Mary Ann Liebert, Inc. Dpublisher

Re:GEN Open Volume 1, Number 1, 2021 DOI: 10.1089/regen.2021.0007

ORIGINAL RESEARCH

A Bibliometric Analysis of Research on CRISPR in Social Sciences and Humanities

Alberto Asquer* and Inna Krachkovskaya

AQ2

Abstract

The rise of CRISPR not only opens up multiple opportunities for genetic editing but also results in potentially threatening or controversial applications. Research needs to be done in order to appreciate how CRISPR affects the identity and role of individuals within society and reshapes social, political, and economic regimes. A bibliometric analysis of articles on CRISPR published in academic journals in the period 2012-2020 helps identify the main research themes on genome editing that have been addressed in social sciences and humanities so far. Results suggest that CRISPR studies have primarily focused on normative and ethical issues, together with more specific attention toward issues of public perception, trust toward science, regulation and governance of critical applications, and, especially, around the manipulation of the genome of human embryos. Results also suggest that issues of commercial, cultural, and geopolitical sorts have been left relatively unattended so far, instead. Attention to the implications of CRIRPS on such areas should inform the future social sciences and humanities research agenda on genome editing.

Keywords: CRISPR; genome editing; social sciences; humanities; bibliometric analysis

Introduction

The fields of molecular biology, biochemistry, and genetics have been revolutionized by the emergence of the CRISPR technique for genetic editing. CRISPR provides a novel approach to edit parts of a genome in a way that is more accurate, efficient, and economical than alternative methods.¹ The opportunities opened up by CRISPR include applications in such different areas, for example, precision medicine, screening and diagnostics, crop improvement, and breeding.2,3 CRISPR, however, also results in potentially threatening or controversial practices, such as, for example, bioterrorism, biohacking, and eugenics.⁴ Issues arise, therefore, around the impact of CRISPR on the society and the economy.

The scholarly literature on CRISPR (and genetic editing more generally) in natural sciences skyrocketed since 2012, when components of the CRISPR-cas9 system were isolated and shown to be programable to

cut specific sites in isolated DNA.⁵ Research in social sciences and humanities proliferated when it became apparent that the new technique would bring about radical innovations and disruptive effects to existing ecological, regulatory, and industrial regimes. The rise of CRISPR triggered a number of questions, for example, around the relationship between genetic editing and ethics⁶, economics⁷, regulation,⁸ and governance.⁹ After about a decade since the discovery of CRISPR, it is timely to look back at social sciences and humanities research done on the implication of genetic editing for humans, other living species, and the environment so far, and to indicate directions for future research.

Engagement of social scientists and scholars from the humanities with genetic editing is welcome because of various reasons. First, the rise of CRISPR provides the opportunity to study the refinement, adoption, diffusion, and regulation of an emerging technology.¹⁰ Second, the

School of Finance and Management, SOAS University of London, London, United Kingdom

*Address correspondence to: Alberto Asquer, Senior Lecturer in Public Policy and Management, School of Finance and Management, SOAS University of London, Thornhaugh Street, Russell Square, London WC1H 0XG, United Kingdom, Email: aa144@soas.ac.uk

[©] Alberto Asquer and Inna Krachkovskaya 2021; Published by Mary Ann Liebert, Inc. This Open Access article is distributed under the terms of the Creative Commons License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

implications of CRISPR are potentially so revolutionary that multiple disciplinary, social and cultural perspectives should be included into the debate about the regulation and governance of genetic editing, in a way that overcomes the limitations that afflicted the Asilomar experience.¹¹ Finally, the issues that arise from CRISPR call for a coordinated policy and regulatory response from different countries and across government layers. Social sciences and humanities research can provide valuable insights into the role of issue framing, policy narrative, policy communication, and other factors that influence how new regulatory policies for genetic editing are made.

This study reviews the research done by social scientists and scholars from the humanities on CRISPR in the period 2012-2020 and, relatedly, provides evidence of main research themes that help shape a future research agenda. Next section will outline the method followed in this study. The following sections will illustrate the results of the analysis and discuss the findings. The final section will draw the conclusions.

Method

The CRISPR opens up venues for applications that pose issues around, for example, mosaicism and other flaws of organisms,12 uncontrolled transmission of genetic edits across countries¹³ and generations,⁸ use of genetic editing for military purposes,14 exacerbation of productivity gaps between gene-edited crops and other varieties,¹⁵ engineering of gene-edited mushrooms that escape regulations,¹⁶ and the birth of genome-edited babies.¹⁷ From a social sciences and humanities perspective, these controversial applications trigger fundamental questions about the regulation and governance of genetic editing, like for example, What should CRISPR be used for? How much risk that arises from unknown effects of CRISPR is tolerable? What institutional regimes facilitate responsible research of CRISPR applications while protecting individuals and the environment from undesired effects? How can coordinated policies on genetic editing be attained at the global scale? Research in social sciences and humanities can help address these questions by investigating the normative and ethical dilemmas that arise from CRISPR applications within specific historical and institutional context conditions.

This bibliometric analysis of research on CRISPR in social sciences and humanities was carried out by searching for journal articles containing the word "CRISPR" in the title or abstract in the period 2012-2020 in three databases, namely, Web of Science (WoS), Scopus, and Dimensions. Search in WoS was limited to the Social Science Citation Index and Arts & Humanities Citation Index. Search in Scopus was limited to the following sections: economics; econometrics and finance; arts and humanities; business, management, and accounting; and social sciences. Search in Dimensions was limited to the following categories: economics; commerce, management, tourism, and services; law and legal studies; studies in human society; and philosophy and religious studies. Other main search engines (Google Scholar and Microsoft Academic) were not used because they do not provide a way to filter search results by discipline or subject area. The research was carried out in adherence to ethical guidelines and approved by the home institution of the authors.

Table 1 provides summary statistics of the search results. Search results were analyzed using R's package Bibliometrix¹⁸ to identify most frequent journal sources and cited articles. In order to map out research on CRISPR, search results were analyzed via a cooccurrence analysis of keywords and bibliographic coupling using VOSviewer.¹⁹ The co-occurrence analysis of keywords resulted in a network of keywords where their relatedness depends on the number of articles in which they occur together. A thesaurus helped consolidate keywords into fewer numbers. The bibliographic coupling analysis resulted in a network of journal articles where their relatedness depends on the number of references that they share. Other methods of analysis (ie, relatedness based on number of coauthored articles or on number of times articles cite each other or on the number of times articles are cited together) were discarded because of the relative newness of studies on CRISPR in social sciences and humanities. Metrics of the networks were obtained using Gephi.

