Introduction

In the spring of 1948 aspiring cancer researcher Robert Briggs received a grant rejection from the National Cancer Institute (NCI). Adding insult to injury, the NCI letter included a comment from a reviewer who called Briggs's proposal "a hare-brained scheme."[1] And perhaps it was. Briggs, who was working at the Lankenau Hospital Research Institute (LHRI), a cancer facility in Philadelphia, had proposed to swap parts between two different types of frog cells: an embryonic cell and an unfertilized egg cell. Briggs intended to harvest the nuclei of each cell—parts that could not survive on their own—and reconstitute them into a newly amalgamated, but living, fertilized embryo. If successful, the reconstructed egg would develop into a normal frog. Briggs insisted that the outcome of the experiment would provide insights into cellular differentiation and, ultimately, cancer. A decade earlier, the renowned embryologist Hans Spemann had called the idea of such an experiment "fantastical," and Briggs notably did not even propose to use cancer cells in the project.[2] The grant reviewers, in other words, questioned whether such an experiment was even feasible, let alone appropriate to be funded by the National Cancer Institute.

Despite the initial rejection, Briggs's proposal eventually gained the NCI's support. Harold Chalkley, the associate director of the grants division, gave the application another look. He visited the LHRI later that year and discussed the

project with Briggs and the administrators.[3] The LHRI had a good reputation as one of the few cancer-focused institutions, and a central mission of the NCI at the time was to increase the number of scientists doing cancer research.[4] Funding young researchers like Briggs, even if their work seemed unconventional, supported the NCI's broader goals.[5] Ultimately, Chalkley decided to approve the project, albeit with the unusual mandate that the "the principal investigator [Briggs] take an active responsible part in the proposed research."[6] If the NCI was going to fund it, Chalkley wanted Briggs directly involved rather than using the grant to hire someone else to do the work and freeing himself up to do other research.

The funding allowed Briggs to hire a postdoctoral fellow, Thomas J. King, and with the help of their laboratory technician Marie Di Berardino, together they successfully carried out the experiment in 1951. When Briggs and King announced the experiment's success in 1952, the "hare-brained" technique was christened *nuclear transplantation*.[7] The *New York Times* hailed it as a breakthrough for cancer research because of its potential as a tool for investigating what controlled differentiation, which offered insight into how cells can go from normal to malignant.[8] The technique would eventually be known by other names, including nuclear transfer and, most notoriously, cloning.

Twenty-five years later, on a rainy morning in May 1978, Briggs found himself testifying in front of the House of Representatives subcommittee on Health and Environment. The agenda for that day focused on "the general issue of cloning," which the chairman, Paul Rogers (D-FL), reminded the group, "is simply one aspect of a general area of cell biology albeit the most sensational." In his opening statements, the Florida congressman justified the hearing, saying, "Among members of the general public there was a concern" about the possibility of human cloning "with regard to the moral, ethical, and legal ramifications of such a breakthrough." He also noted that within the scientific community, "there was a concern that the public would receive the impression that the goal of each scientist working in the area of cell biology was to someday clone a human being." The committee that day heard from scientists themselves to provide "firsthand information on precisely what is being done by legitimate scientists and precisely how this relates to the cloning of a human being."[9] Briggs was one of five scientists to testify.[10]

Clearly, something had changed in the intervening decades between these two episodes. The initial grant rejection was not about the morality of the work, nor did news coverage of Briggs and King's achievement note any ethical

implications. Questions regarding cell differentiation and cancer, not a search for a new form of reproduction, motivated Briggs's experiments. Yet by the late 1970s the narrative of what nuclear transplantation could be used for had dramatically shifted. "We live in interesting times," Congressman Henry Waxman (D-CA) declared at the hearing. "The question is not, can new life survive outside the laboratory, but can our traditional values survive within them?"[11]

What changed over the intervening decades? Did scientists make startling advances with technique that made human cloning possible? Did the motivations for conducting nuclear transplantation research change? Did Briggs, for example, become less interested in understanding developmental processes and more interested in its reproductive potential? Or, was there a larger awakening as to the unintended consequences of nuclear transplantation, consequences not foreseen during its initial development? If so, how did such an awareness emerge and how did a technique that only a handful of laboratories used throughout the world at that time transform from a tool for cancer research to one deserving of public concern?

