# Enter CRISPR: Jennifer Doudna's Autobiographical Assessment of the Science and Ethics of CRISPR/Cas9

#### **Hub Zwart**

Erasmus School of Philosophy, Erasmus University Rotterdam, P.O. Box 1738, Rotterdam, Zuid-Holland, Netherlands, 3000 DR; Tel.: +31 (0)10 408 8993, E-mail: zwart@esphil.eur.nl

ABSTRACT: In 2012, Jennifer Doudna et al. published their landmark article on CRISPR/ Cas9. Five years later, Doudna published an autobiographical retrospective to come to terms with the "tsunami" of events that followed. The subtitle suggests that humans had acquired "unthinkable power" to refurbish life and deflect the course of evolution. Yet the subtitle of the prologue suggests a different view of human agency, seeing CRISPR as a technological pandemic, stressing our powerlessness to develop ethical and governance tools to contain the process. We seem overwhelmed by a surging biotechnological event. Science autobiographies constitute a fascinating genre, providing a window into the context of discovery, revealing what often remains unsaid in more formal academic publications. But they describe events from a decidedly personal and partisan perspective, wavering between self-analysis and self-justification, putting the individual frontstage, obfuscating how research is a collective endeavor. Doudna's memoir is analyzed from three perspectives: knowledge (CRISPR as a shift from reading to reediting genomes), power (memoirs as instruments in controversies over IPR), and ethics. Normative challenges allow researchers to constitute themselves as responsible subjects by developing new skills (bioethical deliberation) while calling forth new practices of the Self (writing science autobiographies). While traditional narrative suggests that, after an increase in dramatic tension, a period of equilibrium sets in, Doudna's retrospective voices the unsettling concern that we may lose control over the disruptive deflection we helped to bring about.

**KEY WORDS:** CRISPR/Cas9, gene editing, science autobiographies, bioethics, philosophy of science

#### I. INTRODUCTION

In August 2012, Jennifer Doudna and colleagues published their now famous *Science* article bearing an enigmatic title: "A Programmable Dual-RNA–Guided DNA Endonuclease in Adaptive Bacterial Immunity." The authors presented a molecular machine, a genome-editing device named CRISPR/Cas9, which would allegedly allow scientists to target and cleave any snippet of DNA, thereby offering "considerable potential for genome-editing applications" (p. 820). Five years later, in June 2017, Jennifer Doudna published an autobiographical retrospective of this breakthrough and its aftermath entitled *A Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution*, written in her own voice (first person singular) but coauthored by Samuel Sternberg, a close colleague. This article presented a critical assessment of

Doudna's 2017 retrospective against the backdrop of the exponentially growing tide of CRISPR/Cas9 discourse. First and foremost, it focused on how *A Crack in Creation* addressed the *bioethical* challenges entailed in CRISPR/Cas9 while also emphasizing the extent to which the bioethical dimension is interwoven with issues of knowledge and power.

The structure of this paper is as follows. In the first three sections I will (1) discuss the pros and cons of autobiographies as source material for bioethical research and (2) provide an outline of the typical narrative structure of science autobiography as a genre. On the basis of this narrative structure, moreover, a short summary of Doudna and Sternberg's book is provided. Subsequently, Doudna's autobiographical reflections on the discovery of CRISPR/Cas9 as a potentially beneficial but also disruptive technology are assessed from three perspectives: epistemological (the knowledge dimension), science politics (the power dimension), and bioethical (scientific research as a practice of the Self). This approach builds on Michel Foucault's famous distinction of three "axes of inquiry": knowledge, power, and the Self.<sup>3</sup>

The knowledge axis emphasises the technicity of scientific research, such as the emergence and adoption of new technologies opening new areas of inquiry. In Doudna's book, the key epistemic event is the shift from *reading* (sequencing) to *rewriting* (editing or optimizing) genomes of multiple species, including our own, thereby transforming genomes into entities that exemplify plasticity rather than stability.

The power axis focuses on tensions and collisions between backstage science (anonymous masses of postdocs and Ph.D.s) and frontstage science (the world of science celebrities and science managers), but also between senior and early-stage researchers, between top universities and midlevel or marginal ones, and between individualization and collectivization (i.e. the paradoxical tendency of contemporary science to emphasize both large-scale collaboration and individual performance). This dimension also encompasses shifting gender roles as well as conflicts over intellectual property rights, reaching a climax in the CRISPR/Cas9 court case (Berkeley v. Broad).

Finally, the ethical dimension revolves around the question of how researchers address emerging normative challenges, thereby constituting themselves as responsible subjects. Doudna's memoir explains how scientists are urged to develop new skills (e.g., bioethical deliberation), calling forth new practices of the Self (e.g., life writing). Precisely here, however, I emphasize how traditional narrative scenarios of science writing (involving pioneer scientists who, by recognizing and assuming their responsibility, contribute to restoring the moral equilibrium) no longer seem to function and become deflected by the unsettling normative features of CRISPR/cas9.

## II. SCIENCE AUTOBIOGRAPHIES AND BIOETHICS: METHODOLOGICAL CONSIDERATIONS

Science autobiographies are a fascinating and controversial genre. On the positive side, they provide a high-resolution window into the "context of discovery"<sup>4,5</sup> of contemporary research, shedding light on the backstage of laboratory life: the dynamics of

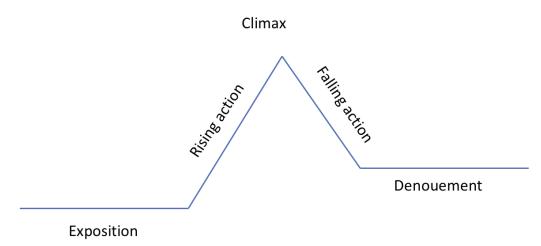
scientific discovery and the politics of cutting-edge inquiry, revealing what tends to remain invisible or unsaid in more formal academic outlets. They describe events from a decidedly personal or even partisan perspective, however, wavering between self-analysis and self-justification and putting the individual frontstage, thereby running the risks of obfuscating the extent to which contemporary research is a collective and networked endeavor.<sup>6,7</sup> In other words, although science autobiographies allow us to study knowledge production processes with microscopic precision, the genre must be handled with care and methodological suspicion.

