The Moral Economy of Genome Editing

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Acknowledgments

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Abstract

This paper lays groundwork for future research on the politics of knowledge by describing the interrelation between structural changes at the interface of academic and industry science and the production of values and value surrounding emergent technologies. Understanding the interplay of the structural and affective conditions from which new technology is constructed contributes to contemporary theories of the affinity between science and capitalism.

Keywords: laboratory ethnography, science and knowledge, technology, neoliberal science

Previous sociological research suggests that whether a new technology is fated to be a flash in the pan or the basis for a durable institution does not just depend on whether scientists or engineers can get the technology to work or not. It also depends on whether reproducible alignment can form between the actors involved in the social construction of a technology. The success of these alignments will also depend on whether a corresponding social order and value framework can be co-produced and normalized (Frickel and Moore 2006; Jasanoff 2004; Klein and Kleinman 2002; May 2006; Pinch and Bijker 1984). This paper describes the system of affect, tension, and value that facilitates the alignment between actors for the case of CRISPR-Cas9 (hereafter CRISPR). CRISPR is an emergent class of biotechnologies that allow researchers to "edit" DNA with unprecedented ease and represents an exceptional case for studying the politics of emergent technology.

With over 20 clinical trials for treating human diseases with genome-editing technologies underway (Henderson 2021; Urnov 2020), scientists and regulators wait anxiously for early evidence of patient outcomes. Alongside the scientists and regulators, investors watch to see which academic teams and companies will be the first to either capture the promised financial gains and scientific accolades of successfully treating patients by modifying their DNA or face sobering clinical results, adverse reactions, or stock buybacks from over-valuation. Academic scientists, research hospitals, biotechnology firms, pharmaceutical companies, regulatory bodies, patients, and patient communities all have a direct stake in the development of genome editing.

Despite this broad set of stakeholders, the field of genome editing is characterized by a narrow mode of alignment: partnerships between academic laboratories and the biotech and pharma industries. These partnerships have become the norm in 21st century biomedicine. The routinization of academic-industry relations is central to the array of practices that universities and their faculty engage in to produce revenue from research. Under the analytic umbrella of *academic capitalism*, sociological research has described how this neoliberal mode of organizing science has become an imperative for both universities and the state (Clark 1998; Etzkowitz 2008; Hackett 1990, 2014; Lave, Mirowski, and Randalls 2010; Moore et al. 2011; Shibayama, Walsh, and Baba 2012). Research in the sociology of organizations has shown that ecosystems made up of universities and technology startups are hubs of production for new biotechnologies. This work illustrates how these arrangements of different kinds of organizations shape scientific work and how well-positioned

actors are able to concentrate both knowledge and capital to set the terms of exchange and production for new technologies (Oliver 2004; Powell, Koput, and Smith-Doerr 1996; Shwed and Bearman 2010). In a separate vein, research has shown how science can shape the production of values and value that can then spread across domains of society and, conversely, how markets can shape the moral order(s) underlying science and medicine (Fourcade and Healy 2007; Healy 2006; Livne 2019; Quinn 2008; Zelizer 2005, 2017).

This paper extends the sociological research on academic capitalism, to study the conditions from which new organizational forms and moral discourse surrounding genome editing are emerging. I begin by surveying the existing body of literature on academic capitalism to describe the cultural impact of the normalization of academic and industry relations. From this survey, I identify an opportunity to examine the relationship between academic capitalism and the construction of technology. To do so, I build on sociological research that has characterized the role of affect and emotion in scientific work (Parker and Hackett 2012). Do partnerships between academic labs and for-profit biotech and pharma industries shape the values that scientists use to advance genome editing? If so, how and to what effect? How are value frameworks produced or adapted to establish moral economies for technologies that are in early stages of development?

After providing background on genome editing, I describe the participant observation and interview data drawn on to describe the micropolitics of CRISPR-based research as it unfolds. Drawing from a larger ethnographic project on the development of genome-editing technology, this paper sifts through a thicket of relationships and interactions between academic scientists, industry researchers, venture capitalists, bioethicists, and clinicians to identify the development of discursive positions and frameworks of meaning that advance human genome editing. In the main body of the article, I argue that academic capitalism has shaped genome editing in two mutually enforcing ways: structurally, when the for-profit and academic actors attempting to control the fate of genome editing become aligned; and affectively, when moral commitments become embedded in market ideologies about what clinical genome editing will look like. Scientists must ultimately manage conflict between competing obligations and feelings of fear and hype when constructing a path for genome editing. This paper lays groundwork for future research on the politics of knowledge by describing the interrelation between structural changes at the interface of academic and industry science and the production of values and value surrounding emergent technologies. I conclude by discussing the theoretical implications of my analysis for the sociology of technology and studies of the affinity between science and capitalism.

THE MORAL ECONOMIES OF ACADEMIC CAPITALISM

Previous work has documented and analyzed the institutional shifts where academic organizations are increasingly adopting the practices and bureaucratic frameworks of for-profit organizations in industry. Building on the theoretical grounds laid by Max Weber and Karl Mannheim, this work argues that beyond the corporatization of higher education (Slaughter and Rhoades 2004) and the establishment of academic entrepreneurs (Jones 2009), academic institutions have shifted ideologically to align with neoliberal economic and social policies. Under the analytic lens of *academic capitalism* this body of scholarship has opened up a line of inquiry into the ways in which these shifts have re-shaped scientific work (Hackett 1990). One key insight has been that it is not that economic incentives are somehow contaminating otherwise "pure" science, but that capitalism is a cultural way of producing, attributing and accumulating multiple forms of value

(Fochler 2016). Like other modes of production, academic-industry relations are facilitated by a *moral economy*.

Building on Fourcade (2017), I here use the concept of moral economy to examine the circulation and exchange of intuitions, feelings, opinions and discourses. This understanding of moral is not normative in the sense of asking whether CRISPR is good or bad, but is instead sociological: What do scientists categorize as moral and what are the justifications that scaffold their own debates about what is meaningful and good? In her extension of the social constructivist program of science studies historian of science Lorraine Daston describes the moral economy[1] as, "a web of affect-saturated values that stand and function in well-defined relationship to one another (…) a balanced system of emotional forces, with equilibrium points and constraints," (Daston 1995). Subsequent work in science studies has illustrated how affective and value commitments shape the epistemic foundations of science (e.g. Strasser 2011). Here, I unpack the ubiquity of the economization and capitalization of academic science and identify the effects of these shifts on how genome-editing technologies are constructed.

Understanding the Capitalist Conditions of Contemporary Science

Within universities, organizational units manage the potential for profitability of scientific discoveries and for managing claims to intellectual property rights (Berman 2012). Technology transfer offices, now ubiquitous, bureaucratically regulate the sharing of research materials and instruments (Colyvas 2007). These changes have put pressure on scientists to patent the products of their work (Fabrizio and Di Minin 2008) and add bureaucratic barriers to the open exchange of research materials between labs.

Interactions between universities and industry can take a variety of forms. For example, scientists in academic and industry may engage in informal interactions where ideas and know-how are shared, such as shared lab meetings, discussions at conferences, and correspondence; labs in academia and industry labs may share research materials and reagents; companies that manufacture equipment for laboratories may beta-test their instruments in academic facilities to learn how their products can be integrated with the workflow of scientists in different specialties (sometimes leading to formal purchase or exchange of these materials as mediated by technology transfer offices of the university); and formal partnerships can be established where capital from companies helps fund the work of academic labs, either via paid salaries of individual personnel, unrestricted funds for general research expenses, or contracted work. Paralleling the increased reliance on for-profit industry investment in academic science, philanthropic funding for biomedical research has also increased since the end of the 20th century (Murray 2013).

