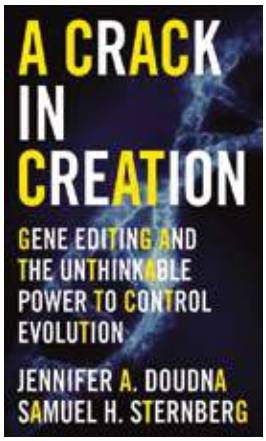
Book Reviews

David A. Bennahum, MD, and Jack Coulehan, MD, Book Review Editors



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

Jennifer A. Doudna and Samuel H. Sternberg
Houghton Mifflin Harcourt; June 13, 2017; 307 pages

Reviewed by David A. Bennahum, MD (ΑΩΑ, 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.

Dr. Bennahum is a member of *The Pharos* Editorial Board, and one of its Book Review Editors. He is Professor Emeritus of Internal Medicine and Resident Scholar at the University of New Mexico's Institute for Ethics. His e-mail address is dbennahum@salud.unm.edu.

The Creative Spark: How Imagination Made Humans Exceptional

Agustín Fuentes
Dutton; March 21, 2017; 340 pages

Reviewed by Jack Coulehan, MD (AΩA, University of Pittsburgh, 1969)

Ever since reading *Lucy: The Beginnings of Humankind* in 1981, I've been a confirmed paleontology junkie.[1] Donald Johanson's 1974 discovery of a partial skeleton of Australopithecus afarensis (Lucy) set off a wave of popular interest in the study of human origins. Since then, the field has rapidly developed as a result of remarkable technical advances, and new finds.

Some of the resulting books focus specifically on the bones. Was Homo habilis a distinct species? How does Homo erectus relate to Homo ergaster? Others, using DNA analysis, track the radiation of our ancestors to all parts of the world, and still others consider the question of why our near cousin, Homo neanderthalis, some of whose genes are part of us, became extinct?

In *The Creative Spark*, Agustin Fuentes sticks to a single narrative, and excludes other branches of the hominid tree. He aims to identify the crucial factor that initiated the long trek toward modern human society. What was the critical brain function that first emerged? Fuentes calls it the "creative spark," which eventually developed into human imagination and an array of other capacities. The creative spark occurred more than 2.5 million years ago, long predating our massive brain enlargement.

Fuentes discovers its earliest traces in the innovation that produced Olduwan tools about 2.5 million years ago. While earlier ancestors, like today's chimpanzees, probably used stones or modified tree twigs, only Australopithecus and the earliest members of the genus Homo invented the sophisticated process of striking one stone against another to create sharp flakes to cut and scrape animal carcasses. A cursory look at photos of these tools leaves the reader unimpressed. It took another million years to initiate a broader and more sophisticated Acheulean toolkit that included a variety of cutters, scrapers, axes, and spear points.

Fuentes sketches the environment and circumstances under which Olduwan tools were made, showing how truly innovative the stone flakes were. The first toolmakers, whether they were Homo or Australopithecus, lived as bands of medium-sized primates who lacked speed and other protective adaptations. They were extremely vulnerable to predators. They learned to identify advantageous stones for chipping; carry them to a safe place where repeated striking would not attract predators; and engage in a series of calculated blows that resulted in knife-sharp flakes. This is a process that modern imitators require considerable time to master.

Fuentes documents power scavenging, which developed about 1.8 million years ago. Our ancestors could not compete with larger, faster predators for prey. The best they could do was passively scavenge whatever meat was left behind by the big cats and vultures. Bands of hominids developed flexible methods of social cooperation that allowed the group to chase predators away from their kills. They quickly employed their stone tools to cut prime chunks of meat, and then run back to safety before the predators were able to attack them.

Shortly after power scavenging, our ancestors developed social organization. Cooperative parenting, whereby some females and perhaps males, would remain in the living space to take care of the children while others gathered edible plants or scavenged for meat, was developed.

Fuentes' deep storytelling describes the transition from a hunter-gatherer lifestyle to early pastoralism and agriculture. Other books tend to present this change as undeniable progress, but don't say very much about how or why it happened, or how long it took. Fuentes discusses multiple steps in the gradual process of animal domestication, e.g. goats (8,000 years to 12,000 years ago) and sheep, pigs, and cattle (8,000 years to 10,000 years ago) in Western Asia. He shows that settled agriculture arose independently in several Old World and New World locations after long periods during which humans had altered edible plants by conscious selection of favorable variants, e.g., those with larger or more easily accessible edible parts. For example, in Central America a species of grass called teosinte was gradually transformed into maize or corn over several thousand years. Likewise, 10,000 years ago in East Asia, sinewy grasses of the genus Oryza had evolved by human manipulation into rice.

Paradoxically, the evidence indicates that settled agriculture was associated, at least initially, with a decline in human fitness. Skeletal remains from pre- and post-agricultural societies in the same geographical settings make it clear that hunter-gatherer bands enjoyed a rich, varied diet and were relatively disease free, while their early farmer descendants were smaller in stature and often malnourished. Why, then, did agriculture flourish? Fuentes discusses several factors, the most compelling of which is population pressure. A settled lifestyle led to rapid population increase followed by the creation of towns and cities. Traditional hunting and food gathering practices could no longer sustain the greater population. Humans became locked in to the new, less nourishing, but still sustainable mode of existence.

What is the essential creative spark that initiated our long road—albeit short on an evolutionary timeline—to human culture and civilization? Fuentes does not attempt to identify the critical mutation or neurophysiological development. There seems to be no way to pinpoint that. However, he makes it clear that the spark occurred much, much earlier than the proliferation of art 40,000 years ago, or the emergence of a fully human skull and skeleton 200,000 years ago.

Fuentes tells a compelling story of deep origins—a

story worth reading. Yet, when all is said and done, the mystery remains.

References

1. Johanson D, Edey M. Lucy: The Beginnings of Humankind. New York: Simon & Schuster; 1981.

Dr. Coulehan is a member of *The Pharos* Editorial Board, and one of its Book Review Editors. He is Emeritus Director of the Center for Medical Humanities, Compassionate Care, and Bioethics at Stony Brook University in New York. His e-mail address is john.coulehan@stonybrookmedicine.edu.

More AΩA member books

The Addiction Solution: Treating Our Dependence on Opioids and other Drugs, by Lloyd Sederer, MD (AΩA, SUNY Upstate Medical University College of Medicine, 1969); Scribner, May 2018, 224 pages

Nuggets from the Golden Age of Medicine: No Relationship to Money, by Kenneth Charles Bagby, MD (AΩA, University of Nebraska, 2005); Outskirts Press Books, June 2018, 99 pages