ASK AN EXPERT

Health Science Inquiry

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REBECCA STEVENS-GREEN is a third year Arts and Science student at the University of Guelph. She is studying Biochemistry and Psychology, and has an interest in bioethics. She is currently working on a research project focusing on the genetics of *Candida albicans* in the Shapiro lab. Rebecca is also working with Dr. Shapiro and Dr. Abraham to investigate the ethics of scientific advancement and genetic engineering.

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The Ethical Implications of CRISPR/Cas9 Gene Editing

The continued development of CRISPR/Cas9 technologies has evoked ethical questions worldwide. The question is no longer whether humans *should* be editing genomes, but rather what regulations should be put in place with the continued use of this technology. Since the discovery of the CRISPR/Cas9 gene editing system, genetic modifications have been used in applications such as improving crop yields, bioengineering malaria-resistant mosquitoes, gene-editing in human somatic cells, and the engineering of microbes for biofuel and drug production [1]. With the advancement of CRISPR/Cas9 systems comes the responsibility of the scientific community to engage with the public for ethical decisions [2].

The CRISPR/Cas9 system allows permanent mutation, deletion and insertion of DNA at precise points in the genome. CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats, which were identified in prokaryotic microorganisms in the 1990s, as a bacterial or archaeal defense system against invading viruses. The Cas9 endonuclease acts as the "scissors" to cut the desired DNA fragment, guide RNAs act as "homing devices" for the CRISPR/Cas9 system to a precise genomic location, and template DNA directs the repair of the cut DNA [3]. This enables targeted genetic editing in almost any living organism. In Dr. Shapiro's lab at the University of Guelph, we study the fungal pathogen *Candida albicans* using CRISPR/Cas9 gene editing technology. *C. albicans* is the most prevalent cause of fungal infections and is of economic importance due to high mortality rates and increased costs of healthcare. Our investigations with CRISPR/Cas9 are helping to uncover important genetic mechanisms by which this pathogen is able to form biofilms and to resist antifungal drugs, with the ultimate goal of discovering new strategies to treat these infections [4].

The genetic manipulation of bacteria, fungi, and plants are potentially less controversial than the recent applications in human embryos. Scientific regulation on genetic engineering has been ineffective since the early development of new technologies in this field. In 1975, the Asilomar Conference brought together biologists, lawyers, and physicians to discuss the biohazards of DNA recombination [2]. Biohazards included the particular fear of creating dangerous new pathogens

through recombinant DNA technologies [2]. The members of the Asilomar conference ultimately decided to halt all DNA recombination experiments [2]. Furthermore, in 2015 there was a worldwide moratorium on embryonic gene editing after documented accounts of embryonic research using CRISPR/Cas9 in China [2]. In both cases, scientists reveled in their transparency, but failed to consider the opinions of the public. The pattern of public scientific discussion is "hitting pause" long enough to diffuse public concern and this has caused a lack of communication on current scientific issues.

In a recent advancement, human embryos were edited by Dr. He Jiankui, using CRISPR/Cas9 technology to mutate the *CCR5* gene in twin girls [5]. Dr. Jiankui mutated the *CCR5* gene in the embryos to render the *CCR5* chemokine co-receptor inactive [5]. This is the co-receptor to which the macrophage-tropic strain of HIV binds. The eight couples selected for the trial were composed of HIV seropositive men and seronegative women [5]. The sperm cells were first tested for HIV, then treated using CRISPR/Cas9 technologies to mutate the *CCR5* gene. This was the first-ever embryo modification on humans, and the procedure violated internationally accepted ethical principles. Additionally, since CRISPR/Cas9 was applied in germline cells, it will be maintained across generations [5]. There are now social, political and ethical issues that need to be addressed, such as the consent process for these trials, the potential medical side effects of CRISPR/Cas9 editing, and the implications for future research using CRISPR/Cas9 on humans [5].

In order for science to continue with technological advances, the dialogue between scientists and the public needs to become more open [6]. Public trust in the scientific discourse and the integrity of scientific investigation are critical in order to democratically create a better future. Restraint should extend to the research agendas instead of eventual applications, with an informed deliberation from the public. Genetic research with CRISPR/Cas9 should continue to solve worldwide issues, but not without the input of law, politics, and the public.

References

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