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CARNEGIE INSTITUTION OF WASHINGTON

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THE DEPARTMENT OF EMBRYOLOGY

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I

INTRODUCTION

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"Embryology," naturally enough, evokes images of embryos. Certainly at the beginning of the Carnegie Institution of Washington Department of Embryology in 1914, there were embryos in abundance. These were human embryos: preserved, sliced and studied in order to construct models that became the basis for human embryology textbooks and medical school training. Primate studies then provided information and understanding of embryo implantation in the mother's uterus, of material exchanges between mother and embryo, and of the entire developmental cycle through studies that would have been impossible with humans. By the second half-century of the Department's work, embryos had receded in importance. Tissue and cell cultures provided new histological information about development. Biochemistry, molecular genetics, and relations of genetics to embryogenesis took center stage. Yet, unlike other university departments, professional societies, and journals, the Carnegie Department did not rush in the second half of the twentieth century to change its name from "embryology" to "developmental biology" or "molecular biology." At heart, the research group remained concerned with the processes of development. And, yes, with embryos, through experimental embryology and then through development and genetics. Now, embryos are in vogue again, vaulted onto the front pages of local newspapers by a cloned sheep named after Dolly Parton, by stem cell research, and by the hopes for improved reproductive medicine.

This book explores the Carnegie Institution of Washington (CIW) Department of Embryology since its inception. Who did what, where, how, and why? What contribution did this department make to the development of biological understanding of embryos, and what is this group doing to lead the way into the future? In this chapter I draw especially on the annual reports from the CIW and on the papers in this volume to provide an introduction to the Carnegie philosophy and to the personality of an institution that is distributed across different places and with people who move in and

out of the story. The CIW could have become an anachronism, a sort of monument to the hopes of the progressive era, frozen in time with the vision of a late nineteenth century rags-to-riches man who made good. But it has not become that. The Carnegie Institution has remained vital because of the underlying principles and the selection of good people to guide programs. The Department of Embryology has helped to keep embryos scientifically alive in the many senses that this volume discusses.

Andrew Carnegie and his Institution

The story begins with Andrew Carnegie, and indirectly with Carnegie's mother. His mother's dominance in his life undoubtedly shaped Carnegie's own drive to succeed and to concentrate on business and community, since she kept him from marrying and developing strong independent ties during her lifetime. Considered a "robber baron" by his critics or a "captain of industry" by his supporters, Carnegie made money in steel – a lot of money. When he succeeded beyond even his imagination, he resolved to put that money to good use. His philosophy of "scientific philanthropy" called for not just scattering funds to individual isolated causes or leaving large sums to one's heirs but rather for investing in the future. Outlined in his "Gospel of Wealth," Carnegie's ideas rested on the assumption that it was better to educate and support than to give handouts on which recipients might become dependent. Wealth must be properly administered, he insisted, and "It were better for mankind that the millions of the rich were thrown into the sea than so spent as to encourage the slothful, the drunken, the unworthy."[2] He gave library buildings, but left it to the community to provide the books and the librarians. He gave to universities, particularly to the Tuskegee Institute, Hampton College, and Berea College rather than to better established schools and made sure that the programming was top quality and the money well invested. And he established the independent Carnegie Institution of Washington to promote scientific research (Fig. 1.1).

In 1901, Carnegie concluded that it was time for an "institution of higher learning" in Washington. Yet he decided against establishing a university there that would compete with other universities. Instead, he settled on an independent research organization. The lovely centennial volume by James Trefil and Margaret Hindle Hazen, entitled *Good Seeing. A Century of Science at the Carnegie Institution of Washington, 1902–2002*, outlines those early discussions and the history of the institution overall. Clearly, Carnegie was inspired by John D. Rockefeller's new medical research institute in New York. His enthusiasm for supporting the individual "genius" pointed to an institution that would allow those individuals to try new ideas in a climate unfettered by the needs to teach or to sell ideas to industry. His goal was to promote both basic research, with "investigation, research, and discovery 'in the broadest

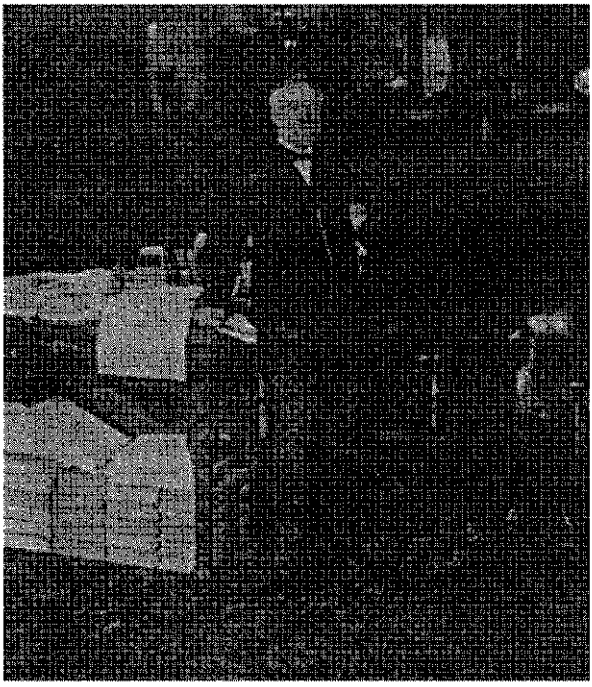

Figure 1.1 Andrew Carnegie "America's Most Eminent Business Man."

and most liberal manner,'" and application, fostering "the application of knowledge to the improvement of mankind."[2] Given Rockefeller's emphasis on medical research, Carnegie resolved to look in other directions and not to include clinical medicine.