Still, science autobiographies may prove a valuable source of information, not only for historians and sociologists but also for bioethicists and philosophers of bioscience. Important bioscientific landmarks—from the discovery of the biomolecular structure of DNA (in 1953) to the invention of PCR (in 1998) up to the Human Genome Project (1990–2003)—consistently resulted in memoirs by key protagonists, as by-products of their ground-breaking research. As to the discovery of the structure of DNA, for instance, beginning with James Watson all involved principal characters/Nobel laureates have published autobiographical retrospectives. 8,9,10,11 And although Rosalind Franklin unfortunately died too early to add an autobiographical account of her own, important biographical studies have been written about her contribution. 12 The Human Genome Project likewise resulted in a series of science autobiographies, notably by John Sulston, <sup>13</sup> Francis Collins, <sup>14</sup> and Craig Venter<sup>15</sup> as well as by others. <sup>6</sup> Thus, rather than being exceptional, Jennifer Doudna's A Crack in Creation represents a flourishing genre. One of the innovative features of her book, compared with previous examples, is that a female researcher now took the autobiographical floor, exemplifying the increasingly important role of women in the global research arena not only quantitatively but also in terms of visibility, leadership, and prominence.

### III. THE TYPICAL NARRATIVE STRUCTURE OF SCIENCE AUTOBIOGRAPHIES

From the point of view of narrative structure, a "typical scenario" can be discerned in the autobiographies just listed.<sup>6,7,16</sup> At a certain point in time, a laboratory researcher (more or less invisible to the outside world) suddenly comes to play a decisive role in a ground-breaking scientific "event" in the philosophical sense of the term *Ereignis*, or *événement*.<sup>17</sup> From that moment onward, epistemic, political, and moral tensions intensify, and things will never be the same. Thus, the rest of the story describes how the scientific protagonist desperately tries to reach a new plateau of relative stability and consolidation, albeit on a higher level of complexity.

Such a scenario reflects the typical narrative structure of autobiographical literature as such. Science autobiographies tend to follow a dramatic pattern first described by Gustav Freytag in his classic *Die Technik des Dramas*, <sup>18</sup> starting with an "exposition" stage, in which key protagonists and their research paradigm are introduced. Typically, this entails descriptions of research equipment and routines: a particular form of laboratory life into which novices (early-stage researchers) are socialized (Fig. 1).



**FIG. 1:** The narrative curve

At a certain point, however, something unexpected happens, such as the introduction of a new and promising technique, that allows researchers to explore new questions or significantly increase the pace and scale of their research. Besides new epistemic opportunities, however, this *novum* also introduces new epistemic and ethical dilemmas, so the researchers' moral and methodological integrity is being tested, resulting in a significant increase in dramatic tension evolving into a climax. Researchers are exposed to hazardous experiences, and, to address them, they must develop new behavioral repertoires and skills. In the end, a new paradigm establishes itself and during the "denouement" stage, researchers reflect on the progress that has been made, the collateral damage that has been done, and the lessons that have been learned. The denouement is typically the moment when science autobiographies are composed. A similar narrative scheme (again encompassing five stages) was introduced by Tsvetan Todorov, commencing with equilibrium (S1), which is disrupted by an unexpected challenge (S2). As soon as the disruption is recognized (S3), attempts are made to repair the damage (S4), resulting in new equilibrium (S5).

Susanna Egan<sup>20</sup> used Todorov's scheme as a scaffold to explore five key metaphors in autobiographical narratives: paradise, crisis, journey, conversion, and reconciliation. In science autobiographies, paradise refers to the quiet, secluded laboratory world, under the sway of an established paradigm, where harsh, messy reality is kept at bay. All of a sudden, there is an intrusion or disruption, however, which gradually evolves into a crisis due to internal factors (the paradigm fails to function, resulting in anomalies and frustrations) or to external factors (a political crisis, the advent of a revolutionary technique, etc.). The crisis entails a number of challenges, and the researchers respond to them by undertaking a journey in the literal sense (accepting positions at other universities, opting for new vocations, visiting remote retreats, etc.) or in the figurative sense (exploring new methodological terrains, developing new forms of transdisciplinary collaboration, etc.). The journey, as Egan phrases it, is a tortuous path of exploration, a

taxing struggle, a trial or test, resulting in new roles (on the individual level) and new paradigms (on the collective level). The journey may result in a conversion, brought about by revelatory insights or new forms of knowledge: a "magic gift" that allows researchers to address the challenge and revivify their field. The end result is reconciliation, as the heroes return home to share their valuable insights with fellow scientists.

#### IV. DOUDNA'S NARRATIVE: A SUMMARY

The dramatic narrative structure just outlined (involving five dramatic stages) is discernible in Doudna's memoir.<sup>2</sup> During the exposition stage, Doudna explains how, while other, more visible (male) colleagues engaged in high-profile research (gene therapy, the Human Genome Project, etc.), she herself remained a more or less anonymous researcher, spending her life inside laboratories, handling Petri dishes ("sequestered away at the laboratory bench" [p. 36]; in "the sealed-off scientific bubble" [p. 197]), studying esoteric questions (such as how RNA molecules fold into elaborate three-dimensional structures).<sup>2</sup>

In 2006, however, she encounters an enigmatic acronym named CRISPR (clustered regularly interspaced short palindromic repeats). A female colleague at Berkeley introduces her to CRISPR's secrets by drawing a mandala-like diagram: an oval (the bacterial cell) with a circle inside (the bacterial chromosome) and a chain of alternating diamonds and squares. At this point, CRISPR research is small-scale, engaging a subculture of devotees.

In 2011, at a conference in Puerto Rico, she meets Emmanuelle Charpentier in a café, Charpentier tells her about a "mysterious" enzyme named Csn1, later rebaptized Cas9. The two researchers decide to partner, and, by coagulating CRISPR with Cas9, they manage to produce a molecular, high-precision genome-editing machine. Doudna describes how, on June 8, 2012, a Friday afternoon, she clicked Confirm on her computer to formally submit her and Charpentier's landmark article to *Science*, where it was published with remarkable swiftness 20 days later, "and nothing after that would ever be the same" (p. 85).<sup>2</sup> The publication unleashes a seismic cascade of events that Doudna alternately describes as a tsunami (she grew up in Hawaii), a scientific revolution, and a roller-coaster. The disruptive crisis (the increase in dramatic action spiraling toward a climax) has set in. Doudna responds to this challenge by trying to broaden her horizons and acquire new skills in order to come to terms with events so that the crisis can be contained and a new equilibrium can set in.

At first glance, Doudna's book seems a recognizable specimen of an established genre initiated by James Watson's trend-setting classic *The Double Helix*,<sup>8</sup> although (as a female protagonist partnering with female colleagues), her memoir discontinues the traditional biographical view of science as the work of singular "great men,"<sup>21,22</sup> with women typically serving as spouses, muses, trusted aides, or enigmatic opponents. Jennifer Doudna actually read *The Double Helix* as a high school student after receiving it as a gift from her father, who thought it was a detective novel, "which it actually was" (p. 10).<sup>2</sup> But whereas in the 1950s female researchers such as Rosalind Franklin were

considered exceptional, Jennifer Doudna's book reflects the extent to which women are advancing in academia. In short, although Doudna's science autobiography indicates a decisive shift in terms of gender roles, her narrative in many ways follows a recognizable narrative path.

