22. The Recombinant DNA Debate and the Precedent of Leo Szilard*

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In 1975, the American Association for the Advancement of Science released its report, "Scientific Freedom and Responsibility."[1] In a section titled "Should There Be Forbidden Areas in the Realm of Basic Research?" the report spoke dramatically of the recent debate over recombinant DNA research:

> Recently in a statement probably unprecedented in the history of science, an eminent group of researchers, headed by Paul Berg of Stanford University, has deliberately renounced, for the time being, the performing of certain experiments of probably great scientific interest, because of potential though unproven hazards to human health.[2] The proposed experiments would involve the use of some newly discovered enzymes, which serve to introduce genetic material of other species into bacteria and other living cells...
>
> Clearly this declaration represents a landmark in the assumption of scientific responsibility by scientists themselves for the possible dangerous consequences of their work.[3]

Yet history provides one obvious precedent to the recombinant DNA debate: Before the Second World War, a group of atomic scientists, led by the Hungarian-born physicist Leo Szilard, attempted to effect a ban on the publication of research into splitting the atom. These physicists, well aware of the "possible dangerous consequences of their work," feared that each publication of an experiment in nuclear fission moved Nazi Germany one step closer to an atomic

*I would like to thank Joel Primack, Clifford Grobstein, and other members of the first U.S. Student Pugwash Conference for valuable discussions on the topic of this paper. Of course, only I should be held accountable for the final product.

[1] "Scientific Freedom and Responsibility: A Report of the AAAS Committee on Scientific Freedom and Responsibility," prepared by John T. Edsall, Washington, American Association for the Advancement of Scince, 1975. (The Edsall Report)

[2] Paul Berg *et al.*, "Potential Biohazards of Recombinant DNA Molecules," *Science*, July 26, 1974, p. 303.

[3] The Edsall Report, pp.13-14.

bomb. Hence, there were extensive and dedicated efforts to prevent the results of fission research from entering the public domain.

This precedent from the 1930s for the DNA controversy of the 1970s is widely noted in the popular literature on recombinant DNA. References are often made to the similar, far-reaching consequences of atomic and genetic science,[4] to the parallels between the physicists' and biologists' attempts to control potentially hazardous results stemming from their basic research,[5] and to the effects, in one author's words, of being "seared by the nuclear flame" upon "confronting the more subtle implications of the innermost language of life. . . ."[6]

A comparison between the roles of the physicists in the 1930s and the biologist in the 1970s should not be made too glibly, however. The differences are substantial. Most obviously, the physicists were attempting to halt *publication* of certain results of fission experiments, whereas the biologists who concerned themselves with the implications of recombinant DNA sought restrictions on certain types of research itself. Nevertheless, the two examples probably represent the strongest and most important attempts at exerting control at the level of basic research that scientists have ever made. A careful analysis of these two examples should help to illuminate the strengths and weaknesses of both "movements," as well as provide a more precise context for drawing comparisons between them.

The attempts of some atomic scientists to control publication of fission experiments originated with the Hungarian physicist Leo Szilard. It was in September 1933 that Szilard, having fled to England to escape the Nazi persecution of the Jews, first conceived of the possibility of using neutrons to create a nuclear chain reaction. Shortly thereafter, Szilard learned of the discovery of artificial radioactivity by Irène Curie and Frédéric Joliot at the Laboratoire de Chimie Nucléaire of the Collège de France. He quickly realized that his conception of a chain reaction might now be tested experimentally and discussed the subject with several other physicists. He was unable to evoke any enthusiasm, however. When he brought the subject to the attention of Lord Rutherford, the famous experimental physicist at Cambridge, the reaction was not favorable: "I was thrown out of Rutherford's office," Szilard later told the physicist Edward Teller.[7]

By this time, Szilard had also foreseen the possibility of the creation of an atomic bomb. As his fears began to grow, he worried that, "unfortunately, it will appear to many people premature to take some action until it will be too late to take any action."[8]

[4]"We are on the brink of scientific breakthroughs that make the atomic bomb seem tame (!)," reads the back cover of *Bio-Revolution: DNA and the Ethics of Man-Made Life,* by Richard Hutton, New York, New American Library, 1978.

[5]See, for example, Nicholas Wade, *The Ultimate Experiment: Man-Made Evolution,* New York, Walker and Co., 1977, pp.36-37.

[6]Clifford Grobstein, "The Recombinant-DNA Debate," *Scientific American,* July 1977, p. 28.