Forgotten Clones explores these questions by following both how biologists used nuclear transplantation to construct embryos in the laboratory and how these embryos were later reconstructed as potential ethical problems. In doing so, a new picture emerges that not only illuminates the importance of the early history of cloning for our understanding of midcentury Anglo-American biology but also exemplifies the changing cultural views of the biological sciences in the decades after World War II. *Forgotten Clones* tells the story of how nuclear transplantation came to be used in radically different ways; whether that use was by scientists in the laboratory to investigate cells or by ethicists in a public discourse to demonstrate the need for their voices.

By connecting the history of the nuclear transplantation in the laboratory to its contested cultural meanings, we gain a more robust picture as to how human cloning became deeply connected to one particular technique. The ethical implications of nuclear transplantation as a tool for reproduction, and particularly human reproduction, were not inherent to it when Briggs, King, and Di Berardino first successfully carried out the work. Rather, the reproductive potential for nuclear transplantation had to be constructed; people not only had to imagine a new use for the technique but had to create a new discourse around nuclear transplantation that promoted it.[12] Saying that it just took time for people to "realize" or to "see" the ethical implications of the research suggests that it was a process of uncovering, of making something visible that had always existed. Such

a view reflects a subtle form of technological determinism, of an inevitability of particular future use. Suffusing nuclear transplantation with all of its meanings from the beginning removes the agency of the people who generated new uses for it, and obscures the reasons for why they did so.

Forgotten Clones does not assume such an inevitability. Rather, it reconstructs the different ways in which people used nuclear transplantation in the middle of the twentieth century and how those uses changed over time. To do so, *Forgotten Clones* traces both how and why scientists developed the technique and how others co-opted it for new purposes.[13] Following this path means that the first half of the narrative takes place mostly within the confines of the laboratory where cloning emerged. The second half of the book examines the construction of public knowledge regarding cloning and how it gained a new meaning in the process.

Nuclear transplantation started as a concept that circulated between biologists who discussed its potential for solving biological riddles and speculated about what it could tell them about the natural world. After biologists successfully transplanted a nucleus they debated how to interpret the results of the experiments, a debate complicated by the shifting theories of development taking place at the same time. Many of the motivations and debates during this period have been forgotten, neglected both because of the way new interpretations in the 1960s made such issues irrelevant and because of how the scientists embraced a narrow history of the technique's development that both elevated the status of the technique and helped protect their work when it later became scrutinized. Similarly, the sensation surrounding the birth of Dolly, the sheep cloned via nuclear transplantation in 1996, particularly in regards to the ethical implications that it seemingly made manifest, has overshadowed the importance of nuclear transplantation during in the middle of the twentieth century, and overlooked the insights that can be gained by analyzing the human cloning controversies that emerged.[14]

A History of Development

Examining how and why biologists developed nuclear transplantation techniques in the laboratory, and how and why nuclear transplantation came to be associated with human cloning, generates a history that defies many of our assumptions about the scientific work and its ethical implications. For starters, nuclear transplantation techniques emerged in the context of cancer research.

Investigating why Briggs worked at a cancer facility, and why transplanting a nucleus was seen as a worthwhile endeavor for cancer research, illuminates a pivotal moment in the history of developmental biology and public health more broadly.