The new Carnegie Institution began in 1902, with Daniel Coit Gilman as President. Gilman had served as first president of the University of California from 1872 until he moved to become first president of the newly founded Johns Hopkins University before then accepting the new challenge of heading the CIW and developing its mission. At first, the institution awarded individual grants. In the biological sciences, some of the most visible funding went to the individualistic Luther Burbank, and some of the most important early support went to George Harrison Shull at the Cold Spring Harbor Laboratory. Burbank was the sort of "genius" Carnegie sought to invest in, but was idiosyncratic and unable to share his individualist approach with others. The Carnegie sent Shull to study with Burbank to learn his scientific methods, but Shull concluded that they were actually not scientific at all and perhaps not very methodical. The resulting "Burbank problem," where Carnegie favored Burbank while the trustees were more skeptical about what Burbank actually offered for the longer term, clearly influenced

the selection process and the organizational structure for further Carnegie awards.[3]

The Carnegie Institution opted for a combination of individual awards to selected geniuses for short-term support and with the apparent expectation that there would be results in the form of reports and publications. Carnegie had written that "You know my own opinion is that no big institutions should be erected anywhere." Instead, "exceptional men should be encouraged to do their exceptional work in their own environment." Carnegie had concluded that "There is nothing so deadening as gathering together a staff in an institution. Dry rot begins and routine kills original work."[4]

Yet this did not mean that the Institution had no place. In 1909, the trustees dedicated an administration building at 16th and P Street in Washington. In addition, various research laboratory sites have come and gone over the century, as appropriate for the work at hand and often in partnership with other institutions and individuals. Genetics found a home at Cold Spring Harbor Laboratory, on Long Island, and in other places like Thomas Hunt Morgan's laboratory at Columbia University. Embryology centered in a sequence of at first borrowed, and then specially-designed, laboratory buildings associated with the Johns Hopkins University.

The Department of Embryology

In 1913 Franklin Paine Mall applied for Carnegie support for his work on human embryos. As Nick Hopwood has documented in an outstanding study, *Embryos in Wax*, close examination of human embryos had gained considerable attention in the preceding decades, notably through the work of Wilhelm His and Franz Keibel.[5] These researchers sought through detailed anatomical and histological studies to trace the changes in structure from the very beginning of embryonic life. That is, rather than just assuming that life really begins at the traditional forty days or at the point when germ layers are well defined as many morphologists had assumed, these embryologists believed that it was at least important to assess the significance of the earliest stages. Presumably, the importance of structure does not begin all of a sudden at a later point, but exists from the beginning. At the very least, we should know more about the entire embryological sequence. To that end, they collected, described, and modeled as many stages of the developmental process as they could find, though initially these necessarily focused on later stages since those were the ones most easily available. Embryos in the earliest stages are nearly invisible, and it took more experience to know even what to look for or to know what the tiny embryonic thing was once it was observed.

Following other leading American anatomists, Mall went to Leipzig to study with anatomist/embryologist Wilhelm His and in his role as anatomist at the Johns Hopkins Medical School began to amass his own collection of

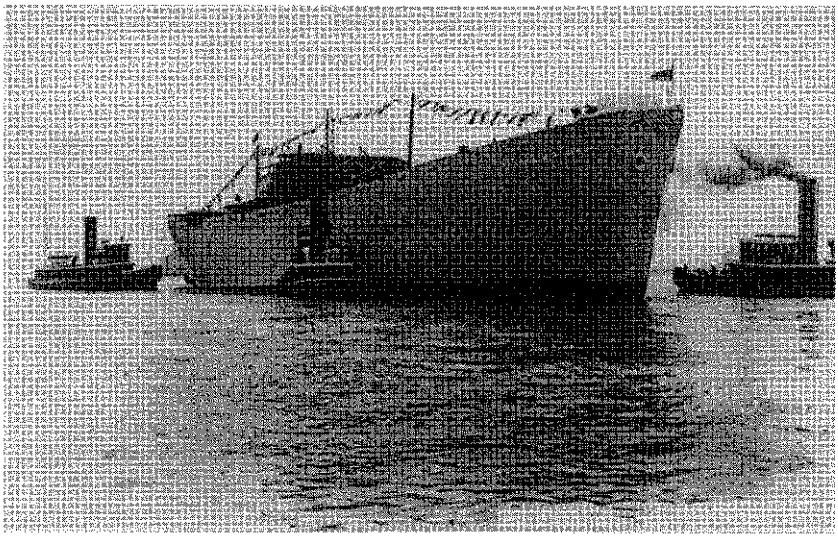

Figure 1.2 The "S. S. Franklin P. Mall," named after the first Director of the Department of Embryology.

human embryos. There is no better way to learn than by doing, he argued, and no better way to teach than with observations of models and specimens to inform study of the static textbooks. On February 20, 1913, Mall received Carnegie Grant No. 874 for $15,000. Work began right away to catalog the existing collections and to secure the collections and records in fireproof facilities. As Mall put it, "A vigorous campaign has been carried on for new specimens of human embryos," reaching half the physicians in the USA and many internationally.[6] This aggressive strategy paid off with new specimens and increased visibility for the collection, presumably helped by the stability afforded by a substantial grant and institutional support from the Carnegie Institution generally (Fig. 1.2).

Mall was made director of a new Department of Embryology, a position he held until his death in 1917. By 1916, Mall was reporting in the annual *Year Book* that while it had taken ten years to get his first 100 embryos, five years for the next 100, three years for the next, and two years for the next, 400 specimens per year had been pouring in since Carnegie support had begun in 1913. He noted that over 500 persons had contributed to the collection (apparently not counting all the mothers who were obviously but in many cases obliviously involved).[7] With Carnegie visibility and authority, the project attracted support from the medical profession generally and even from the State Board of Public Health of Maryland, which instructed physicians in the state to send their specimens to the collection for the purpose of advancing our collective knowledge.