Structural changes within universities and interactions with organizations in biotechnology and pharma have realigned values and norms in molecular biology and biochemistry. These changes put the values scientists receive through their training, such as openness and disinterestedness, in conflict with the values endemic to work with for-profit entities, such as secrecy and corporate ownership over intellectual products (Shibayama et al. 2012). Previous research suggests that this conflict creates ambivalence, alienation, and anomie in academic scientists via competitive and financial incentives and can drive scientists to engage in misconduct or deviant behavior (Croissant and Restivo 2001; Hackett 1990). This process has been characterized by social scientists as an asymmetrical convergence of scientific work and norms in industry and academia, wherein the norms of industry take increasing precedence in universities, rather than academic norms spreading and reproducing in industry (Kleinman and Vallas 2001; Mirowski 2011). In the fields of genetics

and plant biology this leads scientists to become more insular (Campbell et al. 2002; Evans 2010). In others it can shape entire research trends–for example, research on the influence of the pharmaceutical industry on biomedicine has suggested that biased clinical results and regulatory circumvention increase with for-profit partnerships (Dumit 2012; Sismondo 2007, 2008). Moreover, financial conflicts of interest can shape regulation and policy surrounding the uses and ownership of emerging technology (Krimsky and Schwab 2017; Sleeboom-Faulkner 2019).

These modes of organizing science shape and can fortify the epistemic conditions from which technology and knowledge are produced and, in that sense, carry important normative dimensions. For example, academic capitalism shapes the valuation of technology and biological materials. It affects local economies of the sale, donation, exchange and travel of bodies, tissue, blood and individual's biological data (Abadie 2010; Almeling 2011, 2011; Cooper and Waldby 2014; Franklin 2006; Healy 2006; Rajan 2006). Anthropological work in this vein has shown that the effects of academic capitalism vary from country to country in ways that are shaped by global economic and political forces (Deomampo 2016; Greenhalgh 2016; Ocal and Kavak 2018; Rajan 2005). To offer an example outside of biomedicine, in the field of artificial intelligence, whether research is funded through industry partnerships or through national grants can shape which areas of research are valued by scientists and can influence the aims of their work (Hoffman 2017).

What is less understood is the effect that academic capitalism can have on the construction of an emergent technology and the values that justify and legitimate its use. How are value frameworks produced or adapted to create moral economies for emerging technologies? How does the alignment of financial and moral interests between academic scientists, physicians, investors, industry researchers, patients and users shape this production? In addressing these questions, this paper empirically grounds Fourcade's observations on the moral philosophy underlying the "will to progress" in late-stage capitalism: namely, that economic and scientific development is fueled by the belief that technology is inherently egalitarian and democratic, and always aligned with what is seen as morally good (Fourcade 2018). To do this, I draw out the structural and affective dimensions of genome-editing.

DATA AND METHODS

To explain how the local constellation of actors in the San Francisco Bay Area have contributed to the moral economy of genome editing, I draw from data collected from 2015 to 2019 as part of a larger project that traces the institutionalization of CRISPR that combines multi-sited participant observation, in-depth interviews, and archival research. By following proponents of genome editing into their social networks and capturing their engagements in sites of agenda setting, strategic planning, problem resolution and deliberation, this paper develops an empirical account of how and in what ways the development of genome editing has been shaped by partnerships between academia and industry.

Access to closed meetings where scientists spoke freely about their connections to industry was made possible by the rapport and support built for this project over course the of two years as a "house sociologist" in two laboratories in the San Francisco Bay Area. Many of my recorded observations came from attending weekly laboratory group-meetings and project-specific meetings. In a few instances, researchers from other laboratories and biotechnology start-ups would present their work, often as part of a collaborative opportunity. Lab meetings are routinized sites of

interaction where lab members evaluated the epistemic value of practices and techniques and discussed the trajectory of the areas of research they worked on. Beyond the observations of daily scientific work, I paid close attention to selected formative moments—what Hardy and Maguire (2010) call "field-configuring events"—where I could directly observe stakeholders in social context as they attempt to define, assert, and contest genome-editing discourse with each other and their professional communities. In addition to my observations in lab meetings, I attended 20 workshops and conferences on genome editing. At these sites, scientists went on stage on present not only their work, but their visions for the field. Over the course of this fieldwork, 50 semi-structured and ethnographic interviews were conducted with scientists, regulators, and bioethicists using snowball and purposive sampling. These interviews served to deepen my understanding of the projects that post-docs, graduate students, and technicians were working on and to probe about their attitudes regarding genome editing and the lab's relationships with funders and industry partners.

Reflexivity was instrumental in assessing the affective commitments of scientists in social situations with one another. As a social scientist, I sometimes encountered efforts to coopt me into a process of legitimation–for example, I was invited to participate in a meeting with a potential philanthropic funder that was interested in supporting humanistic and bioethics research on genome editing. I participated in lab meetings asking various questions about the reasoning behind experimental techniques and offered suggestions for resolving coordination challenges the lab encountered. As a member of the lab, I presented on the normative dimensions of collaboration in science, disability justice approaches to genome editing, and reported back to the lab from larger conferences and symposia they had not attended. My participation in a bioethics working group held by the institute where I conducted fieldwork also meant that I was actively involved in the production of normative discourse around genome editing. These responsibilities fed into my reflexive positioning as a social scientist.

Data obtained from observations in field notes, transcripts of audio-recorded meeting (where possible), and interview transcripts were analyzed in two iterative stages: First, data was coded manually to generate a set of content themes in line with the theoretical concepts surveyed in the previous literature under the frameworks of sociology of organization, social construction of technology, and academic capitalism. Codes around the affective and moral dimensions of genome editing discourse were identified abductively (Tavory and Timmermans 2014). Second, memos were subsequently produced from field notes and interview summaries to develop these themes and offer a descriptive account of salient cognitive, organizational, and discursive patterns that appeared in the data, as well as a map of the network of actors involved. Together this strategy is well adapted to the observational data of stakeholders developing consensus of the direction of research, contesting the meaning of lexicon, establishing best practices, and arguing over ethical imperatives and the permeability of boundaries between academia and industry.

From this analysis two broad themes were identified: the organizational dimensions of genome editing and the affective experiences of scientists. Understanding the relationship between these two reveals how academic capitalism has shapes the construction of emergent technology. In the discussion, I return to this relationship, where the institutionalized imperative to achieve social impact and alleviate suffering from disease becomes synonymous with commercialization.

BUILDING CRISPR ORGANIZATIONS

The distribution of resources and expertise of academic capitalism in the SF Bay Area have first shaped the creation of organizational structures in which genome editing is practiced. To build

these organizations, academic scientists partnered with philanthropic and industry firms to create reproducible funding streams for developing CRISPR and public events that would legitimize this technology. Public conferences further helped frame CRISPR as a public good to be developed at the intersection of industry and academia. Alignment with commercial entities was advantageous for genome-editing scientists as it opened avenues for the spread and refinement of the technology. Building on the momentum of hype surrounding genome editing and a surge in publications that used CRISPR-based techniques, academic actors sought to develop bridges between their universities, biotechnology startups they had helped found, and more established pharmaceutical companies who were curious about the commercial and research prospects of genome editing. At research sites, key academic actors operated entrepreneurially (Jones 2009) to shape how the organizations producing CRISPR were constructed financially and ideologically.