Beginning in the late 1930s, new institutions emerged that helped reorganize the field of embryology, beginning a crucial conversation that led to the eventual rebranding of the field as "developmental biology" in the 1950s. The LHRI, and particularly the administrators who founded it, played pivotal roles in establishing these new institutional structures. They founded a journal, a yearly symposium, and a new society around the idea of growth, and they did so in order to promote their own cancer research agenda. The LHRI administrators, Stanley Reimann and Frederick Hammett, believed that cancer was a growth problem and therefore needed to be understood within that framework. They spent their careers building the institute with this model in mind, and by doing so supported research that focused on growth from a variety of disciplines, including chemistry, genetics, physiology, and, of course, embryology. The Growth Society eventually disassociated itself with the institute and later was renamed the Society for Developmental Biology in 1965.[15]

Hiring Briggs, whose advisors were among the original leaders of these new growth-focused organizations, made sense for the LHRI administrators in the early 1940s as they expanded their institute. Reimann and Hammett, however, hired Briggs with the assumption that he would continue his postdoctoral work, which was funded by the International Cancer Research Foundation and focused on the development of amphibian tumors. And yet within his first year, Briggs proposed a different project, nuclear transplantation, that the directors approved. Why Briggs was attracted to this problem and why the administrators sanctioned the work also provides insights into the history of biology at this time.

Historians have shown that the role of the nucleus in development is a long-standing question that can be traced back to some of the central figures in science and medicine in the nineteenth century.[16] However, close archival interrogation of nuclear transplantation's genesis exposes how the technique was not inspired by turn-of-the-century debates but rather by a complex set of disciplinary, institutional, and intellectual contexts of the 1940s and 1950s. Before the twentieth century, biologists viewed questions about heredity, evolution, and development as fundamentally interrelated, and the idea that they should be studied separately would have been anathema to them. However, the separation of the fields was exactly what took place in the twentieth century, and tensions built between

embryologists and geneticists as they assumed their ideas were undervalued, in the case of embryologists, or more fundamental, as in the case of geneticists. By the 1940s the disputes had taken on social and institutional implications. For instance, the study of development could potentially be subsumed under the rubric of genetics if it turned out that the chromosomes were indeed the driving force in the process. Nuclear transplantation offered a way to resolve contemporary disputes; it was not simply a technique that could finally put to rest a question from the nineteenth century.

The pressing nature of the problem in the 1940s independently inspired scientists around the world to instigate nuclear transplantation-like projects as the approach offered a rational path to gain clarity regarding what controlled development. Briggs and his associates happened to be the first to successfully carry out the technique in multicellular animals, but notably others had already transferred nuclei of unicellular organisms by that point. This history demonstrates that the NCI rejection calling it "hare-brained" or Spemann's description of the experiment in the 1930s as "fantastical" functions as a red herring, as these descriptors reify the idea that the first successful nuclear transplantation experiment should be seen in a heroic narrative of individual brilliance. Breaking up cells and successfully transplanting the nucleus into an enucleated egg is, of course, a challenging technical feat, and many biologists failed to carry out the experiment. Yet the basic principles that undergirded each of those steps were in place by the 1940s, and mastering and assembling them was the larger task in many ways. *Forgotten Clones* reconstructs the investigative process, reframing the development of the technique as one of trial and error, and emphasizing the important institutions, people, and ideas that have been left out of most histories of cloning.

Forgotten Clones is structured as three parts. Part I focuses on how and why the first successful nuclear transplantation experiment came about when and where it did. In chapter 1, I follow the early career of Robert Briggs, tracing his move from a small New England town to his education in Boston and the first positions he secured after graduate school. I highlight the immediate forces, both disciplinary and institutional, that shaped the trajectory of Briggs's career, and, importantly, help explain why Briggs imagined trying to carry out the technique of nuclear transplantation when and where he did. Chapter 1 also examines the history of the LHRI, and how its focus on cancer provided invaluable support in the development of nuclear transplantation. In doing so, I illustrate that Briggs's influences and motivations stemmed from contemporary debates, colleagues, and the overall goals of the LHRI.