At the same time (as indicated by the subtitle of her book), the traditional scheme no longer seems to function in her case. Although the cycle of equilibrium-disruptionrestored equilibrium can to some extent be discerned, the final stage (reconciliation) becomes increasingly problematic. CRISPR's transformative "power" seems so unsettling that containment and reconciliation may actually be beyond our reach so that "responsible research" runs the risk of becoming an empty signifier. CRISPR/Cas9 is presented as a novum that challenges or even disrupts the narrative pattern of traditional science memoirs. Perhaps the most interesting aspect of Doudna's book is precisely her uncanny apprehension that the global transformation unleashed by CRISPR/Cas9 may actually be beyond repair. Instead of spiraling towards a new stability, the CRISPR wave may result in a drastic rewriting of the biosphere, giving rise to a technoscientific tsunami: a metaphor which, given Doudna's childhood in Hawaii, has strong autobiographical connotations. In other words, the narrative structure of traditional science autobiographies is both reflected and deflected in Doudna's book. Although at first glance A Crack in Creation may seem a feminine version of The Double Helix, the normative challenges implied in the CRISPR technique take us beyond the normal pattern of science autobiography as a genre.

#### V. THE KNOWLEDGE AXIS: FROM QUIETUDE TO CRISIS

This is how, in the prologue of her book, the author introduces herself to her readers: "My name is Jennifer Doudna. I am a biochemist, and I have spent the majority of my career in a laboratory, conducting research on topics that most people outside of my field never have heard of" [p. xii]).2 This motif surfaces repeatedly, emphasizing that this is the memoir of a researcher who, until recently, felt very much at home in the insulated world of Petri dishes. In this artificial ambiance (effectively sealed off from the messy, noisy outside world), she became interested in how bacteria immunize themselves against viral threats by (1) reading viral DNA, (2) rewriting their own CRISPR DNA to mirror the lethal viral genome (splicing snippets of viral code into their CRISPR region), and (3) mounting an immune response as soon as the threat resurges. As Doudna explains, the DNA snippets function as molecular vaccination cards (stored memories of past infectious events), unleashing the Cas9 enzyme as a molecular hedge trimmer to shred intruding viral DNA to pieces. Thus, bacteria are staged as highly efficient biotech engineers and, as Doudna phrases it, can therefore be placed "on equal footing" with human scientists such as herself (p. 59).2 CRISPR/Cas9 exemplifies biomimicry<sup>23</sup> as Doudna and her colleagues adopt and adapt a molecular machine developed by bacteria billions of years ago. CRISPR/Cas9 is one of the many biotechnological techniques currently in use in laboratories worldwide that were developed not by humans but by microbes, the primordial bioengineers. George Church and Ed Regis take this one step

further: "Cohen and Boyer were not the world's first genetic engineers. That distinction belongs to bacteriophages—essentially a string of DNA or RNA wrapped in a protein" (p. 45).<sup>24</sup>

CRISPR/Cas9 also reflects how our understanding of genomes has evolved in the last decades. During the 1980s and 1990s, genomics conveyed a genetic deterministic view of DNA. The genome (a portmanteau of "gene" and "chromosome") was the code or program that provided stability by withstanding entropic environmental influences. Doudna's book indicates how, in the post-genomics era, a different view emerged, seeing genomes of living beings as plastic and malleable, not only epigenetically but also in the sense that living beings (notably bacteria) actively and continuously reedit their own genome. For that is what these bacteria are doing: they actively rewrite their own genetic CRISPR code. CRISPR/Cas9 provides the natural prototype of a programmable molecular machine (p. 67), sequencing, splicing, and destroying specific strands of DNA (which can subsequently be replaced or repaired) with impressive precision.

In Doudna's book, this shift in focus from reading (sequencing) to reediting (rewriting) DNA<sup>26</sup> is described in epidemiological terms, as something that started in a Petri dish in Berkeley and quickly spread from there to other laboratories, evolving into an event of global significance. CRISPR/Cas9 is symptomatic of the fact that, as Doudna phrases it, we are "on the cusp" of a new age: a new era in the history of life on earth (pp. xiii, 117, 243).<sup>2</sup> Although "revolution" has become a stock term in the rhetorical vocabulary of contemporary life science research, we should take it more literally this time. For billions of years, evolution progressed at a slow and natural, Darwinian, pace, but now, Doudna argues, we are about to exercise an unprecedented level of precision control over the genetic composition of the flora and fauna that coinhabit our planet. Via CRISPR/Cas9, evolution becomes human-directed. As a method to "reshape the biosphere" (p. 36),<sup>27</sup> CRISPR/Cas9 is a technology of the Anthropocene par excellence.<sup>28</sup>

The Human Genome Project prepared the ground for this transition, capturing life in letters (A, C, G, T) so that living entities became "obliterated"—replaced by code.<sup>29</sup> While describing her discovery at Berkeley, the *site événementiel* as Badiou<sup>16</sup> phrased it, Doudna presents herself as a vector, transferring molecular mechanisms from microbial nature to human laboratories, where CRISPR/Cas9 evolves into an enabling technology applicable to a broad range of fields, from cancer research and xenotransplantation to agricultural biotech. All of these fields become infected by the CRISPR/Cas9 pandemic. Doudna's book depicts how CRISPR/Cas9, and the various techniques, vocabularies, concepts, metaphors, research practices, moral dilemmas, and IPR conflicts connected with it, spread through research fields worldwide, making Doudna's autobiography a case study of the epidemiology of technoscience.<sup>30</sup>

Most metaphors in Doudna's book are borrowed from the textual realm, presenting the new technology as precision gene editing, gene editing "letter by letter" (p. 93).<sup>2</sup> CRISPR/Cas9 is a "versatile" tool allowing researchers to correct "single-letter mistakes" (p. 100)<sup>2</sup> with unprecedented ease and with "single-letter accuracy" (p. 212)<sup>2</sup>. Because CRISPR/Cas9 is so astonishingly accurate and easy to use, genomes become "as malleable as a piece of literary prose at the mercy of an editor's red pen" (p. 90).<sup>2</sup>

What used to be a metaphor (i.e., the genome as text) is a metaphor no longer. From now on, "gene editing" must be taken quite literally.