Innovative Genomics from Initiative to Institute: the Interstitial Organization

The creation of a center of organizational pull in the SF Bay Area re-ordered social ties between individual academic and commercial laboratories specifically around the practice of CRISPR-Cas9 technology. This center of gravity, the Innovative Genomics Institute (IGI), started as an initiative in 2014 led by Jennifer Doudna, one of the co-inventors of the CRISPR-Cas9 system and Jonathan Weissman, another lead developer. IGI was conceived with the goal of validating, refining, and improving the visibility of genome-editing techniques. It was "dedicated to the enhancement and proliferation of genome editing research and technology in both the academic and commercial research communities" (IGI website Dec. 2014). In this capacity, IGI is an *interstitial organization,* connecting faculty and students at universities with market actors (Ocal and Kavak 2018; Slaughter and Rhoades 2004).

In part because of its interstitial goals the identity and management of the organization was ambiguous to student researchers, employees, and principal investigators. At times the organization operated as collaborative space, encouraging different labs to share resources and tacit knowledge. At others, it acted in the spirit of a company, fighting alongside the UC system for control of the intellectual property rights over CRISPR. Still in other situations, it aimed to act as educational site, offering both practical workshops and training programs for undergraduates, graduate students, and senior researchers, as well as educational outreach efforts in nearby high schools.

At its conception, the initiative was comprised of a small collective of around 10 labs at UC Berkley, UC San Francisco and at Stanford. It received initial funding from a Hong Kong business magnate's philanthropic organization, the Li Ka-Shing Foundation–the second largest private philanthropic foundation in the world. With its name on life sciences and medical buildings at UC Berkeley and Stanford, the Li "Ka-ching!" foundation, as one senior scientist put it, had earned a reputation for starting large research organizations from scratch. As an initiative, the IGI awarded early-stage project funding to labs interested in developing CRISPR-based techniques. In addition to funding, the IGI also began to offer key scaffolding for the practice of genome editing in the form of reagents, protocols, and workshops. Overall, the IGI included work in molecular biology, biochemistry, plant biology, microbial biology, and biomedicine with CRISPR as its keystone, ambitiously attempting to align multiple disciplines and the markets they are connected to. This broad organizational scope reflected both the novelty of CRISPR and its wide applicability across the life sciences.

In January 2016, these ambitious goals paid off. The initiative matured into an institute, after receiving further consecration from the University of California Office of the President and $43

million dollars in funding from gifts, grants, and industry sponsorship, combined with commitments of $30 million and matching contributions of $50 million dollars from the University. Throughout its growth, IGI leadership maintained close ties with emerging biotechnology startups focused on developing CRISPR therapeutics, several of which they themselves had founded. Excluding funds received for the conduct of research from private firms, survey and self-reported conflict of interest data available through state funding bodies shows that scientists involved in developing genome editing tools individually held from $40-$150 thousand dollars in equity in biotech and pharmaceutical companies in any given year (Wei, Waldman, and Armstrong 2019). With the growth of the IGI as an institute, the directors restructured the leadership of the organization, in part to bring together UC Berkeley and UCSF in a co-venture. Throughout this process of maturation, faculty and administrators coordinated across a variety of private and governmental organizations to legitimize and establish the IGI. Access to stably reproducing funding streams also allowed the creation of permanent positions for research scientists, technicians, a biostatistician, a patent specialist, and fundraising personnel directly under IGI management in addition to the lab personnel that made up the laboratories affiliated with the organization. The IGI further matured once it moved to take over a state-of-the-art multi-story building. With a physical hub, came additional coordination opportunities such as regularly occurring events and greater investment in laboratory infrastructure that could advance CRISPR.

The IGI's interstitial characteristics are exemplified by its Entrepreneurial Fellows Program, which professionalizes scientists at the postdoctoral stage of their careers. This program was "designed to catalyze the translation and commercialization of innovative research discoveries for practical benefit, this new program builds strong support networks in which accomplished, entrepreneurial-minded researchers are enabled to make substantial contributions to the biotech economy, and ultimately introduce breakthrough discoveries to the market," (IGI Website, September 2016). The IGI afforded one selected applicant a year up to $250 thousand a year for research for a maximum of two years. In this way IGI leadership aimed to develop the organization into a biotech incubator, linking young researchers with lawyers who can help individuals start their own companies and protect the intellectual property of their inventions.

The interstitial character of the IGI is also manifested in the multi-valence of organization's mission. The public-facing goals of the IGI were highly ambitious: 1) to cure genetic diseases by pioneering what they would call "genome surgery"; 2) to ensure healthy food for the world's growing population by addressing food safety and security; 3) to discover new antibiotics to solve the drug resistance crisis; and 4) to lead policy and bioethics debates surrounding the technology. Bruno Latour's two-faced Janus offers a heuristic for explaining this ideologically (Figure 1.), wherein the IGI promised a CRISPR-panacea to funders and reporters with one face, and with the other, aimed to establish and refine experimental practices with CRISPR in the lab by studying the fundamental molecular mechanisms of the technology.

These aims had a direct bearing on the discourse that would come to construct the dominant imaginary of what CRISPR is understood to be in a broader social context. For example, one of the final drafts of a public handout for dissemination to funders describes the overarching goals of the IGI in relation to CRISPR. In it, CRISPR was defined as "a molecular scalpel with the capacity to correct errors in the genetic alphabet of plants, animals, or people, [it] can be programmed to reach into a genome with unprecedented ease and precision." (Public Handout v.10, May 2017). For the scientists at IGI, the metaphor of the scalpel helped communicate what the technology could be used for.

However, in practice, it was still uncertain whether the technology would be scalable. The metaphor obfuscated the molecular mechanisms underlaying the technology which were still being characterized. In one commentary, a scientist suggested that a more accurate metaphor was a sledgehammer, wherein scientists were "sculpting genomes in the dark," (Conklin 2013). While "ease" and "precision" were hallmarks of the technology for designing and conducting experiments, researchers recognized a wide variety of basic technical challenges that required significant investment to be addressed (Cox, Platt, and Zhang 2015; Doudna 2020; Kempton and Qi 2019; Zhang, Wen, and Guo 2014). Researchers in one lab meeting acknowledged that "the technology does not always work the way it's supposed to on paper, so we're still feeling our way in the dark, what does this do and what does it not do." Scientists outside of leadership generally felt that the internal goals of research programs in the IGI differed in scope from the broader goals of the organization.

This disconnect between the imagined potential of genome-editing technology and the banality of the technical limitations of the technology in practice was characteristic of the discourse around CRISPR and was undergirded by a split in the moral economy underlying scientific practice. On the one hand, the technology may address issues where scientists believed the ethical imperative was clear, such as alleviating patients' suffering from severe genetic diseases or helping cassava farmers dealing with blight. On the other, the ambitious imperatives justified the funding for fundamental and exploratory research to help develop technical protocols that would, in principle, contribute to these broader impacts. As I describe below, this dynamic triggered broader affective expectations about what genome editing was and when its applications would reach those in need. As the IGI continued to mature organizationally by establishing reproducible funding streams and positions for technicians, the scientists in the IGI developed and refined technical protocols that would help push CRISPR out of the laboratory and into the market.

Shaping the direction of research: CRISPR-ventures

When scientists worked to translate CRISPR from an experimental tool used in academic labs to a productive tool in industry, the direction of their research also changed. In this sense, as others research has shown (Hoffman 2011), academic capitalism can shift research priorities. Here I examine a case where the creation of a biotechnology startup coincided with a shift in direction of work in the lab to highlight two ways this can occur: indirectly by determining which applications of CRISPR are likely to yield more medically relevant outcomes and which applications are viable in the market; and directly by shaping the organization of projects in a research program. This doesn't mean that research is being directed by which areas are more profitable or that scientist's choices are driven by a financial incentive, but that scientists' understanding and projections of how market actors will do research and on what diseases informs how they assign value to different areas of application for CRISPR in academia.

