



Jennifer Doudna helped to uncover the CRISPR–Cas gene-editing system.

GENOME EDITING

That's the way the CRISPR crumbles

Nathaniel Comfort finds heroism but little nuance in Jennifer Doudna's account of her co-discovery.

The prospect of a memoir from Jennifer Doudna, a key player in the CRISPR story, quickens the pulse. And *A Crack in Creation* does indeed deliver a welcome perspective on the revolutionary genome-editing technique that puts the power of evolution into human hands, with many anecdotes and details that only those close to her may have known. Yet it does not provide the probing introspection, the nuanced ethical analysis, the moral counterpoint that we CRISPR junkies crave.

After the race for discovery comes the battle for control of the discovery narrative. The stakes for the CRISPR–Cas system are extraordinarily high. In February, the US Patent and Trademark Office ruled against Doudna and the University of California, Berkeley. It found that a patent on the application of CRISPR to eukaryotic cells — filed

by Feng Zhang of the Broad Institute of MIT and Harvard in Cambridge, Massachusetts — did not interfere with Berkeley's more sweeping patent on genetic engineering with CRISPR.

Although that battle is over, the war rages on. Berkeley has already appealed against the decision; meanwhile, the European Patent Office has ruled in favour of Doudna and Berkeley. Doubtless there are many more patents to milk out of this versatile system. And then there's the fistful of 66-millimetre gold medals they give out in Stockholm each year.

So far, the Broad Institute has controlled the CRISPR narrative. Rich in funds and talent, the Broad melds sleek, high-tech sexiness with a sense of East Coast, old-money privilege. Last year, institute director Eric Lander published a now-infamous piece entitled 'The heroes of CRISPR' (*E. Lander Cell* 164, 18–28;

2016). It adopted a tone of magnanimity, crediting Lithuanian biochemist Virginijus Siksnys with observing early on that his findings "pave the way for engineering of universal programmable RNA-guided DNA endonucleases"; and Doudna and her CRISPR co-discoverer Emmanuelle Charpentier with noting "the potential to exploit the system for RNA-programmable genome editing".

Lander's clear implication was that they were laying the groundwork; Zhang's group got CRISPR over the finish line. To many of us, such tactics made Team Broad look like the villains of CRISPR.

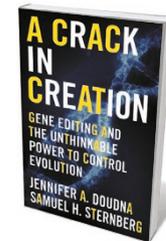
Doudna's book was a chance to deliver a righteous knockout blow. Instead, we get a counter-narrative just as constructed as Lander's article. It is written entirely in the first person; co-author Samuel Sternberg, a former student in the Doudna lab, barely surfaces.

In that counter-narrative, Doudna had always been interested in gene editing. Her early work was on RNA enzymes, or ribozymes. She developed an impeccable pedigree, doing her PhD with Jack Szostak at Harvard and a postdoc with Tom Cech at the University of Colorado Boulder, before joining the faculty at Yale University in New Haven, Connecticut. From the mid-1990s, she writes, she was exploring the basic molecular mechanisms that "would be able to unlock the full potential of gene editing".

Her work on CRISPR dates to 2006 — six years before the key papers were published — and a call from Berkeley geomicrobiologist Jillian Banfield. Over coffee, Banfield described the clustered, regularly interspaced, short palindromic repeats that kept popping up in her DNA databases of bacteria and archaea. The sequences were ubiquitous among these prokaryotes, but unique to each species. This realization "sent a little shiver of intrigue down my spine", Doudna writes. If CRISPR was so widespread, "there was a good chance that nature was using it to do something important". By 2012, she

and her co-workers had characterized the natural CRISPR system, harnessed it as a laboratory tool and developed a modified system that was programmable, cheap and easy to use.

The middle of the book reels off the obligatory breathless list of potential uses, generating everything from malaria-free mosquitoes and police dogs with muscles like Vin Diesel to the canonical cure for



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

JENNIFER A. DOUDNA & SAMUEL H. STERNBERG
Houghton Mifflin:
2017.

cancer. Thankfully, Doudna counterweights sensationalism with a sober accounting of the risks and responsibilities of applications such as altering the genomes of entire populations of organisms with ‘gene drives’. In 2015, she sustained doubts about CRISPR ever being safe enough for clinical trials, but she has come to embrace editing of the human germ line — inheritable DNA modification — once it is proved safe.

But the discussion is ultimately unsatisfying. When it is time to “grapple with tricky ethical issues”, such as human experimentation, she balks, unspooling instead a series of rhetorical questions. Rather than guiding us through the ethical thickets of precision genetic engineering, or providing a candid, warts-and-all look at one of the great scientists of our time, the book mainly polishes her ‘good scientist’ image and rationalizes the unfettered self-direction of human evolution, within liberal bounds of safety, efficacy and individual choice.

