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It is a major task for educators to keep up with the advances in biology that occur almost daily. The National Science Foundation-supported "Advances in Biological Science" program (NSF-ABS), now in its third year, was designed to provide Los Angeles teachers with developments at the cutting edge of the biological sciences and to disseminate this information nationally. The program features scientists, including Nobel laureate Francis Crick, known for outstanding research contributions as well as award-winning teaching.

This article is the second in a series in *The American Biology Teacher* of "Advances" papers based on the NSF-ABS program. Here, we review major developments in areas that are at the cutting edge of biology today. The advances selected for this article represent fields as different as cancer and marine biology, the common thread being that exciting new developments have recently occurred in each.

Human Anti-cancer Gene

The topic of cancer biology and oncogenes was reviewed in a recent article in this journal (Oppenheimer 1987). One series of major new developments was not included because the picture was not complete until after the *ABT* article was already in press. It is appropriate to begin this review with this new development in cancer biology because it can be considered one of the most important true breakthroughs in this area.

Retinoblastoma is a cancer of the eye that strikes about one in 20,000 individuals. It usually afflicts infants and young children, often requiring removal of the eyeball. If the cancer is detected early, it can be cured by less radical treatments, including radiation therapy and sometimes by laser surgery or freezing.

Many of those cured of this cancer in early childhood go on to have children. Much to the surprise of early investigators in this area, the children of retinoblastoma survivors came down with the same cancer at an astounding rate as high as 50 percent.

After a thorough analysis of the histories of 48 retinoblastoma patients, Alfred Knudson at the M.D. Anderson Hospital and Tumor Institute in Houston, TX, concluded that this cancer must be the result of two mutations. Two forms of the cancer exist. In hereditary forms, one of the two mutations is passed on from a parent, while the other occurs spontaneously. In non-hereditary forms, both mutations must occur spontaneously (reviewed in Harris 1986).

The picture began to clear when investigators in the mid-1970s and early 1980s found that some retinoblastoma patients possessed a deletion in chromosome 13. The deletion appeared in a region of the chromosome called q14. Ray White and Webster Cavenee found that cells of retinoblastomas lacked the q14 region. This same deletion was found in osteosarcoma cells, a bone cancer that develops at increased frequency in teenagers who survived retinoblastoma (reviewed in Harris 1986).

By combining all these pieces of evidence, it began to appear that retinoblastoma is caused by the absence of the activity of a gene in the q14 region of chromosome 13. In normal cells, this gene preserves division patterns that maintain the normal state. Each individual possesses two copies of chromosome 13, one from each parent. If the q14 region is missing or damaged on one of the two copies of this chromosome, no cancer develops because the presence of the normal q14 region on the second chromosome produces a gene product in sufficient quantity to preserve the normal state.

The gene in q14 can be called an *anti-cancer gene* because it prevents cancer. In hereditary retinoblastoma, the infant received the missing or damaged anti-cancer gene from one parent on one of its copies of chromosome 13. Once a mutation occurs in the second anti-cancer gene on the other copy of chromosome 13, then and only then will the child develop retinoblastoma. Retinoblastoma, therefore, is caused by a recessive mutation. This is right in line with Knudson's conclusions many years earlier that two mutations are required for the development of

this cancer (Figure 1).

Children with hereditary retinoblastoma carry one mutated gene from a parent and spontaneously developed the second mutation in the other copy of chromosome 13 in eye cells. If they also develop the second mutation in bone cells, osteosarcoma will develop. Thus, both retinoblastoma and osteosarcoma are recessive disorders in which the anti-cancer gene in both copies of chromosome 13 must be deleted or damaged (Figure 1).

A feverish race developed to clone the q14 human anti-cancer gene because only by obtaining millions of copies of the gene can its function be properly studied. Thaddeus Dryja, Stephen Friend and Robert Weinberg succeeded in cloning this gene and reported their findings in the October 16, 1986, issue of the journal *Nature* (Friend, et al. 1986).

An understanding of how this anti-cancer gene works may lead to the eventual prevention or even reversal of human cancers.