Over the course of my fieldwork one of the laboratories affiliated with the IGI pivoted their research program dramatically. Since 2005 the Nielsen Lab's research program had focused on using induced pluripotent stem cells (iPSC) to study cardiovascular diseases by engineering cardiomyocytes–heart cells. Early in the development of CRISPR, the principal investigator (PI) of the lab, Andrew Nielsen, perceived these new techniques to be still too unreliable for widespread use in biomedical research: he believed the innovation needed further proof of concept. This early hesitation to endorse the therapeutic application of CRISPR technologies stemmed from general

uncertainty over the regulation of new techniques and uncertainty over the ability to overcome technical limitations.

During one lab meeting Andrew discussed the emerging landscape of the field of genome editing with another IGI-affiliated PI. The senior scientists at the meeting projected, "therapeutic editing is going to remain a boutique area. But using editing to uncover more about disease etiology [...] every, single, pharma company is doing that." Under the competitive environment of both academic and for-profit genome-editing, researchers estimated that sticking with boutique research projects would be more scientifically productive in the long run. This was because industry research was becoming heavily invested in using CRISPR to characterize diseases to find "druggable targets," molecular sites where small molecules could be used to intervene in biochemical pathways. Each of these small molecules could then be tested in the clinic and turned into a drug. The saturation of this problem space meant unnecessary competition with well-funded industry research.

In 2016, Nielsen and the clinician in his lab, followed this line of reasoning and pivoted away from doing research on heart diseases. They instead identified research areas that more fully embraced the therapeutic potential of genome editing, despite their early hesitation. By early 2017 Nielsen started projects on two rare genetic diseases: Best disease, a kind of macular degeneration that leads to blindness, and Charcot-Marie-Tooth or CMT a hereditary neuropathy that causes progressive loss of muscle function and sensation. Working alongside the clinician in his lab and through discussions with other PIs at UCSF, Andrew chose these two diseases because in his estimation these would serve as a "proof of concept" for therapeutic editing and would keep the lab in that relatively boutique problem area. Because the patient population was small relative to other diseases–prevalence for Best disease in the United States is approximately 1 per 15,000 and CMT is 15.7 per 100,000 (Anon 2021)–Nielsen felt they were unlikely targets for pharmaceutical companies because they represented such a small market. Unpacking the conditions and motivations behind the shift opens up how academic capitalism, as a system of allocation of resources and relations between actors, shapes the organization of inquiry in science.

At one level, this transition was shaped by the specific arrangements of capital in the SF Bay Area. That year, the Chan-Zuckerberg BioHub (CZI) had pledged $600 million for biomedical research that broke the mold of academic innovation. Zuckerberg and Dr. Pricilla Chan said they would invest at least $3 billion over the next decade toward disease cure and prevention. CZI, as an L.L.C., would also be positioned to spend on for-profit companies (Benner 2016). In consultation with the BioHub's scientific advisors, Nielsen put together an application, "Genome Surgery, a Disruptive Approach to Human Genetic Disease" that directly appealed to the CZI's interest in non-traditional science innovation.

In addition to changes in the organizational environment, at another level, Nielsen's individual entrepreneurial goals were aligned with the shift in his research program. During this period, Andrew Nielsen and his colleagues founded a for-profit biopharmaceutical company, Almanor Therapeutics after receiving funding from high-profile biotech venture capitalists. The advertised aim of the company was to develop drugs for heart disease by targeting molecular pathologies heart muscle cells and use cutting-edge research using induced pluripotent cells and CRISPR technologies. The inception and unfolding of this new company, Almanor, offers an example of how alignment is achieved between academic researchers and venture capitalism.

In order to for the new company and the laboratory to align, there had to be a clear articulation of the projects the lab would be working on, who would be working on them and how data and results would be shared with the company. During an interview with a senior member of

the lab, I asked whether a shift to working on Best disease and CMT with CRISPR would prove challenging for the lab and whether it would force Nielsen to find new collaborative opportunities, since most of his work had been aligned with others in the field of cardiovascular disease research.

> "That, sorry? Um no, because the cardiomyocyte stuff is transitioning to Almanor. Which might be a good thing, because theres issues with conflict of interest and ethics, so it makes it cleaner and with interactions. Andrew's thing is not specific to one cell type, he is about the tools like genome engineering and editing so it doesn't really affect the fact that he is transitioning to other cell types […]. So I would say it hasn't. I mean maybe it sort of, maybe he has had to look more outwards to collaborate, […] But he is collaborating on the floor, because of Almanor, they are all founders apart from a couple of PIs, they are still invested in getting [the CRISPR and cardiomyocyte research] to work through Almanor."

The lab member described how because of the emergent partnership with the startup company, the transition made sense, since continuing to work on cardiomyopathies could lead the lab into professionally problematic territory. The metaphor of cleanliness is also indicative of an underlying personal discomfort with industry partnerships. During other meetings, Nielsen also described how Almanor would offer a separate intellectual space where the research on heart diseases could continue. Nielsen and his colleagues conceived Almanor as a collaborative opportunity to share intellectual and material resources in a way that aligned their academic research goals and their commercial aspirations. By building out the products of their research into a company, they hoped their work would be more readily translated into clinical applications.

However, collaborations like this one require legal coordination between organizations to establish terms for assigning intellectual property and allocating any potential profit. Much of this coordination centers on the establishment of a Sponsored Research Agreement (SRA) that delineated boundaries between projects, establishes restrictions on data dissemination, and details ownership of the products of research. Substantively, the Nielsen lab was allotted $1.2 million a year (for 4 years) from the venture funding of Almanor for well-defined projects. Delineating exactly what the deliverables for this project were, i.e., what the lab could spend these funds on, was the meat of the SRA. Early ambiguity in the terms and aims of the company raised tension between the PIs who had founded the company and the members of their labs. For some of the individual graduate students and research assistants who had been working on the projects that would be carried on at Alamanor, the "transition" felt more like capture.

These feelings became exacerbated over the course of a few months where the first few employees of the company leased out space in the Nielsen lab to do early research. The first employees from Almanor worked alongside the Nielsen lab in a leased section of the lab, called a bay, and would be using their instruments for a period of time. To the chagrin of some of the lab personnel, Nielsen delivered some frustrating news in an email,

> "On Wed we will have a lab re-organization to make some more room for Almanor. Although, they have not asked for this space, Almanor is expanding so fast that it is getting too crowded in the shared bay. Since we have room elsewhere in the lab, I am very grateful that we can move, so that Nancy and Nick can work in space that is not shared with the ever-growing Almanor. I think it will be much better for them to have the bench providing a clear boundary. In addition, the Almanor scientists appreciate the space. I apologize for any inconvenience, but none of us anticipated Almanor growing so quickly."

The initial hope, that the lab and Almanor would share the space and exchange know-how in a collegial fashion was quickly replaced by a sense of encroachment and the need to set clear working boundaries.

In one meeting, lab members met with the founding PIs and a representative from Almanor and voiced some concerns. Throughout their exchange, the scientists articulate the some of the tensions that make up the moral economy of not just CRISPR research but academic and industry partnerships more generally,

> **Graduate Student:** I guess, you mentioned the relationship with Gladstone and Almanor being very transparent. I was wondering what the implications are when it comes to who gets credit for the intellectual property over discovery, […] I was wondering what for example, UCSF's role would be there, because some of us are 100% covered by the SRA, which makes it such that whatever they do goes to the company. But some of us are, because of our role here, we are 100% UCSF [appointed]. So, anything that we discover or have credit, is something that we won't claim as intellectual property, but UCSF will definitely try to license that or whatever. And that seems to be a big problem, *which is why people but barriers between industry and academia is to prevent these sorts of situations*. So as much it feels good [to have a collaborative environment], I am worried that will be a thing.
>
> **PI1:** It's less of a worry for the individuals, it's more of a worry for the institutions. It's a grey area, so for any students or physician scientists who maybe from UCSF but training here, it's a grey area that actually hasn't been developed by either institution. […]
>
> **Lab Manager 2:** I still get the impression that the sharing of equipment and the sharing of space makes everything substantially more complicated. So presumably once there is a separation–
>
> **PI1:** –Yeah that's a good point. In their lease agreement, they are paying for the space and we also have a surcharge, knowing that when they are here they are going to be using the equipment here so there is an upcharge for that. And they can use our [facility services], so we charge them an outside rate. So its double what we pay. So you absolutely right though, a non-for profit institution should not be doing anything that would unfairly benefit one commercial entity versus another. That's definitely an issue.

