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Park, Hyung Wook

2015

Park, H.W. (2016). Constructing Failure: Leonard Hayflick, Biomedicine, and the Problems with Tissue Culture. *Annals of Science*, 73(3), 303-327.

<https://hdl.handle.net/10356/87083>

<https://doi.org/10.1080/00033790.2015.1057764>

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Constructing Failure: Leonard Hayflick, Biomedicine, and the Problems with Tissue Culture

Hyung Wook Park

(Nanyang Technologica University; park0717@gmail.com)

Summary

By examining the use of tissue culture in postwar American biomedicine, this paper investigates how scientists experience and manage failure. I study how Leonard Hayflick forged his new definition of failure and ways of managing it by refuting Alexis Carrel's definition of failure alongside his theory of the immortality of cultured cells. Unlike Carrel, Hayflick claimed that every vertebrate somatic cell should eventually die, unless it transformed into a tumour cell. This claim defined cell death, which had been a problem leading to a laboratory failure, as a normal phenomenon. On the other hand, permanent life, which had been considered a normal cellular characteristic, became a major factor causing scientific failure, since it implied malignant transformation that scientists hoped to control. Hayflick then asserted that his cell strains and method would partly enable scientists to manage this factor—especially that occurred through viral infection—alongside other causes of failure in routine tasks, including bacterial contamination. I argue that the growing biomedical enterprise fostered this work of Hayflick's, which had repercussions in both his career and the uses of cells in diverse investigations. His redefinition of failure in the age of biomedicine resulted in the broad dissemination of his cells, medium, and method as well as his long struggle with NIH, which caused his temporarily failed career.

Keywords: tissue culture, failure, biomedicine, Leonard Hayflick, NIH

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Ever tried. Ever failed. No matter. Try again. Fail again. Fail better.
--Samuel Beckett, *Worstward Ho* (1983)

1. Introduction

How and why do scientists fail in their experimental research? Scientists feel that they failed for various reasons. Something went wrong, they say, during the course of their research, which ended up showing artefacts rather than facts of nature. For instance, scientists during their routine laboratory work can perceive failure when their experimental results are too close to what is commonly known as an error and far from their usual expectations based on the systems of theories and assumptions in their field. Occasionally, such results could produce a new theoretical framework for a novel interpretation, but many such findings are eventually abandoned.¹ Failure can also occur at the level of a research project and a career. In a major project they supervise, scientists can fail to produce a result with a clear practical or theoretical relevance. Even their entire career can fail when their problems or mistakes in experimental research seem close to academic misconduct and thus become a problem of ethics.²

Consequently, failure and its causes have commanded scientists' attention. Since Francis Bacon (1561-1626) condemned the 'idols' and Johannes Kepler (1571-1630) studied the nature of observational 'errors', scientists have consistently discussed the problems of failure and its causes.³ Today, researchers teach their students how to avoid possible pitfalls in the labyrinth of protocols, instruments, and chemicals in experimental investigations. Research ethics is another important subject for those who want to build a career in science without being involved in problems that are contrary to the common rules of the research community.

¹ According to Hans-Jörg Rheinberger, a sound experimental system produces many unexpected results, or 'novelties', which are incorporated in constantly changing scientific research. See Rheinberger, *Toward a History of Epistemic Things*. But it is obvious that not all such results engender new lines of investigation.

² For a good example, see Kevles, *Baltimore Case*.

³ Daston, "Scientific Error"; Hon, "On Kepler's Awareness of the Problem."

Failure in science is thus an important subject, and this importance prompted several philosophers and social scientists to explore its nature. Many years ago, Thomas Kuhn stated that failed research might just be a case in which results should be understood outside the current 'paradigm' in a field. With a 'revolution' in the science, researchers would shift their paradigm and redefine the case that had been thought a failure as a successful one.⁴ This view, which provoked long controversies about the meaning of objectivity, was just a first step in the reconceptualisation of the problems of failure. Thereafter, a group of scholars advocating the social construction of scientific knowledge brought forth similar views, despite their significant difference from Kuhn. Stressing the close connections among experimental skill, instrumentation, and the outcome of research, social constructivists have argued that both success and failure are created through negotiations and human interactions under social, political, and material tensions.⁵ For both Kuhn and the social constructivists, experimental failure depends on the epistemic and politico-cultural structures supported or contested by scientific communities or the public.

Failure in science has also been a critical subject among historians, including Gerald Geison and Daniel Kevles. Through his analysis of the Pasteur-Pouchet debate over spontaneous generation in nineteenth-century France, Geison described the political resolution of a conflict between the two scientists with opposite views of failure and success concerning the appearance of germs in an organic soup after boiling.⁶ When Louis Pasteur perceived an experimental failure in germs observed in the boiled soup, Felix Pouchet argued that the germs seen in his own boiled soup successfully demonstrated spontaneous generation. But this success was soon denied in the conservative French Catholic regime that condemned materialism found in Pouchet's theory of spontaneous generation. Scrutinizing a different issue in contemporary biomedicine, Daniel Kevles has also traced the political and cultural

⁴ Kuhn, *Structure of Scientific Revolutions*, esp. 74-6.

⁵ There are numerous publications by these scholars who created the field of STS (Science Technology Studies or Science, Technology, and Society). For some classical books relevant to both social constructivism and this paper, see Collins, *Changing Order*; Gooding, Pinch, and Schaffer, *Uses of Experiment*; Latour and Woolgar, *Laboratory Life*.

⁶ Geison, *Private Science of Louis Pasteur*, 110-42.

landscape around failure.⁷ Through his study of the ‘Baltimore case’, he has illuminated how people who viewed a research problem as resulting from an experimental mistake fought against those who viewed it as a fraud. Kevles has argued that this struggle—which caused the temporary career failure of several engaged scholars, including the renowned biologist David Baltimore—took place in late-twentieth century America where the increasing public expense of biomedical research contributed to greater demands for scientists’ integrity.

This paper does not reiterate the long controversies regarding Kuhn, Pasteur, or the Baltimore case. Rather, I further explore an aspect of scientific failure that these studies have commonly addressed. As they have shown, the creation of artefacts does not necessarily equate to the problems that scientists associate with failure, such as Pasteur’s observation of germs after boiling and Baltimore’s career troubles. Since the meaning of scientific success is subject to continuing negotiation and redefinition, its opposite pole must also be amenable to similarly complex processes. This paper studies how scientists, in accordance with shifting sociotechnical environment, change the meaning of failure and the ways to cope with it, while they might not know the long-term effect of their effort. By ‘failure’, I do not mean a permanent or irreversible loss. After an unsuccessful outcome, scientists could always restart by examining why and how they failed. They then may find their ‘errors’ during an experiment.

Indeed, there has been a substantial scholarship on this subject—‘experimental errors’. Giora Hon and other scholars have investigated various types of errors scientists may commit during their work and their effort to manage them in their everyday practices.⁸ The epistemic, heuristic, and moral implications of errors have also been important subjects of inquiry.⁹ Yet, as a historian, my point of interest is slightly different, since I start from what scientists usually understand as a *consequence* of errors. I think that a focus on ‘errors’ themselves may involve

⁷ Kevles, *Baltimore Case*.

⁸ Hon, “Towards a Typology of Experimental Errors”; “On Kepler’s Awareness of the Problem”; Alchin, “Error Types.”

⁹ Olesko, “Meaning of Precision”; Cadeddu, “Heuristic Function of ‘Error’”; Schickore, ““Through Thousands of Errors.””

a retrospective evaluation of past events from our own standpoint. Rather, I study what scientists in the past called failure within their historical circumstances.

There are several reasons why I do so. Above all, a scientist's successful research can be regarded as a failure by another with a different viewpoint. The Pasteur-Pouchet debate might arguably be the best case illustrating this difference. Moreover, scientists can fail without committing any errors. For instance, a tissue culturist can fail to grow her cells, because of their spontaneous transformation or death, which can occur without any errors in an experiment. Strikingly, scientists might not be able to find even such a natural cause of failure in some situations. As Kathleen Jordan and Michael Lynch have shown, biologists using PCR (polymerase chain reaction) may not be able to identify the cause of their failure, no matter how hard they work to detect possible factors contributing to the disappointing result.¹⁰ In addition, I study the long-term consequences of a scientific work, which may incur moral and legal debates and lead to a researcher's temporarily failed career. This is why I think that 'experimental errors' may not be my research focus. Probably, 'going amiss', a term Hon, Jutta Schickore, and Friedrich Steinle have used in their recent edited volume, is more compatible with my interest, because its broad meaning covers various attempts and their aftermath in diverse cultural and material settings.¹¹

Tissue culture is a good example illustrating my approach. Being a key research method in modern biomedicine, tissue culture has evolved from a cutting-edge technique for prestigious scholars in top-notch institutions into a routinely used tool in many biomedical laboratories engaged in various clinical and experimental tasks.¹² Today, tissue culture is usually a responsibility of graduate students, technicians, and postdoctoral fellows rather than senior scholars. But this current state of affairs concerning tissue culture does not necessarily

¹⁰ See, for example, the problem of 'PCR (Polymerase Chain Reaction) hell', in Jordan and Lynch, "Mainstreaming of a Molecular Biological Tool," 170-4. As a result of this 'hell', the authors claim, scientists often produce diverse variations of the original protocol.

¹¹ Hon, Schickore, and Steinle, "Introduction." I think that this book's perspective is broader than Hon's earlier scholarship on experimental errors. In particular, it successfully deals with 'errors of nature' and the problems of the Whiggish interpretation of history.

¹² Landecker, *Culturing Life*, 107-39; Fujimura, *Crafting Science*, 37-45.

indicate that it has become easy. Culturing cells demands adequate training and careful observance of procedures, without which researchers can often experience failure. As I have just stated, however, some of the causes of failure may have nothing to do with experimenters' errors. Moreover, in certain cases, investigators can never understand the reason why they failed. Such situations, mostly incurred by cells' transformation, contamination, or death, can bring a deep trouble to most investigators, because tissue culture is playing a significant role in biomedicine with an increasing number of available cell lines, diverse culture media, and new technologies like antibiotics and deep freezers. Although scientists, under these circumstances, have tried to identify and manage failure through standardized materials, manuals, and training programs, their efforts have not always been successful.