[7]Stanley A. Blumberg and Gwinn Owens, *Energy & Conflict: The Life and Times of Edward Teller,* New York, G. P. Putnam's Sons, 1976, p. 86.

[8]Spencer R. Weart, "Scientists with a Secret," *Physics Today,* February 1976, p. 23.

Szilard considered several elements as possible candidates for the chain reaction he envisioned. In 1934, he ruled out his initial guess, that of beryllium. Despite his inability to discover an appropriate element, however, Szilard filed a patent containing the words "chain reaction" in the spring of 1934. Not wishing the patent to become public, he assigned it to the British Admiralty.

Szilard saw such patents as one method of maintaining secrecy in atomic research. In a letter to F.A. Lindemann, director of the Clarendon Laboratory at Oxford, Szilard addressed another method as well. Noting that there was ample reason to be "deeply concerned about what will happen if certain features" of atomic physics "become universally known," he wrote:

> ... In the circumstances, I believe an attempt, whatever small chance of success it may have, ought to be made to control this development as long as possible.
>
> There are two ways in which this can be attempted. The more important one is secrecy, if necessary, attained by agreement among all those concerned that another form of publication should be used as far as the dangerous zone is concerned, which would make experimental results available to all those who work in the nuclear field in England, America and perhaps in one or two other countries, but otherwise keeping the results quiet...
>
> The other way, the less important one, is to take out patents.... Obviously it would be misplaced to consider patents in this field private property.... Also one has to avoid applying for patents wherever secrecy is endangered or in countries which are likely to misuse them; so far I have carefully observed this point.[9]

Szilard then turned to indium in his search for an element in which a chain reaction would occur. In the spring of 1936, however, in collaboration with several other physicists, he determined that indium was not such an element.[10] Szilard had hopes of systematically examining the entire period chart, but he was unable to obtain the funding required for such a series of experiments. After expressing his concerns once more to Lord Rutherford and the physicist John Cockcroft, Szilard's fears lay largely dormant until January 1939.

It was late in 1938 that Otto Hahn and Fritz Strassman, working in Berlin at the Kaiser Wilhelm Institute for Chemistry, detected a radioactive barium isotope among the by-products of a uranium target they had bombarded with neutrons. Hahn communicated his results to his colleague Lise Meitner, who concluded that the barium indicated that a new process, atomic fission, had taken place.

Szilard learned of this discovery through Eugene Wigner at Princeton. He realized that, if the fission of uranium released neutrons, the possibility of a chain reaction was moved dramatically closer to reality. If so, he wanted to keep this knowledge from the Germans. He therefore tried to contact Enrico Fermi and Fredéric Joliot, the two physicists he thought most likely to determine if neutrons were, in fact, released.

[9]Spencer R. Weart and Gertrude Weiss Szilard, eds., *Leo Szilard: His Version of the Facts*, Cambridge, Massachusetts, The MIT Press, 1978, pp. 41-42.

[10]These results were eventually published by M. Goldhaber, R.D. Hill, and L. Szilard in *Physical Review*, 55, 1939, pp. 47-49.

On January 26, 1939, Fermi and Niels Bohr had publicly presented the discovery of fission at the Fifth Washington Conference on Theoretical Physics. Through I.I. Rabi, professor of physics at Columbia, Szilard contacted Fermi to speak with him about the implications of this discovery. Fermi's reaction disappointed Szilard:

> From the very beginning the line was drawn; the difference between Fermi's position throughout this and mine was marked on the first day we talked about it. We both wanted to be conservative, but Fermi thought that the conservative thing was to play down the possibility that this [a chain reaction, and hence (perhaps) an atomic bomb] may happen, and I thought the conservative thing was to assume that it would happen and take all the necessary precautions.[11]

In February 1939, Szilard expressed his concerns in a letter to Joliot. "The only reason for my writing you this letter to-day is the remote possibility that I shall have to send you a cable in some weeks," Szilard began. Nevertheless, he made his position clear. Szilard pointed out that, if more than one neutron were liberated in uranium fission, "a sort of chain reaction would be possible. In certain circumstances this might then lead to the construction of bombs which would be extremely dangerous in general and particularly in the hands of certain governments." Szilard informed Joliot that whether censorship on publication should therefore be imposed was being discussed among physicists in the United States. Fermi was conducting experiments at Columbia to determine if there was indeed neutron emission in uranium fission. Had Joliot begun such experiments? Finally, Szilard wrote: "Should you come to the conclusion that publication of certain matters should be prevented, your opinion will certainly be given very serious consideration in this country."[12]

