

Controlling Life: From Jacques Loeb to Regenerative Medicine

JANE MAIENSCHIEIN

*Center for Biology and Society, School of Life Sciences
Arizona State University
Tempe, AZ,
USA
E-mail: maienschein@asu.edu*

Abstract. In his 1987 book *Controlling Life: Jacques Loeb and the Engineering Ideal in Biology*, Philip Pauly presented his readers with the biologist Jacques Loeb and his role in developing an emphasis on control of life processes. Loeb's work on artificial parthenogenesis, for example, provided an example of bioengineering at work. This paper revisits Pauly's study of Loeb and explores the way current research in regenerative medicine reflects the same tradition. A history of regeneration research reveals patterns of thinking and research methods that both echo Loeb's ideology and point the way to modern studies. Pauly's work revealed far more than we readers realized at the time of its publication.

Keywords: Pauly, Loeb, parthenogenesis, regenerative medicine, regeneration, experimentation, control

In 1987, Philip Pauly's book *Controlling Life: Jacques Loeb and the Engineering Ideal in Biology* appeared in a series with Oxford University Press. Unfortunately, the press discontinued the series shortly after, and the book never received as much attention as it should have or as it would if it were published today. The book reflects Pauly's work as a graduate student at the Johns Hopkins University working with Donna Haraway and his time as a Fellow at the Smithsonian Institution. The book also draws on Pauly's deep feeling for American history, and I see now that he was ahead of the time in this as in so many other things. Phil Pauly saw Jacques Loeb's fascination with controlling life as rooted in some of the same impulses as those favoring biotechnological development of the late twentieth century (and since). He painted a picture of Loeb as an iconoclastic German Jewish physiologist in an American world of embryologists and other biologists with different

views about science. While Loeb's driving desire to control rather than to understand life's processes should have fit nicely in the progressive period, his contemporaries were focused on other problems and did not share Loeb's vision.

I read Pauly's book manuscript, then read the book multiple times. I have often gone back to chapters as a reference and reminder. But it is only on re-reading the book again after not having done so for a while that I begin to see additional richness there. The story makes much clearer to me now the struggles Loeb had in finding his role in American biology, and only now do I see the desire to control life expressed by Loeb as reflecting the same set of goals that those enthusiastic about the translational possibilities for regenerative medicine, based on the study of stem cell biology, now have. Pauly's presentation of Jacques Loeb's life and work provides insight into today's desire to control life.

Jacques Loeb

Biographies of Loeb usually start with his arrival in the United States in 1891 to teach at Bryn Mawr College. President M. Carey Thomas and the Trustees made clear that they did not really want to hire this German Jew, but they needed somebody since two of their scientists had just left, and they hoped that Loeb's American wife Anna Leonard Loeb would smooth the way. The arrangement did not work out well, and he eagerly accepted when Charles Otis Whitman recruited him to the University of Chicago in 1892. He also began in 1892 attending summer sessions at the Marine Biological Laboratory in Woods Hole, where Whitman served as Director. This is where the story usually starts with Loeb, and this was the beginning of his professional research and teaching career that helped set Loeb's values and goals. It is his early years in Germany, studying in a practical *Realschule* rather than a *Gymnasium* as required for preparation for college, that Loeb learned about class and social status. He did eventually receive the requisite training and carried out the university and graduate study, with a medical degree that placed him a position for a university appointment. It was clear, however, that being Jewish – even as an atheist – was not going to help him. Nor did the fact that he never really accepted the need to cultivate his superiors in order to move up the very hierarchical German academic ladder. He briefly tried ophthalmological clinical practice but quickly resolved that he and his new wife must move to the United States.