Cellular immortality was a crucial topic representing the problems of failure in tissue culture. The French surgeon Alexis Carrel (1873-1944) first proposed the notion of immortality in the 1910s when he started growing embryonic chicken heart cells, which, according to him, would never die in an adequate culture. That Carrel was a central person showing that animal somatic cells could be maintained outside of the body indicates that tissue culture was intertwined with the notion of immortality from its very inception. Since cells were inherently immortal, Carrel thought, the death of cultured cells was a definite failure caused by researchers' mistakes or incompetence. Conspicuously, most later investigators accepted this view of Carrel's for fifty years until the American biomedical scientists Leonard Hayflick and Paul Moorhead showed that normal somatic cells of vertebrates should always die after a certain number of doublings, which was later called the 'Hayflick limit'.¹³ When their 1961 paper presented this discovery through the culture of human foetal cells, Carrel's earlier work on 'immortal' cells was labelled a failed experiment or, possibly, a fraud.¹⁴ These cells of Carrel's were merely abnormal ones formed after malignant transformation, which was a common cause of failed tissue culture, like other problems such as microbial contamination. After this notable discovery, however, Hayflick's career suffered a considerable setback.

¹³ Hayflick and Moorhead, "Serial Cultivation of Human Diploid Cell Strains"; Burnet, *Intrinsic Mutagenesis*, 60.

¹⁴ Witkowski, "Dr. Carrel's Immortal Cells."

Although he was quite successful until the mid-1970s, he soon came to be involved in a long series of court battles against the National Institutes of Health (NIH), because of its suspicion of several problems in his cells that could potentially lead scientists to fail during their experiments. As a result, Hayflick's career also came close to failure, at least during the six years of litigation. What was the nature and context of Hayflick and Moorhead's work that redefined the previous orthodoxy as wrong and based on failed research? Why did the scientist who conducted this remarkable study then experience such a troublesome affair with a federal institute?

I do not repeat the well-known story of Hayflick and Moorhead's work as a scientific innovation.¹⁵ Nor do I deal with how their study contributed to gerontologists' research on the cellular basis of ageing.¹⁶ Rather, this paper aims at analysing Hayflick's work and career involving tissue culture in twentieth century American biomedicine. On this subject, Hannah Landecker's *Culturing life* stands as an excellent piece of scholarship, which also addresses some of the topics I discuss in this paper.¹⁷ Yet I focus on an issue that she does not discuss in depth, that of the relationship between Hayflick's experiments and career and the practices of identifying and managing failure in biomedicine.

This paper argues that the emerging American biomedical enterprise in the postwar period prompted Hayflick to construct his new definition of failure along with his tools for managing it, which had repercussions on his career as well as general laboratory practices. From social constructivists, I borrow the term, 'construct', to mean that Hayflick's new definition of failure and the dissemination of his tools for its management were made possible in a particular social situation, namely, the rise of biomedicine. I analyse how modern biomedicine after World War II—as characterized by new laboratory approaches to cancer and viral diseases, the circulation of human body parts among hospitals and laboratories that often

¹⁵ Shay and Wright, "Hayflick, His Limits, and Cellular Ageing"; Watts, "Leonard Hayflick."

¹⁶ This has been discussed by some scholars. See Lijing Jiang, "Causes of Aging Are Likely to Be Many," 555-6, 564-5; Moreira and Palladino, "Ageing between Gerontology and Biomedicine," 358-9; Moreira and Palladino, "Squaring the Curve"; Hall, *Merchants of Immortality*, 14-41.

¹⁷ Landecker, *Culturing Life*, 68-106, 166-7,

involved monetary transactions, the extensive funding from the federal government and pharmaceutical companies, and the routinisation of laboratory work including, most notably, tissue culture—led Hayflick to construct his view of failure in tissue culture and the new tools for identifying and regulating it in many lines of research, which involved semi-skilled workers doing routine tasks.¹⁸ I investigate these changes amid uncertainties, opposing voices, and questions, including those that brought about an unfortunate and temporary failure in Hayflick’s career. This story begins with Carrel, whose work Hayflick refuted.

2. Defining Failure

Although Alexis Carrel was not the first to develop tissue culture, he was a major contributor to establishing the technique. After incorporating the basic methodology from the American embryologist Ross Harrison, Carrel showed that animal tissues could not only survive outside of the body but could also proliferate actively.¹⁹ Whereas Harrison was interested in exploring embryological problems in nerve fibre growth through tissue culture, Carrel was attracted by the technique itself, which demonstrated that scientists could make cells continuously divide and increase their kind in a carefully-controlled artificial medium.

As Hannah Landecker and Shelly McKellar have shown, this work of Carrel’s stemmed from his surgical expertise and career.²⁰ He was already famous for his ‘unusual manual dexterity’ in his work at Lyon, France, a city famous for its distinguished surgeons.²¹ However, since he was not able to find a hospital appointment there, he had to leave for North America in 1904. Initially, he moved to Montreal, Canada, where he impressed a number of medical practitioners and researchers with his new vascular surgery. With this reputation, he was able

¹⁸ The birth and growth of biomedicine has been extensively studied. See, for example, Gaudillière, *Inventer la biomedicine*; Keating and Cambrosio, *Biomedical Platforms*; Clarke et al., “Biomedicalization”; Löwy, “Historiography of Biomedicine”; De Chadarevian and Kamminga, *Molecularizing Biology and Medicine*; Lawrence and Weisz, *Greater Than the Parts*. Also see Jordan and Lynch, “Dissemination, Standardization and Routinization.” Some scholars have discussed these as late-twentieth-century phenomena. But Löwy’s, Gaudillière’s, and others’ accounts show that these phenomena of the late twentieth century had already started to emerge as early as the 1950s.

¹⁹ Harrison, “Observations on the Living Developing nerve Fiber”; Carrel, “Rejuvenation of Cultures of Tissues.”

²⁰ Landecker, *Culturing Life*, 68-92; McKellar, “Innovation in Modern Surgery,” 135-50.

²¹ Reggiani, *God’s Eugenicist*, 11; Hamilton, *History of Organ Transplantation*, 90-92.

to move to the United States—first to the University of Illinois, but ultimately to the Rockefeller Institute for Medical Research—where he further developed his method of surgical vascular anastomosis alongside organ transplantation. This technique confirmed his great manual skill and ultimately earned him the Nobel Prize in Medicine in 1912. Significantly, it was this work that led Carrel to appropriate tissue culture from Harrison. To Carrel, Harrison's method was invaluable, because he could use it for investigating the process of healing at the cellular level after surgery. With the culturing technique, surgeons could study how tissues after surgery were restored and might discover a means to facilitate the process.

Carrel's early papers reporting his new tissue culture shows his surgical orientation through methodology and vocabulary. Like most of his contemporaries, he stressed the significance of strict asepsis and the careful maintenance of temperature, humidity, and fluids surrounding the tissues.²² It is thus no coincidence that a photographed scene of his tissue culture experiment resembled that of a surgical operation (Figure 1). Just as Carrel and his assistant looked like surgeons with surgical gowns, the tissues in front of him appeared to be his patients.

[Figure 1]

To Carrel, his surgical training enabled him to handle his cells correctly and made them immortal. This required occasional rejuvenation of aged cells by 'removing from the culture substances that inhibit growth and....giving to the tissue a new medium of development'. This would be

²² Carrel, "Method for the Physiological Study"; Carrel and Burrows, "Cultivation of Adult Tissues and Organs."

accomplished by extirpating with a cataract knife the fragment of coagulated plasma containing the original piece of tissue and the surrounding new cells, which are washed for several minutes in normal or slightly hypotonic Ringer's solution.²³

The 'cataract knife' as well as the careful washing of extirpated tissues in Ringer's solution illustrates that this work was performed by a well-trained surgeon. According to him, the job should be done whenever cultured tissues' 'rate of growth decreased or when large granulations appeared in the cytoplasm of the cells'.²⁴ Since these phenomena indicated that the cells were becoming senile, their transplantation to a fresh and nutritious medium after gentle washing would stop the process and 'rejuvenate' them. If this work was repeated at the right moments, then the cultured tissues would indefinitely survive and proliferate outside of the body. Strikingly, Carrel's team actually cultured one group of their cells derived from an embryonic chicken heart from 1912 to 1946, even after Carrel himself died. For more than thirty years, the cells lived a 'public life' as a piece of material evidence for eternal life at the cellular level.²⁵

Carrel's theory of immortality was not simply a product of his surgical practice. As Landecker has written, 'immortality was not an unusual topic in the biology of this period'.²⁶ Scientists then found immortality in various forms of life. For instance, botanists discovered some plant cells' ability to dedifferentiate and restart the developmental processes.²⁷ The study of invertebrates and protozoa also revealed several instances of their 'rejuvenation', which could make them immortal.²⁸ Alongside these studies, there were some attempts to rejuvenate human beings by transplanting animal sexual organs or glands. That Carrel was a close

²³ Carrel, "Rejuvenation of Cultures of Tissues."

²⁴ Ibid.

²⁵ Landecker, *Culturing Life*, 92-106.

²⁶ Landecker, "On Beginning and Ending with Apoptosis," 43.

²⁷ Hildebrand, "Lebensdauer und Vegetationsweise," 51-134. Plant cells did not seem to have a strict distinction between soma and germ plasm, which applied to all animal cells, as the German zoologist August Weismann argued. See Weismann, *Essays upon Heredity*, 24-32.

²⁸ Conklin, "Size of Organisms"; Child, *Senescence and Rejuvenescence*, 186. From today's standpoint, these phenomena could be called regeneration or heterogamy.

colleague of a champion of this work, Serge Voronoff, was probably not insignificant in starting his immortal cell culture.²⁹ Carrel also closely interacted with scientists interested in rejuvenation and aging, who would later contribute to building the Gerontological Society.³⁰ Carrel's theory of immortality reflected his relationship with these scholars of his time.

But how could ordinary somatic cells could survive permanently? All of them appeared to perish along with the death of the individual body to which they belonged. But Carrel could explain this problem. To him, the cells *in vivo* could not become immortal, because they were not able to eliminate their metabolic wastes quickly and gain a constant supply of quality nutrients in a timely manner, unlike their counterparts in the surgeon's laboratory. Somatic cells' mortality was due to the inherent limitation of their natural multicellular organisation, which could be overcome through Carrel's expertise.

This view highlighted the significance of surgical skill in maintaining immortality. Cells *in vitro*, unlike those *in vivo*, could enjoy an immortal life due to the skill and care of surgical experts like Carrel. Animal somatic cells could rejuvenate only in so far as a competent surgeon or other practitioners with adequate training in tissue culture skilfully controlled cellular life in a laboratory condition. The idea of immortality, which was 'not an unusual topic in the biology of this period', was applied to tissue culture with surgical practice and discourses.

