Fixing Genetic Diseases with Prime Editing

By: Rapid Access International, Inc.

October 2019

Gene editing has been around for some time. In the early days of the mid- to late 2000s, this was a costly endeavor confined to targeted and well-funded areas of research. This was before the Crispr method was unveiled in 2012; a newer approach to gene editing that is "already widely used for scientific research, and in the not too distant future many of the plants and animals in our farms, gardens or homes may have been altered with CRISPR."[1]

What is Crispr?

The technical term 'Crispr' stands for Clustered Regularly Interspaced Palindromic Repeats. Crispr systems – consisting of "a protein with sequence-snipping capabilities and a genetic 'GPS guide' – have "naturally evolved across the bacterial kingdom as a way to remember and defend against invading viruses".[2] Use of the term Crispr generally relates now to the recent discovery by scientists that they can "repurpose that primordial immune system to precisely alter genomes, setting off a billion-dollar boom in DNA hacking."[3]

The large amounts of money being invested in Crispr range across industries: pharmaceuticals, agriculture and energy, to name a few.

Prime Editing: A New Crispr Technique to Fix Almost All Genetic Diseases?

About two years ago, Dr. Andrew Anzalone set out to address some of the challenges faced by Crispr techniques to replace faulty genes with healthy ones.

The problem has been that techniques have required both the programming of a piece of guide RNA to tell Crispr where to cut the DNA, a copy of the new DNA would have to be provided – along with the home that "the cell's repair machinery installs it correctly. Which…it often doesn't".[4]

Dr. Anzalone looked for a way to combine these two pieces, "so that one molecule told Crispr both where to make its changes and what edits to make."[5]

In 2018, Dr. Anzalone joined the lab of chemist Dr. David Liu at the Broad Institute of Harvard and MIT. Drawing on Dr. Liu's recent working developing 'surgical' Crispr systems, or base editors, the two have developed a technique perhaps even more ambitious and capable than Dr. Anzalone had envisioned.

---

[1] Terminology Section. "What is CRISPR?" New Scientist. Available at: https://www.newscientist.com/term/what-is-crispr/. Accessed on December 1, 2019.

[2] Molteni, Megan. The Wired Guide to Crispr. Wired. Posted March 12, 2019. Available at: https://www.wired.com/story/wired-guide-to-crispr/. Accessed on December 1, 2019.

[3] *Ibid.*

[4] Molteni, Megan. "A New Crispr Technique Could Fix Almost All Genetic Diseases". Wired. Posted October 21, 2019. Available at: https://www.wired.com/story/a-new-crispr-technique-could-fix-many-more-genetic-diseases/. Accessed on December 1, 2019.

[5] *Ibid.*

The two scientists have developed what they call 'prime editing': a system that "can for the first time make virtually any alteration—additions, deletions, swapping any single letter for any other—without severing the DNA."[6]

Dr. Liu has likened prime editors to word processors and noted that with such fine-tuned command of the genetic code, prime editing could, according to Liu's calculations, correct around 89 percent of the mutations that cause heritable human diseases.[7] In his lab, they have already been working with human cell cultures and used prime editors to fix the genetic issues that cause sickle cell anemia, cystic fibrosis, and Tay-Sachs disease: three of more than 175 edits they noted in a recent article in the journal Nature.[8]

Going Forward

In short, prime editing is more efficient and less accident prone than Classic Crispr techniques. The system shows much promise.

One large problem in bringing the science of prime editing to patients (so far, mice) is the sheer amount and size of information packed into the editors (in molecular terms). This can present issues as far as 'packing' them neatly into the viruses used to move editing components into cells. And, there could even be issues with clogging of the microinjection needles used for the delivery of these viruses.

To think that the challenges for this technique appear to be logistical in nature is truly amazing. For a category that receives much attention and investment, this new Crispr system of prime editing warrants much attention.

Indeed, Dr. Liu has cofounded a company called Prime Medicine that has licensed the technology from the Broad Institute to develop treatments for genetic disease. His base editing company, Beam Therapeutics, has also been granted a sublicense for certain aspects.

---

[6] *Ibid.*

[7] *Ibid.*

[8] *see* Anzalone, et. al. "Search-and-replace genome editing without double-strand breaks or donor DNA" Nature. Posted October 21, 2019. Available at: https://www.nature.com/articles/s41586-019-1711-4??utm_medium=affiliate&utm_source=commission_junction&utm_campaign=3_nsn6445_deeplink_PID8179212&utm_content=deeplink. Accessed on December 1, 2019. (see also Molteni, Megan. "A New Crispr Technique..." *op. cit*.)