Book Reviews

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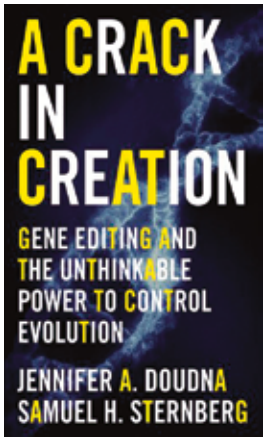

A Crack In Creation: Gene Editing and the Unthinkable Power to Control Creation

Jennifer A. Doudna and Samuel H. Sternberg
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Reviewed by David A. Bennahum, MD (AΩA, University of New Mexico, 1984)

In this timely and well written book, biochemist Jennifer Doudna, with the assistance of her former student and co-author Samuel Sternberg, tells the story of how, since 2015, she and her students and colleagues working in her laboratory at the University of California at Berkley helped discover and create, along with scientists around the world, as she writes "the newest and arguably most effective genetic engineering tool, CRISPR-Cas9 (CRISPR)," and that thereby "the genome—an organism's entire DNA content, including all its genes—has become as editable as a simple piece of text."[pxiii] She describes a few of the early marvels achieved with CRISPR such as hyper muscular beagles, more cashmere wool from Shannbei goats, and perhaps soon a revived woolly mammoth. She notes that there will also be impacts on plant food sources, and human and animal diseases.

The book is divided in two sections: the biochemical work in Doudna's laboratory and in other research centers, around the world, and the potential consequences and ethical questions that have arisen from the discovery of CRISPR.

CRISPR-Cas9 stands for a region of bacterial DNA where clustered regularly interspaced short palindromic repeats are found. Cas9 is the enzyme that the organism uses to snip out an invading virus.

For hundreds of millions of years bacteria have been in a continuous war with viruses that seek to penetrate and take over their DNA. This struggle was first recognized by the British bacteriologist Frederick Twort in 1915, and Canadian-born physician Felix d'Herelle who studied the bacteria that caused Shigella dysentery during World War I. In subsequent decades it was discovered that viruses that attacked archeal and bacterial cells—bacteriophages—are exceptionally abundant. As Doudna writes, "Incredibly, there are many, many more phages on earth than there are bacteria for them to infect: abundant as bacteria are, bacterial viruses outnumber them ten to one. They cause roughly a trillion infections on earth every second, and in the ocean alone, about 40 percent of all bacteria die every day as a result of deadly phage infections."[p48] Thus, "CRISPR was likely part of an archeal and bacterial immune system, an adaptation that allowed microbes to fight off viruses."[p44] Doudna points out how these observations support Darwin's theory of evolution.

Doudna presents a comprehensive and lucid description of the research on CRISPR and other forms of gene editing. Her explanations are greatly enhanced by simple diagrams and drawings. Her writing is enriched by memory as she recalls her studies at Harvard and Yale, and summers as a student in research facilities. Fond memories of her parents and especially of her late father, a professor of English at the University of Hawaii, add an attractive quality to her writing. Recalling a summer spent in a laboratory at the University of Hawaii she writes, "The peace and quiet concentration that characterized Don Hemmes's small research team drew me in, but over the years I became aware of being part of a much bigger community of scientists, each of us seeking, in our own ways, nature's truths." p61

Doudna considers the importance of transplantation to medicine, "Some scientists hope that pigs can offer even more: a vast, renewable source of whole organs for xenotransplantation into human recipients." p140

Doudna points out that, "In the United States alone, more than 124,000 patients are currently on the waiting list for transplants, yet only 28,000 procedures are carried out annually. Gene editing is now being harnessed to shutdown pig genes that might provoke the human immune response and to eliminate the risk that porcine viruses embedded in the pig genome that could hop over and infect humans during transplantation." p141 But, she asks, will we retain a concern for animal welfare?

She also brings up her concern that gene editing will be used for aesthetic reasons, but is not convinced that "this is categorically a bad thing."

Doudna touches on the concept of gene drives stating, "There is one way, at least, in which the power to edit the genes of other species (such as malarial mosquitos) could prove to be more dangerous than any changes humans have made to the planet so far." p148 "With gene editing, however, any off-target DNA sequence, once edited is irreversibly changed. Not only will unintended edits to DNA be permanent, they will also be copied into every cell that descends from the first one. And although most random edits are unlikely to damage the cell, if we have learned anything from certain diseases and cancers, it is that even a single mutation can be enough to wreak havoc on an organism." p179

In considering germ line editing, which of necessity affects future generations, she states, "Essentially, we wanted the scientific community to hit the pause button until the societal, ethical, and philosophical implications of germ line editing could be properly and thoroughly discussed—ideally at the global level." p209

She concludes with the hope that scientists can communicate more honestly, effectively, and openly with the public thereby rebuilding the public's trust. We are lucky to have scientists like Doudna who have both the intelligence to accomplish complex, creative research, but also are not blind to the promethean bargain of which they must always be aware as humans gain ever greater power to alter nature.

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