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Abstract

When announcements by molecular biologists and the biotechnology sector are received negatively by the general public or policy makers, the fault is generally ascribed to a general ignorance of science. This short commentary argues that, on the contrary, the problem may be that an influential portion of the public is actually too well informed to accept blindly what they are told. This awareness does not come from scholarly publications or the media, but more likely from a series of influential books and magazine articles that for the last 3 decades have promulgated a view of molecular biology that diverges strongly from what is generally presented. The actual level of public awareness needs to be taken into account to develop an optimal communication strategy for the discipline.

The recent decision by the Royal Swedish Academy of Sciences to award the 2020 Nobel Prize in Chemistry to Jennifer Doubna and Emmanuelle Charpentier for their contribution to genome editing using Crispr-Cas9 has given rise all around the world to a mixture of both praise and controversy, as tends to be the case with most such awards. In France, in addition, the news has been welcomed by the media with a significant level of unease, the legitimate desire to be proud of French science being tempered by the fact that Emmanuelle Charpentier, a French citizen by birth expatriated in Germany, would have indisputably faced substantial obstacles lately, had she tried to carry out her research in her own country. According to a 2018 ruling of the Court of Justice of the European Union, organisms that have had one or

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more genes edited should be subjected in each country of the EU to the national legislation governing the use of Genetically-Modified Organisms (GMOs), which in France is particularly restrictive. The commercial production of GMOs has been banned in the country since 2008, and research on them is severely controlled. Field trials of GMO crops, for example, are forbidden.

Scientists and executives of biotechnology companies who have been asked recently by the media to comment on this state of affairs often ascribe it implicitly to exaggerated caution, due to a fundamental lack of understanding by policy-makers, as well as by the public at large, of the biology involved. The implication is that if the public were more aware of the basic tenets of molecular biology, there is little doubt that GMOs, and genome editing in particular, would be more widely accepted. "If members of the public understood what biotechnology is all about, they would stop obstructing the path to progress", was a common leitmotif after the decision by Scottish ministers in August 2015 to ban all genetically-modified crops.

However, what if blaming public ignorance is not the right way to look at things? What if exactly the opposite were closer to the truth for a non-negligible portion of the population? Beside the fact that many vocal biotech critics around the world have formal training in biology, there are plenty of reasons to think that a sizeable segment of the public is actually *too well*informed to feel comfortable with the sales pitch of biotech companies as well as with many of the statements made by experts trying to explain in laypersons' terms what they are doing.

Where does this level of information in the public come from? Clearly not from the scientific literature, which was until recently almost entirely inaccessible behind publishers' paywalls, and is in any case written in such a way that it is virtually impenetrable for non-scientists. Media coverage has not done much either to raise public awareness. Whenever daily newspapers and radio or television news programs run stories about recent advances in molecular biology and biotechnology, they systematically attempt to keep things simple, non-technical, and sufficiently positive to attract public interest. For instance, instead of delving into a detailed description of "genetic scissors", including their documented drawbacks, the numerous stories devoted to them by the press in the last few years have tended to project fantastic, Jurassic Park-inspired visions of resurrecting mammoths and other extinct animal species, or of curing vast numbers of diseases by targeting single genes with surgical precision. One could argue that such sensationalist portrayals, with a strong positive bias, have done very little to give to the public an accurate, balanced perspective on scientific advances in the field.

Books and magazines, contrastedly, have been key to communicating detailed information about molecular biology and biotechnology to a wide audience. In particular, a series of bestsellers1-3that Richard Lewontin authored or co-authored starting in 1984 have conveyed

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very effectively the message that many accounts of molecular genetics greatly oversimplify its complexity. In 2002, in a celebrated magazine article4,followed a few years later by another, equally inspired piece5, Barry Commoner attacked what he referred to as the "DNA myth", i.e., the idea that a clear-cut chain of molecular processes leads from a single DNA gene to the appearance of a particular inherited trait. The same message was contained in a very popular book published in 2006 by Denis Noble6, rapidly translated into several languages, and which some readers have hailed as a great antidote to the excesses of what has become referred to as "gene-centrism"7,8. In 2010, both Time magazine (Figure 1) and the German magazine Der Spiegel ran detailed cover stories about how research in epigenetics was revolutionizing our understanding of heredity and of the functioning of cells.