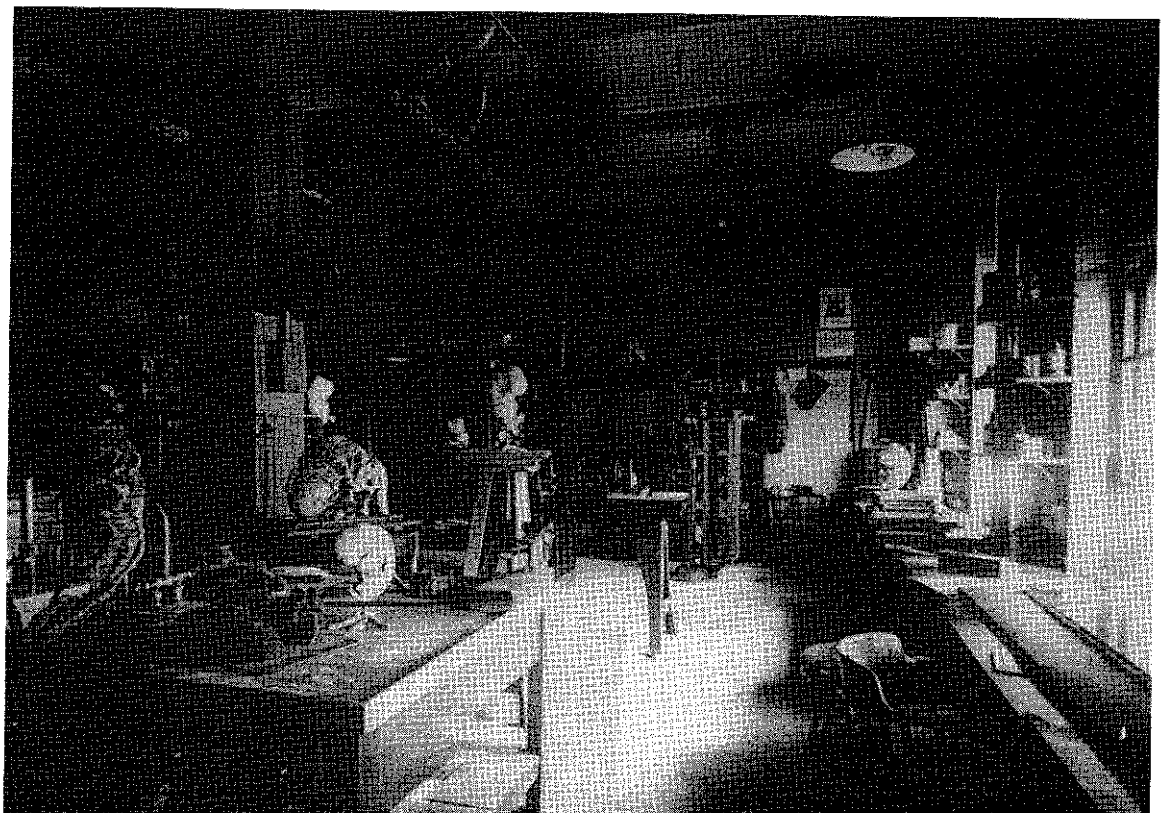

Figure 1.3 Carnegie Laboratory of Embryology, Modeling Department, 1921.

In supporting the project, the Carnegie Institution soon officially opened the Department of Embryology on the Johns Hopkins Medical School campus, with Mall as Director. Within a few years, they were expanding the facilities, adding square footage and facilities for photography, machinery to support making the models, and expanded storage for the collection and the records. By 1915, Mall had formally transferred ownership of his collection of over 2000 specimens to the Carnegie.

Over the next decades, researchers sectioned the specimens, recorded the sections with photographs and drawings, and preserved the materials themselves in fireproof vaults with considerable attention to the acknowledged irreplacability of the collection. In many cases, to augment the specimens themselves and the detailed records about their collection and their analysis, the researchers had models constructed. As His had in Germany to develop his collection, Mall's group hired sculptors to ensure quality and accuracy (Fig. 1.3). By 1914, Mall had hired His's former student and collaborator Franz Keibel from Germany. Keibel had considerable experience in preparing the embryos, so this was a major advance that moved what had initially been a collection of embryos to a major and long-term project of considerable embryological and medical significance. Mall also attracted George Streeter from the University of Michigan, whose work focused on development of the nervous system. And cytologists such as research associate Edmund Cowdry assisted with histological studies while Warren and Margaret Lewis contributed other cell studies.

The result was an impressive group of researchers, established with Carnegie funding and cooperation with Johns Hopkins, at a time when German hegemony in the fields of anatomy and embryology was being considerably undercut by the onset of the First World War. This period of research led to the set of what the group codified as twenty-three distinct stages from fertilization to the eight-week, or fetal, stage. The Carnegie stages, solidified by Streeter, became the standard worldwide for human embryos, and the staff provided a public service for physicians by comparing with the normal stages the abnormal, spontaneously aborted specimens acquired from autopsies sent in by physicians.

Streeter described in the 1918 *Year Book* report the research that Mall had been pursuing at the time of his death in November 1917, including calculations that for every twenty spontaneous abortions, there are eighty full-term births; and that an additional thirty "monsters" are born to every 5,000 pregnancies. In addition, the Carnegie group had made further progress in detailing the timing and sequence of steps in human fertilization and embryo implantation. Streeter was enlisted to serve as Acting Director of the Department for one year after Mall died, and then served as Director until he retired in 1940. As with all the other departments, Carnegie researchers do not receive tenure, and many leave after establishing a research record in this

rich and supportive environment. Fortunately, a few of the leading scientists have remained and have taken on important leadership and administrative positions and stayed with the Carnegie throughout their careers.