The second chapter focuses closely on the institutional and intellectual forces that led Briggs to propose and carry out the first nuclear transplantation experiments while working at a cancer research facility. The institute did not simply supply a funding mechanism for Briggs to carry out the work but rather provided essential motivation and administration. Unbound from the more traditional academic structures, the LHRI fostered an interdisciplinary framework that allowed Briggs and his team to engage in research that might have been more difficult in other settings. It also granted different access to resources, including funding but also people and time, compared to colleagues at other institutions. Finally, working toward a broader understanding and control over cancer provided an additional motivation for Briggs, King, and Di Berardino to carry out their work.

Chapter 2 also demonstrates that Briggs was not alone in tackling this experimental problem in the 1940s, not just in the sense of the people working with him but also in the field more broadly. During this period, scientists in unconnected laboratories embarked on similar research projects, which suggests that the intellectual, technological, and institutional contexts of the 1930s and 1940s supplied the right mix of motivations and support for a number of people to undertake such an endeavor. By uncovering this convergence toward nuclear transplantation, I demonstrate how a straightforward intellectual history of cloning does not fully capture why the technique emerged when and where it did.

Unearthing the immediate contexts surrounding the development of the technique and its early applications both complements and complicates established work that situates the history of nuclear transplantation in a longer history of biology.[17] There are examples of biologists attempting nuclear-transplantation-like experiments in the late nineteenth century in an effort to answer pressing questions of that period.[18] Briggs's work certainly fits into this intellectual genealogy, as the technique could be, and eventually was, applied to answer similar questions. There is much to be said for the history of cloning's ability to connect late nineteenth-century questions and the work of contemporary biology. However, elaborating Briggs's motivations, his approach to the problem, and the debates in the biological community about what the technique could say about the development demonstrates that such histories are only one part of the story. A history of cloning not only can exemplify one way in which biologists have continually returned to big questions but also can be used to illustrate more focused institutional and disciplinary histories that are difficult to see otherwise.

In addition, by examining how the history of nuclear transplantation gets reframed, I demonstrate how privileging only a certain thread of the history, one connected to the great biologists of the nineteenth century, also elevated the status of the work. Nuclear transplantation became a part of one of the great unanswered questions in biology rather than a product of an obsolete debate or an application-focused technique to solve biomedical problems. Such a history elevated the work because of its association with a longstanding problem, and allowed researchers to claim that their experiments had always been rooted in purely scientific motivations when they were confronted with accusations of pushing the world into a new era of human-cloning. *The Forgotten Clones* places cloning techniques within a biomedical framework from the very beginning, rather than framing the technique as only later being applied to biomedical problems.

Nuclear Transplantation at Work

Once the laboratory technique had been successfully carried out, a new phase of experimentation and questioning surrounding nuclear transplantation began. Part II of this book explores the various ways in which scientists engaged with nuclear transplantation research and the initial discourses that developed around it. In chapter 3, I examine one of the central research programs to which the embryologists at the LHRI applied the technique, namely, whether it could be used to initiate development in increasingly more differentiated cells. In the mid-1950s, after several years of experimental results, the team at the LHRI concluded that something in the cell prevented more differentiated nuclei from reinitiating development. A short while later, a graduate student at Oxford University named John Gurdon began to use the technique and came to the opposite conclusion by 1960. Not all scientists, however, immediately accepted his work, and a substantive debate took place between the two research teams over the validity of their results. The legacy of Gurdon (now Sir John in recognition of his scientific contributions), has been shaped by this contest because the cloning work of the 1990s and early 2000s proved that he had the correct interpretation (which also earned him a Nobel Prize in 2012). This perspective, however, has made the contested work of the 1950s and 1960s seem irrelevant to the accepted narrative when it actually provides insights into the questions that the life sciences wrestled with during this period.