Neither Joliot nor his co-workers, Hans von Halban and Lew Kowarski, responded immediately to Szilard's letter. However, shortly thereafter, they published in *Nature* the results of an experiment that showed that neutrons were indeed released during uranium fission.[13]

Evidently Szilard's letter made little impression upon the French. The letter seemed to express the concern of only a single physicist. A note from Enrico Fermi a few days later, informing Joliot that Fermi was working on uranium fission, but making no mention of abstaining from publication, lent credence to this impression. Furthermore, as time passed and Szilard's promised cable did not appear, the French, in Kowarski's words, "considered that probably the whole idea was abandoned. We simply published."[14]

[11]Weart and Szilard, *op. cit.*, p. 54.

[12]*Ibid.*, p. 69.

[13]H. von Halban, F. Joliot, L. Kowarski, *Nature*, 143 1939, pp. 470-472.

[14]Testimony of L. Kowarski before the U. S. Atomic Energy Commission's Patent Compensation Board, Docket 18, 16 March 1967, Energy Research and Development Administration, Germantown, Maryland. Cited in Weart, *op. cit.*, p. 24.

Apart from problems over Szilard's letter itself, Joliot's biographer Pierre Biquard believes that Joliot published on the basis of scientific principle:

In principle the scientist is hostile to any kind of secrecy with regard to fundamental research. International scientific cooperation is an essential condition of scientific progress and cannot be reconciled with secrecy. Thus Joliot, in disagreement with Szilard, continued to publish.[15]

Others take a less idealistic view of Joliot's motivations. Robert Jungk, in his history of the atomic scientists, offers a particularly negative perspective. He writes that Joliot

...was just on the point of experimental realization of the chain reaction to which Szilard's anxious communication had referred. He was determined not to be deprived, under any circumstances, of the credit for being first with this discovery. When the experiment succeeded... he did not entrust the account of it, as in the case of all his previous work, to a French periodical. He sent his report to the British magazine *Nature* because it usually published the work sent in to it more quickly than any other journal concerned with natural science... Kowarski traveled, on March 8, to the airport of Le Bourget, only an hour's journey from the center of Paris, and personally supervised the document's deposit in the London mailbag. To such a race, for the sake of a few days, had atomic research already degenerated by the spring of 1939. A wholly new spirit of keen international competition had now arisen.[16]

Before hearing of Joliot's results, both Szilard and Fermi had performed experiments that independently showed that neutrons were emitted in uranium fission. Soon after this discovery, Szilard, Fermi, and Wigner met in the office of George Pegram, Chairman of the Physics Department and Dean of the Graduate Faculties at Columbia. Wigner expressed the opinion that neutron emission was too important for the scientists to keep to themselves; the government must be informed. On March 16, Pegram wrote a letter to the Navy in which he stated that uranium might "liberate a million times as much energy per pound as any known explosive."[17] Fermi, however, was dubious about such prospects. In any event, nothing came of this initial contact with the government.

The American physicists who were involved in the experiments that showed the emission of neutrons entered into intensive discussions over whether to publish the results. Szilard and Walter Zinn (the physicist at Columbia with whom Szilard had performed the neutron experiments), and Fermi and Herbert

[15] Pierre Biquard, *Frederic Joliot-Curie: The Man and His Theories*, New York, Paul S. Eriksson, 1966, p. 45.

[16] Robert Jungk, *Brighter Than a Thousand Suns: A Personal History of the Atomic Scientists,* translated by James Cleugh, New York, Harcourt Brace Jovanich, 1958, p. 76.

[17] R. G. Hewlett and O. E. Anderson, *The New World, 1939/1946,* Vol. 1, A History of the United States Atomic Energy Commission, University Park, Pennsylvania, Pennsylvania State University Press, 1962, p. 15. Cited in Daniel S. Greenberg, *The Politics of Pure Science,* New York,, The New American Library, 1967, p. 73.

Anderson (a graduate student working with Fermi), each sent a paper to *Physical Review,* but with a request to delay publication.