Carrel often discussed the importance of the care, training, and nimble fingers of those who dealt with cultured tissues in their laboratories. For example, Carrel and Montrose Burrows stressed in 1911,

The condition of the tissue, its size and thickness, the manner in which it has been cut, the period which elapses between the interruption of the circulation and the imbedding in plasma, the duration of the exposure to air, the degree and duration of chilling, etc., may have an influence on the rate and extent of growth. The preparation and the

²⁹ Hamilton, *Monkey Gland Affair*, 8-10.

³⁰ Park, "Refiguring Old Age," 38-51.

preservation of the cultures, and some details of the technique, often affect the growth.

The nature of the plasma, the size and thickness of the drop...the time elapsing between the imbedding of the tissue in plasma and the sealing of the hollow slides, the temperature of the incubator, and the variations of temperature according to the different parts of the incubator, etc., may cause important variations.³¹

Apparently, tissue culture was a very sophisticated art. The authors emphasised that ‘unless great care [was] taken to eliminate...these sources of error’ it was hard to obtain a reliable result through tissue culture. In 1924, Carrel also asserted that ‘the technique [was] delicate and, in untrained hands, the experimental errors [were] of such magnitude as to render the results worthless’.³² Like a failed surgical operation that might kill patients, failure in tissue culture, which would lead to cellular death, was due to lack of enough care and skill of experimenters. Preventing such a failure meant that scientists could make cells stay alive and perpetually proliferate *in vitro*.

3. Rejuvenation and Immortal Cells

Carrel’s emphasis on skill and care as a key to ‘rejuvenating’ cells represented his professional and cultural experience as a surgeon. He reiterated surgeons’ cultural attitude towards touching the ‘territories of the self’, which was translated into a ritualistic procedure for maintaining sterility and asepsis in operating rooms.³³ Yet it seems improbable that later tissue culturists, most of whom had no surgical training, shared the same cultural attitude and practice. It is also unlikely that later tissue culturists attempted to replicate Carrel’s method literally as described in his publications, since actual experimental practices tended to differ in

³¹ Carrel and Burrows, “On the Physicochemical Regulation,” 564.

³² Carrel, “Tissue Culture and Cell Physiology,” 6.

³³ Katz, “Ritual in the Operating Room.” Stefan Hirschauer argues that surgical sterility is to ‘be understood *relative* to the patient-body’, whose boundary must be respected, as we usually respect the boundary of other people’s body in ‘everyday situation’. See Hirschauer, “Manufacture of Bodies in Surgery,” 306-7.

each lab.³⁴ Of course, certain general practices such as aseptic procedures—which were important in a period without antibiotics—were passed on to later tissue culturists, but their actual details did not appear to remain the same. After all, a strict compliance with Carrel’s procedure did not guarantee their success, just as a highly stringent observance of surgical rituals did not completely prevent infection in an operation.³⁵ However, most tissue culturists took one portion of Carrel’s ideas seriously, namely, the relationship between cellular lifespan and the culture condition. For fifty years, they believed that cells could live forever if they were cultured in an ideal condition with extreme caution and care.

This belief continued for several reasons. Some researchers shared Carrel’s idea that humans, through tissue culture, could liberate cells from the limitations of multicellular organisation that inevitably led them to die.³⁶ To others, the reason was geared to the technical challenge of tissue culture itself. After Harrison and Carrel, a large number of researchers began cultivating various animal cells, but many of them, including human cells, simply resisted scientists’ attempts to grow in laboratory conditions.³⁷ If a scientist was not able to culture cells, what was the cause? An easy answer was to attribute the failure to the scientist’s underdeveloped skills or mistakes, and this further buttressed Carrel’s argument. At any rate, Carrel was a Nobel laureate and a member of an affluent medical research institute with cutting-edge facilities. If there was anything wrong in a tissue culture experiment, it was unlikely to be found in the master surgeon’s laboratory.

This situation bespoke what Harry Collins has called ‘experimenters’ regress’.³⁸ Carrel argued that a scientist’s failure with tissue culture was due to his or her ‘untrained hands’, which must have meant the lack of care, sufficient skill, and nimble fingers. But how can we tell if a scientist had such ‘untrained hands’? In accordance with Carrel’s standpoint, it would be decided through the outcome of his or her culture experiment. If cultured tissues died, then

³⁴ For example, see Jordan and Lynch, “Sociology of a Genetic Engineering Technique,” 96-101.

³⁵ Katz, “Ritual in the Operating Room,” 335-6.

³⁶ Lansing, *Cowdry’s Problems of Aging*, chapters 2 and 3; Landecker, *Culturing Life*, chapter 2.

³⁷ Landecker *Culturing Life*, 108-9.

³⁸ Collins, *Changing Order*, 79-111.

the scientist must have such ‘untrained hands’. In other words, the untrained hands caused tissue death, and tissue death was evidence of the untrained hands. This circular logic created an infinite cycle of ‘regress’ for experimenters. Could, then, there be any investigator who was thoroughly trained but still could not sustain the cultured cells permanently? To Carrel, such an investigator could not exist, because experimenters’ skill and the tissues’ indefinite survival belonged to one practical and theoretical package. Researchers who hoped to break this package open needed to tackle his definition of failure. Since this was never easy, ‘scientists were more likely to see the death of their tissues as failure of technique rather than challenges to the idea of life’s indefinite bounds’.³⁹

What, then, happened to the biological studies of immortality and rejuvenation that initially prompted Carrel to propose this ‘idea of life’s indefinite bounds’? Remarkably, Voronoff and others’ work on rejuvenation was rejected by most scientists around the 1930s.⁴⁰ However, the lifespan of plants, protozoa, and invertebrates became gerontologists’ regular study topics. Indeed, most early champions of gerontology—including Edmund Vincent Cowdry and Alfred Cohn, who were also Carrel’s colleagues at the Rockefeller Institute—continued to take cellular immortality for granted in their research and professional discourse.⁴¹

But some of these scholars did eventually challenge Carrel’s work. In 1940, the British scientist Peter Brian Medawar, for example, showed that the rate of duplication in embryonic chicken heart cells consistently declined in a carefully-controlled culture.⁴² Although he did not examine whether this decline actually led to the cell’s death, it was a piece of evidence suggesting that the decrease in the chicken heart cells’ growth was ‘of their own accord’ and

³⁹ Landecker, *Culturing Life*, 92.

⁴⁰ Hamilton, *Monkey Gland Affair*, 120-42.

⁴¹ Park, “Edmund Vincent Cowdry,” 538-40, 546, 551, 557-8; Club for Research on Ageing, Secretary’s Report, p. 2, Box 30, Folder Club for Aging 1943 Feb, Nathan W. Shock Papers, Bentley Historical Library, Ann Arbor, Michigan (hereafter NWS).

⁴² Medawar, “Growth, Growth Energy, and Ageing,” 332-55. For a detailed discussion of the significance of this finding in Medawar’s research, including his evolution theory of aging, see Park, “Refiguring Old Age,” 128-77.

the growth was not maintained forever in accordance with Carrel's argument.⁴³ In 1953, another British scientist, Peter Leslie Krohn, embarked on testing Carrel's immortality theory with a long-term fellowship from the Nuffield Foundation.⁴⁴ However, his project, as well as his scientific career in gerontology, did not turn out to be particularly successful. As British gerontology failed to prosper due to the lack of adequate institutional and public support, Krohn's gerontological research did not consistently progress.⁴⁵

These attempts were not so important to the reception of Carrel's claim as they were to signalling the changed situation during and after World War II. The work of Medawar and Krohn reflected the birth of biomedicine as a major technoscientific enterprise in the western world. Indeed, Krohn's experimental program included both tissue transplantation and culture, reflecting the increasing biomedical attempts to use cells cultured in the laboratory to treat damaged body parts in the clinic.⁴⁶ It is also notable that Medawar started growing his cells in the laboratory of Howard Florey, a major contributor to the early clinical application of penicillin, which was mass-produced during the war to treat wounded soldiers and civilians. The fact that Medawar's career began in Florey's laboratory where penicillin's properties were actively investigated forecast the changing contexts of tissue culture in the age of biomedicine. Carrel's 'immortal cells' could still inspire gerontologists, but tissue culture as a technique became more closely aligned with a different field, biomedicine.⁴⁷

4. Biomedicine and the New Socio-Technical Formations

⁴³ Medawar, "Discussion on Growth," 593.

⁴⁴ Peter Krohn, "The Nuffield Foundation: Nuffield Gerontological Research Fellowship, Proposals for Research," pp. 3-6, Box NF AGE1, Folder Age 18 Nuffield Gerontological Research Fellowship, Nuffield Foundation Archive, London, England (hereafter NF).

⁴⁵ "Professor P. L. Krohn," 11 October 1966, Box NF AGE1, Folder Age 18 Gerontological Fellowships, NF. On the problems in British research on ageing, see Moreira and Palladino, "Ageing between Gerontology and Biomedicine," 357-8; Martin, "Medical Knowledge."

⁴⁶ Peter Krohn, "The Nuffield Foundation: Nuffield Gerontological Research Fellowship, Proposals for Research," pp. 1-6, Box NF AGE1, Folder Age 18 Nuffield Gerontological Research Fellowship, NF.

⁴⁷ According to Tiago Moreira and Paolo Palladino, gerontology forged a domain rather different from biomedicine. See Moreira and Palladino, "Ageing between Gerontology and Biomedicine."

What, then, was biomedicine at the time? Biomedicine was not just a synthesis of biology and medicine or a ‘reduction of pathology to biology’.⁴⁸ Yet its origin could be traced to the new medicine based on biological research in laboratories, which had started in the nineteenth century.⁴⁹ In a sense, biomedicine was an extension of this ‘scientific’ or ‘laboratory-based’ medicine to which major scholars like Louis Pasteur and Robert Koch contributed. But biomedicine involved a further shift in medical practice and research in the twentieth century. The term ‘biomedicine’ itself began to be used only in the interwar period, and World War II became a watershed for its application. This occurred as it became associated with the employment of radioactivity not only in the military but also for civilian medical applications through an alliance among physicians, scientists, governments, and commercial organisations.⁵⁰ After the war, the term soon came to indicate the systematic technoscientific approaches to diseases funded by governments and philanthropies, pharmaceutical companies’ mass-production of drugs, and the extensive movement of human cells and organs between clinics and laboratories, which often involved commercial transactions.⁵¹ When organ transplantation, after its temporary suspension during the 1930s and the 1940s, restarted with Medawar’s study of immunological tolerance, patients’ biopsy specimens began to travel from clinics to laboratories for research and diagnosis.⁵² Some of these specimens were stored for various reasons, including developing therapeutic applications, creating standardized repositories for tissue culture, or preserving biological samples of endangered ‘primitive populations’ in the Pacific Islands and the Amazon.⁵³ The growing medical industry in the mid-twentieth century thus became very different from the medicine in Pasteur’s and Koch’s time.