Results

Search results showed that most frequent venues of publication of articles on CRISPR in social sciences and humanities were journals in the field of ethics (Table 2). Some of the top 10 most cited articles (Table 3) relate to landmark studies on the discovery and development of CRISPR published in *Science*,^{5,24,25,34} *Nature*,¹ *Cell*,²⁶ and Protein and Cell,²³ while others refer to studies on the implications of CRISPR applications on humans, other living species, and the environment.^{20,21,27,30,36} The analysis of co-occurrence of keywords from WoS resulted in a network that consisted of 77 keywords (548 edges, graph density 0.187) grouped into six clusters (Table 4). The analysis of co-occurrence of keywords from Scopus resulted in a network that comprised 207 keywords (4,855 edges, graph density 2.28) grouped into five clusters (Table 5). Search results from Dimensions do not currently include keywords.

	WoS	Scopus	Dimensions
No. documents published in the year			
2012	0	0	1
2013	0	1	1
2014	1	1	4
2015	10	9	45
2016	10	20	104
2017	18	32	166
2018	33	52	267
2019	54	96	304
2020	56	82	351
Total number of documents	182	293	1,243
No. sources	101	106	422
Average years from publication	2.48	2.48	2.62
Average citations per documents	6.281	2.549	3.809
Average citations per year per document	1.606	0.7049	0.9598
Authors	654	599	2,180
Authors of single authored documents	69	149	523
Authors of multiauthored collaboration	585	450	1,657

Table 1. Summary statistics of the search for articles in social sciences and humanities containing "CRISPR" in the title or abstract in WoS, Scopus, and Dimensions from the period 2012 to 2020

Table 2. Top 10 journals by number of articles in social sciences and humanities containing "CRISPR" in the title or abstract in WoS, Scopus, and Dimensions from the period 2012 to 2020

	WoS	Scopus	Dimensions
1	Bioethics (8)	Genetic Engineering and Biotechnology News (54)	American Journal of Bioethics (77)
2	Biology & Philosophy (8)	International Journal of Biological Macromolecules (28)	Frontiers in Genetics (37)
3	Science and Engineering Ethics (8)	Biology and Philosophy (8)	Bioethics (32)
4	American Journal of Bioethics (7)	Science and Engineering Ethics (8)	The Hastings Centre Report (31)
5	Journal of Bioethical Inquiry (5)	AMA Journal of Ethics (7)	Science and Engineering Ethics (23)
6	Journal of Responsible Innovation (5)	Perspectives in Biology and Medicine (7)	Journal of Responsible Innovation (22)
7	Nanoethics (5)	Biolaw Journal (6)	Nanoethics (21)
8	Zygon (5)	Zygon (6)	Cambridge Quarterly of Healthcare Ethics (20)
9	Bulletin of the Atomic Scientists (4)	Bioethics (5)	Perspectives in Biology and Medicine (20)
10	Environmental Communications (4)	Journal of Bioethical Inquiry (5)	The New Bioethics (18)

Bibliographic coupling analysis was carried out on the search results from Dimensions, which largely surpassed, in number of articles, those from WoS and Scopus. The analysis resulted in a selection of 54 articles, but the largest network of connected articles consisted of 38 articles only (125 edges, graph density 0.178) (Fig. 1), which were grouped into six clusters (Table 6). Table 7 shows, for each article (node), the degree (number of links connected to the node), weighted degree (number of links connected to the node, weighted by number of citations), closeness centrality (average length of the shortest path between the node and other nodes), and betweenness centrality (number of times a node is crossed by each of the least cost paths). The nodes are ranked by betweenness centrality, which helps indicate the relative importance of a node to connect different parts of the network.

Discussion

The analysis of co-occurrence of keywords provides some insights into the issues about CRISPR that are tackled in social sciences and humanities research. The analysis of WoS data suggests the presence of research interest toward: public perception and attitudes toward CRISPR, consumer acceptance of genetically edited products, trust toward sciences, risk, and the precautionary principle (in cluster 1); the uses of CRISPR, including preimplantation genetic diagnosis, assisted reproduction, gene therapy, human enhancement, and eugenics (in cluster 2); the experimentation with CRISPR on animals like mice and zebrafish (in cluster 3); the use of CRISPR to research the genetic determinants of disorders like autism and schizophrenia (in cluster 4); the origin of CRISPR as a defense immune system (in cluster 5); and the use of gene drive to tackle infectious diseases like malaria (in cluster 6). The analysis conducted on Scopus data suggests the identification of themes like: how CRISPR works and its effects on genetic materials (in cluster 1); governance issues around the use of CRISPR in humans for various purposes-from infertility to human enhancement (in cluster 2); the mechanisms that underpin CRISPR, such as

