DIRECTOR'S REPORT

In the waning years of the 19th century, the Biological Laboratory at Cold Spring Harbor was expanding its summer program of research and courses that then focused on organism-based biology, encompassing the fields of botany, zoology, bacteriology, and embryology. At the same time, events in Europe would soon have a profound influence on the science at the fledgling laboratory and shape much of biology in the then new 20th century. The hybridist, Hugo de Vries, professor of botany at the University of Amsterdam, completed his extensive, decade-long research on plant hybridization that uncovered quantitative laws of inheritance, research that he first published in 1900. Sparked by the circulation of reprints of the de Vries manuscript, Carl Correns and Erich von Tschermak published accounts of their independent research on plant hybridization in the same year, coming to the same conclusion that traits were inherited as discrete, quantitative units. All three had independently, and to de Vries's disappointment, rediscovered Gregor Mendel's laws of heredity that had remained unappreciated for over three decades. The Darwinian disciple William Bateson, upon receiving de Vries's paper, immediately recognized the importance of the combined discoveries. He soon presented a synthesis of the new field to the Royal Horticultural Society in May of 1900, almost exactly 100 years ago, and, in 1905, coined the term *genetics*.

Charles Davenport, who was by then director of the Biological Laboratory, was aware of these dramatic developments and quickly seized the opportunity to bring Mendelism to Cold Spring Harbor. Davenport was already concerned with understanding inheritance and how it related to evolution. By 1902, he had outlined a plan to the Executive Committee of the Carnegie Institution of Washington for the establishment of a Station for Experimental Evolution, a proposal that was in competition with a rival scheme from the Marine Biological Laboratory at Woods Hole. Fortunately, the Carnegie Institution executive approved Davenport's proposal in 1903, and by 1904, the Station opened with great fanfare. The now celebrated Hugo de Vries was appointed as an honorary associate of the Station for Experimental Evolution and spoke at the opening of the new laboratory. There, he echoed Davenport's belief that understanding the process of evolution necessitates direct experimentation on plants and animals. Remarkably, de Vries chose not to mention Mendel, probably because he considered his 10 or 12 years of studies on plant hybridization to be more extensive and superior to Mendel's work with a limited number of species. Although Mendel was not yet celebrated by those present, Charles Darwin was much in the minds of the assembled, and his revolutionary ideas and studies on evolution of species, by now 45 years old, heavily influenced the goals of the new science. The very name of the station indicated that the principal goal was to understand the laws of inheritance and, thereafter, the secrets of evolution would fall into place.

Evolution and the new science were not only on the minds of the assembled scientists, but clearly were of concern to others present. W.R.T. Jones, brother of the late John D. Jones, one of founders of the Biological Laboratory and governor of the Wawapex Society which owned the Carnegie land, suggested that the new experimental station would revitalize Cold Spring Harbor and its environs, making "our village" well known both at home and abroad. That prediction was more than fulfilled. But Jones also raised concern by stating, "I trust in going back and investigating, as far as possible, the origin and order in creation, it will find nothing to interfere with the doctrine of the church just around the corner, erected largely by the aid of family relatives, in its efforts for improving morals and explaining to the best of its ability life hereafter." This not so subtle plea reflected the tussle between Darwin's ideas and the doctrines of the Christian church that, unfortunately, has not disappeared after 100 years of enormous insight into the nature of life and the process of evolution. Recent pronouncements by misguided educators in Kansas, who eliminated the teaching of evolution from school curriculum because creation was not taught, make it clear that it is still a challenge for some to separate religious beliefs from scientific reason and progress. What is not appreciated by many is that creation, if it should be taught at all, should be taught within the context of religious education, not in the schools as an alternative to evolution. But the very fact that this debate still exits suggests that science will always be a target for attack both because it often challenges accepted opinion and dogma and because it is sometimes difficult for the public to grasp complex new ideas. Thus, it is easy for a vocal few to twist the scientific progress to confuse others.