Szilard, Fermi,and Teller met in Washington to discuss whether or not these results should be published. Szilard recalls:

> Both Teller and I thought that they should not. Fermi thought that they should. But after a long discussion, Fermi took the position that after all this was a democracy; if the majority was against publication, he would abide by the wish of the majority...[18]

It was while they were still in Washington that these physicists learned of Joliot's publication in *Nature.* Szilard again relates:

> At this point Fermi said that in this case we were going to publish now everything. I was not willing to do that... However, from that moment on Fermi was adamant that withholding publication made no sense. I still did not want to yield and so we agreed that we would put up this matter for a discussion to the head of the physics department, Professor Pegram.[19]

While Pegram considered his decision, the physicists in favor of withholding publication intensified their efforts. The editor of *Physical Review* was approached with the request that authors who submit manuscripts dealing with certain areas of fission be asked to contact Szilard's group. Attempts were also made to bring the English into the self-censorship agreement. Victor Weisskopf, a physicist from the University of Rochester visiting Princeton, cabled P.M.S. Blackett, a physicist at Victoria University, Manchester, with the suggestion that papers dealing with nuclear fission be sent to periodicals as usual, but with the request that they not be published until further notice. Nevertheless, Weisskopf suggested, experimental results could still be circulated privately between U.S., English, French, and Danish laboratories. Weisskopf sent a similar telegram to his friend Hans von Halban, asking for Joliot's reaction.

At the same time, Wigner wrote to P.A.M. Dirac, the well-known physicist at Cambridge. Enclosing a copy of Szilard's letter to Joliot, Wigner noted that Fermi's and Szilard's neutron experiments did not dispel the fears of a possibly dangerous application of fission. Requesting Dirac to contact Blackett, Wigner pointed out that self-censorship in the United States alone could not succeed. About a week later, Weisskopf was informed by Blackett that the collaboration of *Nature* and the Royal Society could be expected.

The agreement of Niels Bohr, then visiting the United States, was also obtained. Although he was skeptical of the chances of success, Bohr drafted the following letter to his institute:

> The Columbia group is busy organizing cooperation among all the physics laboratories outside the dictatorship countries, to keep possible results from being used in a

[18]Weart and Szilard, *op. cit.*, p. 56.

[19]*Ibid.*

catastrophic way in a war situation, and I must therefore ask you, if work along these lines is going on in Copenhagen, to wait before you publish anything until you have cabled me about the results and received an answer.[20]

The French, however, declined to join in the self-censorship. Joliot's group sent the following telegram:

SZILARD LETTER RECEIVED BUT NOT PROMISED CABLE STOP PROPOSITION OF MARCH 31 VERY REASONABLE BUT COMES TOO LATE STOP LEARNED LAST WEEK THAT SCIENCE SERVICE HAD INFORMED AMERICAN PRESS FEBRUARY 24 ABOUT ROBERT'S WORK STOP LETTER FOLLOWS

JOLIOT HALBAN KOWARSKI[21]

Szilard immediately replied, noting that Robert's work, as reported by Science Service, concerned only a type of neutron emission that was not dangerous, and furthermore, that his group had already been approached and had agreed to cooperate. Nevertheless, Joliot replied:

QUESTION STUDIED MY OPINION IS TO PUBLISH NOW REGARDS JOLIOT[21]

Shortly after this answer, Pegram decided that it was hopeless to attempt a censorship. Szilard's colleagues at Columbia agreed with Pegram's conclusion, and it was decided to publish.

Thus the effort at self-censorship failed. Ultimately, of course, secrecy was imposed. Indeed, in June 1940, Gregory Breit, who was familiar with Szilard and Wigner's arguments, was named to the National Academy of Sciences in the Division of Physical Sciences of the Academy's National Research Council, where he argued in favor of censorship. Eventually, both the scientific journals and the scientists themselves agreed. But, as Breit wrote the physicist Ernest O. Lawrence, "As recently as six months ago, I should have been opposed to any such procedure, but I feel now that we are in many respects essentially on a war basis."[23]

There are important differences between the atomic scientists' attempt at self-censorship just described and that of the biologists in their quest to restrict DNA research. These differences become apparent in an examination of the early stages of the recombinant DNA debate.

This debate had as its focus the safety of the public and of the researchers themselves, rather than fear of possible dangerous applications of the research. The debate really began in the summer of 1971, when Robert Pollack, a cancer researcher lecturing at the Cold Spring Harbor Laboratory, learned of an

[20]Bohr Scientific Correspondence, cited in Weart, *op. cit.*, p. 26.

[21]Weart and Szilard, *op. cit.*, p. 73.

[22]*Ibid.*, p. 74.