Table 2020	3. Top 10 cited articles in social sciences and	Table 3. Top 10 cited articles in social sciences and humanities containing "CRISPR" in the title or abstract in WoS, Scopus, and Dimensions from the period 2012 to 2020	S, Scopus, and Dimensions from the period 2012 to
	WoS	Scopus	Dimensions
1	Baltimore D, Berg P, Botchan M, et al., 2015 ²⁰	Jinek M, Chylinski K, Fonfara I, et al., 2012 ⁵	Baltimore D, Berg P, Botchan M, et al., 2015 ²⁰
0	Lanphier E, Urnov F, Haecker SE, et al., 2015 ²¹	National Academies of Sciences, Engineering and Medicine, 2017 ²²	Liang P, Xu Y, Zhang X, et al., 2015 ²³
ŝ	Liang P, Xu Y, Zhang X, et al., 2015 ²³	Doudna JA, Charpentier E, 2014 ²⁴	Lanphier E, Urnov F, Haecker SE, et al., 2015 ²¹
4	Cong L, Ran FA, Cox D, et al., 2013 ²⁵	Hsu PD, Lander ÊS, Zhang F, 2014 ²⁶	Jinek M, Chylinski K, Fonfara I, et al., 2012 ⁵
5	Jinek M, Chylinski K, Fonfara I, et al., 2012 ⁵	Ledford H, 2015 ¹	Doudna JA, Charpentier E, 2014 ²⁴
9	Doudna JA, Charpentier E, 2014 ²⁴	Liao SM, 2010 ²⁷	Ledford H, 2015 ¹
7	Ledford H, 2015 ¹	Cong L, Ran FA, Cox D, et al., 2013 ²⁵	Ma H, Marti-Gutierrez N, Park SW, et al., 2017 ²⁸
8	Ran FA, Hsu PD, Wright J, et al., 2013 ²⁹	Jasanoff S, Hurlbut JB, 2018 ³⁰	Cong L, Ran FA, Cox D, et al., 2013 ²⁵
6	Lander ES, 2015 ³¹	Koonin EV, 2019 ³²	Esvelt KM, Smidler AL, Catteruccia F, et al., 2014 ³³
10	Mali P, Yang L, Esvelt KM, et al. 2013 ³⁴	Lander ES, 2016 ³⁵	Lander ES, Baylis F, Zhang F, et al., 2019 ³⁶

those of gene deletion and gene silencing (in cluster 3); and regulatory issues that arise from applications of CRISPR, from agriculture to health to invasive species control (in cluster 4).

The analysis of bibliographic coupling results in a network of journal articles that provides indications of influential studies on CRISPR research. Articles addressed issues concerning human genome editing, human enhancement, and bioethics (in cluster 1), genetic editing in agriculture (in cluster 2), relationships between genetic editing and GMOs and related implications on the bioeconomy (in cluster 3), gene drive and eradication of invasive species (in cluster 4), application of CRISPR in human reproduction (in cluster 5), and security, regulation, and governance (in cluster 6). Those articles that rank higher in betweenness centralitywhich suggests that they play an important role to connect areas of inquiry-especially focus on issues about the use of CRISPR on human embryos,^{70,75} on the application of CRISPR on gene drive,^{63,64,67} and on regulatory policy and governance issues.^{8,39,48}

This bibliometric analysis offers an empirically based approach to map out how CRISPR has been researched in social sciences and humanities so far. Results suggest that the rise of CRISPR triggered a variety of interest. Many studies have been prominently concerned with CRISPR applications that are intended to bring about beneficial effects to individuals (eg, preimplantation genetic diagnosis, assisted reproduction, gene therapy, human enhancement, and eugenics) or to alter the natural environment in ways that are beneficial to individuals or groups (eg, the eradication of invasive species and the improvement of crops). Relatively fewer studies have paid focused attention to CRISPR applications that are intendedly harmful, such as, for example, those related to terrorist threats.⁷⁶ Most studies tackle the normative and ethical implications of CRISPR, primarily focusing on issues not only that arise from the manipulation of the genetics of human embryos but also that relate to the editing of other living organisms that could trigger the extermination or extinction of species or unpredictable harms to ecosystems.

The fact that most studies in social sciences and humanities pay attention to normative and ethical issues arising from CRISPR is hardly surprising. As other waves of innovation in genetics (zinc finger nucleases/ TALENs, gene therapy, GMOs, and recombinant DNA), CRISPR opens up venues for novel applications whose effects and implications are not completely understood yet, or which clash with existing value systems and deontological principles. On the other hand, the bibliometric analysis shows that social sciences and

Cluster	Keywords		
1	Agriculture, attitudes, bioethics, biotechnology, consumer acceptance, future, GMO, governance, health, information, perceptions, policy, precautionary principle, preferences, risk, science, trust		
2	Assisted reproduction, cells, embryos, enhancement, ethics, eugenics, gene therapy, genome editing, germline, human enhancement, noni- dentity problem, preimplantation genetic diagnosis (PGD), reproduction, selection, therapy		
3	Anxiety, behaviour, dysregulation, expression, genes, history, impact, mice, model, mouse, mutations, proteins, regulation, spectrum disor- ders, synaptic-transmission, zebrafish		
4	Autism, autism spectrum disorder, CRISPR, elements, evolution, generation, human genome, morality, pluripotent stem-cells, schizophre- nia, transmission		
5	Biology, conception, defense, disease, DNA, genome, immune-system, repeats, strategies		
6	Endonuclease, gene drive, infection, informed consent, malaria, replacement, synthetic biology, system		

Table 4. Clusters of keywords in articles in social sciences and humanities containing "CRISPR" in the title or abstract in WoS

Table 5. Clusters of keywords in articles in social sciences and humanities containing "CRISPR" in the title or abstract in Scopus from the period 2012 to 2020

Cluster	Keywords
1	Amino acid sequence, bacterial enzyme, bacterial protein, bacterial proteins, bacterial strain, bacterium isolate, biocatalysis, biochemical analysis, biodegradation, biosynthesis, carboxylesterase, catalysis, characterization, chemistry, cloning, molecular, controlled study, detergent, enzyme activity, enzyme analysis, enzyme immobilization, enzyme purification, enzyme specificity, enzyme stability, enzymology, escherichia coli, ester derivative, esterase, esterases, gene expression, regulation, gene overexpression, hydrogen-ion concentration, hydrolysis, immobilization, in vitro study, isolation and purification, kinetics, lipolysis, metabolism, metagenomics, metal, metals, models, molecular, molecular cloning, molecular dynamics, molecular model, molecular weight, nonhuman, nucleotide sequence, organic solvent, ph, phylogeny, protein conformation, protein function, protein motif, protein stability, purification, recombinant proteins, sequence analysis, sequence homology, stereoisomerism, structure analysis, substrate specificity, synthesis, temperature, thermostability, triacylglycerol lipase, unclassified drug, wheat bran
2	Adult, adverse event, Asilomar conference, autonomy, bioethical issues, bioethical enhancement, child, child parent relation, China, clustered regularly interspaced short palindromic repeat, clustered regularly interspaced short palindromic repeats, conflict, CRISPR cas system, designer babies, dissent and disputes, embryo, embryo research, enhancement, ethical analysis, ethical theory, ethics, ethics, medical, eugenics, female, gene therapy, genetic enhancement, genetic therapy, genome editing, genome, human germ cell, germ cells, germ line, history, history, 20th century, human, human cell, human embryo, human enhancement, human experiment, human genome, humans, infertility therapy, knowledge, legislation and jurisprudence, male, medical ethics, molecular genetics, moral status, morality, morals, parents, patent, philosophy, policy, politics, preimplantation genetic diagnosis, procedures, psychology, public opinion, reproduction, reproductive techniques, assisted, trust, uncertainty
3	Animal cell, archaea, article, bacteria, bacterial genome, bacterium, biological model, bombyx mori, cell proliferation, CRISPR associated protein, crispr-cas9 system, DNA, DNA modification, epigenetics, evolution, evolution, molecular gene control, gene deletion, gene expression, gene knockout, gene sequence, gene silencing, gene targeting, genes, genome, genomics, guide RNA, immune system, immunity, Lamarckian, messenger RNA, models, molecular evolution, mouse, polyacrylamide gel electrophoresis, protein analysis, protein expression, RNA, guide, western blotting
4	Agriculture, animal, animalia, animals, Australia, biodiversity, bioengineering, biomedical research, biomedicine, biotechnology, conserva- tion, CRISPR, CRISPR/cas-9, European union, gene drive, gene drive technology, genetically modified organism, germline, germline gene editing, GMO, government regulation, informed consent, invasive species, malaria, medical research, perception, precautionary principle, public health, regulation, synthetic biology, trends, united states