By that time, however, Loeb carried with him a commitment to what Pauly called "an engineering standpoint." Pauly detailed Loeb's studies, his experiments, and his interactions with others during his studies. The first major source of intellectual stimulation was his contact with the botanist Julius Sachs in Würzburg. Like Loeb and unlike most of the medical researchers Loeb had met, Sachs came from a poor family. He found his way to an agricultural context because that is where opportunity lay, but his commitment was to the ideal of *Wissenschaft* and what could be accomplished through application of science. As Pauly put it, Sachs took a "notably active stance toward his organisms." He was not in search of either the empirical classifications of botanical esoterica or the abstract underlying principles of life. Rather, for Sachs "Any transformation that the scientist could perform that would make the plant more useful was good, without regard for the inner nature of the plant." One could control the motions of beans and turnips without worrying about implications for ideas of consciousness, and control of plant development was the central aim of agricultural science. Sachs shared in this drive to manipulate."¹ So, after his contact with Sachs, did Loeb.

It was work on animal tropisms that set Loeb on his track to control. Here was his first example where it was clearly not the internal workings of the organism that dictated the outcome. Rather, the individual responded to the environment. By manipulating the environment, the experimenter could control the results. At least this was true to some extent, but it was a beginning. Loeb looked at various kinds of tropisms, including helio (light), geo (gravity), stereo (friction), galvano (electric), chemo, and other kinds of stimuli. He was committed to the idea of control.

This, Pauly explained, led him to write to the physicist-turned-philosopher Ernst Mach. This began a decade-long correspondence that allowed Loeb to claim Mach as a mentor and to find reinforcement for his views when he felt misunderstood wherever he was at the time. Mach represented an advocate of "scientific positivism" including the basic importance of experimental research while also considering social and cultural implications of science. Note that "positivism" has meant many things to many people, and has often been misunderstood, but the emphasis here is on the combination of science in the context of and in aid of social application. Mach's philosophy fit well with the interest in control of life that Loeb had begun to absorb in contact with Sachs.

¹ Pauly, 1987, p. 35.

For Loeb, Mach represented a rejection of mechanistic explanation as a metaphysical approach. Instead it made sense to look at the dynamics of animal reaction rather than internal mechanistic actions. And it made sense not to see science as uncovering truths about nature, but rather as "a human effort to cope with the environment. For Mach, scientific concepts were tools valuable primarily for their contribution to 'economy of thought.' The measure of economy was efficiency in prediction and control."² Science, for Mach, was "an instrument for action" and was closely tied to technology.³ Loeb was apparently enchanted by Mach's ideas – about science, the need to reform the German educational system to reduce hierarchies, and the desire to raise the status of engineering and technology.

For Loeb, inspired and reinforced by Mach, the work of the scientist was that of an engineer. That meant that the science should certainly not be a search for causes and explanations, nor an effort to understand the metaphysics of nature. Rather, the scientist as engineer "judged concepts by using them in attempts to control nature." This scientist-engineer should engage in action rather than analysis, experimentation rather than theorizing. Yet Loeb deviated from the typical justifications for engineering, in terms of practical application. Instead "there was no need to justify control in terms of utility or to reconcile it with other values. Loeb embraced the engineering impulse as an ultimate value."⁴

How, then, did this conviction play out in Loeb's own research? He had studied tropisms and continued to do so, with an emphasis on the environmental stimulation of an organism's reactions. With work at the Naples Zoological Laboratory in particular, he began to explore regeneration as a reflection of the capacities of organisms to respond to changed environmental conditions, and he discovered what he called "heteromorphosis." Here he showed that by manipulating the conditions it was possible to produce different developmental results. Or as he put it in 1891, "I have succeeded in finding animals in which it is possible to produce at desire a head in place of a foot at the aboral end, without injuring the vitality of the animal."⁵ This, in turn, affected the behavior of the animal – in this case a tubularian. Therefore, Loeb concluded that he had been able to control the behavior by engineering the environmental conditions.

² Pauly, 1987, p. 43.

³ Pauly, 1987, p. 44.

⁴ Pauly, 1987, pp. 47, 48.

⁵ Pauly, 1987, p. 50.

In a letter to Mach in 1890, he wrote that "The idea is now hovering before me that man himself can act as a creator even in living nature, forming it eventually according to his will. Man can at least succeed in a technology of living substance." Yet the process would be slow and "even here I go forward only slowly. I find it difficult not to lose courage."⁶ This, as Pauly pointed out, is absolutely key to understanding Loeb's thinking. Loeb wanted ultimately to create new life forms, and he wanted a science that would be committed to doing that.