One of the first appointments to the Experimental Station at Cold Spring Harbor was Dr. George Shull, who, in 1904, set about preparing the fertile ground for the planting of a variety of species, including species whose seeds were obtained from de Vries. His goal was to confirm the Mendelian laws of inheritance in as many plant species as possible, but within four years, he would clearly state a principle that would change the agricultural economy. By continual self-fertilization of purebred types of Indian corn, the plants reached a state of low vigor that could not be rescued by further selfing of plants of the same type. But superior vigor was obtained routinely by crossing individuals belonging to distinct types, a technique that would dominate agricultural genetics in years to come and cause a revolution in plant breeding.

The new science of genetics progressed rapidly after the rediscovery of Mendel's principles of inheritance, with the period of classic genetics and cytology dominating the 1920s and 1930s. Through the efforts of some of the giants of the classic period, including Thomas Hunt Morgan, Alfred Sturtevant, Calvin Bridges, Herman Muller, and Barbara McClintock (here at Cold Spring Harbor), the chromosomal theory of inheritance was solidified. Units of inheritance were mapped to chromosomes, and their recombination was traced to the physical interchange between chromosomal landmarks. However, it was not until the amazing discovery by Jim Watson and Francis Crick of the double helix that the secret of inheritance was revealed, setting the stage for the dramatic advances in the last half of the 20th century. Two decades after the double helix, recombinant DNA set the stage for remarkable advances in cell and molecular biology, and ushered in the biotechnology era.

It is fitting that just as Mendelism set the stage for the 20th century to become the age of genetics, so determining the complete DNA sequence of the genome of organisms is setting the stage for biology in the 21st century. In just the past five years, the genomes of many microorganisms have been sequenced, as well as those of yeast, the nematode worm *Caenorhabditis elegans*, the first two chromosomes of the plant *Arabidopsis*, and the first human chromosome. Even as I write this, the next milestone—the sequence of the genome of the fruit fly *Drosophila*—will soon be published.

In his 1904 remarks at Cold Spring Harbor, de Vries saw clearly that the new science of genetics would be useful to mankind since "methods would be discovered which might be applied to garden plants and vegetables, and perhaps even to agricultural crops, in order to induce them to yield still more useful novelties." His optimism was fully justified. Manipulation through classical breeding techniques goes back thousands of years to the founding of agriculture itself, but genetics provided a scientific basis for new experimentation leading to such advances as Shull's hybrid corn. Our new knowledge of all the genes of important organisms will have an even greater benefit for all human beings.

Take, for example, what we have learned from the complete sequences of *Arabidopsis* chromosomes II and IV, determined in part by Dick McCombie and Rob Martienssen at the Cold Spring Harbor Laboratory Genome Sequencing Center. This new information has uncovered much about how genomes evolve to create diversity; large regions of duplication of DNA sequences, exchange between chromosomes, and complicated rearrangement of regions within chromosomes have created new genes for nature to exploit. From a practical point of view, what we learn from the *Arabidopsis* genome will tell us much about genes in other plants. The complete sequence of the *Arabidopsis* genome, expected toward the end of 2000, is eagerly awaited, and insights into the structure of the genome of this plant has propelled efforts, of which we are apart, to determine the complete sequence of the rice genome. Similar comparisons will soon be possible with another international effort to sequence the mouse genome and, eventually, to compare it with the human genome. The foresight of David Luke, immediate past chairman of the Laboratory's Board of Trustees, in helping to establish the Genome Sequencing Center has ensured that Cold Spring Harbor Laboratory remains at the cutting edge of genetics, just as the Carnegie investment did in the early years of the last century.