humanities research has been relatively silent toward other implications of CRISPR of commercial, cultural, and geopolitical sorts. These gaps provide some ways to suggest directions for the future research agenda. Each of these areas will be discussed in turn.

First, applications of CRISPR may result in a stream of new food and feed products, which can outcompete existing ones because of higher productivity, less production costs, and higher nutritional content. Successful commercial applications of CRISPR may have important rep on existing industries and international trade in such areas as, for example, patenting of genetically edited seeds and other organisms, certifications, custom controls, and disruption to incumbent industrial regimes. Genetically edited food and feed products may dramati-

cally squash the competitiveness of existing farmers, with potentially devastating effects on the conditions of livelihood especially in developing countries. Various issues would need to be addressed around these implications, such as, for example, how CRISPR products will affect existing agriculture and food markets, how existing regime of patents, health and safety regulations, and international trade agreements will adjust to the rise of CRISPR products, what attitudes the public have toward genetically edited food and feed products, and what policies governments can pursue in order to cope with the rise of CRISPR products.

Second, applications of CRISPR may also result in profound cultural changes. The development of CRISPR applications that deliver enhancements of the human

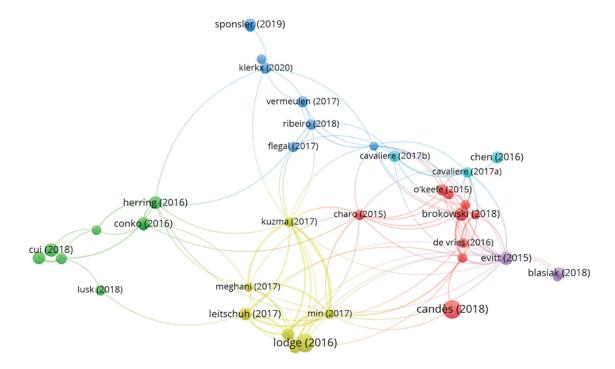


FIG. 1. Clusters of articles in social sciences and humanities containing "CRISPR" in the title or abstract in Dimensions, from the period 2012 to 2020, threshold set at minimum 20 citations. Labels indicate only the first author in case of multiple authors publication.

Table 6. Clusters of articles in social sciences and humanities containing "CRISPR" in the title or abstract in Dimension
resulting from the bibliographic coupling analysis from the period 2012 to 2020

Cluster	Articles
1	Brokowski C, 2018 ³⁷ ; Candes E, Fan Y, Janson L, et al., 2018 ³⁸ ; Charo RA, Greely HT, 2015 ³⁹ ; De Vries RG, Tomlinson T, Kim HM, et al., 2016 ⁴⁰ ; Harris J, 2016 ⁴¹ ; Hildt E, 2016 ⁴² ; Krishan K, Kanchan T, Singh B, 2016 ⁴³ ; O'Keefe M, Perrault S, Halpern J, et al., 2015 ⁴⁴ ; Sparrow R, 2019 ⁴⁵
2	Flegal JA, Gupta A., 2018 ⁴⁶ ; Fraser A, 2019 ⁴⁷ ; Klerkx L, Rose D, 2020 ⁴⁸ ; McLeod C, Nerlich B, 2017 ⁴⁹ ; Ribeiro B, Bengtsson L, Benneworth P, et al., 2018 ⁵⁰ ; Rose DC, Morris C, Lobley M, et al., 2018 ⁵¹ ; Sponsler DB, Grozinger CM, Hitaj C, et al., 2019 ⁵² ; Vermeulen N, Haddow G, Seymour T, et al., 2017 ⁵³
3	Conko G, Kershen DL, Miller H, et al., 2016 ⁵⁴ ; Cui K, Shoemaker SP, 2018 ⁵⁵ ; Herring R, Paarlberg R, 2016 ⁵⁶ ; Lusk JL, McFadden BR, Wilson N, 2018 ⁵⁷ ; Wesseler J, von Braun J, 2017 ⁵⁸ ; Wong AYT, Chan AWK, 2016 ⁵⁹ ; Zetterberg C, Björnberg KE, 2017 ⁶⁰ ; Zilberman D, Gordon B, Hochman G, et al., 2018 ⁶¹
4	Burt A, Coulibaly M, Crisanti A, et al., 2018 ⁶² ; Kuzma J, Gould F, Brown Z, et al., 2018 ⁶³ ; Leitschuh CM, Kanavy D, Backus GA, et al., 2018 ⁶⁴ ; Lodge DM, Simonin PW, Burgiel SW, et al., 2016 ⁶⁵ ; Meghani Z, Kuzma J, 2018 ⁶⁶ ; Min J, Smidler AL, Najjar D, et al., 2018 ⁶⁷ ; Serr ME, 2019 ⁶⁸ ; Scott MJ, Gould F, Lorenzen M, et al., 2018 ⁶⁹
5	Cavaliere G, $2017a^{70}$; Cavaliere G, $2017b^{71}$; Chen SC, Wasserman DT, 2017^{72}
6	Blasiak R, Jouffray JB, Wabnitz CC, et al., 2018 ⁷³ ; Evitt NH, Mascharak S, Altman RB, 2015 ⁸ ; MacIntyre CR, Engells TE, Scotch M, et al., 2018 ⁷⁴