Then he moved to Bryn Mawr and on to the University of Chicago. This seemed a fortuitous set of opportunities for him to expand on his program, and yet he chose to work in environments surrounded by colleagues with quite other views about science and its goals. It is worth understanding this in more detail, since the co-existence of those oriented toward understanding and analyzing nature with those committed to using knowledge to achieve control has reoccurred in different ways, including today with regenerative medicine. It is worth understanding the different approaches and how they worked together (or did not work together) for Loeb.

Loeb in America

It was at the University of Chicago that the tensions began to play out most clearly. Loeb was never one to remain subordinate to others, but Whitman as Director of Zoology sought to relieve tensions by placing Loeb in charge of physiology. It was in a speech in 1896 at the laying of the cornerstone for the long-promised new laboratories for the biological sciences that Loeb set out his vision for physiology. This field was not primarily a service to medicine, he made clear, but it had a higher purpose. Physiology should work with chemistry to solve problems, such as agricultural crop failures, and perhaps to address famine by creating bread "directly from the carbon-dioxide of the air." Physiology should not become bogged down in thinking about such theoretical questions as evolution, but rather get to work in experimental laboratory work. As he had made clear over and over, this meant not the boring work of routine cytological slide preparation and observation, but the real work on experimental manipulation. The biggest objective of all was "to determine whether or not we shall be able to produce living matter artificially."⁷ Loeb had laid it out publicly: for him, science

⁶ Pauly, 1987, p. 51, citing a letter from Loeb to Mach of 26 February 1890.

⁷ Pauly, 1987, p. 92, citing the "Address of Associate Professor Loeb." *University Record* 1 (1896): 288-289.

should be committed not only to controlling but possibly even to creating life.

It seemed to some, including himself, that he had succeeded with his "invention of artificial parthenogenesis" in sea urchins. In 1899, Loeb discovered that changing the salt concentration of sea water in certain ways allowed the unfertilized sea urchin egg to begin developing. He entitled his paper announcing the success as the "Artificial Production," and that is surely how his colleagues saw it, but Pauly makes the case that Loeb considered it an "invention" and that it truly was. This is important. Whereas his embryologist colleagues would largely have seen Loeb as having discovered yet another fascinating fact about development, Loeb saw himself as having engineered and caused a result rather than having discovered it.

No doubt this struck some of his colleagues as arrogant, and the popular news coverage Loeb received undoubtedly aggravated tensions. It did not help when he (too?) candidly told the reporter Carl Snyder that he acknowledged that "I wanted to take life in my hands and *play* with it." That is, he wanted to take life and "handle it in my laboratory as I would any other chemical reaction – to start it, stop it, vary it, study it under every condition, to direct it at my will."⁸ That is decidedly *not* what the leaders among those who called themselves biologists would have said at the time. And they certainly would not have said it to reporters who were, not surprisingly, likely to report the sentiment. Nor would they have called the production of artificial parthenogenesis "immaculate conception" or have allowed it to be likened to the birth of Jesus Christ.

What Loeb did, in fact, was to produce normal pluteus larvae in sea urchins, even though they had not been fertilized. This result strongly suggested that it was possible to control the conditions of life, and to create results at will. It remained for others to reproduce the results (they did, though not without difficulty and not without considerable controversy), and to extend the results to other species to show that this was not just a fluke due to the special nature of sea urchins (it worked in others too, though it took a number of efforts and a number of years to show that definitively). While others debated what the results really meant, Loeb enthused about the possibilities for further such engineering work.

In fact, Loeb actually made some experimental errors. Loeb did not particularly like mucking about doing the dirty work of experimentation himself and he relied on assistants to prepare materials. He was

⁸ Pauly, 1987, p. 102. See Snyder, 1902.

actually working with a different concentration of salt water than he thought. And some contemporaries reportedly suggested that even the experiment of altered salt concentrations was an accident because of Loeb's dislike of collecting himself.⁹

