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INNOVATION

CRISPR: What Managers Need to Know About the Emerging Genetic Revolution

by Andrew Park, Pierre Berthon, Jan Kietzmann, and Leyland Pitt

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Exploring the potential transformative effect CRISPR technology could have on an array of industries.

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CRISPR[1], a novel gene editing technology, is expected to revolutionize a broad array of industries including biotechnology, healthcare, medicine, energy, agriculture, national security and more. It will fundamentally change how we theorize and utilize gene editing.

It has already made a significant impact in therapeutics discovery, having contributed to the development of mRNA vaccines in response to COVID-19. Thus, CRISPR was more than just a 'demonstration in principle', with the aim of verifying that gene-editing had practical potential. It allowed for the development of a novel mRNA vaccine that triggers the human body to produce the COVID-19 spike protein and induce an immune response.

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These mRNA vaccines were developed and deployed at a speed and scale that was previously inconceivable in the traditional biotechnology and drug development industry. Typical drugs that are developed using the incumbent 'blockbuster' drug discovery model require 10-15 years of research and development, clinical trials, and regulatory approval (Maine, 2016; Pisano, 2010). Astoundingly, the first and one of the most widely deployed COVID-19 therapeutics, manufactured by Pfizer/BioNTech, was developed, tested, and received FDA Emergence Use Authorization in less than one year (Pfizer, 2020).

CRISPR is ushering in a new way of creating value, and managers whose industries may be affected by its emergence should prepare now to configure their operational capabilities to capture value from it. In this article, we briefly review the effect that COVID-19 had on the traditional scientific peer review and drug discovery process, and how some firms were better positioned to develop a CRISPR-informed mRNA vaccine than others. We then explore the potential transformative effect that CRISPR technology could have on other industries. We conclude by offering several key managerial recommendations to prepare for this emerging genetic revolution.

The drug discovery process, radically transformed

Pfizer/BioNTech and Moderna's vaccines were developed and deployed at a global scale in only one year (Cleve, 2021). This wholesale reconfiguration of the traditional scientific research, drug discovery and regulatory approval process, triggered by the COVID-19 pandemic, has significant implications for organizations operating in industries that may similarly be upended by unexpected threats. Firms that can anticipate such threats and that have the absorptive capacity to quickly mobilize their operations to mitigate these threats using CRISPR may have a significant advantage over firms that don't. Indeed, traditional vaccine manufacturers such as Merck, GlaxoSmithKline and Sanofi were unable to match the speed with which Pfizer/BioNTech and Moderna deployed their COVID-19 therapeutics (Park et al., 2022; Kuchler, 2021).

One early indication that the crisis presented by COVID-19 had the potential to significantly alter traditional drug discovery was in the recalibration of the scientific peer review process. Research normally takes two to three years to be published in high quality science journals, however, given the pressing nature of the SARS-CoV-2 health crisis, the scientific community utilized a mechanism through which new research could be aggregated and made available in preprint form, prior to peer review. These preprint versions were publicly accessible in the bioRxiv and medRxiv databases. Given the recency of this preprint phenomenon, it is unclear whether the increase in preprinting prior to peer review has contributed to the rapid development of the current rich suite of novel COVID-19 therapeutics, but at least one study suggests that the quality issues arising from the lack of peer-review are partially offset by the expansion of audiences that are able to access and critically examine these studies prior to publication (Kodvani et al., 2022).

The radical reconfiguration of the incumbent regulatory process might be the most important development for managers operating in technical industries. When a US-based biotechnology or pharmaceutical company develops a new drug candidate, they must complete three phases of clinical trials and seek FDA approval, which can take 10 to 15 years or more. However, in response to the global pandemic, the Trump administration announced 'Operation Warp Speed', which provided significant financial support for

research related to a COVID-19 vaccine (US Department of Health and Human Services, 2021). Also, the initiative provided an exemption from the traditional sequential clinical trials process and allowed vaccine candidates to undergo the various phases of clinical trials concurrently. Furthermore, The Department of Health and Human Services and the Department of Defense committed to supporting mass manufacturing and distribution of vaccine candidates once approved, two activities which were traditionally the responsibility of the firm producing the candidate. Lastly, the FDA invoked its Emergency Use Authorization program to provide early access to the newly developed vaccines.