Using other metaphors, Doudna compares CRISPR/Cas9 to precision warfare, presenting it as the molecular biological equivalent of drones that allow scientists to turn viruses into "benign missiles" (p. 19).<sup>2</sup> CRISPR/Cas9 is a "perfect bacterial weapon," a "virus-seeking missile," striking "quickly and with incredible precision" (p. 81),<sup>2</sup> targeting specific phage DNA sequences and destroying them—a molecular missile that can be mobilized to eliminate specific targets and slice up and destroy specific DNA molecules (p. 90).<sup>2</sup> Cas9 is a "warrior protein" (p. 84), ruthlessly shredding adversary DNA into molecular debris. But CRISPR/Cas9 can also become a weapon in the literal sense. Genome editing can be transformed into a weapon of mass destruction.<sup>2</sup>

During the 1990s, genetic determinism emphasized the stability of genomes as biological programs, an idea that gave way to an emphasis on the plasticity and fluidity of DNA. All life (including human life) is constantly exposed to random genetic change, according to Doudna. DNA is constantly changing and "every person experiences one million mutations throughout the body per second" (p. 233),<sup>2</sup> so that any mutations CRISPR may make "pale in comparison to the genetic storm that rages inside each of us from birth to death" (p. 233).<sup>2</sup> In contrast to the classical genomics view, CRISPR conveys a Heraclitean view of life, emphasizing continuous change, permanent warfare, and relentless flux.<sup>31</sup> Warfare rages not only between bacteria and viruses but also between biomedicine and cancer and even between competing research institutes. In other words, this view of life entails a narrative shift from equilibrium (the genome as the stabilizing program of life) to dramatic conflict. Doudna describes how, after having made the decisive step of establishing that Cas9 could be used to cut up any DNA sequence of a specific length, she suddenly found herself "laughing aloud" (p. 84),<sup>2</sup> experiencing the joy of discerning a new truth for the first time: an instance of revelatory laughter, perceiving life and nature in a new light.<sup>32</sup>

#### VI. THE POWER AXIS

In contrast to the other two axes, the power axis is not extensively addressed by Doudna and Sternberg, and yet it is decidedly there as that which remains unsaid. Whoever googles combinations of search terms such as "Doudna" and "CRISPR" will immediately come across the name of Eric Lander, president and founding director of the Broad Institute at MIT. In Doudna's book, however, Lander's name is never mentioned. How to explain this remarkable contrast between search engines (where their names are linked) and the book index, where Lander is not listed?

The answer can be found in the article *The Heroes of CRISPR*, which Eric Lander published in *Cell* in 2016.<sup>33</sup> In this article is a map that raises a number of questions (p. 20).<sup>33</sup> First, only the United States and Europe are represented. What has happened to Asia and the other continents? Why has Europe drifted southward and westward? And why is Boston in the center? These features symptomatically point to what is at stake here, for the map is part of CRISPR politics. Boston is in the center of the map because

is the site of the research institute directed by the author, the place from which the rest of the world is monitored.

Initially, Lander's article aims to demonstrate that scientific discoveries are made not by "lone geniuses cloistered in laboratories" (p. 18)<sup>33</sup> but by large networks of researchers, most of whom are completely unknown outside expert circles. When it comes to understanding scientific progress, we have to study the research "ecosystem," a laudable objective. Indeed, "the giants [on whose shoulders CRISPR research stands] are collective infrastructures and broad research cultures" (p. 2),<sup>34</sup> and the first pages of Lander's article focus attention on researchers working outside leading universities and often experiencing tedious difficulties in competing with academic superpowers (universities in places such as Berkeley and Boston) when it comes to securing sufficient funding for their research or seeing their articles published in top journals. Thus, Lander describes the contributions of CRISPR pioneers such as Francisco Mojica (University of Alicante, Spain), Gilles Vergnaud (University Paris-Sud), Philippe Horvath (Danish food firm Danisco) and Virginijus Siksnys of Vilnius University (all of whom are mentioned and acknowledged by Doudna and Sternberg as well).

At a certain point, however, and at odds with the article's initial objective, the focus of attention shifts from heroes (plural) to one particular hero (singular) or (to use Lander's own terms) from the "research ecosystem" to an "individual genius." And in Lander's version of the story, this individual hero is neither Jennifer Doudna nor Emmanuelle Charpentier (whose contributions are minimized as being of limited significance), but Feng Zhang, a researcher working at the Broad Institute (directed by Lander himself). Zhang receives by far the longest treatment in the story. According to Lander, his contribution was the really decisive one, eclipsing those of Doudna and colleagues.

Although no conflicts of interest are mentioned by the author, at the moment of writing the University of California, Berkeley, and the Broad Institute were embroiled in a fierce and complicated legal battle over intellectual property rights connected with CRISPR.<sup>35</sup> In February 2017, the US Patent and Trademark Office would rule against Berkeley, stating that a patent on the application of CRISPR to eukaryotic cells filed by Feng Zhang (of the Broad Institute) did not interfere with Berkeley's patent on genetic engineering with CRISPR (notably because the Doudna-Berkeley team had not explicitly focused their patent claim on eukaryotic cells).<sup>35</sup> On September 10, 2018, the US Court of Appeals again awarded the intellectual property to the Broad Institute and Harvard University, upholding the previous decision by the Patent and Trademark Office.

Thus, Lander's article and Doudna's memoir should both be regarded as contributions to the patent dispute (as textual missiles). Notwithstanding the initial detour of describing the contributions of less prominent CRISPR researchers, Lander's ultimate objective is to downplay the contributions of Doudna and her team at Berkeley and to highlight the contributions of Zhang at the Broad Institute. The article is a missile sent from Boston to the Bay Area, as it were—perhaps even in anticipation of future discussions, such as who should win the CRISPR Nobel Prize. And there are other biases in

Lander's article. He ignores contributions by researchers located outside the Western world (i.e., not on his map) except for the Korean scientist Jin-Soo Kim, who is granted 22 words in Lander's CRISPR epic, which is significantly less than in Doudna's (pp. 96, 122).<sup>2</sup> A Japanese group (who had observed a repeat sequence in *E. coli*) is briefly mentioned by Doudna and Charpentier,<sup>38</sup> but, according to Lander, they had "made little of the observation" (p. 19).<sup>33</sup> Moreover, although Lander purports to highlight the broader ecosystem, he exclusively focuses on principal investigators and (unlike Doudna) fails to mention or acknowledge contributions by postdocs or Ph.D.s. Finally, Lander's version represents a shift of focus from female to male researchers, reverting to the traditional "male heroes of science" view.