⁴⁸ Keating and Cambrosio, “Does Biomedicine Entail the Successful Reduction.”

⁴⁹ The emergence of ‘laboratory medicine’ has been studied by several historians. See, for example, Cunningham and Williams, *Laboratory Revolution in Medicine*; Geison, *Private Science of Louis Pasteur*.

⁵⁰ Lenoir and Hays, “The Manhattan Project for Biomedicine.”

⁵¹ Gaudillière, *Inventer la biomedicine*; Clarke et al., “Biomedicalization”; Löwy, “Historiography of Biomedicine.”

⁵² Hamilton, *History of Organ Transplantation*, 173-253; Schlich, *Origins of Organ Transplantation*.

⁵³ Landecker, *Culturing Life*, 155-6; Moser, “Modern Approaches,” 393; Radin, “Latent Life.”

In this new era, microbial contamination was a significant problem, but the introduction of antibiotics enabled scientists to manage it and alter the threshold of failure in tissue culture. With antibiotics like penicillin, researchers indeed reduced their rate of failure, because the substances controlled bacterial proliferation in tissue culture. Admittedly, none could completely eliminate contamination. Yet inoculating some amount of antibiotics into the medium did have an effect and contributed to the progression of tissue culture from a special accomplishment of a small cadre of experts to a routine technology amenable to lesser-qualified researchers, such as graduate students and technicians.⁵⁴

There were other factors contributing to the growing use of tissue culture in biomedicine, including the invention of the deep freezing technique and the publication of manuals with detailed protocols and procedures. After William Scherer and Alicia Hoogasian showed that cells could be stored with glycerol at -70°C, many researchers could conduct their experiments with fewer concerns.⁵⁵ Even if the cells died for a reason, such as accidental contamination, a large reservoir of dormant cells were always available in a deep freezer. Scientists simply needed to thaw one ampule of frozen cells and use them for a retrial. The publication of tissue culture manuals and textbooks was also instrumental in wider dissemination of tissue culture. After Raymond Parker, a colleague of Carrel's, published *Methods of Tissue Culture* (1938), a number of additional manuals were published. These manuals spread the techniques to many people engaged in various biomedical projects, especially after the Tissue Culture Association was established in 1946. As the association published manuals and held meetings and conferences, tissue culture became an even more common technique for a wide range of laboratory workers.⁵⁶

The expansion of biomedical research on the problems of viruses and cancer was another factor that facilitated the dissemination of tissue culture as a technique. Although

⁵⁴ Indeed, graduate training in the life sciences had been consistently expanding in America after the late nineteenth century. See Geison, "International Relations and Domestic Elites," 136-47; Pauly, *Biologists and the Promise of American Life*, 126-44; Maienschein, "Whitman at Chicago," 165-8.

⁵⁵ Scherer and Hoogasian, "Preservation at Subzero Temperatures."

⁵⁶ Landecker, *Culturing Life*, 133-4

Carrel and Burrows had proposed the use of tissue culture for cancer research as early as 1910, it became a more established tool for investigating cancer only after World War II.⁵⁷ The viral aetiology of tumours had also been suggested in the 1910s, but it was during the mid-twentieth century that viruses became a key object of cancer researchers' attention along with tissue culture.⁵⁸ In the 1950s, for instance, the 'plaquing' of viruses on cultured animal tissues started, enabling researchers to investigate how viruses killed or transformed ordinary cells.⁵⁹ In particular, normal cells' transformation into tumour cells after viral infection highlighted the importance of the virus in cancer aetiology and contributed to the rise of molecular genetic cancer studies, in which tissue culture played a key role. Behind this development, there was the postwar anti-cancer movement promoted by Congress, the American Cancer Society, NIH, and various pharmaceutical companies. These organisations funded a large number of researchers studying tumour viruses and the molecular characteristics of cancer.⁶⁰ In this collective effort, the results from tissue culture began to be calibrated against those from other new laboratory technologies, such as electron microscopy and ultracentrifugation.

The use of tissue culture for virus and cancer research accompanied the creation of cell lines, including, most notably, HeLa cells. Developed by a Johns Hopkins scientist George Gey and his colleagues in 1951 from a biopsy specimen of Henrietta Lacks, a cervical cancer patient, HeLa was the first human cell line that was put to a diversity of uses, among which cancer research was just one. HeLa cells were employed for examining viral infection, developing the Salk vaccine, and studying the effects of irradiation and intoxication. During these studies, HeLa cells' remarkable ability to survive changing environments allowed scientists to continue using them in various experimental projects. HeLa cells became a new symbol of immortality, long after Carrel's tissues had been discarded.⁶¹

⁵⁷ Carrel and Burrows, "Cultivation of Adult Tissues and Organs," 1381; Fujimura, *Crafting Science*, 37-45.

⁵⁸ Creager and Gaudillière, "Experimental Arrangements"; Fujimura, *Crafting Science*, 45-67.

⁵⁹ Creager and Gaudillière "Experimental Arrangements," 224-9.

⁶⁰ Gaudillière, "Molecularization of Cancer Etiology," 139-70.

⁶¹ Landecker, *Culturing Life*, 159-62; Skloot, *Immortal Life of Henrietta Lacks*.

But the discourse of immortality met a different environment in the 1950s. Postwar scientists involved with tissue culture often asked if the cell lines derived from cancer truly represented the normal human body. Could they really understand the normal physiological mechanisms through such cells? Researchers also began to worry about the ‘primary culture’ of apparently normal cells acquired from volunteers, patients, and aborted fetuses. As these cells moved from clinics to laboratories, tissue culturists asked whether the cells would always remain normal without becoming transformed into cell lines like HeLa. If such a transformation happened to take place, especially during efforts to develop vaccines and drugs funded by NIH or pharmaceutical companies, researchers might not produce a meaningful result and would thus waste their valuable budget. Even when this transformation itself was a research topic for tumour biologists, the cells preceding such a change had to be normal.⁶² In this situation, Joe Tjio and Albert Levan’s 1956 research showing that normal human somatic cells had forty-six chromosomes further prompted researchers’ queries about the differences between normal and transformed cells.⁶³ It seemed that normal and tumour cells did not share the same number of chromosomes. It was then not unusual to ask if normal human cells were as immortal and persistent as HeLa and other cell lines. In other words, immortality, which had once been considered a normal cell’s trait, became a problematic cellular characteristic indicating a possible failure of research projects involving tissue culture.

5. Leonard Hayflick and a Reconstruction of Failure

When Hayflick earned his PhD in medical microbiology at the University of Pennsylvania in 1956, a number of major scientists discussed the problem of cellular transformation in tissue culture and ways to examine and prevent its occurrence. For instance, Raymond Parker and his colleagues reviewed how normal somatic cells in culture underwent changes in phenotype and chromosomal structure through the effects of carcinogens and

⁶² Fujimura, *Crafting Science*, 41-5.

⁶³ Tjio and Levan, “Chromosome Number of Man.”

‘deliberate neglect’.⁶⁴ The authors stated that the altered cells ‘continue to multiply indefinitely, even in cultures in which the parent cell type disappears’. This characteristic could be ‘related to carcinogenesis’. In contrast, Jerome Syverton, chair of the Cell Culture Collection Committee sponsored by the National Cancer Institute, assured his readers that ‘biologically verified instances of *in vitro* neoplastic transformation’ seemed quite rare, since there were only ‘three reports over a period of two decades’.⁶⁵ Nevertheless, neoplastic transformation of cultured cells was a subject of serious concern among many people. Indeed, Theodore Puck’s team at the University of Colorado proposed a new means to monitor cultured cells’ chromosomal constitution alongside a technique for maintaining the genetic normality of cultured cells with a strict control of pH, temperature, and other factors.⁶⁶ To Puck and his co-workers, these conditions were very important, because most transformed cells ‘with more favourable growth potential could outgrow the euploid [normal] cells in the culture’.⁶⁷ Such an outgrowth would obviously make an experimental study fail.

In a similar vein, H. Moser at Columbia University stressed the biomedical significance of keeping cells normal and non-cancerous during continued tissue cultures. A chromosomal aberration was definitely an ‘artefact induced in the conventional suboptimal culture environment’.⁶⁸ Therefore, maintaining ‘in long term culture mammalian cell strains with normal and stable chromosome constitution’ was a ‘major achievement’ and ‘one of the keys to the establishment of functional cell banks for therapeutic applications (bone-marrow banks, skin-cell banks) and for other uses (*in vitro* production of antibodies, hormones, and viruses)’. Keeping normal cells with the usual chromosomal constitution was crucial in the new therapeutics relying on ‘functional cell banks’ in the age of biomedicine, when human body parts were shuffled across various laboratories and clinics.

⁶⁴ Parker, Castor, and McCulloch, “Altered Cell Strains,” 305.

⁶⁵ Syverton, “Comparative Studies,” 339.

⁶⁶ Tjio and Puck, “Genetics of Somatic Mammalian Cells.”

⁶⁷ Puck, Cieciura, and Robinson, “Genetics of Somatic Mammalian Cells,” 952.

⁶⁸ Moser, “Modern Approaches,” 392.

During his early career, Hayflick also extensively used tissue culture and investigated the problems of cellular transformation together with another critical issue in biomedicine, namely, contamination. In his postdoctoral training at the University of Texas, he joined a team investigating the changes caused by gamma irradiation upon human cells.⁶⁹ This project measured the chemical and morphological alterations of irradiated cells in culture. He also studied the problem of contamination of cultured tissues with the pleuropneumonia-like organism (PPLO). PPLO was found in nongonococcal urethritis and Reiter's syndrome and was known to be a common agent contaminating cultured mammalian cells.⁷⁰ It seemed to be bacteria, but was also similar to viruses because it appeared to enter a cell and could live within it as an internal parasite. Since antibiotics were not very effective in eradicating the organism, Hayflick thought that there should be a new and more effective measure, which he proposed in 1960. According to him, a hyperthermic treatment at 41°C, which simply meant a short-term elevation of temperature of culture dishes, would kill PPLO without disturbing cultured cells, because of differential sensitivities to heat.⁷¹ This was a new method of preventing problems in tissue culture due to microbial contamination.