body and capabilities—possibly alongside therapeutic benefits—has been already contemplated as posing normative and ethical issues. In addition, affordability of the CRISPR technique opens up venues for carrying out genetic editing of humans in ways that are unpractical to monitor and relatively uncontrollable. Individuals and groups could become able to undertake genetic editing of themselves and possibly of acolytes of transhumanist movements. The risk that individuals inflict threats of mosaicism and other genetic flaws to themselves and to others would pose issues around the design of regulatory policies that prevent self-inflicted harms. The option to edit own human genome would likely pose cultural issues on such themes as the control of one's (and possibly one's progeny) biological identity and the democratization of the selection of desirable biological traits.

Table 7. Degree, weighted degree, closeness centrality, and betweenness centrality of nodes of the network of articles in social
sciences and humanities containing "CRISPR" in the title or abstract in Dimensions, resulting from the bibliographic coupling
analysis from the period 2012 to 2020

Node	Degree	Weighted Degree	Closeness Centrality	Betweenness Centrality
Evitt NH, Mascharak S, Altman RB, 2015 ⁸	19	32	0.57	132.72
Herring R, Paarlberg R, 2016 ⁵⁶	9	11	0.48	122.59
Klerkx L, Rose D, 2020^{48}	7	7	0.49	113.65
Kuzma J, Gould F, Brown Z, et al., 2018 ⁶³	14	42	0.58	99.22
McLeod C, Nerlich B, 2017 ⁴⁹	12	13	0.51	67.63
Charo RA, Greely HT, 2015 ³⁹	12	14	0.52	58.22
Zilberman D, Gordon B, Hochman G, et al., 2018 ⁶¹	5	14	0.36	54.38
Min J, Smidler AL, Najjar D, et al., 2018 ⁶⁷	11	58	0.53	45.53
Leitschuh CM, Kanavy D, Backus GA, et al., 2018 ⁶⁴	10	27	0.51	44.78
Cavaliere G, 2017a ⁷⁰	11	22	0.47	43.53
Rose DC, Morris C, Lobley M, et al., 2018 ⁵¹	2	2	0.34	36.00
Sparrow R, 2019 ⁴⁵	11	25	0.46	32.88
Meghani Z, Kuzma J, 2018 ⁶⁶	10	24	0.51	32.63
Conko G, Kershen DL, Miller H, et al., 2016 ⁵⁴	4	6	0.42	24.55
Wong AYT, Chan AWK, 2016 ⁵⁹	4	5	0.37	23.05
Lusk JL, McFadden BR, Wilson N, 2018 ⁵⁷	2	2	0.37	13.97
Hildt E, 2016 ⁴²	11	25	0.47	11.35
Cavaliere G, 2017a ⁷¹	5	10	0.43	10.82
Flegal JA, Gupta A., 2018 ⁴⁶	4	5	0.43	10.03
Ribeiro B, Bengtsson L, Benneworth P, et al., 2018 ⁵⁰	6	9	0.45	9.59
Brokowski C, 2018 ³⁷	10	14	0.46	5.50
Krishan K, Kanchan T, Singh B, 2016 ⁴³	8	12	0.44	2.99
De Vries RG, Tomlinson T, Kim HM, et al., 2016 ⁴⁰	6	6	0.41	2.54
Scott MJ, Gould F, Lorenzen M, et al., 2018 ⁶⁹	8	27	0.47	1.98
Cui K, Shoemaker SP, 2018 ⁵⁵	3	5	0.28	1.43
Burt A, Coulibaly M, Crisanti A, et al., 201862	8	36	0.47	1.13
Cetterberg C, Björnberg KE, 2017 ⁶⁰	3	5	0.39	0.67
Harris J, 2016 ⁴¹	8	8	0.45	0.63
Lodge DM, Simonin PW, Burgiel SW, et al., 2016 ⁶⁵	7	8	0.46	0.00
D'Keefe M, Perrault S, Halpern J, et al., 201544	7	7	0.44	0.00
Vermeulen N, Haddow G, Seymour T, et al., 2017 ⁵³	4	4	0.43	0.00
Candes E, Fan Y, Janson L, et al., 2018 ³⁸	2	2	0.38	0.00
Vesseler J, von Braun J, 2017 ⁵⁸	2	10	0.27	0.00
Blasiak R, Jouffray JB, Wabnitz CC, et al., 201873	1	1	0.37	0.00
err ME, 2019 ⁶⁸	1	1	0.37	0.00
Fraser A, 2019 ⁴⁷	1	1	0.33	0.00
Chen SC, Wasserman DT, 2017 ⁷²	1	1	0.32	0.00
Sponsler DB, Grozinger CM, Hitaj C, et al., 2019 ⁵²	1	1	0.25	0.00

Researching the effects of CRISPR on culture will require sensitive attention toward nuances in contemporary discourses as well as in forms of creative expression such as novels, movies, and art.

Cultural implications of CRISPR also call for more intense research effort on the issue of communication of scientific and technological advancements on genome editing to the public. Public perception of opportunities and threats of genome editing would have various consequences on, for example, consumer behavior, attitudes toward environmental integrity and preservation, and policy preferences toward research freedom and funding. Uncertainties about the effects of CRISPR applications could trigger cautionary reactions, which might induce the adoption of restrictive policies toward the use of genome editing and the commercialization of genetically edited products. Research in social sciences and humanities could address these issues and explore the effects of CRISPR communication to public perceptions and policy preferences.