[23]Lawrence Papers, Bancroft Library, Berkeley, California, cited in Weart, *op. cit.*, p.30.

experiment planned by Professor Paul Berg, of the Stanford University Medical School. Berg intended to insert the DNA of an animal tumor virus (SV40) into a bacteriophage and then recombine this DNA in the host bacterium *Escherichia coli.* Pollack was alarmed by the proposed experiment, both because SV40 was known to cause cancer in mice (although it seemed harmless to man), and because *E. coli* commonly resided in the human gut. Pollack feared that the SV40 genetic material might somehow cause its host bacterium to activate cancer, which—since *E. coli* flourishes in man—could have grave consequences should any of the bacteria escape Berg's laboratory. He therefore called Berg to express his concern over the proposed experiment.

Berg was sufficiently impressed with the potential hazards of his experiment that he then began to question other biologists about its safety. At MIT, David Baltimore, later to be a Nobel laureate in medicine, voted against Berg's proposed experiment. Maxine Singer, at the National Cancer Institute (NCI), expressed similar criticism.

Berg also talked with Andrew Lewis, a virologist at the National Institute of Allergy and Infectious Diseases (NIAID),who had once made the distribution of a hybrid SV40 virus to other scientists conditional upon the recipients' promises to obey certain safety precautions. At the time, several prominent biologists—including Berg, had initially refused to agree to such conditions. Now, Berg and Lewis found that they had mutual concerns.

As news of Berg's proposed experiment spread, other scientists expressed their fears. Wallace Rowe, also of NIAID, commented that "the Berg experiment scares the pants off a lot of people, including him."[24] George J. Todaro, of NCI, felt simply that Berg's experiment "is one of those which I think just shouldn't be done."[25]

Six months after Pollack's initial telephone call, Berg informed Pollack that the experiment was postponed indefinitely.

By the summer of 1973, the power of recombinant DNA techniques had increased greatly, largely through the work of Herbert Boyer and Robert Helling, of the Department of Microbiology at the University of California at San Francisco, and of Stanley Cohen and Annie Chang, of the Stanford University School of Medicine. Using these new techniques, Cohen and Chang found that they could introduce genes that had provided resistance to penicillin for their original parent bacteria into *E. coli.* It was found that the *E. coli* then also became resistant to penicillin.

In July 1973, Cohen and Chang performed an even more dramatic experiment. They found that genes from *Xenopus llevis*, a South African toad, would be reproduced after insertion into bacteria. This experiment represented the crossing of tremendous evolutionary distances.

[24]Nicholas Wade, "Microbiology: Hazardous Profession Faces New Uncertainties," *Science,* November 9, 1973, p. 567.

[25]*Ibid.*

Both these experiments depended upon a particular cloning vehicle, pSC101, which had been first obtained in Cohen's laboratory. Cohen and Chang soon found themselves inundated with requests from other scientists for pSC101. Before providing samples of pSC101, however, Cohen and Chang asked that it not be used for certain potentially hazardous experiments. Moreover, in order to maintain some control over the spread of pSC101, they requested that those receiving samples not pass pSC101 on to other laboratories.

More formal attempts at exerting control in recombinant research were initiated in the summer of 1973. In June, at the Gordon Research Conference on Nucleic Acids, Herbert Boyer presented a paper that discussed the techniques he and Cohen had developed for recombining DNA. In particular, he described the experiment in which the gene for penicillin resistance had been inserted into *E. coli*. The issue of possible biohazards arose, and Maxine Singer and Dieter Söll, cochairpersons of the session, agreed to consider the safety issues raised by the new technique. In a fifteen-minute session on the last day of the conference, a majority of the remaining participants agreed to send an open letter to the National Academy of Sciences (NAS) and the National Institute of Medicine. The letter, which was published in the September 21 issue of *Science*, read in part:

> We are writing to you, on behalf of a number of scientists, to communicate a matter of deep concern. Several of the scientific reports presented at this year's Gordon Research Conference of Nucleic Acids... indicated that we presently have the technical ability to join together, covalently, DNA molecules from diverse sources... This technique could be used, for example, to combine DNA from animal viruses with bacterial DNA, or DNA's of different viral origin might be so joined. In this way new kinds of hybrid plasmids or viruses, with biological activity of unpredictable nature, may eventually be created. These experiments offer exciting and interesting potential both for advancing knowledge of fundamental biological processes and for alleviation of human health problems.
>
> Certain such hybrid molecules may prove hazardous to laboratory workers and to the public. Although no hazard has yet been established, prudence suggests that the potential hazard be seriously considered.
>
> A majority of those attending the Conference voted to communicate their concern in this matter to you and to the President of the Institute of Medicine (to whom this letter is also being sent). The conferees suggested that the Academies establish a study committee to consider this problem and to recommend specific actions or guidelines, should that seem appropriate...[26]

After the receipt of this letter, an official of the NAS contacted Singer, who suggested that the NAS speak to Paul Berg. Berg, in turn, contacted James Watson, Nobel laureate and director of the Cold Spring Harbor Laboratory. Together they decided to call an international conference to examine the recombination experiments being performed and to consider appropriate safety

[26] Maxine Singer and Dieter Soll, "Guidelines for DNA Hybrid Molecules," *Science*, September 21, 1973, p. 1114.

precautions. In preparation for this conference, they held a preliminary meeting of eight concerned scientists[27] at MIT in April 1974.