Hayflick's remarkable paper of the following year should be understood as an extension of these early studies amid the deepening concern over neoplastic transformation and contamination. Indeed, when he returned to Philadelphia in 1958 as an associate member of the Wistar Institute of Anatomy and Biology, Hayflick created a team with chromosome specialist Paul Moorhead to investigate the problem of transformation and contamination. After intensive research funded by the National Cancer Institute, Hayflick and Moorhead published a paper in 1961 that started by stating, 'only limited success has been obtained in developing strains of human cells that can be cultivated for long periods of time *in vitro* and that still preserve the diploid chromosomal configuration'.⁷² Most cells in long-term cultures, including cells lines, shared 'many of the properties of malignant cells' such as the extensive chromosomal

⁶⁹ Pomerat et al., "Irradiation of Cells in Tissue Culture."

⁷⁰ Hayflick, and Stinebring, "Intracellular Growth."

⁷¹ Hayflick, "Decontaminating Tissue Cultures."

⁷² Hayflick and Moorhead, "Serial Cultivation of Human Diploid Cell Strains," 585.

aberration. Moreover, reflecting the emerging discourse on the viral aetiology of cancer, Hayflick and Moorhead suggested that this change might have something to do with viral contamination of cultured cells. If the tissues were transformed or infected, how could medical researchers then use them for the development of vaccines or drugs? There must be a standard procedure for producing cells without such problems.

Conspicuously, Hayflick did not conduct this research in a gerontological context, although it would ultimately become important to students of ageing. He was then not a member of the Gerontological Society, and was not well aware of major gerontological literature, some of which still reiterated the ideas of immortality.⁷³ That his and Moorhead's 1961 paper cited no scientific papers in gerontology meant that the context of his research was quite different from that of Carrel and his gerontologist colleagues.⁷⁴

Hayflick's experiment then had a distinct objective, namely, a delineation of 'clean' and normal human cells' characteristics in the context of biomedicine.⁷⁵ He obtained such cells after mincing and trypsinising aborted foetal tissues acquired from a local hospital. The biomedical traffic of human body parts between clinics and laboratories provided Hayflick with the lung, muscle, kidney, heart, and skin of 19 fetuses. Created from these normal human bodies, Hayflick's cells were deemed adequate for an intense biomedical investigation.

By growing these cells with a new method—namely, cultivating the cells in Eagle's medium supplemented with calf serum, penicillin, streptomycin, and sodium bicarbonate, and then subculturing them whenever they formed a confluent sheet in a culture bottle—Hayflick and Moorhead found that there were three stages in the lives of normal human cells (Figure 2). 'Phase I' was the period when 'the cells have been freed from the intact tissue and are just

⁷³ GSA's official record shows that Hayflick joined the society in 1964. For gerontological literature in the 1950s and the 1960s discussing immortality and rejuvenation, see, for example, Lansing, *Cowdry's Problems of Aging*, esp. chapter 3; Strehler, *Time, Cells, and Aging*, 33-40.

⁷⁴ See Moreira and Palladino, "Ageing between Gerontology and Biomedicine," 358-9. Hayflick stated, 'I did not consider myself a biogerontologist when I published my paper in 1961. I am not certain but I think that it was in about 1964 that I joined the GSA [Gerontological Society of America]. In the early 1960s researchers on aging were not considered to be serious scientists. The scientific mainstream was not interested in aging and ridiculed those who were. For a young scientist like me at that time to admit to be doing research on aging was equivalent to committing academic suicide'. Leonard Hayflick, email message to author, February 5, 2014.

⁷⁵ Hayflick and Moorhead, "Serial Cultivation of Human Diploid Cell Strains," 619.

establishing themselves on glass'. 'Phase II' covered the time during which the freed cells underwent rapid duplication in the culture medium. But this active cellular multiplication ended with the start of 'Phase III', when researchers could observe a consistent decrease in the doubling rate of cultured cells, which produced a large amount of intracellular debris. During this phase, 'the cells become much less polarized, more spread out' as their loss of mitotic activity presaged impending death.⁷⁶ However, some cells could avoid this phase by undergoing a transformation to 'cell lines'. Since these cell lines had the properties similar to those of cancer cells with abnormal karyotype, Hayflick proposed that his 'clean' cells should be called by a different name. They were the 'cell strains' rather than cell lines. His cell strains, which he named with a serial number following the initial 'WI' (Wistar Institute), did not develop into tumours when they were transplanted into hamster cheek pouches and the bodies of six terminal cancer patients. Nor did they grow in liquid suspension cultures, unlike HeLa and other cell lines.

[Figure 2]

These observations shifted the definition of success and failure in tissue culture. To Carrel, cellular immortality was normal, and achieving this state meant that tissue culture had succeeded. In contrast, tissue death was a failure, and occurred because of a scientist's 'untrained hands'. However, Hayflick and Moorhead argued that the death of cultured tissues after twelve months' was a perfectly normal phenomenon, belonging to 'Phase III' in cellular life. This phenomenon was observed 'many times', and any 'attempts to reverse Phase III have been uniformly unsuccessful'.⁷⁷ It was thus clear that what Carrel called immortality was only a deviant and perhaps pathological phenomenon caused by a cell strain's transformation into cell lines with some cancerous characteristics. This condition indicated that something had

⁷⁶ Ibid., 598.

⁷⁷ Ibid., 598.

gone wrong, perhaps spontaneously or due to viral infection. Scientists might fail, if they continued their experiments with these cells. Unfortunately, the chromosomal aberration characteristic of cancer cells occurred ‘haphazardly and under influences poorly understood’.⁷⁸ The only way to deal with this problem was a regular monitoring of the cells’ chromosomal condition.

However, Hayflick and Moorhead argued that their cell strains and methodology would enable researchers to control the problem at least partially. Since malignant transformation often occurred with viral infection, his cells, free from any ‘latent viruses’, could substantially reduce the rate of failure in tissue culture. Although spontaneous transformation into tumour cells could not be completely prevented or predicted, the virus-induced transformation would certainly be managed. Furthermore, Hayflick and Moorhead’s cells did not have any bacteria or PPLO, which might also ruin tissue culture for experimental research or clinical work. Since the cell strains did not appear to have any microbial contaminants or agents of infectious disease, they were ideal and safe materials for biomedical research and treatment.

Hayflick and Moorhead suggested that their cell strains were like inbred model animals that could be used for a variety of purposes. Since their strains were devoid of viruses or bacteria and were all homogeneous with no malignant cells found among them, they might be used for wound repair without provoking the fear of attaching possible tumour cells or pathogens to a patient’s body. Their cell strains were also excellent materials ‘for the production of killed or attenuated human virus vaccines; and in particular poliovirus vaccines’.⁷⁹ In effect, Hayflick and Moorhead grew many human viruses causing infectious diseases—including adenovirus, measles virus, rabies virus, and influenza virus—in their WI-1 and WI-10 strains, finding clear plaques and cytopathic effects. These indicated the usefulness of the cell strains for wide-ranging biomedical research projects involving viruses. Like the rats

⁷⁸ Ibid., 613.

⁷⁹ Ibid., 616.

produced in his Wistar Institute, Hayflick's cell strains would contribute to the advancement of biomedicine.⁸⁰

But what would happen if these cell strains suddenly died before proving their ability to manage failures? Was Carrel still right when he said that 'untrained hands' would bring forth a failure in an experiment? To Hayflick and Moorhead, Carrel was only partially right. Of course, cell death could always happen. However, the advent of antibiotics in the 1940s had already begun to control its occurrence. Moreover, Hayflick suggested, tissue death did not necessarily mean that there was an error on the part of investigators. The death of cells—especially human foetal cells—could occur simply because of an early start of Phase III, which depended not on 'absolute calendar time' but on the number of doublings, which was roughly, but not precisely, fifty.⁸¹ The cellular degeneration 'did not appear suddenly, but took place over a period of from 1 to 3 months'.⁸² In any case, all normal cells were expected to die naturally, and researchers were not at fault in that situation.

This view reconfirmed that tissue culture was becoming a routine job that anybody with some training could conduct. Hayflick and Moorhead wrote the following.

The experiments herein described illustrate the simplicity with which strains of human fibroblasts can be kept in serial cultivation for long periods of time with maintenance of the integrity of the diploid karyotype. It is apparent that the exacting conditions by others...are not critical in order to achieve this result.⁸³

The nimble fingers and utmost care that Carrel had emphasized were not needed in a modern tissue culture experiment, since it was no longer a highly 'delicate' art. By defining cell death as a usual phenomenon in a cell's life rather than a result of mistake, Hayflick reframed the meaning of failure in the daily practices of biomedicine, whereby an increasing cadre of

⁸⁰ For the experimental rats produced by the Wistar Institute, see Clause, "Wistar Rat."

⁸¹ Hayflick, "Limited In Vitro Lifetime," 616.

⁸² Hayflick and Moorhead, "Serial Cultivation of Human Diploid Cell Strains," 598.

⁸³ Ibid., 612.

‘inexperienced workers’ replaced a master surgeon.⁸⁴ These workers could often observe cellular death, but it might have nothing to do with their mistake or lack of skill. At least temporarily, he thus provided a means to manage the infinite ‘regress’, when he disseminated his cells and method as well as this new definition of failure to the community of tissue culturists.⁸⁵

But wasn’t the limited cellular lifespan itself a cause of failure? Wouldn’t researchers be in trouble if all their cells entered Phase III during a long-term research project? Even in such a case, according to Hayflick, there was nothing to worry about. He placed the foetal cell strains in a deep freezer at -70°C, and thawed them to prove that these cells showed the same average length of life. Most of his human foetal cells, without regard to the experience of freezing, died approximately after fifty doublings. Significantly, this finding had an implication for the amount of cellular resources, since it led him to infer that ‘if all the surplus cells from each subcultivation were stored in the frozen state a potential yield of 20 metric tons of cells could be obtained from any single strain’.⁸⁶ Even though the current batch of cells that scientists were using had undergone some doublings and became aged, an enormous number of cells could still be retrieved for subsequent culturing from a deep freezer. Therefore, the limited lifespan of normal cells did not imply that scientists would lack a sufficient cellular resource for their biomedical research. In the new laboratory setting, the definite duration of cell life ceased to be a reason for failure of tissue culture, because ‘almost an unlimited supply’ of cells was feasible at any time.

Yet it was still possible that an experiment failed solely because of a researcher’s mistake that contaminated the cells. This could be a problem if the frozen stocks had not been prepared. However, Hayflick devised a reasonable method to cope with it, even though he did not publish it. It was not necessary to blame anyone or restart the whole process in that case;

⁸⁴ Hayflick, “Hayflick’s Reply,” 131.