Finally, more attention could be paid, within social sciences and humanities, to geopolitical issues that arise from CRISPR applications. Scientific and technological leadership on genome editing may have important effect on countries' economic competitiveness, military prowess, and strategic advantages. CRISPR applications—for example, from the development of drugs to the one of ethnic bioweapons—can result in tactical advantages to advance a country's interest within the international arena. Accordingly, governments may pursue industrial policies that help advance their countries in the technology race by attracting investment capital and know-how on genome editing, or promoting the cultivation of domestic expertise. Issues that will deserve attention include how genome editing could raise up on a government agenda, what policy design helps stimulate R&D on genome editing, and how CRISPR would eventually impact the balance of power in the international arena.

Conclusions

This study offers a bibliometric analysis of research done in social sciences and humanities on CRISPR in the period 2012-2020. It also provides some considerations about the future research agenda on the implications of genome editing on the society and the economy. The method of the bibliometric analysis consisted of a co-occurrence analysis of keywords and a bibliographic coupling of journal articles. The results indicate that social sciences and humanities research on CRISPR has primarily addressed normative and ethical implications of the application of genetic editing in various areas. Considerable attention has been placed, in particular, on applications of CRISPR on human embryos and on gene drive. Future research on the implications of CRISPR, instead, could address issues that arise from the commercialization of CRISPR applications, from the cultural effects of the rise of CRISPR, including the role of communication and public perception, and from the geopolitical consequences of CRISPR.

The present study contains some limitations that should be acknowledged. First, bibliographic analysis provides a systematic way to map out the state-of-the-art of scholarly research, but more focused literature reviews in specific areas of inquiry are needed in order to appraise the debate on the effects of CRISPR applications and inform policy choices on the governance and regulation of genetic editing. Second, the present study focused on academic journals only, which may often address relatively narrow issues that arise from CRISPR. Future research may extend attention to monographs, edited books, policy papers, and other documents that could offer alternative insights into perspectives toward CRISPR. Furthermore, the present study focused on academic journal articles that exhibit "CRISPR" in the title or abstract, but part of the social sciences and humanities literature on genome editing might not explicitly refer to CRISPR technology. Future research may extend attention to scholarly works done on the social and economic implications of genome editing more generally. Finally, the present study looked at CRISPR research published in English, but future work could be done on non-English literature which could provide a complementary perspective on genome editing, especially from the Global South.

Authorship Contribution Statement: Both the authors declare that they equally contributed to the

research and drafting of the paper. They both share responsibilities for the manuscript. They have both reviewed and approved the manuscript prior to submission.

Authors' Confirmation Statement: Both the authors confirm that the manuscript has been submitted solely to this journal and is not published, in press, or submitted elsewhere.

Authors' Disclosure Statements: Both the authors declare that no actual or potential competing interests or personal financial interests exist.

Funding Statement: No funding was received for this study.

References

- Ledford H. CRISPR, the disruptor. Nat News 2015; 522(7554): 20–24. DOI: 10.1038/522020a.
- Barrangou R, Doudna JA. Applications of CRISPR technologies in research and beyond. *Nat Biotechnol* 2016; 34(9): 933–941. DOI: 10.1038/ nbt.3659.
- Barrangou R, Horvath P. A decade of discovery: CRISPR functions and applications. Nat Microbiol 2017; 2(7): 1–9. DOI: 10.1038/nmicrobiol.2017.92.
- 4. Sarewitz D. CRISPR: Science can't solve it. Nat News 2015; 522(7557): 413–414. DOI: 10.1038/522413a.
- Jinek M, Chylinski K, Fonfara I, et al. A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. *Science* 2012; 337(6096): 816–821. DOI: 10.1126/science.1225829.
- Nestor MW, Wilson RL. Beyond mendelian genetics: Anticipatory biomedical ethics and policy implications for the use of CRISPR together with gene drive in humans. *Bioeth Ing* 2020; 17(1): 133–144. DOI: 10.1007/s11673-019-09957-7.
- Wesseler J, Politiek H, Zilberman D. The economics of regulating new plant breeding technologies-implications for the bioeconomy illustrated by a survey among Dutch plant breeders. *Front Plant Sci* 2019; 10: 1597. DOI: 10.3389/fpls.2019.01597.
- Evitt NH, Mascharak S, Altman RB. Human germline CRISPR-Cas modification: Toward a regulatory framework. *Am J Bioeth* 2015; 15(12): 25–29. DOI: 10.1080/15265161.2015.1104160.
- Asquer A, Krachkovskaya I. Uncertainty, institutions and regulatory responses to emerging technologies: CRISPR gene editing in the US and the EU (2012–2019). *Regul Gov* 2020; in press. DOI: 10.1111/rego.12335.
- Rotolo D, Hicks D, Martin BR. What is an emerging technology? *Res Policy* 2015; 44(10): 1827–1843. DOI: 10.2139/ssrn.2743186.
- Fredrickson DS. Asilomar and recombinant DNA: The end of the beginning. In *Biomedical Politics*. Washington, DC: The National Academies Press, 1991:258–292. DOI: 10.17226/1793.
- Mehravar M, Shirazi A, Nazari M, et al. Mosaicism in CRISPR/Cas9-mediated genome editing. *Dev Biol* 2019; 445(2): 156–162. DOI: 10.1016/ j.ydbio.2018.10.008.
- 13. Alphey L. Can CRISPR-Cas9 gene drives curb malaria? *Nat Biotechnol* 2016; 34(2): 149–150. DOI: 10.1038/nbt.3473.
- Greene M, Master Z. Ethical issues of using CRISPR technologies for research on military enhancement. *Bioeth Ing* 2018; 15(3): 327–335. DOI: 10.1007/s11673-018-9865-6.
- Khan MZ, Zaidi SSEA, Amin I, et al. A CRISPR way for fast-forward crop domestication. *Trends Plant Sci* 2019; 24(4): 293–296. DOI: 10.1016/ j.tplants.2019.01.011.
- Waltz E. Gene-edited CRISPR mushroom escapes US regulation. Nat News 2016; 532(7599): 293–293. DOI: 10.1038/nature.2016.19754.
- Greely HT. CRISPR'd babies: Human germline genome editing in the 'He jiankui affair. J Law Biosci 2019; 6(1): 111–183. DOI: 10.1093/jlb/lsz010.