By July, this group had reached several conclusions. Most important, it was decided to call for a moratorium on certain types of recombinant research believed to be the most hazardous. Furthermore, the group proposed that the National Institutes of Health (NIH) establish guidelines for scientists working in this area of research. Finally, the scientists officially called for an international meeting of involved researchers to discuss ways to deal with the possible hazards posed by recombination.

The group made its conclusions known in two ways. On July 18, it took the biohazard problem directly to the public in the form of a press conference. Later that month, the group, now with the title of Committee on Recombinant DNA Molecules of the National Academy of Sciences, published its concerns in the form of a letter in *Science* magazine. For this letter, the group had also obtained the signatures of several well-known West Coast biologists, including Stanley Cohen and Herbert Boyer. The letter thus represented the opinion of the most prominent recombinant DNA researchers on both coasts and invoked the prestige of the Academy. The letter read:

> Recent advances in techniques for the isolation and rejoining of segments of DNA now permit construction of biologically active recombinant DNA molecules *in vitro*...
>
> Several groups of scientists are now planning to use this technology to create recombinant DNA's from a variety of viral, animal, and bacterial sources. Although such experiments are likely to facilitate the solution of important theoretical and practical biological problems, they would also result in the creation of novel types of infectious DNA elements whose biological properties cannot be completely predicted in advance.
>
> There is serious concern that some of these artificial recombinant DNA molecules could prove biologically hazardous. One potential hazard in current experiments derives from the need to use a bacterium like *E. coli* to clone the recombinant DNA molecules and to amplify their number. Strains of *E. coli* commonly reside in the human intestinal tract, and they are capable of exchanging genetic information with other types of bacteria, some of which are pathogenic to man. Thus, new DNA elements introduced into *E. coli* might possibly become widely disseminated among human, bacterial, plant, or animal populations with unpredictable effects.
>
> ...The undersigned members of a committee, acting on behalf of and with the endorsement of the Assembly of Life Sciences of the National Research Council [of the NAS] on this matter, propose the following recommendations.
>
> First, and most important, that until the potential hazards of such recombinant DNA molecules have been better evaluated or until adequate methods are developed for preventing their spread, scientists throughout the world join with the members of this committee in voluntarily deferring the following types of experiments.
>
> *Type 1:* Construction of new, autonomously replicating bacterial plasmids that might result in the introduction of genetic determinants for antibiotic resistance or bacterial toxin formation into bacterial strains that do not at present carry such determinants....

[27] Paul Berg (chairman), David Baltimore, Herman Lewis, Daniel Nathans, Richard Roblin, James Watson, Sherman Weissman, and Norton Zinder.

> *Type 2:* Linkage of all or segments of the DNA's from oncogenic [tumor-causing] or other animal viruses to autonomously replicating DNA elements such as bacterial plasmids or other viral DNA's. Such recombinant DNA molecules might be more easily disseminated to bacterial populations in humans and other species, and thus possibly increase the incidence of cancer or other diseases.
>
> Second, plans to link fragments of animal DNA's to bacterial plasmid DNA... in light of the fact that many types of animal cell DNA's contain sequences common to RNA tumor viruses... should not be undertaken lightly.
>
> Third, the director of the National Institutes of Health is requested to give immediate consideration to establishing an advisory committee charged with (i) overseeing an experimental program to evaluate the potential biological and ecological hazards of the above types of recombinant DNA molecules; (ii) developing procedures which will minimize the spread of such molecules within human and other populations; and (iii) devising guidelines to be followed by investigators working with potentially hazardous recombinant DNA molecules.
>
> Fourth, an international meeting of involved scientists from all over the world should be convened early in the coming year to review scientific progress in this area and to further discuss appropriate ways to deal with the potential biohazards of recombinant DNA molecules.
>
> The above recommendations are made with the realization (i) that our concern is based on judgements of potential rather than demonstrated risk since there are few available experimental data on the hazards of such DNA molecules and (ii) that adherence to our major recommendations will entail postponement or possibly abandonment of certain types of scientifically worthwhile experiments. Moreover, we are aware of many theoretical and practical difficulties involved in evaluating the human hazards of such recombinant DNA molecules. Nonetheless, our concern for the possible unfortunate consequences of indiscriminate application of these techniques motivates us to urge all scientists working in this area to join us in agreeing not to initiate experiments of types 1 and 2 above until attempts have been made to evaluate the hazards and some resolution of the outstanding questions has been achieved.[28]

