A Search for Context:
Cloning Techniques and the Work of Paul Weiss, 1930s-1960s

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Judging from the fellow researchers that I encountered during my few weeks at the Rockefeller Archive Center in the fall of 2010, it is clear that the Rockefellers – through the university, their foundations, or the actions of the family – impacted the twentieth century in a variety of disparate and seemingly unconnected ways. Many historians writing about the twentieth century can easily connect their work to some influential aspect related to the Rockefellers. For other researchers, the Rockefeller family and their institutions provide a rich contextual background for historical work in the twentieth century. I visited the RAC with the goal of the latter, but quickly found my research situated in the former category. As it turns out, the name "Rockefeller" has even found its way into the history of cloning.

My doctoral thesis, "Cloning Practice, Cloning Fear: A 'Fantastical' Experiment for Biologists and Society, 1952-1982," examines the history of an experimental technique that moved from laboratory bench to congressional floor in the span of a few decades. The scientific and social narratives surrounding cloning experiments during these years reflect a shift in biological practice and the public evaluation of science. In 1938, Nobel Laureate Hans Spemann conceived of a 'fantastical' experiment to settle the long-standing debate over what controls cellular development: the nucleus or the cytoplasm. Soon afterwards, biologists began honing a

technique by which the nucleus of one cell is extracted and placed into an embryo whose original nucleus has been removed. The resulting embryo, and ensuing organism, becomes a genetic duplicate of the donor. At first, biologists employed this technique — nuclear transplantation, or cloning — specifically to answer Spemann's pressing scientific problem. However, in the decades that followed, nuclear transplantation research became more utilitarian, eschewing the theoretical questions in favor of their biomedical promises. The increasingly practical goals for nuclear transplantation reflected broader patterns in biology, precipitating debates among scientists, and in society at large, about the nature of biological research. An analysis of these debates illustrates the ways in which Americans became skeptical about the motivations of biologists and direction of biological sciences. As funding for cloning experiments shrank in the wake of intense social and scientific concerns in the early 1980s, biologists jettisoned nuclear transfer methods in favor of new genetic engineering techniques that had been developed in the 1970s.

The early breakthrough in cloning came in 1952, when embryologists Robert Briggs and Thomas King, intending to answer basic questions about development, pioneered successful nuclear transfer experiments with frogs. Their breakthrough came during a time when the field of embryology was in significant flux, moving from a defined discipline with very specific tools and approaches to being incorporated in the up-and-coming field of "Developmental Biology." The larger field of developmental biology sought to unify an array of perspectives, disciplines, and technical approaches that were used to study the broader idea of development from early embryos to senescence. Like any burgeoning discipline, there were theories and personalities that helped to define the structure, direction, and attitudes of the field. One such person, who both produced important coalescing theories, and provided leadership for the field, was

Dr. Paul Weiss, whose papers are housed at the Rockefeller Archive Center.

Paul Weiss (1898 – 1989) was an Austrian-born biologist who immigrated to the United States in 1930. Weiss worked on a wide variety of biological phenomena, but became particularly known for his theories of early development, regeneration, and neurobiology. In 1933 he became a professor at the University of Chicago, where he worked diligently and effectively for twenty years, earning a reputation as not only one of the foremost minds in biology, but also as someone who possessed the political skills and ambition to rise to the highest positions in the profession. In 1954, Weiss accepted a position at Rockefeller University in New York where he remained affiliated until his death in 1989. Dr. Weiss had been elected to the National Academy of Sciences seven years prior to his move to Rockefeller University. While at Rockefeller University, Dr. Weiss strengthened his already strong reputation as a scientist and continued to be a leader in the field. In 1979 President Jimmy Carter awarded Weiss the National Medal of Science, the highest scientific honor in the United States.

In his career, Paul Weiss held some of the more influential positions in the profession. He served as chairman to several National Academy of Sciences committees as well as president and editor to some of the most prestigious societies and journals in the biological field. In 1939 he wrote *Principles of Development*, an influential developmental biology textbook in which he laid out his inspiring, but controversial ideas concerning the role of morphogenetic fields in development.[1] In the 1940s and 1950s, during which the techniques and theories of cloning were developed, Paul Weiss was one of, if not the most, well-known and influential developmental biologists.