AO4

Asquer and Krachkovskaya

- Aria M, Cuccurullo C. Bibliometrix: An R-tool for comprehensive science mapping analysis. J Infometr 2017; 11(4): 959–975. DOI: 10.1016/ j.joi.2017.08.007.
- 19. van Eck NJ, Waltman L. VOSviewer Manual. Leiden, The Netherlands: Universiteit Leiden, 2013.
- Baltimore D, Berg P, Botchan M, et al. A prudent path forward for genomic engineering and germline gene modification. *Science* 2015; 348(6230): 36–38. DOI: 10.1126/science.aab1028.
- 21. Lanphier E, Urnov F, Haecker SE, et al. Don't edit the human germ line. Nat News 2015; 519(7544): 410–411. DOI: 10.1038/519410a.
- National Academies of Sciences, Engineering, and Medicine. Human Genome Editing: Science, Ethics, and Governance. Washington, DC: National Academies Press, 2017. DOI: 10.17226/24623.
- Liang P, Xu Y, Zhang X, et al. CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes. *Protein Cell* 2015; 6(5): 363–372. DOI: 10.1007/s13238-015-0153-5.
- Doudna JA, Charpentier E. The new frontier of genome engineering with CRISPR-Cas9. Science 2014; 346(6213): 1258096. DOI: 10.1126/ science.1258096.
- Cong L, Ran FA, Cox D, et al. Multiplex genome engineering using CRISPR/cas systems. *Science* 2013; 339(6121): 819–823. DOI: 10.1126/ science.1231143.
- Hsu PD, Lander ES, Zhang F. Development and applications of CRISPR-Cas9 for genome engineering. *Cell* 2014; 157(6): 1262–1278. DOI: 10.1016/j.cell.2014.05.010.
- 27. Liao SM. The basis of human moral status. J Moral Philos 2010; 7(2): 159–179. DOI: 10.1163/174552409X12567397529106.
- Ma H, Marti-Gutierrez N, Park SW, et al. Correction of a pathogenic gene mutation in human embryos. *Nature* 2017; 548(7668): 413–419. DOI: 10.1038/nature23305.
- Ran FA, Hsu PD, Wright J, et al. Genome engineering using the CRISPR-Cas9 system. Nat Protoc 2013; 8(11): 2281–2308. DOI: 10.1038/nprot.2013.143.
- 30. Jasanoff S, Hurlbut JB. A global observatory for gene editing. *Nature* 2018; 555: 435–437. DOI: 10.1038/d41586-018-03270-w.
- Lander ES. Cutting the gordian helix—Regulating genomic testing in the era of precision medicine. N Engl J Med 2015; 372(13): 1185–1186. DOI: 10.1056/NEJMp1501964.
- Koonin EV. CRISPR: A new principle of genome engineering linked to conceptual shifts in evolutionary biology. *Biol Philos* 2019; 34(1): 1–30. DOI: 10.1007/s10539-018-9658-7.
- Esvelt KM, Smidler AL, Catteruccia F, et al. Emerging technology: Concerning RNA-guided gene drives for the alteration of wild populations. *Elife* 2014; 3: E03401. DOI: 10.7554/eLife.03401.
- Mali P, Yang L, Esvelt KM, et al. RNA-guided human genome engineering via Cas9. Science 2013; 339(6121): 823–826. DOI: 10.1126/ science.1232033.
- Lander ES. The heroes of CRISPR. Cell 2016; 164(1–2): 18–28. DOI: 10.1016/j.cell.2015.12.041.
- Lander ES, Baylis F, Zhang F, et al. Adopt a moratorium on heritable genome editing. *Nature* 2019; 567: 165–168. DOI: 10.1038/d41586-019-00726-5.
- Brokowski C. Do CRISPR germline ethics statements cut it? CRISPR J 2018; 1(2): 115–125. DOI: 10.1089/crispr.2017.0024.
- Candes E, Fan Y, Janson L, et al. J R Stat Soc B 2018; 80(3): 551–577. DOI: 10.1111/rssb.12265.
- Charo RA, Greely HT. CRISPR critters and CRISPR cracks. Am J Bioeth 2015; 15(12): 11-17. DOI: 10.1080/15265161.2015.1104138.
- De Vries RG, Tomlinson T, Kim HM, et al. The moral concerns of biobank donors: The effect of non-welfare interests on willingness to donate. *Life Sci Soc Policy* 2016; 12(1): 1–15. DOI: 10.1186/s40504-016-0036-4.
- Harris J. Germline modification and the burden of human existence. *Camb Q Healthc Ethics* 2016; 25(1): 6–18. DOI: 10.1017/ S0963180115000237.
- 42. Hildt E. Human germline interventions-think first. Front Genet 2016; 7: 81. DOI: 10.3389/fgene.2016.00081.
- Krishan K, Kanchan T, Singh B. Human genome editing and ethical considerations. *Sci Eng Ethics* 2016; 22(2): 597–599. DOI: 10.1007/s11948-015-9675-8.
- O'Keefe M, Perrault S, Halpern J, et al. Editing' genes: A case study about how language matters in bioethics. *Am J Bioeth* 2015; 15(12): 3–10. DOI: 10.1080/15265161.2015.1103804.

