safe for a person's lifetime. Occasionally we can reach consensus without full understanding.**

**It may be irrelevant to distinguish between a disease treatment and an enhancement, because if one thinks in terms of well-being, the boundaries are blurry. The questions of safety and precision of the interventions are key.**

**There are differing stages all over the globe in terms of governance and oversight, and different starting points of what we think is acceptable. We should be talking about preparedness for genome and emerging technologies in terms of governance.**

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