By the next year, after his first full year as director, Streeter had had time to reflect on the directions of the Department. He reported that they remained focused on human embryology as their primary problem, including microscopic study of cell structure and gross anatomy of organ systems to understand the body as a whole. They were discovering the value of comparing not only the standard normal, but also pathological specimens to appreciate the factors involved in producing abnormalities. This was obviously of medical importance though not involving clinical research directly and once again reflects the practical aspects of the Carnegie mission. Already there were plans for a new building to provide more space. Warren Lewis had been made a research associate to the Department and had, with his wife Margaret, developed valuable tissue culturing techniques that had already proved innovative for culturing embryonic tissues and expanding cytological studies. Under Streeter, the embryological work continued, but Streeter's own contributions soon brought that line of research to a natural end that pointed in new directions.

By 1973, the emphasis of the Department had changed so much that the collections were really no longer used. They were moved to the University of California at Davis, and then again in 1990 to the National Museum of Health and Medicine of the Armed Forces Institute of Pathology, where they reside today. The collection has recently been digitized and is available through the internet as a resource for the medical and research community and for historians.[8] Adrianne Noe discusses this phase in the history of the Department both in this volume and in her other work cited there.

Primate and comparative studies

Following the emphasis on anatomy with the human embryos came comparative studies with other animals such as chicks, pigs, cows, and then primates, with a focus on physiology. Elizabeth Hanson's chapter in this volume, chapter 3, describes and explains the importance of the primate colony for the CIW study of embryology. It was during Streeter's chairmanship of the Department that the monkeys arrived. One of Mall's students, George Corner, studied anatomy and had become particularly interested in the cycle of reproduction in mammals. He began his studies of rhesus monkeys in a laboratory at the Johns Hopkins, and continued that work through the CIW. He then moved to head the Department of Anatomy at the University of Rochester Medical School from 1923 to 1940.

The initial small group of monkeys became a large colony of rhesus macaques, and the Carnegie researchers' continuing studies achieved such success that the Department recruited Corner to return and follow Streeter

as Director of the Department from 1941 to 1955. Corner's role as Director indicates the direction of research during this period. As Hanson shows in chapter 3, Corner's rhesus monkey colony made possible detailed study of this mammal thought to be closely related to humans and with a menstrual cycle like that in humans. The studies played an important role in focusing serious biological attention on reproductive biology. Adele Clarke's chapter in this volume, chapter 4, demonstrates the nature and importance of that reproductive study, which shaped and even substantially helped to create a disciplinary field of study. Hanson shows that the decision to establish and sustain such a monkey colony required considerable continued investment. As Clarke demonstrates, that investment paid off well in both basic and practical knowledge, in this case to benefit women as part of the Carnegie objective of seeking "improvement of mankind." Although the primate colony was eventually transferred, as Hanson explains in chapter 3, the reports of the 1930s and 1940s are full of discoveries about endocrinology, physiology, and neurology (related to primate) and gynecology (related to human).

Streeter noted in his report for 1936 that there were differences of opinion about just how far the researchers ought to be pressed to develop the medical applications of their work, and about how to organize that work. "The question is raised as to how much freedom should be given to the independent investigator." Should there be dedicated institutes just for the study of cancer, for example? This approach would be too regimented, Streeter concluded. He noted that in pursuing other studies the Department of Embryology had made important discoveries about the nature of tumor development, for example, and the Department of Genetics had added knowledge about tumor heredity even though cancer research was not their primary mission. This argued against single-mission medical laboratories and called for the importance of supporting research into "the fundamental facts upon which an understanding of the nature of cancer must eventually rest," or a call for basic research.

Furthermore, different groups, working quite independently of each other, were making discoveries that complemented each other and added up to significantly advanced knowledge. Therefore, "It is obvious that intercommunication between the groups should be frequent and full, in so far as this can be brought about without infringement upon the backgrounds and approaches of the respective groups. Such an intergroup awareness is facilitated by our administrative organization as a division."[9] Distances between the individual labs, such as Embryology at Johns Hopkins and Genetics at Cold Spring Harbor, should not be allowed to become a barrier to exchange of ideas and free and open cooperation. Any university today would be happy with that emphasis on collaboration, which is something they all seek – or at least say they do.

The CIW sought to realize those hopes by coordinating the Department of Embryology and the Department of Genetics, plus the Nutrition Laboratory

in Boston and the Tortugas Marine Laboratory in the Florida Keys, into a Division of Animal Biology starting in 1934. Streeter served as Chairman and explained that the separate biological studies had been "in each case located where it seemed they could be best conducted." The tendency to overlap and to relate to one another had become sufficiently strong, however, that by 1934 formal coordination had seemed desirable.[10] Yet, as Garland Allen explains in chapter 6, this volume, this spirit of cooperation at times remained more rhetorical than real across the areas of embryology and genetics. By 1941, reports once again came from the separate departments.

Recording cell and tissue development

Hannah Landecker explains the contributions of Warren Harmon and Margaret Reed Lewis in chapter 5, this volume. Rather than theoretical originality, they brought technical skills to the study of cells and tissues. In particular, the techniques to culture tissue and cells outside the body afforded the opportunity to record what happens in the culture. Ross Harrison had developed the very first tissue culture techniques, using hanging drops to culture nerve fibers and demonstrate that they experience protoplasmic outgrowth that appears to be just like that in normal development.[11] Harrison first pursued this work at Johns Hopkins, before moving to Yale, and he worked with the Lewises. While Harrison gave up the technique as not central to the problems he wished to pursue, the Lewises carried development of the technique further. Landecker's account of their work focuses on the intriguing decisions to record the steps of development on film.