De Vries could not have imagined the remarkable discoveries of recombinant DNA and the ability to manipulate plant genomes with high precision. But we now have available techniques that enable rational design of desired characteristics that were previously acquired only through prolonged breeding and selection. Genetically modified plants are the future of agriculture and the possibilities they offer are both exciting and unlimited. Creation of disease-resistant crops that do not require the spraying of large amounts of chemicals into the environment makes plain sense. Production of plants that provide much-needed dietary supplements, particularly in the third world, is a moral imperative. Production of varieties that reduce the need for vast amounts of fertilizer also contributes to a better environment and reduces costs to farmers. In the third world, crops that can better survive under adverse conditions will become a necessity as populations expand. The much-touted methods of organic farming are a luxury that only wealthy individuals in economically privileged societies can indulge in, for they cannot serve the needs of the masses. Organic farming on a large scale will be nothing short of an environmental disaster. The developments of 20th-century genetics make all of these possibilities a reality.

Unfortunately, this reality has triggered a reaction from some, particularly in Europe, that is the cause of great concern. The opposition to the use of genetically engineered (GE) food is most often irrational and not targeted at the science, but at peripheral issues that suit the agendas of minority groups. Genetically engineered food has become a sitting duck for groups that are opposed to such diverse issues as the potential dominance of multinational corporations, the demise of the local farmer, scientists playing God, the economic dominance of the United States over technically challenged states, and even international trade. Perhaps more justifiable concerns are whether the technology is safe and what are the long-term consequences of modifying crops. There are even rational arguments for the cultivation of genetically modified, long-lived plants that are designed to be infertile to ensure that they do not mix with native or wild species. But even these concerns are due to not understanding the technology or are based on fear of the unknown. If this type of thinking prevails in society, then we are never going to make any advances, technical or otherwise.

The anti-GE food groups have been quick to jump onto a growing bandwagon that attacks science indirectly. Often, they use the results of scientific investigation to suit their own purposes and in doing so misrepresent the scientific process. Such was the case following the publication in the journal *Nature* of a study from Cornell University of the forced feeding of pollen from corn that had been genetically engineered to produce an organic, naturally occurring toxin, *Bt*. The study subjected monarch butterflies to a choice of eating milkweed covered with the pollen or nothing at all and reported that about half of the butterflies died in the experiment. The experiment confirmed other studies that insects die when they consume *Bt.* The publication was heralded by a misguided publicity machine from Cornell and was immediately picked up by the anti-GE groups as their *cause célèbre*. The paper has since been criticized by colleagues of the original authors and deemed to be an unlikely event in the field because *Bt* is rapidly inactivated by sunlight not present in the laboratory studies. Moreover, *Bt* has been used for many years, and no adverse effect has been recorded. Despite the fact that further experimentation and studies have not found any support for the demise of monarch butterflies, the anti-GE groups continue to flutter around with multicolored wings, pushing their agendas. Such irrational behavior has induced the further inexplicable decisions of a few major corporations to abandon the use of GE crops, even after they have been using the technology safely for years. Moreover, such protests gloss over the clear documentation of the adverse effects of the use of chemical pesticides.

In the early 1970s, the recombinant DNA debate reached the public forum, and misunderstanding of the science and a fear of the unknown fueled exaggeration of the issues. Now, with the benefit of hindsight, genetic engineering technology has proved to be one of the safest to have been used for the benefit of humankind. Perhaps we should learn a lesson from the recombinant DNA debates about how science, when it receives the attention of the public, should be discussed. First and foremost is that scientists should make every effort to educate the public and keep society abreast of the emerging science. Such efforts eventually won the day in Switzerland, where political events drove the country into referenda about the use of recombinant DNA technology. Here, improved communication between scientists and the public resulted in a slim majority rejecting the excessive claims of the naysayers. Although the issue has not disappeared in Switzerland, the fact that Swiss scientists did not have to leave the country to continue to do their research is due to their efforts in public education.

Genetics and genomics have great promise for the future, both for the insight they will provide into the ways of nature and for the tangible benefits to mankind. For the most part, the scientific community pursues its research and develops technologies in isolation. We are driven by curiosity to shed light on the unknown, but for biology, times have changed, and we must do this as members of a broader society. We also have responsibilities as scientists. There are times when scientists must take a stand against those who seek to manipulate the scientific harvest for purposes that have nothing to do with the science itself. Otherwise, once encouraged by success, science will forever be abused.