Too often the discovery of DNA's structure and the rise of molecular biology overshadows the post–World War II period, making it a convenient explanation

for many changes in biology.[19] *Forgotten Clones* shows how the emergence of gene-regulation theories in the 1960s created a new way to interpret the value of nuclear transplantation as an experimental technique. In doing so, gene-regulation theories made the original motivations for nuclear transplantation obsolete, as those questions no longer made sense for how biologists framed debates about development. Instead, only a small part of what drove researchers before the 1950s was, and still is, held up as the motivating force for cloning technologies. In other words, the history of cloning is a powerful example of the way in which the continual reevaluation of scientific work for contemporary problems erases its own past in the process.

Histories of cloning are quick to move from the milestone experiments of Briggs and King in 1952 and Gurdon's work in the early 1960s to the first mammalian cloning in the 1980s.[20] In doing so, one ignores how scientists applied the technique to answer a variety of questions and explored its use to further research programs around the world. However, given some of the idiosyncrasies of the technique, it belied easy adoption, and tracing how it moved in the following decades from laboratory to laboratory and from species to species highlights the plasticity that some scientists saw in the technique, and also how local conditions and contexts affected its adoption. Drawing from a contemporary embryological database, in chapter 4 I showcase how nuclear transplantation can be used to see aspects of the inconspicuous scientific networks of the mid-twentieth century.

Salvaging this past not only realigns the historical trajectory of the science, which includes a number of different research programs, but also allows us to recognize the important contributions of those who helped make it work and why. Privileging a narrative of labor over brilliance allows the various people who participated in that labor to be more visible. The early success of nuclear transplantation, for instance, was highly dependent on the work of women as technicians, assistants, and as teachers of a technique that demanded significant hands-on knowledge, and yet our histories have overwhelmingly tended to focus on the published milestones of the work that honor fewer people, and mostly men.

Imagining what problems nuclear transplantation could be used for was not only confined to the scientists that employed the technique. In that regard, chapter 4 also details how the public knowledge of nuclear transplantation was initially constructed in the 1950s, and the uses that it was perceived to have. The press did indeed cover the work as an important breakthrough, although they couched it in terms that reflected the science journalism of the day—mostly supportive and uncritical. In other words, writers assumed that the technique

was relevant for the reasons that the LHRI scientists and funders championed: for understanding development and, hopefully, to cure cancer. Here, the cultural histories of the public perception of science become important as they help contextualize why some experimental embryology in the past, such as Jacques Loeb's work on artificial parthenogenesis, became immediately relevant for the way in which it could potentially affect society, whereas it took decades before similar visions emerged for nuclear transplantation.[21]

Notably, several years after the LHRI pioneered the technique, one French public intellectual, Jean Rostand, a man whose career more closely resembled that of a nineteenth-century natural philosopher than a mid-twentieth-century scientist, did imagine the possibility of using nuclear transplantation for reasons other than answering questions about development, namely, using it to potentially reproduce humans. Some noticed his passing mentions of the idea, which were equal parts science and philosophy in the way he presented it, but his visions of nuclear transplantation's future use did not become widely circulated. The idea required not only more elaboration but also a shift in the public perception of science.

Cloning during the Biological Revolution

Part III examines both the shift in how the public viewed the biological sciences and how nuclear transplantation became a prominent topic within those discussions. For a group of scientists, white Anglo-American men mostly, during this period, biology became a socially transformative science in the same way that physics had with the creation of the atomic bomb—with all the positive and negative repercussions that came with such an event. Certainly there had always been a belief in the transformative power of biology, but the experience of the atomic bomb, and the perceived failures of eugenics, reshaped what some biologists felt was their responsibility to the public.[22] Chapter 5 details how in the late 1950s and early 1960s several prominent biologists spoke openly about not repeating the mistakes of physicists, who supposedly had not effectively articulated the extraordinary power that resided inside atoms. Instead, atomic bombs had shocked the world and reshaped the social-political landscape of the twentieth century. Biology seemed to them to be standing at a similar precipice, and a few, and particularly a young Nobel Prize winner named Joshua Lederberg, felt a responsibility to inform the public of work going on in biological laboratories across the world that could potentially cause a similar disruption.