Clearly, embryonic development is a process, and it takes place through time. The fascination with capturing the movement is obvious. The idea that following cells and tissue changes during every step of the process rather than just at defined "stages" must have been compelling. Furthermore, the attraction is enhanced by the possibilities for speeding up and slowing down the film to observe details even better. As Landecker explains, the Lewises contributed to a significant shift in anatomical and embryological studies, toward seeing the cell as a dynamic contributor rather than passive respondent in the developmental process. This work began while Streeter was Director, during the 1920s, and continued under Corner's direction into the 1940s.

What the Lewises contributed, as Landecker shows so nicely, was techniques. They helped to develop infrastructure that allowed the research to succeed. The embryo collection, the primate colony, and the tissue culturing and video recording all provided considerable support for investigations by others, both within and beyond the CIW. The Lewises therefore provide a beautiful example of the wisdom of the Carnegie philosophy. Investing in people and supporting their innovations and encouraging them to work together produced a lively intellectual community. The case of the Lewises

makes clear that within this context, not everyone has had to be a leader in advancing theory, yet they could still be central players in a team built on the healthy cooperation, collaboration, and mutual respect that still characterizes the CIW Department of Embryology philosophy.

Embryology at 25 years

On April 4, 1939, in the Department's twenty-fifth year and his last as Director, George Streeter reflected on their contributions. They were receiving about 600 embryos a year, he noted, and providing a service to the physicians who had sent them through the accumulated collation of embryological knowledge and detailed descriptions of developmental stages. Therefore, retaining strong connections with the medical community, facilitated by the Johns Hopkins location, was essential. In addition, the researchers had been busy. In the first quarter century, he counted 1,148 articles by staff members and associates, plus twenty-seven monographs in the Carnegie *Contributions to Embryology* series.

The research had not always gone as expected, Streeter noted, for "Apparently the progress of research can be predicted only to a limited degree and we must recognize that opportunism plays a large part in discovery." Indeed, "advantageous alterations in course" are important, and "it is well to be aware of the limitations of rigidly planned and far-flung research."[12] He acknowledged that the Department had taken up work and moved in directions not originally foreseen. Yet there nonetheless remained a driving goal by the Department of Embryology underlying all the changes, namely to study embryonic structure and how it develops. This included the structure and function of component parts, and the factors that shape them throughout a lifetime. Yet within this broad mandate, it was wisest to invest in the best people and let them do their work. That is the recurring message from the CIW leadership.

By 1939, there was already tremendous interest in genetics and the mechanisms of heredity. Many felt that the mechanisms of reproduction would be found in genetics. Yet Streeter urged that "there still exists a large gap between where the geneticist leaves off and where the embryologist begins." We do not know the forces that direct embryogenesis, nor how genes affect or effect their control, if they in fact do. Geneticists have techniques for demonstrating correlations but not yet for establishing causes. Embryologists do have techniques for following how one stage gives way to the next, or the appearance at least of causal connection, and Streeter's message was that it was incumbent upon embryologists to continue their work. Biochemistry, endocrinology, genetics, study of growth in cancers: all are important and part of understanding development. There are "stimulating advantages of such interchange of ideas and cooperative investigation. There can be no

doubt of the great value of the combination of genetics and embryology in the important undertaking which is now occupying so large a share of our thought."[13] Let us not lose sight of the embryos, Streeter seemed to be saying.

He also noted the research on primates that had begun in the 1920s. With humans we can only work with those embryos that happen to become available when physicians bring them in. Yet there is great advantage in understanding the full reproductive cycle in humans as well as other animals. Researchers associated with the Department had studied how an egg fastens to the uterine lining and the early stages of placental formation. They had already made considerable progress in understanding exchanges between mother and developing embryo.

In addition, with animals including primates, researchers could carry out tissue cultures and cell cultures. They could extract cells and culture them, thereby allowing research on living materials rather than just the dead and dissected materials afforded by the preserved specimens. Observing many specimens in animals allowed them to interpret what they saw in the few human cells and embryos to which they had access. Warren Lewis's development of a system to capture the observation in film using the relatively new techniques of making motion pictures led to increased data and understanding of the character and details of cell movements.

Streeter pointed to possible future research directions, including the prospects for using radioactive tracers to track the movement of materials from mother to embryo. Yet he also warned that they must not become like Aesop's dog, which in the excitement of seeing its reflected image with bone in the water, dropped the bone it already had. By implication, the CIW Department should not drop important ongoing work to chase trends and fads. They should therefore retain their solid foundation in first-rate scientific exploration while pursuing innovations where and only where they made sense. Above all, what CIW could offer this research was the capacity to work across disciplinary boundaries, the flexibility to promote cooperations, as between geneticist and embryologist, and to incorporate techniques and tools from a wide diversity of fields, and thus the ideal climate for incubation of innovations. Streeter retired with an optimistic outlook on the CIW efforts.

The Department's wartime effort

In his 1944–5 report, Director George Corner noted that in the fourth year since war had begun, he had to offer the smallest review of research since the Department had been established. His staff had been diminished, and had been distracted by "emergency duties" and by "the general disturbance." Nonetheless, Corner reported on new microtomic techniques used by the

modeling and technical team, the continuation of the monkey colony, and participation in cooperative efforts stimulated by the war effort. Indeed, he cited "Embryology as a cooperative science" in the title of his report.

