Collective Intelligence

Pitfalls and Progress in Genome Editing

Takeaways From the Third International Summit on Human Genome Editing

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Societal issues take center stage

This month, the Third International Summit on Human Genome Editing was held at the Francis Crick Institute in London, bringing together 500 experts from around the world, plus another 1,600 online, to discuss advances and challenges in the fast-evolving field.

Five years ago, the second such summit, in Hong Kong, was mired in controversy when Chinese scientist He Jiankui announced he had created the world's first gene-edited babies – breaching a legal red line against editing human eggs, sperm or embryos, and landing him in jail. Today, scientists and bioethicists are still dealing with the fallout, with governance a major topic at the London meeting. But wider societal issues – particularly equity and access – were also a key focus, reflecting the rapid pace of research and development, which could see US approval for the first genome-edited product later this year.

For a few individuals in clinical trials, the promise of genome editing is already transforming lives. The conference heard from **Victoria Gray**, the first sickle cell patient to receive genome editing treatment, who has now gone four years without needing a blood transfusion and is free of the painful symptoms she described as "like being struck by lightning and hit by a freight train at the same time."

The following were some of the key discussion topics at the London summit, as tracked by the Brunswick Healthcare & Life Sciences team.

Clinical trials advance as CRISPR takes off

The science of genome editing has advanced substantially in the past five years. The CRISPR/Cas9 genetic "scissors" technology, which secured the Nobel Prize in Chemistry in 2020 for Jennifer Doudna and Emmanuelle Charpentier, has more recently been complemented by next-generation tools like base, prime and epigenetic editing. **David Liu** of the Broad Institute said these new tools significantly increased the capabilities of genome editing, opening more possibilities for correcting genetic variants linked to disease with greater precision and efficacy. Overall, there are over 130 clinical trials involving genome editing underway around the world, and the first product based on CRISPR genome editing technology is now being submitted for approval to treat sickle cell disease and beta thalassemia. **Victor Dzau** of the US National Academy of Medicine said the science had made remarkable strides in a few short years, with therapies under development for diseases ranging from blood disorders to sight loss and cancer.

Delivery and cost: twin challenges to equitable access

Despite the advances, however, the new science will not truly benefit humanity unless it is widely accessible, said **Linda Partridge** of Britain's Royal Society. Sickle cell disease underscores the point: the condition affects millions of people worldwide, but most live in sub-Saharan Africa, where healthcare capacity is severely limited. The first CRISPR editing therapies will therefore be out of reach for most of the global sickle cell community – a function of the expense and complexity of delivery, which involves invasive procedures to extract cells for editing, intensive chemotherapy and lengthy hospital stays. **Emily Turner** of the Bill & Melinda Gates Foundation said that work needs to start now toward the "aspirational" goal of developing more convenient in vivo treatments that could meet the needs of patients in low- and middle-income countries. If genome editing is to become the standard of care for the many diseases that it could theoretically treat, addressing the pricing conundrum will be critical. Scientists recognized that scaling up delivery and reducing costs has to be done in a way that maintains the engagement of life-science companies and their investors. In the last two years, six gene therapies have been dropped by commercial manufacturers for nonmedical reasons. US launch prices of $1 million to $3.5 million per patient proved too much for other countries. "People want to say 'yes' to gene

therapies but they are going to struggle to do so," said **Steven Pearson**, founder of the Institute for Clinical and Economic Review.

Engaging stakeholders in a controversial field

Right now, CRISPR is used in research almost exclusively for editing somatic cells, meaning changes cannot be passed on to future generations. There is consensus that alterations to heritable cells leading to live births should remain out of bounds for the foreseeable future, which limits research on embryos. **Robin Lovell-Badge** of the Francis Crick Institute said any decision to eventually allow heritable genome editing would require a properly informed discussion among all stakeholders, and it would be contingent on demonstrating it could be done safely, which he said was "still a big if." Public engagement is also unlikely to produce simple "yes/no" answers, requiring scientists to adapt to nuanced, conditional and evolving societal feedback.

China has tightened oversight, but critics still see gaps

While He Jiankui's edited-babies experiment was already illegal under existing laws in 2018, China has accelerated the pace of biomedical regulation in the past five years. **Yoajin Peng** of the Chinese Academy of Sciences said there had been a slew of new laws and guidelines, with the latest measures on the ethical review of life science research issued on February 27, 2023. However, **Joy Zhang** of the University of Kent said China's regulatory changes were "significant but not sufficient." She expressed concern that governance measures are still largely confined to academic institutions and do not directly address how privately funded research is conducted in China.

Microbiome is next frontier for genome editing

Future applications of genome editing are set to expand beyond altering patient cells to changing the DNA of bacteria that live in the guts of humans and other animals – opening new avenues for fighting disease and even fighting climate change. CRISPR pioneer **Jennifer Doudna** of the Innovative Genomics Institute said this would lead to "a whole new area of biology." Her team is working to characterize and understand whole microbial communities. The aim is to develop microbial community-editing technologies that will make it possible to target individual genomes; for example, within the human gut. This approach opens the door to much wider therapeutic applications, because the microbiome is increasingly linked to all kinds of diseases, from infections and asthma to neurodegeneration. It could also revolutionize agriculture if a way is found to reduce methane generation in cow rumens, thereby cutting greenhouse gas emissions and efficiently converting animal feed to meat or milk.

Closing statement from the organizing committee

The summit's organizing committee said in a closing statement that heritable human genome editing remained unacceptable "at this time." It also called for an urgent global commitment to make treatments affordable and equitable.

How Brunswick can help

Through its worldwide team of experts in the healthcare and life sciences sector, Brunswick is well placed to help companies tell their value story. Our advice is rooted in an understanding of the changing corporate, regulatory, scientific, social and political landscape, and includes in-depth experience in the field of rare diseases.

To continue the conversation:

Contact ukhealthcare@brunswickgroup.com.