Lander's account highlights the extent to which historical accounts and retrospectives take position in a force field of claims and contentions. A position "from nowhere" does not exist. After the race for discovery comes the battle for control over the discovery narrative. The question is therefore not whether the author has a stake in the affair (this evidently applies to Doudna's book as well) but rather to what extent the (inevitable) interestedness of the author is convincingly included in self-reflection and self-analysis. In Lander's account, self-reflection seems underdeveloped. What about Doudna?

In the 2012 Science article, whose title echoes the "frontier of science" metaphor,<sup>37</sup> Doudna included a map of her own<sup>38</sup> visualizing how two research fields merged. The 2012 discovery (that Cas9 is an RNA-programmable DNA endonuclease) is presented as the turning point, leading to an "explosion" of subsequent articles beginning in 2013 with one by Zhang's team in Boston in which CRISPR/Cas9 is used to modify genes in human and other types of cells. In A Crack in Creation, Zhang's work is acknowledged on several occasions. Still, although the role played by Zhang's team is acknowledged more generously compared with how the work of Doudna's team is acknowledged by Lander, Doudna does portray her own 2012 article as the decisive turning point, or événement.<sup>38</sup> The Broad-Berkeley court case is mentioned in A Crack in Creation only once, quite briefly and in passing as it were, deploring how her academic articles and publication dates would be "dissected" to support "a dispute over CRISPR patent rights in a disheartening twist" (p. 97). My interpretation is that, with regard to the power dimension, Doudna tries to uphold an ideal of pure (untainted) science, keeping the threatening world of patent politics at bay. If CRISPR/Cas9 proves patentable, the entire biosphere may become a target for appropriation, may be reframed as a collection of potentially proprietary entities resulting in a legal tsunami whose unsettling dynamics may prove difficult to contain. Philosophically speaking, Doudna positions herself as a beautiful soul who allegedly refuses to show any interest at all in "disheartening" patent politics. As Comfort phrases it, the book polishes Doudna's "good scientist" image and presents us with "a persona so flawless that it seems more concealing than revealing"  $(p. 31).^{36}$ 

And yet, from a power perspective, Doudna's book serves a purpose similar to that of Lander's article—namely, reinforcing her position when it comes to claiming patents, perhaps even boosting her chances of winning the Nobel Prize: "The larger purpose of A

*Crack in Creation*, clearly, is to show that Doudna is the true hero of CRISPR" (p. 31).<sup>36</sup> Both Lander's article and Doudna's autobiography are more deeply entangled in the force field of contemporary IPR politics than either is willing to admit, although Doudna acknowledges, indirectly, the link with the fight for the Nobel Prize by identifying with two previous Nobel laureates: James Watson, whom she emulates by writing an autobiography, and Paul Berg, who functions as her guide and exemplar on the ethical level.

#### VII. CRISPR AND CONSCIENCE

As to ethics, a chronic ambivalence pervades Doudna's memoir, reflected in the chapter titles she uses. On the one hand, the book is a traditional autobiographical narrative of a previously unknown scientist who introduces a new and powerful technology to the world and who now sees her responsibility as fostering its containment (restoring equilibrium). To achieve this, she immerses herself in bioethical literature, organizes conferences, goes to meetings she had never attended before, and publishes a coauthored ethics article in *Science*, entitled "A Prudent Path Forward,"<sup>27</sup> on how the CRIPSR revolution can be responsibly managed. The subtitle, however, raises serious doubts whether "we" human beings will be able to come to terms with this "unthinkable power" to control evolution and refurbish life. CRISPR seems to entail an *anthropocenic* role for human-kind: resetting the future course of evolution but in the absence of a moral compass.

The subtitle of the prologue to a *Crack in Creation* ("The Wave") frames humans in general and scientists in particular as overwhelmed by a surging biotechnological tsunami. Doudna grew up in Hawaii, and the tsunami motif recurs on various occasions, notably in one of the dreams recorded in her book. The wave metaphor suggests a more passive role for human beings. It voices the concern that CRISPR, once unleashed, may become an uncontainable tide, gaining an unsettling momentum of its own. CRISPR is bound to have "seismic implications" (p. xii),² and Doudna's reaction to this is one of growing unease. While her conscious deliberations focus on responsibility and prudence, in her dream life the experience of unease is amplified, to the point where she is "paralysed by fear" (p. xi).² On various occasions, she voices her unsettled awareness that human beings serve merely as vectors. The ultimate actor, bound to transform the world as we know it, is the CRISPR technology *as such*. In other words: because of CRISPR, genomes become editable and genes can be upgraded into superior versions, but it is questionable whether "we," as a "fractious species," will be able to handle this "awesome power" (p. xvi).² CRISPR seems to be using *us* rather than vice versa.

Thus, two storylines can be discerned. In one, Doudna stages herself as a responsible scientist who sees it as her obligation to "help lead" (p. xvii)² public deliberations on how this versatile method for repairing ailing genomes and faulty biocodes is to be used: restoring equilibrium, containing the dramatic climax. Notably, she becomes involved in bioethics conversations about "designer babies" and "super-humans." To play this new role, Doudna must acquire new vocabularies and new skills, and develop new practices of the Self, shifting attention from laboratory research to ethical debate. For years, she explains, her comfort zone ended at the rim of Petri dishes (p. xvii).² She

had never worked with animal models or with patients and is not used to asking herself bioethical questions or writing bioethical prose. She had always preferred working in the lab, talking with specialists and thus falling into the "trap" (p. 197)<sup>2</sup> of scientists who feel comfortable when surrounded by peers who speak the same language and worry about the same issues, insulating themselves inside their scientific bubble while keeping the public realm at bay. But now that an ethical storm is brewing around this easy-to-use technology that she helped to create, she inevitably realizes how little the denizens of the scientific and public worlds seemed to know about each other. CRISPR experts should actively contribute to the debate on whether and how to redirect the future course of evolution.

At the same time, Doudna suggests that the phrase "human-directed evolution" is far too anthropocentric. Neither humans in general nor scientists in particular consciously function as agents of change. Rather, the uncanny suggestion running through her memoir (and surfacing in her dreams) is that the actual agent of change is the technology *as such*. Although CRISPR/Cas9 is a "thing" (p. 40) that Doudna "helped to create" (p. 198), it is now taking on a momentum of its own.<sup>2</sup> A game-changing technology is unleashed into the world, and this raises the question of agency because, rather than conveying an anthropocentric message, human beings seem to become increasingly marginalized by the unfolding biotechnological epidemic.

CRISPR/Cas9 is not only very precise but also exceptionally easy to use, so that it can quite easily become perverted (p. 200), a concern that Doudna voices "subconsciously" (p. 198) via dreams.<sup>2</sup> In one dream, Doudna is asked to teach someone how gene editing works, but when she enters a room to meet her student, she sees Adolf Hitler in the flesh, seated in front of her (p. 199),<sup>2</sup> eagerly awaiting his first introductory lesson.