In the few histories that have examined the history of cloning, none have properly contextualized the science or its goals. Considering the importance of Paul Weiss to the field,

both as a leader and as a theoretician, the Weiss papers provide one of the best ways to understand how the development of nuclear transplantation techniques fit within the broader profession. For instance, were Briggs and King working on the peripheries, or well within the experimental boundaries of the field? What were the theoretical underpinnings of their work? And, how did the work of Briggs and King undermine or bolster contemporary theories?

The archival material found in the collection of Paul Weiss provides ample means to build a coherent scientific context of the late 1940s and early 1950s. The lecture notes from a summer class taught by Weiss in 1950 provide some of the most useful material.[2] These notes offer a meaningful window into the context of developmental biology in that era and offer insights into Weiss's personal and intellectual commitments. For instance, the class appears to be designed for those who had a firm foundation in the biological sciences and were interested in learning more about the development of multi-cellular organisms. This format allowed Weiss to outline the established theories of development without being bogged down by explanations of the basic biological functions associated with them. However, Weiss did not teach the class from a textbook in the traditional manner. Instead, Weiss created his own topic outline and lectured about the latest theories surrounding specific topics in developmental biology such as nerve regeneration, immunology development, and aging.

In this first lecture, Weiss remarked "I decided that the best thing maybe that I can do for you is to tell you about the things that are not published and that you wouldn't be able maybe to find. So I will avoid repetitions of the text-books. I take it for granted that you all can read and I'll simply refer you to this [sic] respective references."[3] Over the course of the semester, Weiss outlined a variety of cutting-edge theories that biologists were using in experimental practice and to understand new phenomena. Like most cutting-edge theories, many of them were not

universally accepted nor would they become entrenched within the field in the future. These theories, however, represented the currents of the field in 1950, illuminating the ways in which experimental approaches and explanations the developmental biologists thought of were the most fruitful in answering and uncovering new questions.

The 1950 lectures offer a glimpse into the importance of genes to the field (they were not), the value of physio-chemical approaches (very valuable), and whether reductionism offered all the solutions (it could not). For historians, these lectures uncover a picture of developmental biology that is often hidden. Published scientific papers often lack the larger theoretical explanations in favor of limited explanations concerning the phenomena and data at hand. Grand theorizing is difficult to pass through the scientific review process without massive amounts of data. Though such generalizations are absent in many of these articles, they nonetheless underpin the contemporary objectives of the biologist. Without further access to personal papers or oral histories, it is difficult for historians to confidently identify such intellectual motivations. Weiss's lectures, however, make these ideas accessible in a new way.

Moreover, many of the biological sciences in the late 1940s and early 1950s were on the cusp of a major transformation. In 1953, Watson and Crick discovered the structure of DNA, which tripped a cascade of technical and theoretical advances over the proceeding decades. Science, as a rule, only acknowledges those theories that "won out." That perspective, however, misrepresents the historical process of how science develops. During the late 1940s and early 1950s, many of the prominent competing theories and experimental approaches contemporaneous with the discovery of DNA had been downplayed and forgotten, distorting our ability to properly contextualize developmental biology theories at this time. The fourteen

transcribed lectures from Weiss's 1950 summer class offer an anchor in which to build a robust context in which the first cloning experiments can be placed within.

As expected, the RAC offered unique and enriching materials through the Rockefeller University collections. The surprise came when I took extra time to delve into the papers of Rockefeller Foundation (RF), and in particular, those of Gerard R. Pomerat, the program officer in charge of funding projects in the biological sciences. As the primary agent for doling out funding, Pomerat traveled extensively to review and tour laboratories, keeping careful diaries of his conversations and contacts with biologists throughout the world. Through these diaries, a fascinating picture arises of the biological community.