Lederberg believed that society might best cope with these possibilities if everyone was aware of what might come. Lederberg's deep belief in the rapid progress of the biosciences and his concern about how unprepared society was drove him to search for work that he could use to generate public awareness. He chose to use the potential of human cloning via nuclear transplantation as his exemplar of how seemingly benign experimental techniques could soon have the power to transform society. However, it was not any particular advance beyond the development of the core technique in Briggs's laboratory that inspired Lederberg's decision to publicize this new potential use for nuclear transplantation. Although he was not the only one who discussed the possibility, as a highly visible scientist who embraced his role as a public spokesman, his ideas became central to creation of a new public consciousness surrounding the potential for nuclear transplantation.[23]

As Lederberg promoted a new potential for nuclear transplantation, the role of science in American society also changed. In the early 1950s, science and scientists occupied culturally and socially prestigious positions, more often celebrated and trusted than doubted. By the end of the 1960s that had changed. Enough examples of unrealistic expectations, poor judgment, self-righteous belief, and hypocritical actions had marred the scientific establishment and undermined its prestige by the 1970s.[24] Science journalism became more skeptical, moving from a role that educated the public of the great advances of the age to one that critically informed them of the potential consequences of science. Cloning via nuclear transplantation became one of their choice examples, as they sought to draw readers in with salacious stories about the potential for a gaggle of Britt Eklands or a football team of Joe Namaths, while also scaring them with visions of a room full of cloned Adolf Hitlers. In chapter 6 I detail the specific ways in which nuclear transplantation and human cloning became linked in the public mind over the course of the 1960s and 1970s.

The rhetoric of the transformative potential of the biological sciences also caught the attention of theologians, philosophers, and related scholars who turned a critical eye to such topics, forming the basis of a new field of study: bioethics. Pioneers such Paul Ramsey, Leon Kass, and Joseph Fletcher used cloning in the late 1960s and early 1970s as one of the main subjects in which they could effectively build expertise on the ethics associated with biomedicine. In other words, cloning debates played a foundational role in the establishment of bioethics as a field, a point often overlooked in histories of bioethics.[25] Ramsey and Kass, in particular, set up Lederberg and his discussions of cloning via

nuclear transplantation as their primary antagonist. Lederberg's position became representative of the need for other voices besides scientists to direct science. Cloning would fade as a central villain as the 1970s wore on, but by that point it had already been useful in establishing the need for bioethicists.

In the wake of bioethical scandals, environmental regulation reform, and Vietnam protests, cloning via nuclear transplantation also became an easy target for critical voices against mainstream science such as Science for the People and reformers in Congress who sought to regulate the directions and actions of scientists. Thus, in 1978, when a science journalist claimed to have witnessed the cloning of a wealthy businessman, many were already primed to take such claims seriously and to investigate them.[26] That is how Briggs and several scientists in the field found themselves testifying before a congressional subcommittee that year on the uses of nuclear transplantation techniques. As a shield, they deployed their own history of nuclear transplantation's development as a part of a longstanding intellectual history rather than as born within an intentionally socially transformative public health establishment.

Forgotten Clones ends in the late 1970s, as by that point the cornerstones for a history of cloning had settled in their foundations. The scientific origin stories for nuclear transplantation and its uses for theoretical purposes had become a repeated, and protective, refrain. Human cloning via nuclear transplantation had also gained a layer of cynicism. Its use in scaremongering about the direction of science had become trite. Enough science fiction, even if passed off as nonfiction, had leveraged the concept of cloning so much by that point that it had become unimaginative. The 1980s and 1990s would bring about its own set of exemplars to generate public discourse, and many of the cloning debates in the 1960s and 1970s, particularly the context for them, would be forgotten.