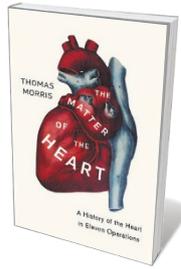
Rather than dispel the cartoon-character feel of this epic battle, Doudna elaborates on it. She presents us with a persona so flawless that it seems more concealing than revealing. She waves away the bloody patent fight as a “disheartening twist” in the story, but the entire biomedical world knows that it was much more. As I read *A Crack in Creation*, I was reminded of Benjamin Franklin’s “benevolent man”, who, he wrote, “should allow a few faults in himself, to keep his friends in countenance” — and, I would add, to give him- or herself more depth.

The narrative often substitutes melodrama for dramatic tension. A conference in Puerto Rico sees Charpentier and Doudna strolling the cobbles of Old San Juan, with Charpentier saying earnestly, “I’m sure that by working together we can figure out the activity” of what became the Cas enzyme. “I felt a shiver of excitement as I contemplated the possibilities of this project,” Doudna writes. When first wrestling with the ethical dilemmas of gene editing, she dreams of meeting Adolf Hitler, who demands to know the secrets of her technique. She wakes, of course, freshly determined to ensure that CRISPR is not put to nefarious use.

The larger purpose of *A Crack in Creation*, clearly, is to show that Doudna is the true hero of CRISPR. And ultimately, despite the book’s flaws, I’m convinced. Nominators and the Nobel Committee will need to read this book. But CRISPR binge-watchers like me still await a truly satisfying account — one that is insightful, candid and contextualized. ■

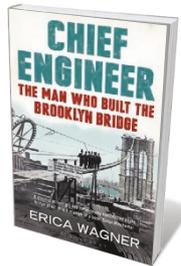
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Books in brief



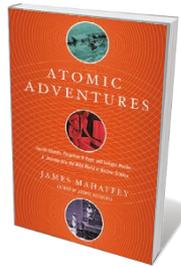
The Matter of the Heart: A History of the Heart in Eleven Operations *Thomas Morris* BODLEY HEAD (2017)

With the cut and thrust of cardiac surgery now demystified, we forget that venturing into the thoracic cavity once seemed as daunting as polar exploration. Or more so: as Thomas Morris reveals in this stirring chronicle, even touching a beating heart was long viewed as impossible. Told through 11 pivotal operations, it’s a tale of ingenuity, from Henry Dalton, who in 1891 became the first US surgeon to suture a pericardium, to artificial aortic valves implanted by robots. It’s rich, too, in alarming details — not least, the injections of strychnine and whisky that featured in early surgery.



Chief Engineer: The Man Who Built the Brooklyn Bridge *Erica Wagner* BLOOMSBURY (2017)

At its 1883 debut, the Brooklyn Bridge was by far the world’s longest suspension bridge — its construction a bravura feat founded on a deep understanding of geology. The life of chief engineer Washington Roebling also has a certain monumental quality, as Erica Wagner proves in this engrossing, exhaustive biography. The project took the lives of at least 20 workers and of its designer, Roebling’s truculent father John; Roebling himself was left with decompression sickness. But, as Wagner reveals, the central structure and main cables remain a rock-solid testament to engineering acuity and vaulting ambition.



Atomic Adventures

James Mahaffey PEGASUS (2017)

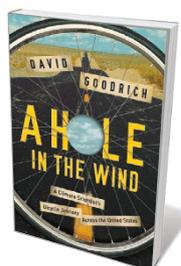
Nuclear scientist James Mahaffey’s gloriously nerdy tour of atomic research ranges over projects from the dead-end to the hare-brained (see also M. Peplow *Nature* **506**, 292–293; 2014). Here, for instance, are “obscure, third-tier scientist” Ronald Richter — who wasted US\$300 million of Argentinian government money on a crackpot scheme to build a fusion power plant in the early 1950s — as well as Mahaffey’s own serious work on the lost dream of cold fusion. You’ll learn, too, how to use a smartphone as a Geiger counter and what to pop in case of atomic attack (phosphorylated aminothiols, apparently).



The Sum of Small Things: A Theory of the Aspirational Class

Elizabeth Currid-Halkett PRINCETON UNIVERSITY PRESS (2017)

US economist Thorstein Veblen’s 1899 *Theory of the Leisure Class* held a mirror up to rich Americans deep-dyed in Gilded Age ostentation. Here, Elizabeth Currid-Halkett updates Veblen’s analysis, arguing that the leisure class is now aspirational, and that consumption has become inconspicuous — all heirloom vegetables and electric cars. Yet, ‘smart’ elites contribute to inequality just as surely as yesterday’s luxury addicts. A key companion to Robert Putnam’s survey of dwindling US social mobility, *Our Kids* (Simon and Schuster, 2015; see B. Kiser *Nature* **520**, 155; 2015).



A Hole in the Wind

David Goodrich PEGASUS (2017)

At the end of a high-level career in climate science, David Goodrich cycled from Delaware to Oregon looking for a “hole in the wind” — a human future in the unrelenting march of climate change. Over a rain- and sweat-soaked 6,700 kilometres, he encountered Pennsylvanians at the fracking frontline, forest fires in Wyoming and scores of people in diners, labs and schools profoundly concerned about coming realities. Ultimately, he sees humanity’s capacity for economic transformation and reform as up to the job. **Barbara Kiser**