⁸⁵ I do not argue that Hayflick prevented ‘experimenters’ regress’. But Hayflick certainly lessened the problem as he circulated his cells and method in the tissue culture community. As STS scholars have shown, the regress can be managed through scientists’ interactions within their community. See Shapin and Schaffer, *Leviathan and the Air-Pump*, 225-82.

⁸⁶ Hayflick and Moorhead, “Serial Cultivation of Human Diploid Cell Strains,” 619.

scientists or technicians could simply ‘decontaminate’ their cells with antibiotics to reverse the unfortunate incidence, and the cells would be ready to be used again.⁸⁷ In a sense, this process was an extension of his earlier proposal of heat shock as a way to ‘decontaminate’ cells infected with PPLO.⁸⁸ Unlike Carrel, who stressed an ultimate perfection of researchers’ skill throughout the entire procedure, Hayflick thus permitted occasional mistakes or losses that could be remedied by antibiotics, a key reagent in modern biomedicine. At any rate, Hayflick thought, antibiotics were a normal component in his culture medium, and their use in later decontamination would not be a problem.

6. Materials and Methods in the Community of Tissue Culturists

Tissue culturists with diverse aims and schemes responded to Hayflick’s research. Yet some of them were quite critical. Above all, some scientists attacked Hayflick’s argument that normal diploid cells should always die after a certain number of doublings. For example, G. T. M. Cummins and J. D. Ross at the University of Minnesota argued that ‘evidence on the finiteness of viability of normal cells [was] not decisive’.⁸⁹ Nelly Auersperg at the British Columbia Cancer Institute also asserted that ‘while human diploid cultures [did] not survive indefinitely’, permanent diploid lines had ‘been established from other species such as pig...and Chinese hamster’.⁹⁰ These scientists cited the papers of Jean Ferguson, Ann Wansbrough, Frank Ruddle, and others who had cultivated pig, monkey, rabbit, and horse cells for long periods of time.⁹¹ Among them, Ruddle cultured pig kidney cells with apparently normal diploid chromosomes for five years without incurring death and degeneration. In 1964, Robert Krooth’s team at the University of Michigan also found that 85% of normal rat cells underwent neither malignant transformation nor degeneration after 15 months of culture.⁹² For Krooth, the unlimited lifespan of tumour cells that Hayflick took for granted was questionable,

⁸⁷ Hayflick, “Hayflick’ Reply,” 131.

⁸⁸ Hayflick, “Decontaminating Tissue Cultures.”

⁸⁹ Cummins and Ross, “Colonial Study of Cells,” 1589.

⁹⁰ Auersperg, “Long-Term Cultivation,” 147.

⁹¹ Ferguson and Wansbrough, “Isolation and Long-Term Culture”; Ruddle, “Chromosome Variation.”

⁹² Krooth, Shaw, and Campbell, “Persistent Strain of Diploid Fibroblasts.”

too. He noted that ‘two or three months following the heteroploid change, an ever increasing number of cells...[died]—or at least [ceased] growing’.⁹³

These challenges pointed to a key problem in Hayflick and Moorhead’s 1961 work. They had then studied only the cultures of human cells from nineteen foetuses, and never claimed that their conclusion would apply to other species or other human individuals. But Hayflick grew confident that his argument was true for a broader range of cells. In 1965, he claimed that ‘Carrel’s experiment’ had ‘never been confirmed’ because ‘regardless of the vertebrate tissue of origin, cell populations derived in vitro could be kept in an active state of multiplication for a varied but finite period of time’.⁹⁴ However, he did not test this idea using all available vertebrate cells, although he cultured rhesus monkey cells alongside human cells for the purpose of exploring the end of cellular life.⁹⁵ In general, he remained a specialist of human cells throughout the 1960s, and other scientists could always claim that somatic cells from different species or different groups of humans showed dissimilar behaviour and lifespans in culture. How could he be sure that his theory was applicable to all vertebrate cells, as he had claimed in 1965?

With this question, the real issue was not so much about Hayflick’s theory as his materials, methods, and the community relations surrounding his effort to render his cells equivalent to model organisms like the standardized fruit flies, mice, or nematodes.⁹⁶ His assertion that his cells were much like these inbred laboratory animals played a crucial role in incorporating his research into the tissue culture community.⁹⁷ In effect, the process of establishing a model organism was connected to the belief that the same or at least a similar result would be obtained in different laboratory organisms.⁹⁸ Hence, it is no wonder that his endeavour to make his cell strains equivalent to model organisms encouraged an expectation

⁹³ Krooth, “Future of Mammalian Cell Genetics,” 26. Krooth’s view was partially correct, because some tumour cells *in vitro* did stop growing and die naturally. See Fujimura, *Crafting Science*, 23, 41, 246-7.

⁹⁴ Hayflick, “Limited In Vitro Lifetime,” 628. This belief became stronger over time. See Hayflick, “Immortality.”

⁹⁵ Hayflick, “Discussion,” 64.

⁹⁶ For historical literature on model organisms for experimental research, see Kohler, *Lords of the Fly*; Rader, *Making Mice*; Creager, *Life of a Virus*; Ankeny, “Wormy Logic.”

⁹⁷ Hayflick and Moorhead, “Serial Cultivation of Human Diploid Cell Strains,” 613.

⁹⁸ Creager, *Life of a Virus*, 5; Ankeny, “Wormy Logic,” 46-47.

that other types of normal vertebrate cells would behave similarly in the culture medium, even though he never proved this. In the era of biomedicine that demanded a constant supply of standardized research material, his effort to spread his cells as a kind of model organisms led to the proliferation of research relying on them, which would ultimately overwhelm the objections raised by some scholars.⁹⁹

Hayflick utilized his scientific community to disseminate his cells, just as Thomas Hunt Morgan shared his fruit flies with other geneticists in his academic community and Clarence C. Little sold his mice as a standard laboratory material to his associates in the field of cancer research.¹⁰⁰ In fact, Hayflick's work was quite similar to Little's, because both scientists created their biomedical business networks using their study subjects, with the federal government as their major patron.¹⁰¹ Initially, Hayflick distributed his cells to his colleagues for free. He also attended several meetings on tissue culture—including the Syverton Symposium sponsored by the Tissue Culture Association and the meetings of the Committee on Cell Cultures of the International Association of Microbiological Societies—where he advertised the use of his cells for a variety of tasks, including vaccine production, tumour virus research, anticancer drug development, and making normal human cell banks.¹⁰² Simultaneously, Hayflick, like Little, contacted the federal biomedical authorities in the Bureau of Biologics and NIH to persuade them to adopt his cells for various research purposes. But a more crucial job Hayflick did at the time was to start a company, named 'Cell Associates', to sell his cell strains to biomedical workers interested in using normal and clean cells from human fetuses.¹⁰³ As a result, his cells, especially the WI-38 and WI-26 strains, came to be

⁹⁹ From 1961 to 1965, seven among the 164 papers citing Hayflick raised a question on his claim.

¹⁰⁰ Kohler, *Lords of the Fly*; Rader, *Making Mice*.

¹⁰¹ Rader, *Making Mice*, 135-60. Hayflick did not seem to create a moral economy of researchers as Morgan did. Hayflick's work was similar to Little's, but the two are not the same. In addition to what I discuss in the next section, the two were quite different, especially with regard to bioethical problems. Little's mice provoked no controversy on bioethics, while Hayflick's cells did. Whereas antivivisectionists did not care much about the mice which were regarded as a pest, Hayflick's cells, due to their origin from aborted human fetuses, became a subject of concern among anti-abortionists and the Catholics. See Wadman, "Cell Division," 425.

¹⁰² Hayflick, "Discussion," 63; Hayflick, Perkins, and Stevenson, "Characterization and Uses of Human Diploid Cell Strains"; Perkins and Hayflick, "Cell Cultures."

¹⁰³ Wade, "Hayflick's Tragedy," 125. The earliest paper mentioning the purchase of Hayflick's cells is Mufson et al., "Effect of Neutralizing Antibody," 580.

used by many researchers in America and Europe. Even those who could not use Hayflick's cells for various reasons still found that his culture method or medium was useful.

Amid this process, Hayflick and Moorhead's 1961 paper became a citation classic. According to Google Scholar, this paper has been cited more than 5400 times.¹⁰⁴ During the first five years after publishing this paper, it was already cited 164 times, excluding Hayflick's self-citation, duplicate publications, and some false positives (Table 1).

Research using Hayflick's cells	Research on non-tumour virus	35	47
	Tumour-related research	8	
	Study of chromosomal aberration	1	
	Research on normal cellular function	3	
Research using Hayflick's method or culture medium	Research on non-tumour virus	12	27
	Tumour-related research	7	
	Study of chromosomal aberration	5	
	Research on normal cellular function	3	
Research citing Hayflick's work as a background fact	Research on non-tumour virus	8	59
	Tumour-related research	27	
	Study of chromosomal aberration	1	
	Research on normal cellular function	17	
	Study of cellular drug response	2	
	Other research	4	
Theoretical papers, reviews, textbooks, and manuals	Theoretical papers	1	29
	Reviews	18	
	Textbooks and manuals	10	
Unavailable			2
Total			164

Table 1. A tabulation of publications citing Hayflick and Moorhead's 1961 paper from 1961 to 1965. 'Other research' indicates the studies marginally relevant to Hayflick and Moorhead's

¹⁰⁴ Hayflick's second paper on cellular lifespan, 'The limited in vitro lifetime of human diploid cell strains' (1965) was cited more than 4500 times.

paper as well as those that explicitly rejected their argument. 'Unavailable' are the publications that could not be acquired by any means.

Among the 164 papers, 47 papers reported research using Hayflick's cells, while 27 studies used his culture medium or technique. To them, Hayflick offered a useful tool for growing viruses *in vitro*, measuring their cytopathic effects, and exploring the process of tumour formation from normal tissues. As early as 1963, some already called Hayflick's diploid cells 'a standard culture system' for their research.¹⁰⁵ For others, the cells were 'attractive' because of their 'inability to form tumours', lack of 'extraneous viruses', standardized characteristics, and continued availability.¹⁰⁶ There were also researchers employing Hayflick's culture method to increase the number of cells acquired from patients with hereditary aneuploidy before chromosomal analyses. These researchers probably believed that his method would preserve the current chromosomal condition of the cells without causing further aberration.¹⁰⁷

To most users of his cells, Hayflick's success in culturing normal cells for one year was more important than his ascertainment of their unavoidable degeneration and its implication for ageing *in vivo*. At least during the first five years after the publication, Hayflick's work was deemed relevant not so much to the nature of cellular ageing as to the possibility of culturing clean human cells for an extended period without viral and bacterial contamination or karyotype aberration.¹⁰⁸

Many of the investigators citing Hayflick emphasized the convenience of using his cells and culture method. He forged an easy means to control the possible causes of failure in

¹⁰⁵ Bloom et al., "Relationship of Rhinovirus Infection," 38.