- Sparrow R. Yesterday's child: How gene editing for enhancement will produce obsolescence—and why it matters. Am J Bioeth 2019; 19(7): 6–15. DOI: 10.1080/15265161.2019.1618943.
- Flegal JA, Gupta A. Evoking equity as a rationale for solar geoengineering research? Scrutinizing emerging expert visions of equity. *Int Environ Agreements* 2018; 18(1): 45–61. DOI: 10.1007/s10784-017-9377-6.
- Fraser A. Land grab/data grab: Precision agriculture and its new horizons. J Peasant Stud 2019; 46(5): 893–912. DOI: 10.1080/ 03066150.2017.1415887.
- Klerkx L, Rose D. Dealing with the game-changing technologies of agriculture 4.0: How do we manage diversity and responsibility in food system transition pathways? *Glob Food Sec* 2020; 24: 100347. DOI: 10.1016/j.gfs.2019.100347.
- McLeod C, Nerlich B. Synthetic biology, metaphors and responsibility. Life Sci Soc Policy 2017; 13(1): 1–13. DOI: 10.1186/s40504-017-0061-y.
- Ribeiro B, Bengtsson L, Benneworth P, et al. Introducing the dilemma of societal alignment for inclusive and responsible research and innovation. *J Responsible Innov* 2018; 5(3): 316–331. DOI: 10.1080/ 23299460.2018.1495033.
- Rose DC, Morris C, Lobley M, et al. Exploring the spatialities of technological and user re-scripting: The case of decision support tools in UK agriculture. *Geoforum* 2018; 89: 11–18. DOI: 10.1016/ j.geoforum.2017.12.006.
- Sponsler DB, Grozinger CM, Hitaj C, et al. Pesticides and pollinators: A socioecological synthesis. *Sci Total Environ* 2019; 662: 1012–1027. DOI: 10.1016/j.scitotenv.2019.01.016.
- Vermeulen N, Haddow G, Seymour T, et al. 3D bioprint me: A socioethical view of bioprinting human organs and tissues. J Med Ethics 2017; 43(9): 618–624. DOI: 10.1136/medethics-2015-103347.
- Conko G, Kershen DL, Miller H, et al. A risk-based approach to the regulation of genetically engineered organisms. *Nat Biotechnol* 2016; 34(5): 493–503. DOI: 10.1038/nbt.3568.
- Cui K, Shoemaker SP. Public perception of genetically-modified (GM) food: A nationwide chinese consumer study. NPJ Sci Food 2018; 2(1): 1–8. DOI: 10.1038/s41538-018-0018-4.
- Herring A, Messana A, Bara AM, et al. Generation of a TLE1 homozygous knockout human embryonic stem cell line using CRISPR-Cas9. *Stem Cell Res* 2016; 17(2): 430–432. DOI: 10.1016/j.scr.2016.09.009.
- Lusk JL, McFadden BR, Wilson N. Do consumers care how a genetically engineered food was created or who created it? *Food Policy* 2018; 78: 81–90. DOI: 10.1016/j.foodpol.2018.02.007.
- Wesseler J, von Braun J. Measuring the bioeconomy: Economics and policies. Annu Rev Resour Econ 2017; 9: 275–298. DOI: 10.1146/annurevresource-100516-053701.
- Wong AYT, Chan AWK. Genetically modified foods in China and the United States: A primer of regulation and intellectual property protection. *Food Sci Hum Well* 2016; 5(3): 124–140. DOI: 10.1016/ j.fshw.2016.03.002.
- Zetterberg C, Björnberg KE. Time for a new EU regulatory framework for GM crops? J Agric Environ Ethics 2017; 30(3): 325–347. DOI: 10.1007/ s10806-017-9664-9.
- Zilberman D, Gordon B, Hochman G, et al. Economics of sustainable development and the bioeconomy. *Appl Econ Perspect Policy* 2018; 40(1): 22–37. DOI: 10.1093/aepp/ppx051.
- Burt A, Coulibaly M, Crisanti A, et al. Gene drive to reduce malaria transmission in Sub-Saharan africa. J Responsible Innov 2018; 5(Suppl. 1): S66–S80. DOI: 10.1080/23299460.2017.1419410.
- Kuzma J, Gould F, Brown Z, et al. A roadmap for gene drives: Using institutional analysis and development to frame research needs and governance in a systems context. J Responsible Innov 2018; 5(Supp. 1): S13–S39. DOI: 10.1080/23299460.2017.1410344.
- Leitschuh CM, Kanavy D, Backus GA, et al. Developing gene drive technologies to eradicate invasive rodents from islands. J Responsible Innov 2018; 5(Supp. 1): S121–S138. DOI: 10.1080/23299460. 2017.1365232.
- Lodge DM, Simonin PW, Burgiel SW, et al. Risk analysis and bioeconomics of invasive species to inform policy and management. *Annu Rev Envi*ron Resour 2016; 41: 453–488.
- Meghani Z, Kuzma J. Regulating animals with gene drive systems: Lessons from the regulatory assessment of a genetically engineered mosquito. J Respnsible Innov 2018; 5(Supp. 1): S203–S222. DOI: 10.1146/annurev-environ-110615-085532.

AQ1 Research on CRISPR in Social Sciences and Humanities

- Min J, Smidler AL, Najjar D, et al. Harnessing gene drive. J Responsible Innov 2018; 5(Suppl. 1): S40–S65. DOI: 10.1080/23299460.2017.1415586.
- Serr ME. Towards a Genetic Approach to Invasive Rodent Eradications: Assessing Reproductive Competitiveness between Wild-Derived and Laboratory Mice. PhD dissertation, North Caroline State University, Releigh, NC, 2019.
- Scott MJ, Gould F, Lorenzen M, et al. Agricultural production: Assessment of the potential use of Cas9-mediated gene drive systems for agricultural pest control. *J Responsible Innov* 2018; 5(Suppl. 1): S98–S120. DOI: 10.1080/23299460.2017.1410343.
- Cavaliere G. A 14-day limit for bioethics: The debate over human embryo research. *BMC Med Ethics* 2017a; 18(1): 1-12. DOI: 10.1186/ s12910-017-0198-5.
- Cavaliere G. Genome editing and assisted reproduction: Curing embryos, society or prospective parents? *Med Health Care Philos* 2018; 21(2): 215–225. DOI: 10.1007/s11019-017-9793-y.
- Chen SC, Wasserman DT. A framework for unrestricted prenatal wholegenome sequencing: Respecting and enhancing the autonomy of prospective parents. *Am J Bioeth* 2017; 17(1): 3–18. DOI: 10.1080/ 15265161.2016.1251632.
- Blasiak R, Jouffray JB, Wabnitz CC, et al. Corporate control and global governance of marine genetic resources. *Sci Adv* 2018; 4(6): eaar5237. DOI: 10.1126/sciadv.aar5237.
- MacIntyre CR, Engells TE, Scotch M, et al. Converging and emerging threats to health security. *Environ Syst Decis* 2018; 38(2): 198–207. DOI: 10.1007/s10669-017-9667-0.
- Herring R, Paarlberg R. The political economy of biotechnology. Annu Rev Resour Econ 2016; 8: 397–416. DOI: 10.1146/annurev-resource-100815-095506.
- Kosal ME. Emerging life sciences and possible threats to international security. Orbis 2020; 64(4): 599–614. DOI: 10.1016/ j.orbis.2020.08.008.