Applicability to Other Industries Amenable to CRISPR

The case of the COVID-19 mRNA vaccines, the development of which was informed by our increasingly sophisticated understanding of CRISPR, is likely a precursor for similar disruptions in other industries. An unexpected threat could upend the traditional operational and regulatory structures of other sectors, and accelerate the development timelines of radical, new products and services. For example, in the agricultural setting, work is already being conducted globally to make crops more resilient to climate change, nutrient deficiencies, droughts and pests, and be more productive. Researchers have used CRISPR to make tomato plants resistant to fungi such as *Pseudomonas syringae* and *Phytophthora capsica* (de Toledo Thomazella et al., 2016). Similarly, researchers have used the technology on cacao plants to make them resistant to the pathogen, *Phytophthora tropicalis* (Fister et al., 2018).

CRISPR could also revolutionize the energy industry, and a significant amount of work is already being conducted on developing more efficient and sustainable biofuels. In 2017, ExxonMobil and Synthetic Genomics used CRISPR to deactivate a gene in algae that down regulated fat production, essentially creating a strain of algae that could produce high-energy fat cells indefinitely (Rimmer, 2021).

As a final example, CRISPR has been targeted as a potentially powerful tool in military applications, particularly surrounding the development of new bioweapons. Numerous scientists and policymakers have contemplated and debated the threat of CRISPR in the

creation of artificial pathogens of unprecedented lethality, including issues surrounding the dual nature of help and harm in CRISPR-enabled antibiotic resistance, and the creation of chimeric molecules (where they serve as both a benefit and detriment to human health) (Vogel & Ouagrham-Gormley, 2018; Gerstein, 2016; Jasonoff, 2015).

Managerial recommendations

We conclude with three recommendations for managers whose industries may be disrupted by CRISPR-based technologies. First, managers must be acutely aware of repositories of preprint studies and understand that as a result, future technologies may be shaped earlier and more quickly than they may be accustomed. It appears that both the publication of, and the consumption of non-peer reviewed, preprint studies is here to stay, and organizations that have the technical ability and capacity to discern the quality of unvetted research and absorb them effectively into their product and service pipelines will likely enjoy a competitive advantage in product development.

Second and relatedly, organizations that are willing to invest in, and embrace novel CRISPR-based technologies and ascertain the risk associated with them will be in an advantageous position to create and capture value from unexpected threats. In the case of COVID-19 vaccines, it has been posited that the reason the traditional major vaccine producers such as Sanofi, Merck and GlaxoSmithKline were outcompeted by Pfizer/BioNTech and Moderna was due to their skepticism and reluctance to accept the previously untested mRNA technology.

Third, and possibly most importantly, managers should not assume that long established regulatory structures and value chain configurations are immutable. In fact, they should assume that they can be radically and rapidly reconfigured. Managers might want to prepare for potential changes in regulatory regimes by seeking alliance partners who may complement their organizations' core capabilities. For example, a research-based organization that focuses on developing new products may begin to seek partnerships that allow them to quickly scale-up manufacturing and distribution of CRISPR-based products, particularly if there is a possibility that the future regulatory environment will allow easier and direct access to end-users.

1. CRISPR Cas9. CRISPR is an acronym for ‘clustered regularly interspaced short palindromic repeats.’ Cas9 is a bacterially derived enzyme that snips DNA, and CRISPR is a collection of DNA sequences that tells Cas9 precisely where to cut.

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Andrew Park

Andrew Park, PhD is an Assistant Professor of Information Systems at the Gustavson School of Business, University of Victoria, Canada. His work centers around how Open Innovation mechanisms impact value creation of firms within the emerging Personalized Medicine ecosystem.

Pierre Berthon

Pierre Berthon, PhD holds the Clifford F Youse Chair of Information Design at Bentley University, USA. Professor Berthon has held academic positions at Columbia University in the US, Henley Management College, Cardiff University and University of Bath in the UK. His research focuses on the interaction of technology, corporate strategy and consumer behavior.

Jan Kietzmann

Jan Kietzmann, PhD is a Professor of Innovation and Information Systems at the Gustavson School of Business, University of Victoria, Canada. The focus of Jan's work is on organizational and social perspectives related to innovation and emerging technologies.

Leyland Pitt

Leyland Pitt, PhD is the Dennis Alumni Chair of Business in the Beedie School of Business, Simon Fraser University, Vancouver, Canada. He has also taught on executive and MBA programs at schools such as Columbia, London Business School, and the Graham School of Continuing Studies at the University of Chicago.