Yet Pauly explained very clearly that the errors did not matter for Loeb, even though they would have been serious for his colleagues Thomas Hunt Morgan or Edmund Beecher Wilson. As Pauly put it, "It mattered little that his technique was sloppy and that the data were often inconsistent. Loeb was guided by the desire to produce fatherless sea urchins, not to reduce fertilization to a particular chemical process. Analytical difficulties were subordinated to the search for control of development. Loeb invented artificial parthenogenesis because of his search for an engineering biology, and artificial parthenogenesis served as an exemplar for the further development of that approach."¹⁰

The rest of the story plays out in Philip Pauly's excellent book, and everybody should read it again today, two decades and a great deal of biotechnological developmental later. Pauly made clear that Loeb's views evolved, despite his rejection of evolution as important to biology. And Loeb never quite found a completely comfortable fit either in academic settings or in the independent research environment of the Rockefeller Foundation, where he had what most would consider a dream job without teaching responsibilities and with the explicit permission to pursue whatever research he wanted. The only pressure was to be innovative and to produce results of some sort. Loeb apparently felt that pressure keenly and worried, though he was productive.

Loeb did not, however, produce the control that he had sought. In the end, he spent his time moving toward articulating a "mechanistic conception of life," despite his earlier rejection of such analytical reflection. Loeb's was the life of a complex man, an iconoclast who does not so much reveal what is typical about American biology in the early twentieth century as show us a bold vision that was not realized at the time.¹¹ It is only later that establishment science has returned to the vision, and it is worth exploring the similarities and differences. I only regret that Phil Pauly is no longer here to help us with this thinking.

⁹ This rumor pops up in stories by Edwin Grant Conklin and others at the Marine Biological Laboratory.

¹⁰ Pauly, 1987, p. 99.

¹¹ Pauly at the end of his book discussed some individuals who were influenced by Loeb: J.H. Northrop, John B. Watson, B.F. Skinner, H.J. Muller, W.J. Crozier, and Gregory Pincus.

Controlling Life through Genetic Engineering?

There were, of course, various efforts to develop biotechnologies after Loeb, including through pharmaceutical companies and industrial efforts to use chemistry to produce nutritious food, drugs, hormones, or to engineer other additives to support life. Biophysical enhancements provided prostheses of various sorts from eye glasses to substitute limbs or other organs. All these explicitly applied products came out of different traditions than Loeb's desire to learn to control life as a biologist, however. So did the medical applications, including Alexis Carrel's work on tissue culture and organ transplantation. It was really with genetic engineering in the 1970s, reinforced by the Human Genome Project, that the biological research community began to embrace ideas similar to Loeb's.

There are other histories of genetics and genomics, so for purposes here, I will briefly note the language of control and the hopes for engineering that came starting in the 1970s with the capacity to recombine DNA.¹² The early episodes of recombinant DNA raised controversy. Was the technique safe? What if recombined *E. coli* bacteria escaped the lab and invaded the human gut? What if scientists did not heed warnings like those from physicists who had unknowingly participated in producing an atomic bomb that killed and injured many people? If scientists had once known sin, as J. Robert Oppenheimer put it, then it could happen again. Shame on those scientists who were warned but did not heed the cautionary message and became Frankensteins or worse. Some called for limits or at least protections on what kinds of recombining of DNA could occur and how and under what circumstances. Others admitted the concerns but called for academic freedom of inquiry, even into areas of the scientifically unknown.

After much debate, scientists worked with the National Institutes of Health to develop a set of guidelines to enforce appropriate and moral research behavior. With time, when nothing bad happened and increased knowledge suggested that many of the scenarios could not happen, skeptics became advocates. By the time of a 1977 hearing by the National Academy of Sciences, a number of the scientists who had worried the most were lobbying for an end to restrictions and open research.

The sentiment shifted from concern about not going too far to concern about not going far enough. Perhaps there should be a research

¹² For an overview of some of the core issues, see Maienschein, 2003. On the history of the recombinant DNA debates, see for example: Krimsky, 1982; on later developments see such works as Cook-Deegan, 1994.

imperative. If, in fact, study of human genetics and of recombination could even lead to gene therapies, where “defective” or “disease-causing” genes could be replaced, that would be a wondrous thing. At least some advocates began to argue in that direction. In addition, they saw that Big Biology was very, very enticing, with its promises of substantial support from the federal government to carry out basic research into fundamental processes of heredity. Academic scientific researchers who considered themselves biologists began to endorse the goal of biology as controlling life. Perhaps with knowledge, biologists could eliminate genetic disease by eliminating “bad” genes or by replacing their function.