The PI's deferral to the institutional offices of the two organizations is ultimately meant to remove responsibility from the individual scientists, an attempt to organizationally silo ethical concerns. Still, the PI's idea of having a collaborative environment came into conflict with graduate student's ethics trainings, as one of the lab managers pointed out, "the case scenarios [in the NIH ethics and misconduct course] are exactly like this one." The competitive environment of commercialization and patenting in genome editing further fueled lab members' paranoia over the legal terms of the SRA. One of the ways senior researchers attempted to quell the concerns of lab members was by reifying a division between the goals of a for-profit biotechnology company and the goals academic laboratory.

The division one PI drew aimed to establish a division of labor between the laboratory with the company. With this division, he carved an epistemic and organizational boundary between the two entities. As this PI explained to group,

> **PI2:** I think from a goal standpoint there is a clear separation. That is another issue, *I think we don't necessarily want there to be overlap on goals.* And so, it's easy to monitor right now and I think by the time that, over time that will evolve but *I think their focus is to develop a drug*, they are going to be solely focused on [that]. They have to get it as quickly as they can, not just figure out gene networks. They've got a time limit. Within three years they need to reach some inflection point, were they have to go to people and say, "this is something that could got to the next stage and we therefore need to get more money, or a higher valuation to bring this to a therapeutic," *not to knowledge*. So, to the extent that they are trying to develop knowledge, to get to a future pipeline, that will be valuable. They will be, form our sponsored research agreement, relying on us to provide knowledge that will feed into that product development. That's where the symmetry lies.

This separation of goals strategically drew on a definition of knowledge that decouples tacit know-how and the products of scientific work. In doing so, this PI was also reproducing an idealized distinction between for-profit science and exploratory, non-profit science.

The fuzziness of the distinction becomes apparent through an example of how CRISPR was used. In one lab meeting, one of the postdocs from the Nielsen lab who was hired as one of the first employees at Almanor, Naval, presented on how his expertise using genome editing techniques would fold into the goals for Almanor. He explained, "I'll be employing CRISPR interferase and high throughput chemical screens to identify gene networks that are dysregulated in a diseased state. And to be able to validate assays and then validate druggable targets." This application of genome editing, CRISPR interferase or CRISPRi, was not itself being developed as a therapeutic, but rather was a tool for discovery and learning more about the molecular mechanism of disease. A portion of the funding the Nielsen lab was receiving was to produce heart cells that could be used in Naval's CRISPRi experiments.

For the Nielsen lab and Almanor to partner in this way, their interests needed to be aligned both legally and epistemologically. After Naval's presentation, Nielsen described how this work should be organized, "there's sort of general organization around this but the organization at this point actually has to do with the IP (intellectual property) people wanting to make sure that the scope of each of these things was narrow enough that we could actually deliver it without causing any trouble." Trouble could arise when the deliverables of the lab, engineered heart cells, are produced by or contain multiple proprietary parts. This was likely, however, since the Nielsen lab hadn't invented the CRISPRi technique, but collaborated closely with the labs that did. Nielsen elaborated, "So for instance, here, the deliverable is a method to make CRISPRi in iPS cells, in iPS cardiomyocytes. So if there's a problem with transferring cells from, like there's some technology that is from [one of our collaborators] or some other sorts of things where you can't physically [transfer them to Almanor]. The cells are made, and we can publish on them, but for some reason we can't transfer the cells because the cells contain other proprietary things or something like that. That has to be worked out at one point. *The only thing that is important on this front is really the knowledge*." Here, Nielsen explains how norms governing the transfer of technology between organizations can easily become entangled with the research aspirations of for-profit partnerships. Because the materials of science are routinely the products of multiple organizational actors, Nielsen recommended relying on the transmission of protocols and know-how as a way to circumvent the challenges of physically transferring materials.

This strategic separation of *knowledge* from the *materials* of science helped justify the alignment between the academic laboratory and the biotechnology start up by providing an

epistemic approach that accommodated the legal requirements of the partnership. Because CRISPR was seen as a revolutionary technology, the experience using it and the tacit knowledge required to carry out new experimental protocols was highly coveted by researchers in industry who hoped to test the potential of the technology. This shaped the agreement: the deliverable to the company from the Nielsen lab was a method, not the specific products of research; and Naval was the right hire for the startup precisely because his experience with CRISPRi allowed him to produce the data that the company would need during its first phases of research and development.

Taken together, the growth of the IGI, an interstitial organization, and the creation of Alamanor, begin to exemplify how the alignment of academic and industry organizations in the field is coupled with the articulation of an epistemic and moral order. This order is experienced differently by different scientists, resulting in a set of affective tensions that is stratified by one's position in the laboratory. The tensions that arose from this, however, were overridden by a) the commitment to genome editing as an inherent moral good, and b) the authority of senior scientists who reified an ideological distinction between *experimental knowledge* and *experimental materials*. The exchanges I observed between lab members illustrated how the benefits of collaborative relationships with emerging start-ups can come into conflict with the values and goals of younger, less-established scientists and how the moral economy of genome editing intersected with the interests of both senior scientists and their universities who stood to gain a great deal from licensing technologies developed in their laboratories. Partnering with industry was, in fact, good science because it funded the production of the experimental techniques and protocols needed to use CRISPR technology in the lab and then translate these into what scientists saw as socially impactful products. As one of the senior scientists put it, "a Nature paper is not the ticket to the real world."

AFFECTIVE AND MORAL ORDERING

In addition to shaping the structural arrangements between the actors surrounding CRISPR technology, the ubiquity of academic-industry partnerships shapes scientists' views about what CRISPR technology is and the moral imperatives that drive what it will be. Because CRISPR has such a wide array of applications, the scope of the technology was a matter of active contestation. With some proponents advocating for CRISPR to be used solely on rare genetic diseases and others advocating for CRISPR to be used to also address common diseases. Academic scientists at the center of the development of CRISPR and the technologies derived from it saw market forces as necessarily shaping what the outcome of this contestation would be. These forces were experienced and internalized by scientists as anxieties and fears about the future of the field and the risks of accidents or misuse. When counterbalanced by the hype and promise of CRISPR-cures, the push and pull of these affective commitments shaped how leading scientists approached the commercialization of their work.

Fear and "Real-world" Genome Editing

In one workshop for scientists in the Bay Area who wanted to develop new genome editing techniques, one scientist in IGI leadership with extensive experience in industry expressed,

> "I will admit my sort of deep anxiety for CRISPR is sort of the story... and don't laugh, I'm dead serious... is sort of the story of the Segway. If you've ever ridden a Segway, it's amazing. I mean, it takes five seconds to learn, it's super-fast, it's super safe, it's amazing! It's just… nobody uses it. I mean, police do use it and tourists in

> San Francisco. So once upon a time, there was a world where people thought that everybody would be riding Segways everywhere, and it has become a niche thing. *So my raison d'etre is to try to make sure that pretty much CRISPR everything*, at least that is impactful to the real world, is not niche, and is in fact quite widespread."