¹⁰⁶ Pearson et al., "Growth Characteristics of Three Agents," 49.

¹⁰⁷ See, for example, Chandra and Hungerford, "Aberrant Autosome."

¹⁰⁸ See, for example, Fraser and McCall, "Culture of Synovial Cells," 358; Chu, "Chromosomal Stabilization of Cell Strains," 58; Mellman, "Chromosome Analysis." In these years, only five articles cited Hayflick and Moorhead's 1961 paper with regard to research on ageing. Among them, only two were original research papers. See Childs and Legator, "Lactic Dehydrogenase Isozymes"; Soukupová, Holečková, and Cinnerová, "Behaviour of Explanted Kidney Cells." Hayflick's idea was considered useful for gerontologists only after the publication of his 1965 paper.

biomedical research, such as cells' malignant transformation and contamination. Sudden cellular death was not a great problem, either; it could be a mere natural phenomenon or the result of a minor mistake that could be easily remedied with cells in a deep freezer. In this sense, Hilary Koprowski at the Wistar Institute stressed that 'any laboratory equipped for work with viruses' could use Hayflick's cells.¹⁰⁹ John Foley and Byron Aftonomos at the University of Nebraska also mentioned 'the ease with which fibroblast-like cells' of Hayflick's could 'be isolated and propagated serially in culture', which contrasted sharply with the remarkable difficulty of growing epitheloid cells.¹¹⁰ Similarly, the Canadian scientists Juan Embil and Ruth Faulkner mentioned the merits of Hayflick's cells, which appeared to 'be easy to prepare and maintain, retain its primary characteristics, be susceptible to a broad spectrum of viruses, and contain no carrier or latent viral agents'.¹¹¹ In a similar vein, William Mellman at King's College of London wrote that researchers did not need to worry about the limited lifespan of the diploid cell strains, because 'some of the cells may be frozen at any early passage and used to re-establish actively growing cell populations as they are needed'.¹¹² Hayflick's cells were also superior to fresh primary tissues, because the latter were heterogeneous and might contain latent viruses.¹¹³ Even Robert Krooth, who was sceptical of Hayflick's claim, admitted that his human cell strains 'would eventually yield more than 50 metric tons of cellular material', an amount enough for most investigators who might occasionally fail to culture cells properly.¹¹⁴

These scientists' remarks implied that Hayflick's cells and culture method were becoming a well-received means to avoid 'pitfalls' or manage 'errors'. As many historians and philosophers have discussed, scientists develop such a means as their field of research matures.¹¹⁵ This is necessary, because they need to establish protocols for their daily practices,

¹⁰⁹ Koprowski, "Live Poliomyelitis Virus Vaccines," 1154.

¹¹⁰ Foley and Aftonomos, "Growth of Human Breast Neoplasm," 217.

¹¹¹ Embil and Faulkner, "Human Diploid Cell Strains," 111.

¹¹² Mellman, "Chromosome Analysis," 1065.

¹¹³ Iyengar, "Cell Systems for Production of Viral Vaccines," 218.

¹¹⁴ Krooth, "Future of Mammalian Cell Genetics," 25.

¹¹⁵ Hon, "On Kepler's Awareness of the Problem"; Olesko, "Meaning of Precision"; Ravetz, *Scientific Knowledge*, 94-101.

which might be considered a kind of ‘craft’.¹¹⁶ In fact, tissue culture was a craft as well as a science from the beginning, and thus demanded certain ways of managing errors or pitfalls, which Hayflick supplied. But Hayflick did worry about some people’s occasional reports of their difficulties in culturing WI-38 and WI-26. Thinking that the central problem was the method of fostering the right condition for cellular life, he and his colleagues published a paper in *Nature* to elucidate further details of the standard procedure for producing an effective culture medium.¹¹⁷

Admittedly, the WI strains did not dominate the resource market. Biomedical investigators continued to use various cell lines as well as primary tissues in their research. But the WI strains did become a useful reference for many scholars studying viral infection, tumour formation, genetic disease, cell physiology, and drug response (Table 1). Although these scholars used other cells because of their specific merits, including higher plating efficiency and permanent cultivability, they found Hayflick’s research relevant as a meaningful case showing normal human cells’ behaviour and function. The characteristics of Hayflick’s cells, including the absence of microbial contamination and chromosomal aneuploidy, were important as a background fact concerning normal human cells.¹¹⁸

The growing significance of Hayflick’s cells and method could also be seen in the textbooks and manuals citing his work as an excellent way to culture human diploid cell strains. Between 1961 and 1965, ten articles in textbooks and manuals citing Hayflick were already published (Table 1). These publications also reflected the increasing significance of those in lower academic positions who took charge of the task of cell culture. For instance, one of these manuals, *A postgraduate course in cell culture* (1963), cited Hayflick and Moorhead’s 1961 paper many times and detailed the method of establishing ‘diploid cell strain from skin biopsy’ in a separate chapter.¹¹⁹ The editor of this book described the changed situation after Carrel.

¹¹⁶ Ravetz, *Scientific Knowledge*, 94-101.

¹¹⁷ Hayflick, Jacobs, and Perkins, “Procedure for the Standardization of Tissue Culture Media.”

¹¹⁸ For a paper stressing plating efficiency and permanent cultivability as the reasons for choosing heteroploid lines, see De Carli et al., “Cytogenetic Studies.” From 1961 to 1965, there were only two such papers.

¹¹⁹ White, *Postgraduate Course in Cell Culture*, Experiment 11.

Since the days of the great Alexis Carrel, who pioneered the field in the pre-antibiotic era, cell culture has been regarded by the outsiders with a certain amount of awe. The fortuitous combination of Carrel's black hoods and gowns, his strict security precautions...inevitably led to talk of Carrel's 'tissue cult'. We have come a long way since the days of Carrel.¹²⁰

The new age demanded a set of fresh techniques, including the antibiotics not available to Carrel as well as Hayflick's method that scholars-in-training could use.¹²¹ These techniques were standardized and included in manuals for those who needed to avoid failure as far as possible in their routine biomedical work.

Nevertheless, in this new age, another major problem emerged as a possible cause of failure in many biomedical studies involving tissue culture: the spontaneous transformation of normal cells into malignant cells. At the Syverton Symposium, Ernest Chu at the Oak Ridge National Laboratory raised the following issue after a short discussion on growing diploid mammalian cells in culture.

The battle, however, in maintaining diploid lines is only half won. In primary cultures and relatively stable diploid cell lines occasional aneuploidy and polyploidy do exist. In addition, chromosomal aberrations of spontaneous nature occur in appreciable frequencies...The problem of accumulation in pure cultures of naturally occurring genetic variants confronts all biologists alike.¹²²

Before Hayflick, the primary 'battle' was fought against cellular death. The new biomedical context in the postwar era changed the configuration of this battlefield, rendering cells'

¹²⁰ White, "Principles of Cell Culture," 171.

¹²¹ Ibid., 175.

¹²² Chu, "Chromosomal Stabilization of Cell Strains," 59-60.

spontaneous transformation as a main adversary. This adversary stood in an unintelligible and uncontrollable sphere, while failure due to contamination and cell death became manageable and intelligible. This adversary could occasionally bring deep troubles to tissue culturists who might not be able to understand why and how they failed to maintain the normality of their cells.

7. Failure in Tissue Culture and a Career Problem in Biomedicine

But the emergence of this new problem improved Hayflick's career prospects, because he was a key contributor to the changed perception and technique behind the problem. Most of all, he moved to Stanford University as a tenured professor in 1968. He also became well-known among an increasing number of investigators using his cells. Meanwhile, the Medical Research Council of the United Kingdom forged another human cell strain named MRC-5, which was to be a competitor in the market.¹²³ At the same time, a growing number of scientists began to study programmed cell death as a natural end of cellular life, when many gerontologists started considering Hayflick's theory of limited lifespan of cells a basis of explaining aging at the cellular level.¹²⁴ While it took a long time for sceptical gerontologists to accept Hayflick's idea, it ultimately became the dominant opinion regarding the mechanism of senescence in the 1970s.¹²⁵

This development accompanied substantial repercussions. Carrel's argument on cellular immortality was thought to be wrong; his results had probably been due to unintended contamination or intentional fraud. This view, together with his notorious eugenic and racist remarks, led to a complete reassessment of his entire scientific career.¹²⁶ However, Hayflick's subsequent career also was not without problems. Through a report by management accountant James W. Schriver, NIH made serious allegations in 1976 regarding Hayflick's handling of

¹²³ Jacobs, Jones, and Baille, "Characteristics of a Human Diploid Cell."

¹²⁴ Landecker, 'On Beginning and Ending with Apoptosis,' 46-52.

¹²⁵ See Box 8, Folder Correspondence Hayflick, NWS. Compare Bernard Strehler's *Time, Cells, and Aging* (1962) with Strehler, *Time, Cells, and Aging*, 2nd edition (1977), 37-55.

¹²⁶ Reggiani, *God's Eugenicist*; Witkowski, "Dr. Carrel's Immortal Cells."

cells.¹²⁷ According to Nicholas Wade, who discussed Schriver's report in *Science*, Hayflick earned \$67 000 from his sales of WI-38 and 'entered into a large contract with...Merck & Co., Inc.', although he was not supposed to earn profit from the cells that were created under NIH's grant and therefore were government property.¹²⁸ Moreover, Wade wrote, some of the cells that Hayflick offered to NIH were contaminated with microbes, and others were 'cleaned-up' after contamination through the use of antibiotics. Strangely, NIH authorities felt, Hayflick had never mentioned this 'cleaning-up' to them. Furthermore, it was found that the remaining stock of WI-38 cells would last only for a few additional years, and NIH was now seeking an alternative. Even the label of the number of passages of his cells was not correct, and this would mislead some scholars who needed to know the precise number, especially for their research on ageing.¹²⁹

Facing these charges, Hayflick filed a formal rebuttal and published an article in *Science* to tell the story from his own perspective. To Hayflick, NIH violated the Privacy Act through its public charge against him, which was also unfair due to the lack of a proper peer review. He claimed that NIH announced its allegations to the public as if they were already confirmed by reliable evidence. Moreover, he argued, NIH never asked an opinion of his professional colleagues, even though the charges were about scientific problems and should thus be decided by an academic community. Hayflick also stressed that the cells belonged to him, because Leon Jacobs, associate director for collaborative research at NIH, confirmed Hayflick's ownership, and 'competent, independent legal counsel' had concurred.¹³⁰ Otherwise, NIH had no reason to pay for the cells, and 'several commercial organizations' selling his cells would also be in trouble.