This becomes a theme: cooperation and teamwork, for "Among the gains brought by this way, in partial compensation for its destruction and misery, surely not the least is this cross-fertilization of the various sciences, which results not only in immediate practical advantages, but also in new thinking about fundamentals. The synthesis of ideas thus achieved is not lost even if in times of peace the pendulum swings again necessarily toward individualistic research." This was a notable change of tone for the CIW, emphasizing the interactions more than the individual research efforts. Reports of the next years continued to stress the prospects for interconnections and cross-fertilizations as a justification for the various separate lines of research. "At any moment," Corner noted, the results of "pure" science may become useful. Indeed, "The understanding of man's place in the animal world," such as those promoted by the embryological group, "necessarily influences the whole structure of human education, lawmaking, and philosophy."[14]

By a decade later, Corner was reporting a huge influx of researchers from around the world. The recitation of publications, description of research, and list of researchers was impressive, indeed, and showed how far the Department had come in these glorious post-War years. Usefulness was measured far more clearly in terms of value to the understanding of embryology and fundamental biological problems than to external applications.

Carnegie at 50

Vannevar Bush was president of the CIW during its fiftieth year, in 1951–2. The event promoted reflection. The Institution continued to proceed in just the way the founder had envisioned, promoting mutually beneficial basic and applied research. The focus also remained on the individual scholars, with investment in the talented expected to yield results. Bush believed strongly in such investment, with the primary responsibility to invest in fundamental research without regard to the potential payoff or industrial application that would follow if and when appropriate. Much remained the same, therefore.

Yet the departments were continually evolving, and that was good. After all, though the scientists might each differ "in what they are trying to accomplish," they conducted scientific research the same way. Piece by piece, the selected individual researchers have added to our pool of knowledge that is available for public good. The CIW programs have begun with basic research, publishing openly, with laboratories open to any serious-minded visitors and open to opportunities for developing patents should those arise. Perhaps the Institution could and should help to hasten the time from research to development, Bush reflected, since the bridge between basic and applied research

is often ineffective with too many hurdles. In particular, he pointed to George Shull's pioneering work on hybrid corn at Cold Spring Harbor and the time it took before the idea made it to market. Perhaps the Institution should have promoted the development more directly, but it was not clear how. Other devices to help with childbirth and information for textbook training of physicians provided more evident moves from the lab to the practical world.

Notably, when Bush turned to the contributions from the Department of Embryology for that year, it was already organs rather than embryos that received top billing. Discoveries of neural crest cell formation shed light on development of the eye and the neurology of vision. Kidney formation in humans provided another example. "In this respect, as in many other details of embryonic development," Bush noted, "our species is more like other mammals than has sometimes been thought." X-ray studies, and in particular X-ray motion pictures were revealing details about umbilical arteries, and combined with studies of the chemistry of uterine muscle contractions were illuminating many details of the reproductive process. CIW researchers were "getting very close to the fundamental problems of the specific manner in which hormones exert their extraordinary physiological effects upon their target organs."[15]

This might be "fundamental research," but Bush and the CIW research staff remained very aware of the potential benefits for greater understanding of important biological processes and also for potential medical applications. The fundamental or basic science easily merged with the applied, Bush emphasized, even in detailed and specific studies. Together the individual studies asking different questions with different techniques combined, through communication and cooperation, to advance knowledge for the "improvement of mankind."

In his last report as Director in 1954–5, Corner had reflected on the first forty-two years of the Department, outlining a formidable portfolio of diverse studies. As Donald Brown discusses in chapter 7, this volume, Corner had raised questions about future directions for the Department and how best to remain innovative and adaptive to changing environments. The decisions made reflect the impact of focusing on techniques and infrastructure, and the value of investing in people and allowing them enough time and support to incubate innovations without demand for immediate results.

The selection of Mall, Streeter, and Corner as the first three Department Directors reflects the strong medical connections of the Embryology Department. Embryology was a practical and medical science, and the CIW researchers saw it that way. They brought to bear studies of cells, tissues, and other basic biological tools and questions. Yet the emphasis remained medical and the ultimate goals practical through this time. That changed with the next director and after the mid-1950s and the advent of DNA studies.

The second half-century of the Department of Embryology has therefore looked quite different from the first, demonstrating the wisdom of retaining flexibility and mobility in investment that Carnegie and the early trustees had emphasized from the beginning.

Genetics and evolution

In this volume and elsewhere, Garland Allen has discussed the CIW's investment in genetics and experimental evolution. Most notably, this occurred through individual grants to fund Thomas Hunt Morgan's fly room at Columbia and for Nettie Stevens' studies of chromosomes at Bryn Mawr, and through institutional funding for the Department of Genetics at Cold Spring Harbor. For Cold Spring Harbor, Charles Davenport had a vision of a Station for Experimental Evolution. He saw the importance of studying heredity, since inherited variations are the raw material for the evolutionary process. Clearly, he concluded, traits run in families and therefore are inherited. Therefore, Davenport suggested that to promote intelligent evolution, we should begin with data about which families carry desirable and which undesired traits. Eugenics made perfect sense to Davenport, and was consistent with commitment to advancement of the general public health. Surely a visionary like Andrew Carnegie and his Institution's trustees would be committed to this interpretation of the "improvement of mankind."

So they were. As Allen explains in chapter 6, this volume, Davenport approached the Institution for funding in 1902. At first, the CIW funded Davenport through the Station for Experimental Evolution at the Cold Spring Harbor Laboratory, begun in 1904. Then in 1918, that station was combined with Davenport's separately funded Eugenics Record Office into the Carnegie Institution Department of Genetics. Though the Department continued until 1962, after 1940 the Eugenics Record Office was closed and the emphasis placed on the genetics research of a few individual investigators, including two of the most important genetic researchers of the twentieth century, Alfred Hershey and Barbara McClintock. In 1962, Carnegie president Caryl Haskins in effect gave the Department to the Cold Spring Harbor Laboratory, with the understanding that the CIW would continue to fund those two researchers. From 1962 to 1971, what was called the Genetics Research Unit continued, headed by Hershey, who along with his predecessor Milislav Demerec had considerably raised the quality of research pursued.

