Shifting Perceptions of CRISPR: From Controversial Gene Editing Tool to Indispensable SARS-CoV-2 Variant Surveillance Tool

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INTRODUCTION

More than 20 cell and gene therapies are now available to safely minimize genetic diseases such as retinal dystrophy (LUXTURNA), some B-cell lymphomas (YESCARTA), and B-cell lymphoblastic leukemia (KYMRIAH).[1] One such gene-editing tool is Clustered Regular Inter Spaced Palindromic Repeats (CRISPR) and its associated proteins or CRISPR-Cas. Jennifer Doudna and Emmanuelle Charpentier described CRISPR's potential as an accurate genome editing tool in 2012. The FDA approved the first cell and gene therapy in 2017.[2] The FDA is continually approving more CRISPR clinical trials, including therapies to treat sickle cell anemia, cancer, and HIV.[3]

Amid the COVID-19 pandemic, the broad potential applications of CRISPR have extended beyond gene editing. CRISPR is being used in rapid diagnostic testing to determine not only whether an individual becomes infected with SARS-Cov-2 but also the specific variant.[4] As with many diagnostic tests, scientists still face challenges like speed, sensitivity (the ability of the test to detect viral load), and robustness (the ability of the test to give accurate results in the field).

Nonetheless, these tests could revolutionize surveillance of the virus and help curb the spread of new variants as they arise. According to the Centers for Disease Control and Prevention, there are SARS-CoV-2 variants of interest, variants of concern, and variants of high consequence. In varying degrees, these may impact the efficacy of different vaccines and treatment plans.[5] Knowing which variant an individual has or is circulating within a population informs public health policy.

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I. Public Perceptions of Gene Editing Throughout the Decades

Perceptions about gene editing have fluctuated, especially since the 1970s. Support has varied for recombinant DNA in which editing a bacterial genome produces human insulin to treat diabetes, genetically modified plants such as antibiotic resistant tobacco, and other genetically modified organisms. Human gene editing has a tainted past: consider the teenager Jesse Gelsinger who tragically died in a gene therapy clinical trial in 1999.[6] Another gene therapy trial led to the development of leukemia in several young children.[7] In the last two decades, there have been significant improvements in safety and reliability. Though scientists have developed various gene therapies over the years, such as viral vector delivery of therapeutic transgenes, transcription activator-like effector nucleases (TALENS), and zinc finger nucleotides, CRISPR far surpasses them by safety, accuracy, and ease of use.[8]

II. Shifting Perceptions and Broader Applications

CRISPR is controversial due to concerns of safety, misuse for non-therapeutic purposes, and uncertainty about the science and technology. Yet, there is also an underlying assumption that gene editing for therapeutic purposes would be a good use of CRISPR. There is an ethical imperative to use CRISPR therapeutically to safely reduce suffering for people with debilitating genetic diseases if proven safe. However, there is more variation in what would be considered *good* about uses beyond therapeutic applications, such as enhancement purposes. Enhancement is a broad and conceptually laden term. For example, Julian Savulescu defines enhancement as any change in the person's state – biological or psychological – which in turn is experienced or judged by the person or people as good.[9] Thus, enhancement could include any gene-editing relating to physical, cognitive, aesthetic, or moral enhancement. For example, the public and the scientific community reacted with outrage to the 2018 scandal of He Jiankui, a Chinese scientist who gene-edited two baby girls to make them HIV resistant. Rather than therapeutic gene-editing, this example was widely considered enhancement. The public may perceive the uses of CRISPR for enhancement as negative, but improved public perception of CRISPR overall would be beneficial to promote its therapeutic uses.

CRISPR opened an array of possibilities and consequential decisions that lie in the hands of the consumer. A qualitative study done to gauge opinions on Twitter found that "#CRISPR babies" elicited responses of sentiments ranging from positive and neutral to negative, spiking in 2018 with mostly neutral and negative sentiments.[10]

As cell and gene therapies move to market treating a small number of people with rare genetic diseases, public perceptions of these technologies are already shifting and may shift more over time. The factors influencing this shift toward acceptance might include trust in science,[11] trust in the technology or the brand[12] that brings it to market, and proven safety and efficacy over time.

Meanwhile, in this COVID-19 pandemic, CRISPR's beneficial services for the detection of different variants in individuals and populations may positively impact the way it is perceived and accepted by the public. Mammoth Biosciences[13] and Nanyang Technological University have developed rapid diagnostic tests called DETECTR and VaNGuard, respectively, to detect variants.[14]

CRISPR and its associated proteins act as molecular scissors that have the ability to cut a specific section of genetic material with accuracy. It is the exploitation of a bacterial defense mechanism. When a virus infects bacteria, it uses CRISPR-associated proteins to cut out the bacteriophage's RNA. The bacteria then insert some of the virus RNA into its own genome to detect and destroy it in the future. In the VaNGuard diagnostic test, the enzyme enAsCas12a targets specific sections of the SARS-CoV-2 genome. Guided by two guide RNAs, it snips a section of the virus and can detect the virus as well as two mutation sites in the virus.

CONCLUSION

CRISPR's application as a diagnostic testing tool is different from its gene-editing use. However, people may not distinguish the different applications when forming their perceptions of CRISPR. Public confidence in certain technology needs only a push in a certain direction to sway opinion toward mass consumption or disapproval. Research investigating people's perceptions is becoming central to the debates about new technologies.[15] The WHO's Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing, in their Position Paper (2021), calls for "education, engagement, and empowerment."[16] They call on the United Nations to establish an interagency working group to facilitate global dialogue. The National Academies of Sciences, Engineering, and Medicine Consensus Study Report (2020), also calls for public engagement and education about these technologies.[17] DIY and biohacking communities have shown an inclination to understand and apply these technologies with or without the guidance of regulators, scientists, or academia.[18] Perhaps as CRISPR is used to saved lives during the pandemic, this is a pivotal moment to educate people about CRISPR and its broad applications.

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