Since 2010, other books and magazine articles have also challenged the gene-centric paradigm, and have reached a wide audience as well. Concomitantly, the content of all these texts has also been widely cited and discussed on the web, amplifying their impact even more. As of April 9, 2021, searches with a web browser for "Lewontin DNA" and "Barry Commoner DNA" give access to about 472,000 and 465,000 sites, respectively. Many videos of public lectures by Lewontin, Commoner, Noble, and others are also available on the internet.

A recent book by Stuart Ritchie9may bring public awareness to a higher level still. It is currently attracting a tremendous amount of attention, and is therefore likely to have a significant impact. In this remarkable book, the author analyzes the many problems that he argues currently plague scientific research, including negligence, bias, and hype. He uses the "candidate gene approach" to illustrate some of the deleterious consequences of negligence, in this case because researchers did not pay sufficient attention to the low statistical power of their analyses. As a result, many of the research efforts carried out from 2000 to 2010 to identify close associations of specific individual genes with complex traits or diseases resulted in "building a massive edifice [...] on foundations that we now know to be completely false". Ritchie points out how, over the last decade, large-scale genome-wide association studies (GWAs), have cast serious doubt on many of the candidate genes identified previously10,11and have demonstrated that most complex traits are massively polygenic, as predicted theoretically by Fisher12 more than a century ago.

It would be a stretch to pretend that, at this stage, through the various books and magazine articles mentioned above, every member of the public now has a good grasp of the state-of-the-art in molecular biology and biotechnology. That is not the case. Nevertheless, a non-negligible portion of the population definitely is aware of the fact that things are enormously more complicated in these disciplines than was thought to be the case 20 or even 10 years ago, and that, in particular, as Noble put it succinctly, "there are no biological functions that depend on the coding provided by a single gene". People having read this statement in the

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past, or having gone recently through Ritchie's description of the evidence of massive polygenicity that emerges from many GWAs, are likely not to be very receptive any more to the idea, still advocated in a variety of contexts, that, in and of itself, the straightforward sequencing of a genome or metagenome can provide definitive answers to all kinds of questions13. Similarly, any proposal to modify an organism by acting on a single gene to obtain a desired trait is liable to be received with suspicion or unease. To assuage these feelings, definitely in documents forwarded to legislators and the press but in scholarly articles as well, proposers of novel genetic manipulations or genome editing procedures should systematically demonstrate that they are vigilantly checking for unexpected off-target effects, be they mutations elsewhere in the genome that can have deleterious effects14,15,16, or unwelcome changes in one of the multitude of functions, other than the targeted one, in which it is probable that the modified gene be involved. In other words, given the level of awareness of a portion of the public (including researchers in other disciplines) and of policy-makers, it is not a sound communication strategy in the long term, for the purpose of getting research advances to pass successfully through regulatory hurdles and to be implemented widely, to present things as if they were far less complicated and uncertain than they are in reality. That strategy is bound to largely backfire now, and seems very likely to do so even more in the future, which in turn could affect negatively how researchers in other fields as well are viewed by the public. Such an outcome would be utterly damaging when humanity is facing great challenges, calling for the swift adoption of significant breakthroughs in science and technology in years to come.

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Figure 1.Cover of the January 19, 2010, issue of Time Magazine, devoted to a story on the new science of epigenetics. (Reprinted with permission). A few months later, the German magazine Der Spiegel also had a provocative cover, focusing on a story on epigenetics entitled "The victory over genes" (available online at https://www.spiegel.de/spiegel/print/d-73109479.html, last retrieved February 25, 2021).

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