In order to prevent nefarious misuse, Doudna joins elite gatherings such as the World Economic Forum in Davos, Switzerland, to discuss with both civic and private-sector leaders how to tweak the *Homo sapiens* gene pool in a "prudent" manner (p. 160) and how to assume control over and responsibility for "our own evolution" as a self-directing species.<sup>2</sup> On such occasions, Doudna tends to adopt the view that we can and should restore normative equilibrium by refraining from using CRISPR/Cas9 technologies to permanently alter human genomes "until we have given a broader range of stakeholders the opportunity to join the discussion" (p. 182).<sup>2</sup> Elsewhere, however, such a course of action is depicted as pointless.

Doudna's "trepidations" about CRISPR are notably invoked by the possibility of rewriting the DNA of future human beings. Now that (because of IVF) human life can be created in a Petri dish (the same type of sterile environment where gene-editing technologies are developed), it seems inevitable that CRISPR and IVF will converge (p. 191).<sup>2</sup> This implies that humans are about to become the coauthors of their own genetic constitutions (p. 189).<sup>2</sup> Indeed, as Robert Sinsheimer argued in 1969,<sup>39</sup> we are imperfect, flawed creatures who may someday use biotechnology to perfect a product of two billion years of evolution. But, Doudna argues, if at all, this should be done in a careful, prudent, and well-considered manner.

Predictions such as Sinsheimer's build on the presupposition that we humans have the governance power to manage and contain the way in which the CRISPR "menagerie" (i.e., the organisms whose genomes are consciously gene-edited) will evolve. Even the prudent conviction that "we should think twice and think again" before gene-editing the human germline presupposes that such thinking may have a significant impact on the future course of events. Yet "whether we will ever have the intellectual and moral capacity to guide our own genetic destiny is an open question" (p. 183). This is the second storyline running through Doudna's autobiography, which explicitly questions the viability and credibility of the "responsible research" scenario (technology steered by prudent humans).

For Doudna, there is something unsettling about the rapid spread of powerful new CRIPSR-related techniques (p. 113).<sup>2</sup> She is taken aback by the pace of the dissemination of the tool she helped to create (p. 100).<sup>2</sup> CRISPR (an "almost effortless" way to edit genes in nearly any organism) is exploding and morphing quickly from an esoteric technology into a DIY tool. The "democratisation" of CRISPR (p. 113) seems impossible to contain. CRISPR has lowered the technical barriers to self-directed evolution. Genomes will be flooded with thousands of new genes, and species will become increasingly plastic. CRISPR will revolutionize the world (p. 117),<sup>2</sup> giving rise not only to miniature designer pets, extra-muscular beagles, and frankenfish but also to "humanized pigs" as a resource for xenotransplantation.

Initially, in order to contain this threat, Doudna adheres to the archetypal narrative structure of life writing in science: she departs on a journey through the land of bioethics in order to acquire new insights that will allow her to restore the equilibrium. Now that scientists have "crossed the Rubicon" (p. 200),<sup>2</sup> public discussion should not fall too far behind, and Doudna sees it as her task to send out a wake-up call, even if this means stepping out of "comfort zones" such as her lab (pp. 205, 243) to enter the sphere of public debate.<sup>2</sup> She is hesitant to do so because she has never before played this kind of role (p. 206), but compares her position to that of Paul Berg, the Stanford biochemist and Nobel laureate with whom she clearly identifies (p. 202).<sup>2</sup> Four decades earlier, in 1973, Berg had taken the initiative to organize the Asilomar conference at Monterey, resulting in a landmark letter in Science<sup>40</sup> advocating a moratorium on hazardous forms of recombinant DNA research. This precedent provides a scaffold, allowing Doudna to enact her new role by endorsing Berg. Thus, she decides to host a similar meeting, again at a pleasant location (in Napa, California, not that far from Monterey), where she initiates the Innovative Genomics Institute (IGI) Forum on Bioethics. IGI is an organization cofounded by Doudna with the goal of advancing gene-editing technologies). Besides Doudna and Sternberg, the group includes leaders of the original 1970s discussions about recombinant DNA research at Asilomar, including David Baltimore and Paul Berg, and the conference likewise results in a Science article: "A Prudent Path Forward for Genomic Engineering and Germline Gene Modification."<sup>27</sup> Scientists are "strongly discouraged" from making heritable changes in the human genome, but the use of the signifier "moratorium" is consciously avoided so that the moral message is much less clear (the article basically concludes that "there is an urgent need for open discussion of the merits and risks of human genome modification," [p. 37]).<sup>27</sup>

Already during this meeting, however, the strategy of prudence and responsibility is called into question. While the participants avidly discuss whether human embryos should be exposed to gene editing, the news reaches them that a manuscript describing gene-editing experiments with human embryos is already circulating among journals. And on April 18, 2015, the rumored article would be published.<sup>41</sup> More recently, this branch of research had resulted in Chinese scientist He Jiankui's claim that he altered the DNA of two human embryos to create the world's first genetically edited babies, thereby "defying a broad consensus against hereditary tinkering." The problem, as Doudna sees it, is that CRISPR has made gene editing far too easy (p. 187)<sup>2</sup>: "This possibility gnawed at me. CRISPR had the potential to turn all future genomes into a collective palimpsest upon which any bit of genetic code could be erased and overwritten depending on the whims of the generation doing the editing" (p. 188).<sup>2</sup> The post-discovery events call her initial enthusiasm into question:

What had we done? Emmanuelle and I, and our collaborators, had imagined that CRISPR technology could save lives ... Yet as I thought about it now, I could scarcely begin to conceive of all the ways in which our hard work might be perverted. Overwhelmed by how fast everything was moving ... I began to feel like Dr. Frankenstein. Had I created a monster? (p. 200)<sup>2</sup>

These lines not only allude to Mary Shelley's famous classic, published two centuries ago, but literally echo her prose. For this is precisely the question Victor Frankenstein asks himself on the famous first pages of Chapter 5. After having worked hard for years, the doctor suddenly beholds the "thing," the "miserable monster whom I created ... a thing such as Dante could not have conceived" (p. 319). And CRISPER, like Frankenstein's monster, is about to escape from the lab and into outside world, which seems completely unprepared for this event.