¹²⁷ J. W. Schriver, 'Investigation of activities relating to the storage, distribution, and sale of human diploid cell strains, WI-38 and WI-26. Working papers' (Division of Management Survey and Review, National Institutes of Health, Bethesda, MD, 1976). I have tried to acquire this document from the National Archives and Records Administration and the NIH Library. But neither of them was able to locate the document in their collection.

¹²⁸ Wade, "Hayflick's Tragedy," 125.

¹²⁹ In Hayflick's methodology, the passage number of a cell approximately equals to its total number of divisions after its removal from the foetus.

¹³⁰ Hayflick, "Hayflick's Reply," 129.

Hayflick claimed that bacterial contamination was not a problem, either. Since it was a common occurrence in the laboratory, scientists often ‘decontaminated’ their cells with antibiotics as ‘an accepted procedure’.

Virtually all cell cultures in use today...are ‘cleaned-up’ because they or their progenitors have been grown in filtered and antibiotics-contained media. Almost every pool of bovine serum, trypsin, and synthetic media in which cells are grown is ‘cleaned-up’ by filtration; serum is usually initially contaminated with from 10^5 to 10^8 bacteria per millimeter. Antibiotics are used at some stage in the preparation of almost all human virus vaccines, thus the use of ‘cleaned-up’ cultures containing the cadavers of dead microorganisms is a universally accepted practice—even for the manufacture of human virus vaccine.¹³¹

In fact, even MRC-5, an alternative to WI-38 that NIH was now willing to adopt, also had a number of contaminated ampules. Furthermore, there was no need to report the contamination to NIH, because few at the institutes then seemed interested in it and he did not want to generate ‘unnecessary alarm’.

For Hayflick, the other charges were similarly false or irrelevant. Most of all, the prospect of the remaining stock of WI-38 was seriously misunderstood. He asserted that the current WI-38 stocks would ‘satisfy the needs of vaccine manufacturers for at least 10 years’, because ‘about 2000 frozen ampules of WI-38 at passage levels below 17 [were] stored in laboratories throughout the world’ including those in Canada, Japan, and the United States. Likewise, the passage number disparity was not a serious issue, since such a degree of disparity conformed to the international consensus and guideline.

Unfortunately, Hayflick’s troubles did not end with this rebuttal. Since NIH did not accept his explanations, he was then in litigation against them for six years, which temporarily

¹³¹ Ibid., 131.

damaged Hayflick's career and research. When Stanford University started its own investigation of the problem in 1976, Hayflick resigned from his professorship. He then remained unemployed until he got a marginal post at Children's Hospital Medical Center in Oakland. Fortunately, in 1982, an out-of-court settlement was reached, and this settlement designated that the charges concerning him were in 'reasonable dispute'. Hayflick was allowed to 'keep the money from cell sales' and NIH was able to maintain 19 ampules of Hayflick's cells.¹³² In that year, he also obtained a full-time tenured faculty post at the University of Florida. But the officials at NIH still did not admit that there was anything wrong in their previous judgment, while Hayflick felt 'exonerated' from the charges. Accordingly, Philip Boffey at *The New York Times* stated that the settlement failed to shed 'much light on who was right and who was wrong in this bitter, tangled affair'.¹³³ However, Bernard Strehler and 84 gerontologists declared that NIH's charges were definitely unsubstantiated and unjust. These charges had brought about 'the near destruction of an outstanding career'.¹³⁴

From a historical perspective, the charges stemmed from the biomedical situation that also prompted Hayflick's work. Above all, the main allegation against him, the commercial transactions of cells originating from aborted foetal tissues, was a central feature of biomedicine, which would often incur conflicts regarding ownership.¹³⁵ When NIH claimed that WI-38 was government property, Hayflick argued that he was the true owner. But at least one of Hayflick's colleagues believed that the cells belonged to the entire scientific community, whereas the parents of the aborted foetus might have claimed that the cells were theirs.¹³⁶ Who, then, was right? This question was fundamentally biomedical in nature, because—as Kevles has shown—it was related to the escalating federal expenditure for biomedicine and the

¹³² Holden, "Hayflick Case Settled."

¹³³ Boffey, "Fall and Rise of Leonard Hayflick."

¹³⁴ Strehler, et al., "Hayflick-NIH Settlement," 240, 242.

¹³⁵ For a review of the politico-economic problems and ownership issue in bio-industry, see Thackray, *Private Science*. For the rise of the biogerontology business, see Hall, *Merchants of Immortality*.

¹³⁶ Medvedev, "Hayflick's Tragedy," 1182; Wadman, "Cell Division," 423.

consequent concern about the possible abuse of the public money.¹³⁷ This concern became deeper and more serious, as human tissues moving between clinics and laboratories became a commodity with no clear agreement over the problem of ownership. The contamination and depletion of the cells was another critical matter. Although Hayflick claimed that his cell strains were ‘clean’ and guaranteed their abundant supply, NIH found that some of them were contaminated and would soon be exhausted. Notably, biomedical scientists’ worries about contamination and uninterrupted supply of clean cells were factors prompting his creation of his new cell strains that would be used to manage possible problems in tissue culture. But these worries also temporarily interrupted his career.

A closer look at Hayflick’s ‘decontamination’ of cells reveals another topic. He argued that decontamination using antibiotics was a ‘universally accepted practice’. But how universal was it? Most tissue culture manuals of the 1970s recommended ‘decontamination’ of infected cultures only as a last resort.¹³⁸ Some urged readers to discard ‘infected cultures’ right after discovery, because their ‘treatment is usually difficult’.¹³⁹ Another manual described a procedure for ‘recovering’ contaminated cells with antibiotics, but also claimed that this was ‘worth attempting’ only when cells were truly irreplaceable and the degree of contamination—which might be subjectively determined—was not very substantial.¹⁴⁰ From Hayflick’s standpoint, however, decontamination was a more straightforward task. Since bacteria existed everywhere including the human body where cultured cells originated, antibiotics had to be used in every step. Obviously, the cleanliness of his cells was not their inherent feature but a product of constant intervention against a factor leading to failure—contamination. Yet this intervention was local rather than universal, because some people did not rely on it. Hayflick himself never mentioned it in his research papers, unlike other procedures in his technique.

¹³⁷ Kevles, *Baltimore Case*, 96-117. While Kevles dealt with the problems in the 1980s, these problems or their precursors already existed in the 1960s and the 1970s.

¹³⁸ I examined *Medical Cytogenetics and Cell Culture* (1977), *Animal Cell Culture Methods* (1970), *Animal Tissue Culture* (1972), *Methods in Enzymology, Volume LVIII: Cell Culture* (1979), and *Cell and Tissue Culture* (1975).

¹³⁹ Priest, *Medical Cytogenetics and Cell Culture*, 274.

¹⁴⁰ Wasley and May, *Animal Cell Culture Methods*, 92, 97.

Hayflick's trouble partly stemmed from this localised nature of his work for avoiding failure. Indeed, as Jordan and Lynch have shown, the routine procedures of sterilisation may vary widely even within a single laboratory. Moreover, knowledge on sterilisation may be 'tacit' in nature, since researchers might not be able to or would not like to explicate their method to others.¹⁴¹ Investigating a materials science lab, Cyrus Mody has also shown that contamination plays diverse roles in research, and its occurrence and degree is an inter-subjective matter.¹⁴² But an intervention of 'organisational bureaucracy' could change the situation, as Barbara Rawlings has claimed.¹⁴³ A strict compliance with the published protocols might be expected when bureaucratic personnel came to interrogate the procedures of sterilisation that were often subjectively managed. In light of this literature, it seems possible to say that Hayflick's decontamination was in a grey area, because it made sense to him and his colleagues but might not be publishable or unanimously acknowledged. Unfortunately, NIH, a form of 'organisational bureaucracy', failed to recognize this area. Could a peer review, which he requested to NIH, have made a difference? Perhaps. But there was no guarantee that everyone in the field would approve his method.

8. Conclusion

What Hayflick contributed to and experienced was a part of a broader phenomenon that can be called the growth of biomedicine after World War II. His research was driven by the mounting concerns about failures in cell cultures used in this new environment, including the malignant transformation and microbial contamination of human tissues moving among clinics and laboratories funded by NIH, pharmaceutical companies, and other patrons. Hayflick's new definition of failure in tissue culture and its reception reflected the increasing researchers, cells, grants, and institutions in the new technoscientific era. His work then allayed the fear of resource depletion and inexperienced handling, which might lead to failure in tissue culture. By

¹⁴¹ Jordan and Lynch, "Sociology of a Genetic Engineering Technique," 96-101; Collins, *Tacit and Explicit Knowledge*.

¹⁴² Mody, "Little Dirt Never Hurt Anyone."

¹⁴³ Rawlings, "Coming Clean," 289, 292.

contributing to the reduction of anxieties of many semi-skilled workers involved in the routine laboratory practices, he crafted a 'right tool for' a variety of biomedical 'jobs'.¹⁴⁴

This tool embodied Hayflick's theory. His theoretical claim that all normal somatic cells of vertebrates should eventually die implied that cell death might not be caused by a tissue culturist's fault. As the cells tended to die even in the best possible condition, scientists did not need to blame anyone, and could simply manage this misfortune using deep freezers or other techniques. Hayflick's scientific theory of a limited cellular lifespan was intertwined with the use of his cultured cells as a routine tool in laboratories.

But Hayflick's tool was bearing certain problems stemming from its origin in biomedicine. As his professional hardships from 1976 to 1982 showed, Hayflick and NIH disagreed over the ownership of the cells that he cultured, distributed, and sold. The cleanliness of his cells was another problem. His cells, far from being inherently and always clean, were an embodiment of his local laboratory practices managing mistakes and inexperience that might lead one to fail in routine practices involving tissue culture. Unfortunately, these features of his cells fuelled NIH's suspicion in the age of biomedicine, when both the public expenses and commercial motivations prompted bureaucratic inquiries into researchers' proper conduct. With an increasing amount of public money and intensifying concerns about the contamination, malignancy, and ownership of cells, the rising biomedical enterprise shaped Hayflick's definition of failure in tissue culture as well as his job as a scientist and toolmaker. At the same time, this enterprise led to his temporarily failed career.

(Word Count: 16 898)

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