For him and other scientists, the fate of previous technologies in the market informed their fear of obsolescence. If CRISPR were to become niche in the market, their access to research funding would plummet. In one weekly lab meeting, a postdoctoral student expressed a similar worry. Remarking on the organization of projects in the lab, he argued that their relevance hinged on CRISPR being the most cutting-edge technology. His fear was that someone would invent the iPhone for CRISPR, "Steve Jobs, he killed the iPod with the iPhone. Killed it. What if we are the iPod?" This fear was multifaceted in that it reflected insecurity about the continuity of relevance, funding, and individual scientists' careers. It was also a fear that evinced an inflection in the meaning of science identified by Max Weber that, at its heart, science "*cries out* to be surpassed and rendered obsolete," (Weber 1919, p. 11). Under the conditions set by academic capitalism, instead, scientists working in the fast-paced field of genome editing expressed a near constant preoccupation with new techniques outpacing the technologies they were committed to or their competitors in other laboratories laying claim, via publication or patent, over more efficient, or powerful genome editing tools.

The alternative fate that scientists hoped for, that CRISRP would stay relevant, reflected their understanding of commercialization as a means through which to bring about societal benefits with CRISPR technology. In the same workshop above, the IGI scientist explained, "The tiles of IGI interest whether by medicine, plant, microbe, tools, and society all wrap around CRISPR-Cas. The mission, in sort of an emic form is to discover, then develop, and then deliver CRISPR-Cas solutions that improve the human predicament." For medicine, this meant their goal was to, "make sure that the CRISPR footprint in biomedicine is as broad as possible." A graduate student probed into the imperative with a frustrated tone, "but what does that mean?" The speaker responded, "Well, so that means we are going to perform both structured and unbiased discovery. If we see something interesting, we will try to convert that into a proof of concept. Then, critically, and this is the last step that I think might surprise some of you... […] we're hopeful to go from that proof of concept to something that's actually *real-world robust*," [italics added].

This scientist's account of "real-world robustness" boiled down to whether and how CRISPR technology developed in academia would be taken up by industry. In walking us through this, he illustrated for the small audience of grad students, postdocs and PIs how the scope conditions for genome editing technologies were shaped by the biotech and pharmaceutical industry. He explained how in order to fulfill its mission of ensuring biomedical applications of CRISPR were as broad as possible, the IGI needed to navigate the research and product pipelines of for-profit entities in a shared competitive field. His presentation then surveyed the firms in the genome-editing industry, "at least on the publicly-held front, these five [companies] are putting editing into the clinic and are public. […] There's a large number of companies that are starting now to use CRISPR for various biomedical applications. Sort of the practical reality is that if you look at the pipeline of these, […], certainly what's in the pipeline for these for the next five years is, round numbers, maybe 10 diseases. 10. One, zero. That's not very many." In other words, industry was treating CRISPR as though it had a narrow scope of application.

The main obstacle to the broad adoption of CRISPR in the real world, this researcher went on to argue was fear,

> I'm going to walk you through what the obstacle is and what we're doing to try to address it. The first obstacle, why there are not more diseases, is this: It's fear. […] a key factor in the sloth of adoption of editing, in particular in pharma pipelines, is frankly fear. Pharma is afraid. This is not a small molecule. This is not a biologic. This is strange. And I speak to big pharma a lot, and let me assure you, it is really hard to convince somebody from a company with a hundred-billion-dollar market capitalization that they should be investing in this sort of stuff.

While the novelty of genome editing was experienced by scientists as a point of excitement, to the pharmaceutical industry this risk of adoption was greater. This was, in part, because the material components of CRISPR-Cas9 technology (an enzyme that cuts DNA, called a nuclease, and a set of genetic instructions for where to cut, called a guide RNA) didn't have clear pre-existing regulatory standards of efficacy and safety. The there was a deeper anxiety shared between academic scientists and industry: the risk of an "adverse event."

Senior scientists in the field inherited the anxiety of an "adverse event" from their observation or, in some cases, participation in the technological predecessor to genome editing, gene therapy. As briefly reviewed above, gene therapy is a different molecular approach to treating human genetic diseases where DNA is inserted into patient's cells using a virus. On multiple occasions, both in bioethics workshops and in technical scientific talks, the trajectory of development of gene therapy was a touchstone. As one scientist put it during a lab meeting, "My worry is that you will kill people in trials, […] the same thing that happened for gene therapy." In both this lab meeting and the workshop above, the senior scientists recounted the case of Jesse Gelsinger, a teen-age patient who died in 1999 in a clinical trial for gene therapy, one of them explained, "[Gelsinger's] disease was treated by gene therapy, conventional gene therapy, not editing, and there was a severe adverse event due to insertion mutagenesis. And the field of gene therapy felt as if somebody poured liquid nitrogen over it. The FDA just shut the thing down." Senior scientists shared this history with younger scientists, explaining how for several years this resulted in a public loss of confidence in the approach, funding losses and extensive regulation of any gene therapy products. These histories informed how senior scientists managed the uncertainty over how the tools of the lab bench would be translated into the clinic. One aspect of the Gelsinger case that was seldom part of scientists' recounting was that a financial conflict of interest on the part of academic scientists was found to have influenced academic scientists' assessment of the risks of the trial (Yarborough and Sharp 2009).

While the field of gene therapy had begun to recover, the threat of regulatory freeze pervaded. This reflected how scientists understood the conditions of their field. As one scientist put it, "the biggest victory in all of this is not the fact that we are sort of in the clinic, but the fact that nobody has died. […] We, therefore, right now, are living in this sort of halo where things are still okay while perpetually being afraid that something bad might happen. This is just the name of the game for clinical development. It's just how things work." This fear of an adverse event, and the orientation towards risk it represents, is part of the moral economy of clinical trials in general and is not unique to CRISPR (Corrigan 2002; Hedgecoe 2014; Petit 2023).

Scientists in universities made their own market predictions to assess the direction of research and construct a pathway of development for CRISPR technology. In discussing which of the 4,000 genetic diseases they should study outside of the 10 that industry had decided to focus on, one university scientist argued, "the question is which ones... what's the cost to develop and which ones have a positive return on investment because anyone... if you think this is cookie-cutter, any disease that has a positive return on investment should just be more capital and then it should be a

solvable problem." I further probed into this logic during the Q&A of the workshop and asked the group of researchers why the IGI should broaden the biomedical footprint of CRISPR to, "CRISPR everything." To the scientists at the meeting, my question was naïve,

> **Senior Scientist:** Well, I think my response to that would be that once something's proven in principle, it's profitable by a very generous definition. There is capital and things can scale quickly, and that's the difference between the world 200, 300 years ago and now. When something is proven in principle, the ability to replicate it, scale it, deploy it is pretty simple.
>
> **Senior Scientist 2:** The biggest advance or kind of most radical thing that has happened in biomedicine is in vitro fertilization, […], but before it was actually done a lot of people just thought it was basically criminal, and there was no research funds for it [sic.]. But as soon as kids started getting born, then it just changed the way people look at it. So, you have to realize that I think the advance of somebody who really has a serious disease and is better (from treatment with CRISPR), and then having more and more of those, that that kind of success is, I think, very powerful.
>
> **Senior Scientist 3:** I cannot agree with you more strongly. […] I am convinced that the next half century will see editing therapies for common disease. These will be cardiovascular, neurological, gastrointestinal, musculo-skeletal, so the broad categories of killers. I think that the technology will have to be de-risked largely through the monogenic space and cancer first.