As we know, the Human Genome Project has generated tremendous amounts of data, but gene therapy has not worked to produce medical solutions. Not yet, and maybe not ever in the way the original advocates were imagining. This reminds us that Jacques Loeb’s vision may have been rather naïve, yet the central goal of controlling life remains. Using genetic-based knowledge to produce therapies will likely not be a matter of introducing “good” genes to replace bad but more likely to use genetics to gain more information and then to induce appropriate replacement function. Controlling life and, certainly, the ambitious goal of creating life are likely not to work out the way we imagine. Indeed, genetics only takes us a little bit of the way to life. Stem cell research and cloning have brought the realization that it is not just genetics but also development and regulation that matter for life. This brings us to regenerative medicine.

Controlling Life through Regenerative Medicine?

Regenerative medicine brings together three research traditions: study of regeneration, study of stem cells, and the demand for translational medicine. It also requires techniques of transplantation to make regeneration work. In addition, to be regenerative and medicine depends on a commitment to controlling life, or something like the translational imperative that the National Institutes of Health has adopted in the United States. I will take each of these in turn.¹³

First, regeneration. Fascination with the powers of regeneration began with the tales of Prometheus. Tied to a rock for eternity, Prometheus was being punished for giving the power of fire to man. Each day an eagle came and ate his liver, which should have killed him. Yet

¹³ For further discussion, see Maienschein, 2008.

each night, the liver regenerated and the eagle would eat it again the next day. And so on. This tale is usually presented as a warning to behave or else you will be condemned to be tied to a rock and suffer as your liver is eaten again and again forever.

Regeneration has always held fascination. In the eighteenth century, researchers began to ask how and why some animals and some body parts under some circumstances regenerate. When a hydra's head is chopped off, what happens? Why does it grow back, but not always exactly in the same way? Why can earthworms regenerate from pieces? Was the form already preformed in some way so that it simply grew back and replaced the missing part, or did the remaining parts of organism somehow know that something was wrong and from internal forces self-organize to replace the missing or injured part? Discussion of regeneration has often played central roles in debates about whether development occurs as guided by some sort of preformation or through epigenetic responses to changing internal and external conditions.

By 1900, so many researchers had poked and prodded and chopped off pieces of various organisms to watch them regenerate and had developed so many competing theories that Thomas Hunt Morgan gave a series of lectures at Columbia University and then summarized in his book *Regeneration*.¹⁴ Here he described earlier studies and their implications, and also focused on current views. He rejected what he saw as the unwarranted theorizing, especially by August Weismann, who saw regeneration as a product of evolution. For Weismann, those parts most likely to be injured have a set of reserve hereditary units to guide regeneration. Morgan rejected that idea and instead pointed to internal factors within the cytoplasm as holding the capacity to initiate regeneration. For Morgan, regenerative capacity was not pre-programmed but rather a response to internal environmental conditions. His own ideas did not persuade many and he soon set them aside, but his investment in the topic shows the wide fascination with the powers of regeneration.

What Morgan's work also shows is that regeneration was very much a central biological phenomenon. As Mary Sunderland has demonstrated, Morgan saw regeneration as a window into problems of generation that were very difficult to access under normal conditions.¹⁵ This has remained the focus until recent decades. Those studying regeneration of lost tails in salamanders, for example, sometimes ask "why can't we humans do that too?" But the primary focus for those studying

¹⁴ Morgan, 1901.

¹⁵ Sunderland, 2007; 2008.

regeneration is on fundamental questions about development and differentiation.