As several members of the Committee on Recombinant DNA made preparations for the proposed international meeting, the moratorium they had thus invoked was enjoying the observation of biologists worldwide. Nicholas Wade writes:

> As it turned out, the moratorium was scrupulously observed throughout its requested duration, from July 1974 until the convening of the conference seven months later. As far as is known, it was heeded by scientists in Europe and the Soviet Union as well as by those in the United States. In England the Medical Research Council (the equivalent of the National Institutes of Health) ordered its scientists not to undertake any of the experiments in the Academy group's letter.[29]

The International Conference on Recombinant DNA Molecules was held at the Asilomar Conference Center in February 1975. The conference included

[28] Berg *et al., op. cit.*, p. 303.

[29] Wade, *The Ultimate Experiment*, p.39.

ninety American and fifty foreign scientists, as well as representatives of the press and several lawyers concerned with the public policy aspects of science. The conference all but unanimously agreed to several levels of physical and biological precautions in DNA experiments. Moreover, the conference passed a motion calling for the banning of the most dangerous types of experiments. In June 1976, the NIH finally presented detailed and specific guidelines for recombinant DNA research, based largely upon the conclusions drawn at Asilomar.

Thus, it can be said that the biologists attempting to restrict research in recombinant DNA succeeded in their aims. Although the NIH guidelines by no means satisfied everyone involved in the debate, they did represent the culmination of a collective attempt by the scientists concerned to inject caution into their own area of resarch.

While the recombinant DNA debate shared with Szilard's movement such a collective attempt, it clearly differed both in motivation and, indeed, in its level of success. The biologists were concerned with specific health hazards arising from their work, and, despite efforts by some scientists to expand the debate,[30] on the whole it maintained this narrow focus. The controversy in nuclear fission, on the other hand, grappled with the broad questions of secrecy in scientific research in the light of international politics. Such questions would seem less easily addressed.

Thus, secrecy was the essential concern of Szilard, whereas such an issue never entered the DNA controversy. Szilard and the other concerned physicists wanted to prevent dangerous applications of their research, as opposed to incidential hazards encountered during the research itself.

One severe problem both the biologists and the physicists clearly shared was that of the intense competition at the frontiers of scientific research. We have already noted Jungk's analysis of Joliot's motives for continuing to publish: Joliot "was determined not to be deprived, under any circumstances, of the credit for being first with this discovery," for "a wholly new spirit of keen international competition" had arisen. An analogous problem presented itself to those attemtping to restrict research in recombinant DNA. One observer has written:

> One reason why safety was being neglected is the high-pressure atmosphere and intense rivalry of modern science, particularly in such fast-moving fields as molecular biology. The fierce pace of competition, though highly efficient at getting results, does not encourage researchers to handicap themselves with excessively rigorous safety precautions.[31]

[30]For example, "there arises a general problem of the greatest significance, namely, the awesome irreversibility of what is being contemplated. You can stop splitting the atom; you can stop visiting the moon; you can stop using aerosols; you may even decide not to kill entire populations by the use of a few bombs. But you cannot recall a new form of life. Once you have constructed a viable *E. coli* cell carrying a plasmid DNA into which a piece of eukaryotic DNA has been spliced, it will survive you and your children and your children's children. An irreversible attack on the biosphere is something so unheard-of, so unthinkable to previous generations, that I could only wish that mine had not been guilty of it. The hybridization of Prometheus with Herostratus is bound to give evil results." See Erwin Chargaff, "On the Dangers of Genetic Meddling." *Science*, June 4, 1976, pp. 938–940.

[31]Wade, *The Ultimate Experiment,* pp. 30-31.

Indeed, when the eight-member Committee on Recombinant DNA met at MIT in 1974, it received a letter from the virologist Andrew Lewis, who observed:

> It is unlikely that in the competitive atmosphere in which science functions that broad unenforceable requests for voluntary restraint will contain the potentially hazardous replicating agents which arise from the widespread application of the plasmid recombinant technology.[32]

Yet the moratorium proposed by this committee did gain widespread, even universal, acceptance. Why should this have been the case? More important, why did the biologists succeed in this attempt at "requests for voluntary restraint" while Szilard's group failed?