For genome-editing scientists working under the moral economy of academic capitalism, the Latourian mantra, "once the machine works, people will be convinced," takes on a distinctly market-based quality. Taken together, the responses this group of scientists reflect an expectation of inevitability in the progression of both technology and the market. Scientists' arguments of what kinds of diseases should be treated with genome editing were sometimes warranted by a belief I heard echoed throughout my observations: that, "if I don't do it, someone else will." Moreover, the optimism with which these scientists responded to my question also serves to counterbalance their fear of a severe adverse event, resulting in a speculative epistemology supported by a belief that once one successful case of therapeutic recovery occurs or a clinical trial is completed and consecrated by the FDA, other biomedical applications will quickly follow.

Re-framing Genome Editing Discourse: The Genome Surgery Center

To bring about its goals, the IGI attempted to develop a framework of meaning and an organizational model to support the expansion of clinical genome editing. To address the costs of clinical development some scientists in the IGI proposed the idea of a Genome Surgery Center that would partner with pharmaceutical companies for chemical manufacturing. In this imagined center, scientists hoped to enroll patients to test genome-editing therapies outside of the traditional pharmaceutical-clinical context with the idea that medical universities would stand to gain from greater autonomy when engaging in partnerships with industry. Scientists begun to call therapeutic genome editing "surgery" with three aims in mind: First, the metaphor could make the practice of genome editing more legible to physicians and patients by proving a familiar framework of meaning. Second, it brought connotations that were distinct from CRISPR as a drug, for example, it could instead be thought of as an urgently needed intervention or a one-time procedure to correct a "mistake" in a patient's DNA. Some scientists thought this would work as a discursive strategy to

construct CRISPR as a medical device instead of a drug, potentially changing its regulatory pathway. Third, with the language of "surgery" they hoped distinguish their applications of CRISPR from those being pursued by larger for-profit CRISPR companies. This section draws from observations at a series of meetings held to develop a plan for the Genome Surgery Center to unpack scientists' affective commitments around the translation of experimental bench practices into clinical practices.

The metaphor of surgery was first proposed to describe the technique of directed DNA mutagenesis, but one scientist cited sociologist Paul Starr's book *The Social Transformation of American Medicine* (Starr 2017) to explain the distinction:

> It is also different regulation, different funding models, and so on. When you think historically about physicians and surgeons you actually realize that it's actually quite different. […] They came from very, very different schools and very different approaches towards treatment, and they have very different traditions. Even today though, they're very different in the sense that physicians and medicine think about making drugs, […], where surgery is actually where you make new devices essentially on rare diseases.

This difference he explained, also contrasted in terms of the economic differences between surgery and medicine. "Surgeons when they did the first heart transplant, the first thing on their mind was not how to monetize the heart transplant, right? That was just not even on the table. […] The issue was how to do the next one, and how to do the next one, and each one was different in an iterative way. And so, we felt that this actually was a better sort of metaphor for how we go forward in terms of thinking about this process, because actually in genetic disease every single person is quite different and really need to have custom tools, custom scalpels." The model of surgery, he additionally argued, was better fit for efforts to treat rare genetic diseases, commonly described as "orphan diseases" which the pharmaceutical industry had historically neglected developing treatment for because they represent a small market. Under the model of genome surgery, the IGI could perform experimental gene surgeries under a framework of "compassionate use" and not charge patients.

During a regular bioethics workshop, one of the senior scientists who advocated for the metaphor explained that the IGI needed an organizational model to address the narrow and risk-averse focus of industry. He explained with sarcasm, "so you have four large companies looking at editing a 30-base region in the genome that will increase fetal hemoglobin [for the treatment of sickle cell and thalassemia] and probably have a therapeutic value. But this is the genie in the bottle. […] 30 bases out of three billion bases (in the human genome). So, let's just say that there's a little bit of opportunity." In other words, the human genome is so large that potentially any genetic variation that has pathogenic consequences or is associated with an increased risk of disease is a possible target for surgical intervention.

From the outset, however, the discourse around clinical applications advanced by IGI scientists produced a set of affective expectations especially among those who would stand to benefit the most from genome-editing therapies: patients with genetic diseases. In practice, alignment with the needs of patient communities was only a priority further downstream of the process of technological development. The interaction between researchers and this interested public illustrates the effects of the moralized goals of genome-editing technology development. Since the burgeoning of CRISPR in the media, the biochemists and molecular biologists in the field have received thousands of emails and phone calls from patients, their advocates and interested members of the public. In these communications, patients described the popular sources through

which they had heard of CRISPR and its therapeutic potential and sought treatment from academic bench scientists. In one email, for example, a patient described, "I have a haplotype form of Cystic Fibrosis. My genetic variation is c.1477C>T. You might be able to manipulate this gene in the lab. It might be an easy breakthrough research project for yourself or one of your assistant researchers?" These hopeful messages reflected the public facing discourse that stressed the precision and ease of genome editing, which was often simplified and hyped by reporters and documentary film makers who bridged scientists' work with broader audiences.

At stake in the online interactions between patients and bench scientists was the production of affective expectations around a yet undefined and promissory technology. Unlike physicians, however, biochemists and molecular biologists do not receive training in clinical ethics, patient care or genetic counseling. This results in a capacity gap when the work of the lab bench is quickly translated into the work of clinical bedside. Unsure of how to address the concerns of patients on a case-by-case basis in a way they felt was sincere and truthful to the way CRISPR is used in practice, IGI researchers sought the guidance of bioethicists. In consultation with a bioethicist specializing in therapeutic misestimation, the IGI developed an organizational response by creating an online portal on the IGI website for triaging and addressing public inquiries. This work was then taken up by graduate students who had then transitioned into science communication positions for the IGI. In most cases, the solution was to direct individuals to patient advocacy groups, rare genetic disease foundations, more clinically focused research organizations, and professional medical associations. The portal was additionally flooded by inquiries from high school students working on projects about the ethics and science of CRISPR.

Within the IGI, the medical needs voiced by patients were a strong motivator for the continuation and acceleration of their work. For the scientists I observed, this moral imperative was closely aligned with the imperatives of academic capitalism. For example, for one IGI scientist, their motivation for delivering on the promise of genome surgery and their sense of how to do it tied both patients' experience of the severity of rare genetic diseases and the for-profit landscape. To kick off his lecture at of the meetings of the imagined Genome Surgery Center the scientist offered an anecdote about a patient with a rare neurological disorder, Rett syndrome,

> "All right, so I know there are many clinicians in the room. I am not one, but I want to show you again as a *profession de foi*, something that has driven me passionately. Many people who speak about editing for disease or therapy of disease, start with patients. I always think this is a little bit manipulative, because why are you doing this?
>
> We all know the disease is bad. I don't know how many of you have seen a Rett's child, I want to show you a movie of a Rett child having a seizure to really highlight and to remind us all that when we think about, for example, safety, or when we think about urgency, we really have to frame those two issues in the context of what the patients are going through."

The scientists' hesitation with "being manipulative" suggests evidence of a recognition that biomedical researchers use patient suffering as an affective device to value their work for different audiences. Despite the recognition, he continued,

> "Rett is particularly pernicious for two separate reasons, it effects one in 10,000 girls, so it's as prevalent as hemophilia A, […] girls born with MECP2 mutations on the X chromosome develop completely normally until age two. They're in

> fact happy children and then they slow down, […] really horrific symptoms. So, I don't want to spend too much time on this, the next slide shows Alexa having a seizure. This was sent to me by her mom. Alexa gets these about 10 or 15 times a day, you will also hear her hold her breath. Again, this is super hard watching, I don't want to be manipulative, I want to be deeply respectful of the child and her mom, but I really want us to remind ourselves what we're doing."