Through most of the twentieth century, this meant careful study of cells and organ development. The last few decades have brought increasing study of the genetic role. Which genes are involved in allowing regeneration, and what regulatory and transcription factors are involved? In some labs, such questions of gene control dominate discussion. In others, such as Alejandro Sanchez Alvarado, an HHMI researcher at the University of Utah, the traditional morphological and genetic lines of research come together. Sanchez Alvarado focuses on study of planarians, long a favorite of biological researchers. There are others, of course, but Sanchez Alvarado is relatively rare in his appreciation for the history of the field and his awareness that the questions and approaches past researchers have used may offer valuable clues for researchers today.¹⁶

The second line of work contributing to regenerative medicine is transplantation. If we cannot transplant cells, tissues, or organs from one place to another, we are very limited in how we can be able to make regeneration work for medical therapies. Since regenerative medicine has come to focus on stem cell research, this is even more the case. The great hope for stem cell applications is that we can make undifferentiated stem cells differentiate properly into the "right kind" of cell and then transplant them into the place where they are needed. Therefore, translational regenerative medicine will depend on transplantation.

Transplantation research as a branch of biology began seriously at the end of the nineteenth century. Eduard Pflüger and Gustav Born in Germany, each for different reasons, began transplanting bits of frog embryos and tadpoles from one individual to another. Most famously, Ross Granville Harrison and Hans Spemann took up this work and took it to the forefront of experimental embryology.¹⁷ Both were very much biologists, interested in fundamental questions about development. They were seeking to control life only in the sense of controlling conditions of an experiment in order to be able to come to solid answers to research questions.

Spemann and Harrison each worked with frogs. Spemann took pieces of the embryo that were known to give rise to ears or eyes under normal developmental circumstances and asked "what will happen if I

¹⁶ See the website of the American Society for Cell Biology for such lectures and a great deal more on current research: www.ascb.org.

¹⁷ For more discussion of this episode in the history of embryology, see Maienschein, 1991.

remove that bit of tissue?" No ear or no eye. Or what will happen if I move it and transplant it to a different frog?" In some cases, there was a new ear or a new eye vesicle – but now in the "wrong" place. There seemed to be some sort of induction going on, in which the tissue must already be determined or at least inclined to become a particular part and could induce the specified result, wherever it actually was. Of course, there were many limits to such induction, and Spemann's lab in particular took up exploration of what factors allow which parts to induce what results. Controlling as many variables as possible helped lead to results. This work led Spemann to the concept of the "organizer," as discussed by Spemann's student-turned-historian Viktor Hamburger.¹⁸

Spemann was concerned especially with questions about causes of differentiation and the conditions that drive each step of developmental processes. So was Harrison. Harrison also transplanted bits of frog embryos, and also pieces from later developmental stages of frog to discover what would happen. He went one step further than transplantation and carried out an explantation experiment. This involved actually explanting, or removing, a piece of tissue from the frog embryo and placing it not into another living frog but into an artificial culture medium.

In 1907, Harrison first removed neuroblast cells from his frog embryo.¹⁹ These neuroblasts normally would have given rise to neural cells as the frog developed, with nerve fibers reaching out from each cell and making contact with other nerve cells. Harrison wanted to discover how much they would develop by themselves, epigenetically in response to their surrounding medium, and how much they needed to be part of the whole organism to know what to do. He wanted to resolve an ongoing debate about whether nerve fibers develop as a result of protoplasmic outgrowth from the neuroblast itself or only in the context of protoplasmic bridges that pre-existed in the egg and laid out the neural paths as a sort of pre-formed design. He had a very particular embryological problem in mind, and he designed a research method to address it.

The result was that the nerve fiber grew out by protoplasmic outgrowth, even when he put the neuroblasts into a quite artificial medium of frog lymph, then suspended them in a hanging drop to reduce the possibility that it was gravity or perhaps some structure in the depression slide that was guiding the cell. Even in such abnormal conditions,

¹⁸ Hamburger, 1988.

¹⁹ Harrison, 1907; 1910. On Harrison, see Haraway, 1976; Billings, 1971; Maienschein, 1991.

the nerve cells seemed to do the same thing they did normally. Harrison had carefully controlled his variables, as Spemann did, wherever possible. The result was a beautiful and compelling experiment. It settled Harrison's embryological question in favor of epigenetic development.