The two storylines (the two interpretations of the meaning of CRISPR/Cas9) result in moral ambivalence. Ethical deliberation is called for, but seems meaningless now that gene editing is already being applied not only to human embryos but to a quickly growing "menagerie" of animals (p. 205). This gives rise to an alternative set of responses, building on the conviction that genomes will become "as malleable as a piece of literary prose at the mercy of an editor's red pen," in a scenario that now seems inevitable (p. 90). Once this game-changing technology is unleashed into the world, it will take control of evolution one way or another (p. 227). Gene editing is not really new, for our DNA is constantly changing, as we have seen. Every person experiences one million mutations per second. Each one of us begins life with fifty to one hundred random mutations *de novo* and any CRISPR mutation performed will pale in comparison to the genetic storm that rages inside each of us from birth to death (p. 223). In other words, gene editing is not unnatural but in accordance with nature ( $\kappa \alpha \tau \acute{\alpha} \ \phi \acute{\nu} \sigma \imath \nu$ ), and human bioengineers merely serve as vectors.

Even bioethics may become a vehicle for infecting the biosphere with this new technology, for although technoradical Steven Pinker, in his stereotypical portrayal, suggests otherwise, arguing that the primary "imperative" for today's bioethics is to get out of the way,<sup>44</sup> the ethical landscape often reveals a reversal of roles. While Doudna and her coauthors advocate prudence and caution, influential ethicists such as Julian Savulescu argue that it is a moral imperative that CRISPR/Cas9 (experimentally as may be) should move forward.<sup>45</sup> To intentionally refrain from engaging in life-saving research, Savulescu argues, is to be morally responsible for foreseeable deaths. In other words, gene-editing of human embryos is not seen as an option (although questionable) but is framed as inevitable (p. 218).<sup>2</sup>

Doudna's retrospective reflects a basic anthropocenic experience. In terms of technological power, human beings have a disruptive, irreversible, and omnipresent impact on the global biosphere, but the sense of responsibility to which this gives rise is frustrated by the apparent inability of ethics and governance tools to steer or contain this power in a prudent manner. In terms of narrative structure, instead of curving toward a new equilibrium (denouement), the dramatic climax becomes increasingly intense.

#### VIII. CONCLUDING REMARKS

Science autobiographies provide a case history perspective on transformations in knowledge production, but must be treated with care. In her assessment of the CRISPR revolution (the knowledge dimension), Doudna claims that genomes (of all species, including humans) have become malleable, resulting in the increased plasticity of living beings. Her vision of the CRISPR menagerie, however (malaria-free mosquitoes, ultramuscular dogs, cancer-curing viruses, humanized pigs, draconic or miniature designer pets, etc.), may fall into the trap of overestimating the engineering view of life (visible in the synthetic biology literature of recent years), in this way underestimating the complexity and recalcitrance of living systems. Doudna seems to extrapolate the effectiveness of an engineering, laboratory approach to life (based on the manageability of microbes in Petri dishes) into the sociobiological environment, endorsing the idea that life as such can finally be fabricated (p. 7).46 In the real world, the translation of laboratory technologies into life-world applications often proves hazardous and complicated. Techniques and insights produced in the drastically simplified environments known as laboratories are not that easily transferrable into messy reality, where countless intruding factors come into play. In short, the gap between the lab and the real world seems obfuscated in Doudna's announcement of the technological reproducibility of life.

As to the power dimension, power games are presented in Doudna's retrospective as an intrusive factor, as something foreign and external: a "disheartening twist" (p. 97).<sup>2</sup> Thus, the authors maneuver themselves into what Hegel<sup>47</sup> once referred to as the position of the beautiful soul (*schöne Seele*), bemoaning the fact that lab work is besieged by legal controversies but obfuscating the extent to which Doudna herself is actually deeply *involved* in the very controversies she claims to deplore. More specifically: the beautiful soul position obscures the extent to which writing and publishing memoirs may be seen as strategic moves in the context of such controversies. Indeed, her memoir may even (to some extent at least) be seen as a response to them. One of the motives for writing the memoir may have been the desire to reinforce the Berkeley version of the discovery

narrative, favoring the Doudna camp. As Comfort phrases it, the purpose of *A Crack in Creation* is to show that Doudna is the true heroine of CRISPR.<sup>36</sup> Thus, although legal controversies are hardly addressed as such, there is an undeniable link between the Berkeley-Broad feud and the decision to publish and the timing of her book.

As to the ethical dimension, life writing emerges as a practice of the Self: an effort by the author to come to terms with her experiences. This is a process that in psychoanalysis is known as working through (Durcharbeiten), involving the acquisition of new skills and new vocabularies to contribute to, or even take a leading role in, public debate on CRISPR's seismic impact. Yet, notwithstanding the attention given to the ethical dimension in quantitative terms (the number of words and pages, especially when compared with the virtual absence of the power dimension), an unresolved tension can be discerned in the manner in which the ethical dimension is addressed. Doudna's account focuses on her contributions to invited elite initiatives (IGI, Science, Davos), but hardly involves other voices and perspectives from outside scientific expert circles, so that many of the ethical questions raised in A Crack in Creation sound fairly formulaic and predictable (echoing the 1974 Science article by Berg et al.). Moreover, the intriguing ambivalence running through Doudna's arguments—her reliance on two apparently incompatible narrative vocabularies, both stressing and downplaying the role of human individuals—is never explicitly addressed by Doudna herself. She remains a "divided subject," psychoanalytically speaking, and her narrative trajectories are like the two sides of a Möbius Ring. At times she positions herself as the prudent, responsible researcher; at times (the reverse side), she experiences herself as a mere vehicle or vector. These narratives seem incommensurable, never converging into a comprehensive view.

Precisely this, I would argue, is what makes science autobiography a fascinating genre. Retrospectives such as *A Crack in Creation* are interesting not only because of their moments of lucidity and transparency but also because of their blind spots: components that decidedly play a role but are not explicitly addressed. Flaws and tensions are no less interesting and revealing than frankness and confession. Moreover, we should not expect *A Crack in Creation* to be the final word. Other memoirs (by other prominent players) are bound to appear, no doubt partly endorsing and partly challenging Doudna's "fractious" narrative.

#### **REFERENCES**

- Jinek M, Chylinski K, Fonfara I, Hauer M, Doudna J, Charpentier E. A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. Science. 2012;337(6096):816–21. DOI: 10.1126/science.1225829.
- Doudna J, Sternberg S. A crack in creation: gene editing and the unthinkable power to control evolution. Boston: Houghton Mifflin Harcourt; 2017.
- 3. Foucault, M. Histoire de la sexualité 2: L'usage des plaisirs. Paris: Gallimard; 1984.
- Reichenbach H. Experience and prediction: an analysis of the foundations and the structure of knowledge. Chicago: University of Chicago Press; 1938.
- 5. Schickore J, Steinle F. Revisiting discovery and justification: historical and philosophical perspectives on the context distinction. Dordrecht: Springer; 2006.