Carnegie in the post war era of expanding science

The 1950s brought changes, of course, with the rise of the National Science Foundation, increased funding for the National Institutes of Health,

democratization of the universities as soldiers continued to use their GI Bill benefits to pursue education and a promised better future. It was a period of adjustment, with the CIW guided by Vannevar Bush. In 1956, Caryl Haskins became President at the same time that James Ebert became Director of the Embryology Department. By 1961, with the sixtieth anniversary of the Institution, the changes had become more visible.

In his presidential report in the 1961–2 *Year Book*, Haskins grew reflective. He cited the early decisions to make the CIW largely an operating rather than granting institution, with localized smaller laboratories around the separate departments but with flexibility as well. This had served the Institution well, for each unit remained relatively independent and "able to seize the initiative in new and appropriate fields as they appear, yet all sufficiently connected so that they may be of mutual assistance as the needs arise." Organization in itself is not important, except in that it gives a framework for the research.

The philosophy of an institution matters, and the CIW philosophy was to promote the creative individual, assuming that the result would be incubation of original thinking and innovative science.

> And with this goes the philosophy, equally deep-seated and equally important, that this freedom from fixed commitment applies to fields of endeavor as well as to men: that high mobility within specific fields, that of unfettered crossing of fields, that the fashioning of unconventionally wide-ranging programs, are subject only to the limitations imposed by Nature and by the judgment of the gifted and discriminating investigators, and that making this mobility and this flexibility possible is the principal objective of the Institution.

Again, any twenty-first century research institution would be pleased to point to a history of successful promotion of such creativity and would love to know how they could achieve the successes that the CIW experienced.

Haskins realized that the world had changed since Andrew Carnegie had first laid out his vision. By 1961, science had seen tremendous growth and was obviously going to continue its extraordinary expansion of personnel and intellectual development. Could it possibly be that the reliance on small and mobile groups of individual researchers, encouraged to be creative and innovative, was no longer the way to promote scientific discovery? "Is it possible that we are witness to a profound revolution in the very character of research itself," and must we develop larger and differently organized teams? This question about organization "touches on the nature of scientific truth itself," Haskins thought, and it touches on the CIW faith in the "distinguished, unfettered individual." Was this the end of an era after "only" sixty years?

No, of course not. Yes, there was room for other ways of organizing science as well. But the most recent research in genetics, for example, showed that it

was "abundantly clear that the essential qualities and requirements of inquiry at the very frontiers of man's knowledge of his universe do not now, and in all probability will not in the foreseeable future, differ significantly from those of our classical scientific past." Surely scientific inquiry would continue as it had, and the Institution should continue its wise investment in people, providing them whatever material and human support might be required for the production of knowledge. There is a heroic quality in the expressions of faith. And an inspiring conviction that the CIW leaders carried a "heavy responsibility of the keeper of a vision." It was their task to facilitate creativity, remove obstacles, and encourage the "priceless jewels" that individual innovators represented to continue their work. Quoting Chaucer, Haskins reminded his readers that it made sense to continue the CIW traditions rather than rejecting what had proved to be a sound philosophy, for "Out of the old fields cometh the new corn."[16]

Meanwhile, James Ebert was pointing the Department of Embryology in new directions. Not at all giving up traditional problems of embryology, he saw the Department as embracing new techniques of genetics and molecular biology to attack those problems. Even before they began their terms, by 1955, Ebert and Haskins had apparently agreed to phase out the human and primate embryological work.[17] Instead, the Embryology Department would explore the most fundamental embryological problems of differentiation, growth, and morphogenesis with new techniques. Clonal cell lines would provide material for exploring genetic transduction. Biochemistry, physical chemistry, and optical methods would allow close examination of the fine structure of cells.

Whereas Mall and Streeter had emphasized morphology and anatomy, Corner had brought physiology, biochemistry, and biophysics to embryology. In turn, Ebert brought genetics to development and helped transform embryology at CIW. Rather than correlations, population studies, or the role of transposable elements pursued by the Department of Genetics and particularly by Barbara McClintock at Cold Spring Harbor, the Embryology Department would focus on "genetics by gene isolation" as researcher and later Department Director Donald Brown put it. Gene amplification, isolated purified genes, and RNA all provided material for the study of the role of genes in development. Brown's chapter in this volume discusses the period that began after Ebert arrived and that so notably redirected the Department. Brown provides further detail and insight into the biological inquiry of this important transformational era for the Department of Embryology and for embryology itself. He also emphasizes that science remained the focus of the Department and the Directors (Fig. 1.4).

In addition, as science became more complex and called for multidisciplinary approaches, the CIW cultivated an emphasis on innovation along

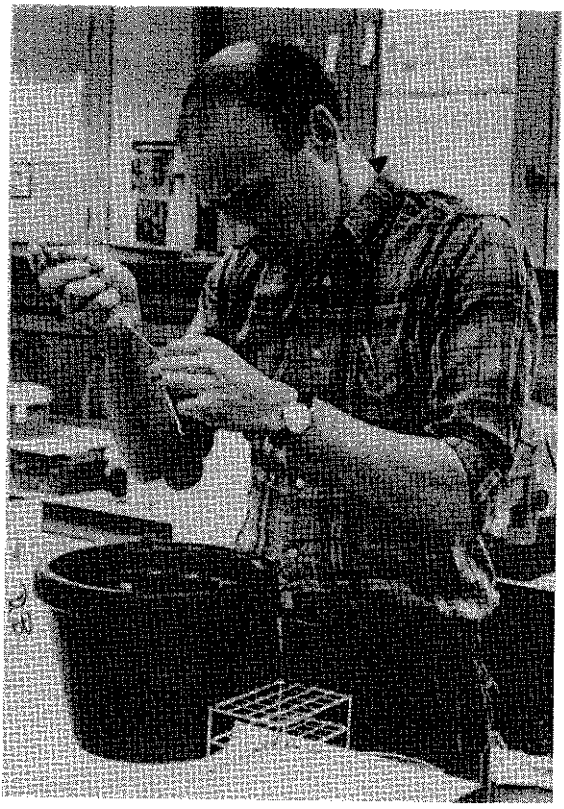

Figure 1.4 Donald Brown, Department of Embryology's fourth Director, at the bench.