Yet Harrison's and Spemann's control was very different from Loeb's. They were asking questions about development. They wanted to understand causes, patterns, and processes of development and differentiation. There is no evidence that either wanted to be able to control the progress of development in order to control its results, and even less did they give any indication that they would want to create life with their experimental procedures. In fact, Harrison developed this first ever tissue culture and then gave up that line of research. He no longer needed the technique, since it had answered his question and he was moving on to other embryological problems.

Others did take up tissue culture, and Alexis Carrel at the Rockefeller Institute in New York became the center for such research. As Darwin Stapleton and especially Hannah Landecker have shown, Carrel saw the possibilities of using scientific knowledge and medical techniques to promote regeneration and even immortality at will.²⁰ Carrel may have come as close as any other researcher in the life sciences at the time to sharing Loeb's ambitions for biology. Yet he remained very much to his own, like Loeb never quite fitting neatly into American academic research and indeed settling into a medical rather than biological research setting. Like Loeb, he was an iconoclast, who never quite accepted the ideas or the academic ways of American scientists.

This reinforces the point that it was necessary for the goal of controlling life to achieve much wider acceptance before we could get to the enthusiastic push for regenerative medicine that we see today. Along with regeneration as a biological phenomenon and transplantation as a technique, in order to get to regenerative medicine we need the felt imperative to control life in Loeb's sense. This imperative came with the National Institutes of Health's call for translational medicine at just the time that stem cell research was becoming successful enough to look as though it could promise results.

When Elias Zerhouni took over as the NIH Director in 2002, he quickly developed a "Roadmap" for the Institutes, with a focus on translation of scientific discoveries into clinical applications in the forms of drugs, treatments, and methods of prevention.²¹ This goal of moving work from the laboratory bench to the clinical bedside, not just in

²⁰ Landecker, 2004; 2007.

²¹ Maienschein et al., 2008.

clinical trials but in actual developed therapies, became his campaign. Stem cell science offered tremendous promise for progress in such a translation. Yet as we all know, stem cell science for a while seemed likely to founder on the shoals of political contention.

Indeed, after the announcement in 1998 by both James Thomson and John Gearhart that they had developed "immortal" lines of pluripotent stem cells, first U.S. President Bill Clinton and then President George W. Bush took questions about the ethics of stem cell research to their respective bioethics committees.²² They sought counsel about whether and how to support such potentially promising research. We see in the range of reactions both extremes of reaction to the idea that with stem cell science we could control degenerative diseases by controlling the capacity of the individual to regenerate. Stem cell research and its applications became a significant public issue because of the background of abortion politics, of course, and because of different public views about what an embryo is and what rights it might have. The debates also shaped up as advocates favored the sort of controlling life that Loeb had envisioned, while critics opposed the implications of human hubris in making such claims and instead sought to control the biologists who wanted to control life itself.

Many issues have played out together with stem cell research, making it a highly contested and socially quite fascinating case of biological science in society. What is important for our purposes is to note that the state of California and afterwards other states have voted in favor of funding stem cell research in order to control degeneration through regenerative medical applications. And the U.S. Congress has voted twice in favor of explicitly allowing or authorizing stem cell research. There are no U.S. laws governing the research, however, because George W. Bush vetoed the Congressional bills in 2006 and 2007, though most lobbyist on both sides as of pre-presidential election 2008 expect the Congress to succeed in passing an authorization bill in the next Congress. There may also be an appropriations bill which would not just explicitly allow but also provide public funding for stem cell research in order to promote regenerative medicine. We shall see how far the public is prepared to go, but just as there has been tremendous change in our understanding of the underlying biological processes of development, there has already been considerable change from 1998 to now with respect to the public enthusiasm for regenerative medicine. More than a century later, we are much closer to Jacques Loeb than his embryologist colleagues must have thought would ever be likely.

²² See Maienschein, 2003 for a review of this episode and the literature discussing it.

Conclusion

The changes in political climate also signal a change in scientists' attitudes. Some researchers are keen to follow the funding, of course, but others have become sincerely persuaded by the prospects for clinical application of the stem cell scientific discoveries. They see real prospects for taking the developmental biological results and making them clinically real. They see the possibilities of controlling life, and they are excited by the prospects. These researchers, and there are increasingly many of them, are embracing the vision that Jacques Loeb laid out over a century ago. The time was not right, his approach was not effective, the technical skills and understanding of basic science was not ready for the sorts of results he imagined. Perhaps we now are. And it is worth reflecting more carefully on what such controlling means and whether, when, and why we want it. As a society, how far are we ready to embrace an engineering ideal?