- 6. Zwart H. Understanding the Human Genome Project: a biographical approach. New Gen Soc. 2008; 27(4):353–76.
- Zwart H. From playfulness and self-centredness via grand expectations to normalisation: a psychoanalytical rereading of the history of molecular genetics. Euro J Med Health Care Philos. 2013;16(4):775–88.
- 8. Watson J. The double helix: a personal account of the discovery of the structure of DNA. New York: Simon and Schuster; 1968/1996.
- 9. Crick F. What mad pursuit: a personal view of scientific discovery. New York: Basic Books; 1988.
- 10. Wilkins M. The third man of the double helix: an autobiography. Oxford: Oxford University Press; 2003.
- Zwart H. The third man: comparative analysis of a science autobiography and a cinema classic as windows into post-war life sciences research. Hist Philos Life Sci. 2015;37(4):382–412. DOI: 10.1007/s40656-015-0080-z.
- 12. Maddox B. Rosalind Franklin: the dark lady of DNA. New York: HarperCollins; 2002/2003.
- 13. Sulston J, Ferry G. The common thread: science, politics, ethics and the human genome. London: Bantam/Corgi; 2002/2003.
- Collins F. The language of God: a scientist presents evidence for belief. New York: Free Press/Simon and Schuster; 2006.
- 15. Venter JC. A life decoded: my genome my life. New York: Viking/Penguin; 2007.
- 16. Badiou A. L'être et l'événement. Paris: Éditions du Seuil; 1988.
- 17. Freytag G. Die Technik des Dramas. Leipzig: Hirzel; 1863.
- Zwart H. Limitless as a neuro-pharmaceutical experiment and as a Daseinsanalyse: on the use of fiction in preparatory debates on cognitive enhancement. Euro J Med, Health Care Philos. 2014;17(1): 29–38.
- 19. Todorov T. The poetics of prose. Ithaca: Cornell University Press; 1977.
- 20. Egan S. Patterns of experience in autobiography. Chapel Hill: University of North Carolina Press; 1984.
- 21. Ostwald W. Große Männer. Leipzig: Akademische Gesellschaft; 1909.
- 22. Lenard P. Great men of science. London: Bell & Sons; 1933.
- 23. Benyus J. Biomimicry: innovation inspired by nature. New York: HarperCollins; 1997.
- 24. Church G, Regis E. Regenesis: how synthetic biology will reinvent nature and ourselves. New York: Basic Books; 2013.
- Nelkin D, Lindee S. The DNA mystique: the gene as a cultural icon. Ann Arbor: University of Michigan Press; 1995/2004.
- 26. Zwart H. On decoding and rewriting genomes: a psychoanalytical reading of a scientific revolution. Euro J Med Healthcare Philos. 2012;15(3):337–46.
- 27. Baltimore D, Berg P, Botchan M, Carroll D, Charo A, Church G, Corn J, Daley G, Doudna J, Fenner M, Greely H, Jinek M, Martin S, Penhoet E, Puck J, Sternberg S, Weissmann J, Yamamoto K. A prudent path forward for genomic engineering and germline gene modification. Science. 2015;348(6230):36–8. DOI: 10.1126/science.aab1028.
- 28. Zwart H. From the nadir of negativity towards the cusp of reconciliation: a dialectical (Hegelian-Teilhardian) assessment of the anthropocenic challenge. Techné: Res Philos Technol. 2017;21(2–3):1–24. DOI: 10.5840/techne20176565.
- 29. Zwart H. The obliteration of life: depersonalisation and disembodiment in the terabyte age. New Gen Soc. 2016;35(1):69–89. DOI: 10.1080/14636778.2016.1143770.
- 30. Serres M. Hermes II: L'interférence. Paris: Les Éditions de Minuit; 1972.
- 31. Zwart H. In the beginning was the genome: genomics and the bi-textuality of human existence. New Bioeth Multidisc J Biotechnol Body. 2018;24(1):26–43. DOI: 10.1080/20502877.2018.1438776.
- 32. Zwart H. Ethical consensus and the truth of laughter: the structure of moral transformations. Kampen: Kok Pharos; 1996.
- 33. Lander E. The heroes of CRISPR. Cell. 2016;164:18–28. DOI: 10.1016/j.cell.2015.12.041.
- 34. Capps B, Chadwick R, Joly Y, Mulvihill J, Lysaght T, Zwart H. Falling giants and the rise of gene editing: ethics, private interests and the public good. Human Genom. 2017;11(1):20. DOI 10.1186/s40246-017-0116-4.

- 35. Reardon S. CRISPR patent battle goes to court. Nature. 2015;540:326–7.
- 36. Comfort N. That's the way the CRISPR crumbles. Nature. 2017;546:30–1.
- 37. Ceccarelli L. On the frontier of science: an American rhetoric of exploration and exploitation. East Lansing: Michigan State University Press; 2013.
- 38. Doudna J, Charpentier E. The new frontier of genome engineering with CRISPR-Cas9. Science. 2014;346. DOI: 10.1126/science.1258096.
- 39. Sinsheimer R. The prospect of designed genetic change. Amer Sci. 1969;57:134–42.
- 40. Berg P, Baltimore D, Boyer HW, Cohen SN, Davis RW, Hogness DS, Nathans D, Roblin R, Watson JD, Weissman S, Zinder ND. Potential biohazards of recombinant DNA molecules. Science. 1974;185:303.
- 41. Liang P Xu Y, Zhang X, Ding C, Huang R, Zhang Z, Lv J, Xie X, Chen Y, Li Y, Sun Y, Bai Y, Songyang Z, Ma W, Zhou C, Huang J. CRISPR/Cas9-mediated gene editing in human triponuclear zygotes. Protein Cell. 2015;6:363–72.
- 42. New York Times. Should scientists toy with the secret to life? 2019 Jan 28; https://www.nytimes.com/2019/01/28/opinion/crispr-genes-babies.html.
- 43. Wollstonecraft SM. Frankenstein; or, the modern Prometheus. Harmondsworth: Penguin; 1818/1968.
- 44. Pinker S. The moral imperative for bioethics. Boston Globe. 2015 Aug 1.
- 45. Savulescu J, Pugh J, Douglas T, Gyngell C. The moral imperative to continue gene editing research on human embryos. Protein Cell. 2015;6:476–9.
- 46. Bensaude-Vincent B, Benoit-Browaeys D. Fabriquer la vie: Où va la biologie de synthèse? Paris: Éditions du Seuil; 2011.
- 47. Hegel GWF. Phänomenologie des Geistes. Werke III. Frankfurt am Main: Suhrkamp; 1807/1973.