with the attitude of cooperation and collaboration. As current Department Director Allan Spradling says in his chapter in this volume, chapter 8, the current Department research team is proud to say "we do not know." He notes that researchers are expected to generate first-rate and ground breaking science, not necessarily more publications or more grants just for the sake of having more. Follow the research and innovations, and be patient in waiting for results if necessary. Spradling gives us insights into the current opportunities and limitations for a Department of Embryology in this era of translational genomics and developmental genetics. As Spradling put it so perfectly in a recent annual report, "Genomic research is frequently viewed by the public, and even in some scientific quarters, as a relatively new development. In reality, though, this institution and the Department of Embryology have been striving to decipher gene structure and function for most of the last 100 years"[18] (Fig. 1.5). In different ways at different times, researchers have continued to work toward methods and approaches for answering the

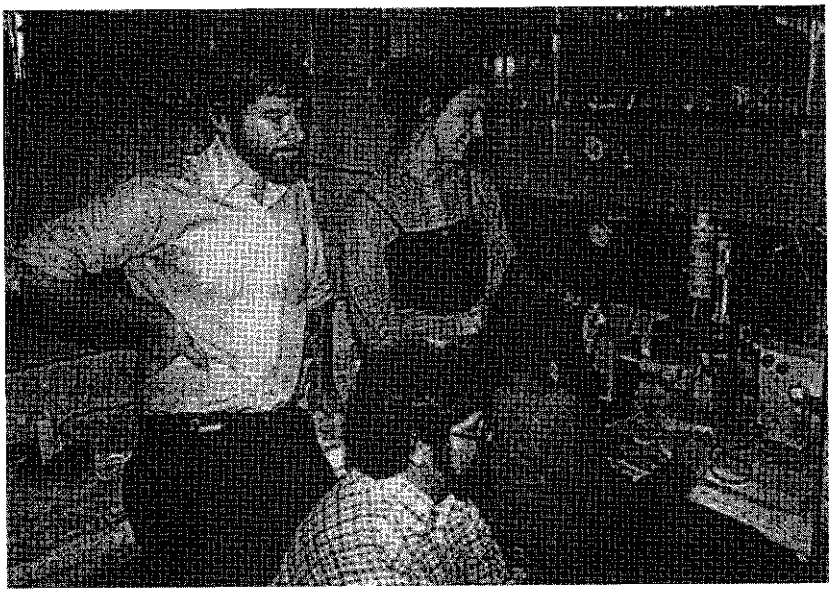

Figure 1.5 Members of the Allan Spradling Laboratory team introducing purified genes into fruit fly embryos, 1983, including Terry Orr-Weaver (postdoc, standing), Suki Parks (graduate student, seated), and Joe Levine (technician).

fundamental questions about embryonic development. For 100 years, the CIW Department of Embryology has been a leader in cooperation, innovation, and incubation of new ideas in a changing world.

Notes

1. Andrew Carnegie, "A Gospel of Wealth," cited in James Trefil and Margaret Hindle Hazen, *Good Seeing. A Century of Science at the Carnegie Institution of Washington*. 1902–2002 (Washington, DC: Joseph Henry Press, 2002), p. 16.
2. Trefil and Hazen, especially pp. 21–35.
3. Trefil and Hazen, pp. 31–33.
4. Trefil and Hazen, p. 33.
5. Nick Hopwood, *Embryos in Wax. Models from the Ziegler Studio* (Whipple Museum of the History of Science, University of Cambridge, 2002).
6. Franklin Paine Mall, Carnegie Institution of Washington *Year Book* 13 (1913–14), p. 290.
7. Franklin Paine Mall, Carnegie Institution of Washington *Year Book* 16 (1916–17) p. 109.
8. http://nmhm.washingtondc.museum/collections/hdac/Education_Projects.htm for the Visible Embryo Project.
9. George Streeter, Carnegie Institution of Washington *Year Book* 37 (1936–7), pp. 3, 4.
10. George Streeter, Carnegie Institution of Washington *Year Book* 34 (1934–5), p. 3.

11. Jane Maienschein, *Transforming Traditions in American Biology, 1880–1915* (Baltimore: Johns Hopkins University Press, 1991), especially chapter 9.
12. George Streeter, "Carnegie Institution of Washington. Memorandum on Department of Embryology," 4 April 1939, CIW Archives, memo, pp. 3, 4.
13. Streeter, 1939 memo, p. 7.
14. George Corner, Carnegie Institution of Washington *Year Book* 44 (1944–5), pp. 90, 91, 93.
15. Vannevar Bush, Carnegie Institution of Washington *Year Book* 51 (1951–2), pp. 16–17.
16. Caryl Haskins, Carnegie Institution of Washington *Year Book* 61 (1961–2), pp. 5, 6, 16, 25.
17. Philip Abelson, Carnegie Institution of Washington *Year Book* (1976–7), 75th year, p. 33.
18. Allan Spradling, Carnegie Institution of Washington *Year Book* 99/00 (1999–2000), p. 43.

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