This brings us back to Prometheus. The story is usually presented as a cautionary tale. If you do what you are told not to do, you suffer. Yet it can also be seen as a triumphant tale about the powers of regeneration. Look: again and again, the liver regenerates. This living organ, the liver, has tremendous and undying regenerative power. Even on its own, it can regenerate. This is the way the introduction to a recent report by the NIH presents the case.²³ See the wonders of regeneration. Then the report suggested that if only we can control this regenerative process, we can do wondrous things. For this, we need stem cell research. For this, we need a mandate to translate our scientific research into clinical results. For this, we need an engineering ideal for biology and the goal of controlling life. If we decide we want to do so.

References

- American Society for Cell Biology for such lectures and a great deal more on current research: www.ascb.org.
Billings, Susan F. 1971. "Concepts of Nerve Fiber Development, 1839-1930." *Journal of the History of Biology* 4: 275-305.
Cook-Deegan, Robert. 1994. *The Gene Wars: Science, Politics, and the Human Genome*. New York: Norton.
Hamburger, Viktor. 1988. *The Heritage of Experimental Embryology. Hans Spemann and the Organizer*. New York: Oxford University Press.

²³ NIH, 2006.

- Haraway, Donna. 1976. *Crystals, Fabrics, and Fields. Metaphors of Organicism in Twentieth-Century Developmental Biology*. New Haven: Yale University Press.
- Harrison, Ross Granville. 1907. "Observations on the Living Development Nerve Fiber." *Anatomical Record* 1: 116-118.
- . 1910. "The Outgrowth of the Nerve Fiber as a Mode of Protoplasmic Movement." *Journal of Experimental Zoology* 9: 787-846.
- Krimsky, Sheldon. 1982. *Genetic Alchemy: The Social History of the Recombinant DNA Controversy*. Cambridge: MIT Press.
- Landecker, Hannah. 2004. "Creating a Tradition of Biomedical Research. Contributions to the History of the Rockefeller University." Darwin Stapleton (ed.), *Creating a Tradition of Biomedical Research Contributions to the History of the Rockefeller University*. New York: Rockefeller University Press.
- . 2007. *Culturing Life. How Cells Became Technologies*. Cambridge: Harvard University Press.
- Maienschein, Jane. 1991. *Transforming Traditions in American Biology, 1880-1915*. Baltimore: Johns Hopkins University Press.
- . 2003. *Whose View of Life: Embryos, Cloning, and Stem Cells*. Cambridge: Harvard University Press.
- Maienschein, Jane, Sunderland, Mary, Ankeny, Rachel and Robert, Jason. 2008. "The Ethos and Ethics of Translational Research." *The American Journal of Bioethics* 8: 43-51.
- Maienschein, Jane. Forthcoming 2008. "Regenerative Medicine in Historical Context." *Medicine Studies* 1.
- Morgan, Thomas Hunt. 1901. *Regeneration*. New York: Macmillan.
- NIH. 2006. *Regenerative Medicine*. Department of Health and Human Services. <http://stemcells.nih.gov/info/scireport/2006report.htm> (with 2007 update added); NIH 2008. <http://nihroadmap.nih.gov/overview.asp>.
- Pauly, Philip J. 1987. *Controlling Life. Jacques Loeb and the Engineering Ideal in Biology*. New York: Oxford University Press.
- Snyder, Carl. 1902. "Bordering the Mysteries of Life and Mind." *McClure's Magazine* 18: 386-396.
- Sunderland, Mary. 2007. "Regeneration and cloning," paper presented at the workshop on the History of Cloning, Max Planck Institute for the History of Science, Berlin.
- . 2008. "Comparing Regulative Processes to Understand Development: An Examination of John Tyler Bonner's *Morphogenesis*," paper presented at the Joint Atlantic Seminar for the History of Biology, Princeton.