The small audience of high-profile scientists, senior gene therapy researchers, clinicians, a fundraising expert, and I quietly watch the short clip taken with a phone camera. There is a short pause, and then the scientist continues,

> "So, where are we? The mutation was discovered when I was a post-doc at NIH, so this was 20 years ago and for the subsequent 18 there was absolutely nothing. To the best of my knowledge no pharma is working on a small molecule modulator of this. There was no gene therapy effort and there was no gene editing effort, despite the fact that we know the mutation and we know the fact that the mutation is restorative.
>
> Very recently, in the past year, AveXis, which as you know was bought by Novartis for eight point something billion dollars, have very promising late stage data for SMA (spinal muscular atrophy) using AAV9 (a viral vector). They have disclosed that they may advance an AAV9 based treatment for that. The good news is they dosed non-human primates and there are no adverse findings. Hypothetically suggesting that there will not be an adverse effect from excess dosage, but nobody knows.
>
> The deep tragedy here, is that, and I can tell you having just worked in one, is that no editing biotech will take Rett on as a project until the AveXis phase one completes. First of all, this will be Novartis, so this will be slower. Second, so best scenario (is) three years. […] And AAV9 is tied up IP-wise for that modality."

The urgency of genome surgery, from the perspective of this scientist, was that despite a complete understanding of the molecular basis for Rett syndrome, there have been few therapeutic options for patients. Moreover, the competitive nature of industry was further delaying clinical development. For him, the affective basis for genome surgery weds a moral imperative to alleviate suffering with the neglect of the disease by industry. Instead, he recommended a hybrid model, the Genome Surgery Center, which would draw from the innovative potential of universities in the Bay Area to develop partnerships with chemical and pharmaceutical manufacturing firms under a non-profit model. In imagining this center, this researcher aimed to circumvent dominant market forces that shaped the decisions of scientists in industry and identify novel pathways to develop CRISPR's therapeutic potential.

In short, the affective commitments expressed by researchers as fears and aspirations for CRISPR feed back into the development of organizational structures that support genome-editing work. While patient needs are framed as a priority by scientists, these needs were overridden by concerns about the practicalities of commercialization and competition between different university-industry partnerships. This dynamic matters to construction of genome-editing technology because the discourse used to frame and describe CRISPR and its applications reflects the imagined alignment between different stakeholders. As a "surgical tool," for example, the biotechnology could be wielded outside of the perceived constraints of drug commercialization. By emphasizing the

moral imperative to address rare diseases, scientists fortified CRISPR clinical importance in hopes that proof of concept would eventually allow for the expansions of CRISPR's scope of application to other disease areas, and thus larger markets.

Discussion and Conclusion

[Morality and markets

- Capitalism and knowledge production: against the creative side of markets (Fourcade and Healy)
- Technological progress: moralizing (Parthasarahy)
- Going beyond the critique of neoliberal science as motivated by profit (it is cultural and internalized)
- Momentum and inertia in organizations?]

[Social construction of technology: organizational alignment, but individual alienation. Discourse and metaphors as moral and ordering]

The cases analyzed in this paper highlight the affective tensions that come with the organizational alignment of university laboratories and biotechnology startups. When new interstitial organizations like the IGI are founded, alignment with broader moral goals helped draw in philanthropic donors and helped legitimize genome-editing technology. By leaning into the hype around CRISPR, scientists set in place a set of affective expectations about the epistemic, moral, and clinical value of genome editing. Patients and their communities who learned about the ease with which CRISPR was being used in the lab perceived the clinical translation of the lab tools to be imminent and began reaching out to academic scientists for individual treatment. However, clinical translation, as understood by senior scientists, had to happen in partnership with industry firms from biotech and big pharma. The "real world robustness" of CRISPR hinged on whether it could be commercialized. In the case of Almanor, scientists aimed to take the practices and techniques developed in the lab and use them as the foundation for a venture capital-backed start up. This decision, however, created tensions between the values that new scientists were receiving through their academic training and the norms of industry partnerships. Senior researchers alleviated these tensions by siloing moral concerns about conflict of interest to local organizational bodies tasked with managing the intellectual property agreements and appealing to an ideological division of interests between academia and industry; where academia is focused on developing "knowledge" and industry is focused on developing "products".

This paper has additionally illustrated how scientists' understanding of and speculations about the biotechnology and pharmaceutical market can shape how different areas of research are valued. This, in turn, shaped scientists' decisions about what diseases would be valuable targets for the development of therapeutics. Moreover, in the case of the Genome Surgery Center, scientists assessed the competitive dynamics between industry firms and their fears of potential market failures in developing the organizational model for developing CRISPR-Cas9 into a biomedical platform with broad scope. These ambitions, however, were closely followed by a set of anxieties about the decline of CRISPR, whether brought about by a regulatory freeze in response to a severe adverse event in a clinical trial or because it may be superseded by an, as of yet, undeveloped technology.

These tensions, between promise and fear, and between multiple forms of value, were constitutive of a moral economy where scientists' intentions and commitments to advancing genome editing for the good of patients is entwined with speculative capital and market competition. The continued relevance of genome editing rests on this alignment between industry and academia, where the interplay between, "once the machine works, people will be convinced" and "once all the relevant people are convinced, the machine will work" becomes a fervent driver of scientific work.

[Broader questions about other technology: Benjamin

- Technological beneficence
- Algorithms (L Amoore)
- Philanthropy capitalism

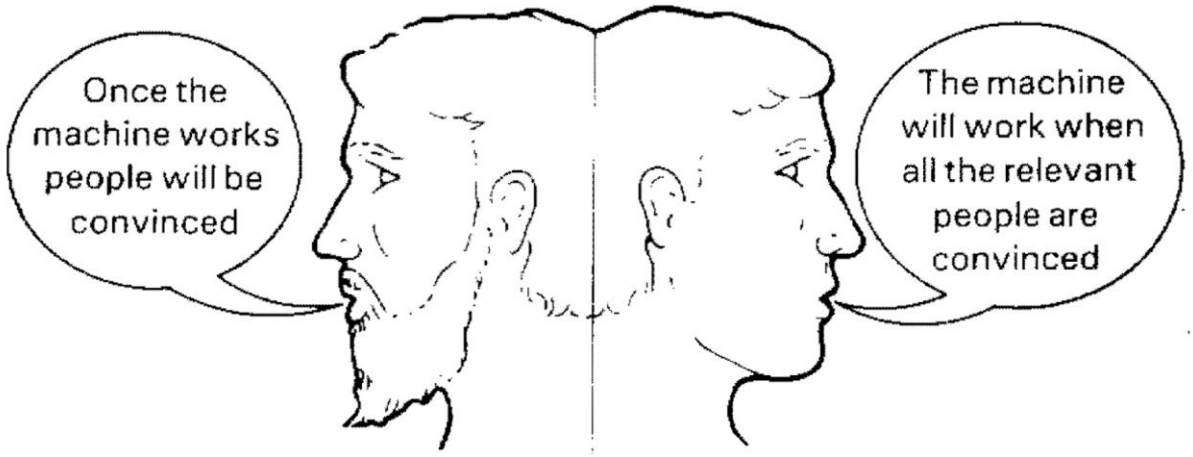
"Values do not distort science, they are science." p.6

NOTES

[1] Though not entirely separate, the concept of moral economy has two distinct intellectual origins. On the one hand, the concept was introduced to sociology via the writings of E.P. Thompson (1971) and James C. Scott (1977) who used it to describe the role of norms and obligations in the exchange of goods and services. The second origin is that highlighted in this paper, proposed by historian of science Lorraine Daston with the aim of formalizing the analysis of emotion and values in scientific work. Though the concept's origin is distinct, these two sources have since been made commensurate with one another (Carrier 2018; Fassin 2020; Fourcade 2017).

FIGURES

Figure 1. The Third Dictum of science's Janus (Latour 1987)



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