I examined Pomerat's diaries from 1949 through 1959, focusing particularly on the developmental biology community.[4] Through opinions of Pomerat and the detailed conversations that he had with various biologists during this decade, it became clear as to which laboratories and researchers were most promising from a RF perspective, not forgetting that, despite their protestations to the contrary, the RF officers had agendas as well.

In recording every conversation with scientists in almost every laboratory he visited, Pomerat's diary made me aware of cloning research that I did not know previously existed. In his frequent visits to English laboratories, Pomerat had detailed conversations with scientists at King's College London. In June of 1950, Pomerat met with James F. Danielli, a cell biologist who had completed pioneering work on cell membrane structure in the early 1940s. As Pomerat wrote, Danielli's new project dealt with nuclear transplantation experiments. Danielli's plan was to perfect the technique in amoeba and sea urchins first, and then apply it to mammals.[5]

Danielli's work has been overlooked in the histories of this field. However, his work is important for a variety of reasons, none of which have to do with whether he was successful.

The fact that Danielli conducted similar experiments concurrently with Briggs and King implies that nuclear transplantation studies were seen by multiple researchers as a valid way to answer pertinent questions in the field. Cloning, it seems, had multiple independent beginnings, with researchers in very different settings conducting similar experiments to answer similar questions. Danielli never became the father of cloning because he met significant hurdles in applying the technique to mammalian embryos. Briggs and King worked with frog embryos, which proved to be much easier to work with than mammalian cells. In fact, though many researchers advanced nuclear transplantation studies in the 1950s and 1960s after Briggs' and King's first experiments, mammals were not cloned until the early 1980s. In effect, Danielli's choice to move from the simplistic model of single-celled organisms to the highly complex developmental patterns of the mammal without working with on simpler complex organisms greatly contributed to his failure to be play a significant part of cloning's history.

Gerard Pomerat's conversations with Danielli uncovered other valuable information for the history of cloning. Briggs' and King's first paper, published in 1952, appeared in the *Proceedings of the National Academy of Sciences*.[6] For a paper to be published in the journal, a current member of the National Academy of Sciences had to sponsor it. Charles W. Metz, a prominent cell biologist at the University of Pennsylvania sponsored the paper for Briggs and King. It was assumed that the city of Philadelphia provided the connection between these researchers given that many of the biologists at Lankenau Hospital Research Institute, where Briggs and King worked, had joint appointments with local universities, including the University of Pennsylvania. However, Pomerat's diary shows that Metz was a visiting fellow at Danielli's laboratory in Kings College London in the late 1940s. With this information, the connection between Briggs' and King's work and Metz becomes much clearer. Metz's familiarity with

Danielli's work probably allowed him to immediately see the significance of Briggs' and King's research.

Overall, Pomerat's diaries and Weiss' papers highlight and uncover new connections in the history of cloning. The development of science does not occur in solitude at a laboratory bench, but rather is deeply affected by the movement and interaction of people and ideas. As a historian, it is my job to contextualize, trace, and identify the influences that shape my story. The Rockefeller Archive Center has allowed me to do so.

ENDNOTES:

[1] Paul A. Weiss, *Principles of Development*. New York: Henry Holt and Company, 1939.
[2] Rockefeller University, RG 450 W436: Paul A. Weiss Collection, Series 5: Lectures, Box 49.
[3] Rockefeller University, RG 450 W436: Paul A. Weiss Collection, Series 5: Lectures, Box 56, "First Lecture, June 24, 1950."
[4] Rockefeller Foundation, RG: 12.2, Officer's Diaries, "Pomerat, Gerard R."
[5] Rockefeller Foundation, "Diary entry - GRP Diary, June 7, 1950 – London," RG: 12.2, Officer's Diaries, "Pomerat, Gerard R." Box 68, Folder – "1950."
[6] Rockefeller Foundation, Robert Briggs and Thomas J. King, "Transplantation of Living Nuclei from Blastula Cells into Enucleated Frogs' Eggs." *PNAS* 38 (May 15, 1952), pp.455-463.