The answer would seem to lie in the broader-based origin of the recombinant DNA debate. Nicholas Wade emphasizes the importance of the role of a prestigious leader, in this case Paul Berg.

> There is a direct line of descent from Berg's first scruples to the decision reached by the Asilomar conference...but the sequence of events was by no means a foregone conclusion. Probably few other people could have asked for a moratorium, got it to stick worldwide, and then handled the issue with the openness and disinterest that disarmed resentment and led the world's scientific community to a notable and generally harmonious consensus.[33]

Yet this analysis is clearly insufficient. Berg was only one force in the debate. The letters of both the Gordon Conferences on Nucleic Acids and the Committee on Recombinant DNA indicated broad support among the most prominent American biologists for placing controls on the research. Not only were many individual biologists represented, but the letter from the Committee on Recombinant DNA indicated the support of the National Academy of Sciences as well.

As the techniques involved in recombinant DNA research originated in the United States, this represented strong restraint on the part of those most able to benefit from the techniques in question. Yet these biologists did not hesitate to expand the debate to an even broader base in the form of the international Asilomar Conference.

Szilard's group suffered from the absence of precisely these strengths. The atomic scientists' efforts were undeniably primarily the work of one Hungarian physicist. While Szilard was successful in drawing more scientists into the debate, his success was never sufficiently communicated to the French. One author has written that the French

> could scarcely believe that everyone would adhere to an unprecedented pact, a pact pushed forward, so far as they knew, only by two Central European refugees on the

[32]Lewis to the Committee on Recombinant DNA, Natural Academy of Sciences, November, 29, 1974, cited in Wade, *The Ultimate Experiment,* p. 32.

[33]Nicholas Wade, "Genetics: Conference Sets Strict Controls To Replace Moratorium," *Science,* March 14, 1976, p. 935.

outskirts of the Columbia scientific community. (Had Fermi, Bohr or a leading American scientist written them about the scheme, the French might have found it more plausible.)[34]

Szilard's group never published an impressive letter in a leading scientific journal in the manner of the letters published by the biologists in the 1970's. Of course, it is highly unlikely—given the necessity for secrecy—that such a letter would ever have been possible. Similarly, the atomic scientists did not enlist the official endorsement of a government agency. Jungk writes:

> In the first place he (Joliot) had not taken Szilard's letter seriously simply because he had supposed it to be a solo performance by his Hungarian colleague. Weisskopf's telegram . . . had strengthened this impression that the proposal had been made unofficially by a minority of scientists. So important a matter, in the opinion of the formally minded French, should have been broached by the American Academy of Sciences instead of being raised by a few "individualists" and "outsiders."[35]

Thus, the very nature of the restraints Szilard wished to impose limited his effectiveness. Ultimately, the biologists, while overcoming problems similar to those faced by Szilard, had the distinct advantages of a broader, more visible base, official sanction, and, perhaps, a different perspective among themselves than that held by most scientists of Szilard's day. This new perspective was addressed by Sidney Brenner (of the Medical Research Council laboratory of Molecular Biology in Cambridge, England) at the Asilomar Conference:

> The issue that I believe is central is a political issue. It is this: we live at a time where I think there is a great anti-science attitude developing in society, well developed in some societies, and developing in government, and this is something we have to take into consideration. . . . Who really believes that natural science will increase your GNP? Maybe this is the end of this era. It is very hard to tell in history where you really are. . . . I think people have got to realize there is no easy way out of this situation: we have not only to say we are going to act but we must be seen to be acting.[36]

Ultimately, any "anti-science attitude" among the public must owe much to the onset of nuclear weaponry. Thus, Szilard's failure may ultimately have increased the likelihood of the biologists' success.

[34]Weart, *op. cit.*, p. 28.

[35]Jungk, *op. cit.*, p. 77.

[36]Wade, "Genetics: Conference Sets Strict Controls To Replace Moratorium," p. 935.

SCIENCE AND ETHICAL RESPONSIBILITY

Proceedings of the U.S. Student Pugwash Conference
University of California, San Diego, June 19-26, 1979

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1980
ADDISON-WESLEY PUBLISHING COMPANY
ADVANCED BOOK PROGRAM
Reading, Massachusetts

London • Amsterdam • Don Mills, Ontario • Sydney • Tokyo