The Impact of Recombinant DNA Techniques on the Detection of Huntington Disease Carriers

Huntington Disease is an inherited trait that is typically expressed after the affected individual has had children. Because the trait is dominant, a person undergoing the physical and mental deterioration characteristic of the disease could be advised that each of his or her children has a fifty-fifty chance of suffering the same fate. In the past, identifying individuals who carry the dominant allele leading to disease before the onset of symptoms has been impossible. Recently, techniques used to manipulate DNA for genetic engineering have allowed detection of such individuals with a high degree of accuracy.

When DNA is isolated and exposed to enzymes called restriction endonucleases, the molecules of DNA are broken at specific nucleotide sequences. For example, one such endonuclease called Eco RI (because it was the first such enzyme isolated from *Escherichia coli* strain R) cleaves DNA wherever the nucleotide sequence is

GAATTC
CTTAAG

Because this sequence occurs randomly along any particular DNA molecule, fragments of varying lengths are produced. DNA fragments are readily separated on the basis of size by electrophoresis through an agarose gel; small fragments migrate faster, and thus move farther from the origin than larger fragments. Any DNA thus broken and subjected to electrophoresis produces a reproducible pattern of separated fragments. Interestingly, if DNAs are isolated from two different persons, the

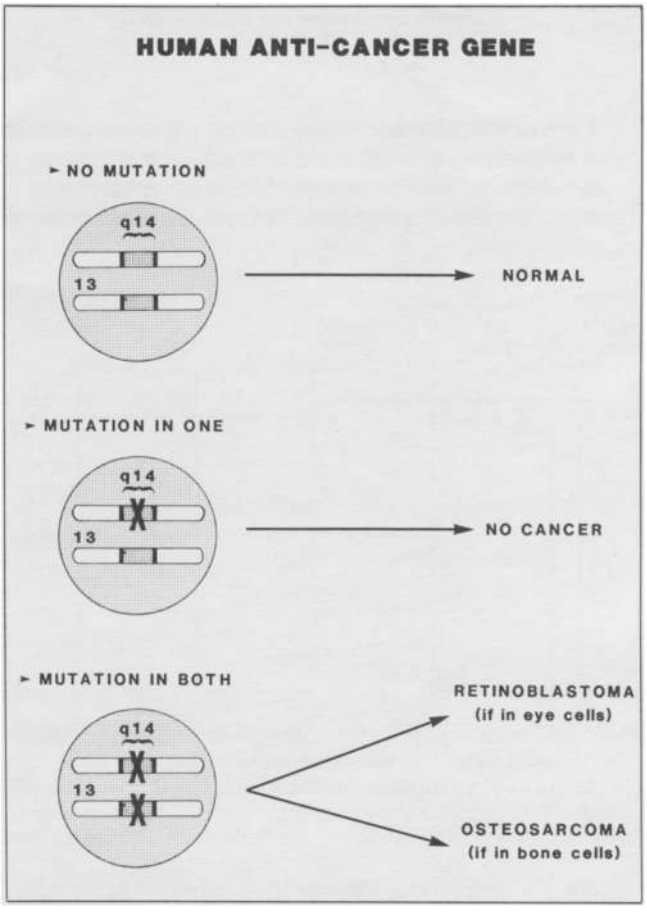

Figure 1. Human Anti-Cancer Gene. Cells are normal if no mutations occur in the q14 region of chromosome 13. If a mutation in the anti-cancer gene in q14 occurs in only one of the two chromosome 13s, cancer is not induced. If, however, such a mutation occurs in both chromosome 13s, retinoblastoma is induced if it occurs in eye cells, while osteosarcoma develops if it occurs in bone cells. The gene in question can be called a human anti-cancer gene because normality is maintained when at least one copy of the gene is functional, while cancer is induced if both copies are inactivated.

patterns may differ slightly. This makes sense, for we know that each person possesses a set of allelic forms of human genes that is different from anyone else, and alleles typically differ by one or a few nucleotides. If, by chance, the nucleotides that distinguish one person's DNA from another's possess a changed sequence recognized by the restriction endonuclease, one DNA will be broken at the sequence and one will not. Such differences in patterns of fragments observed in the DNAs isolated from different individuals are referred to as Restriction Fragment Length Polymorphisms or RFLPS. Such differences are inherited and can be followed in a human pedigree like any other inherited trait.

The breakthrough in identifying carriers of the Huntington Disease allele came when the disease was observed to show close linkage to a particular restriction fragment called G8 (Gusella 1985). In a

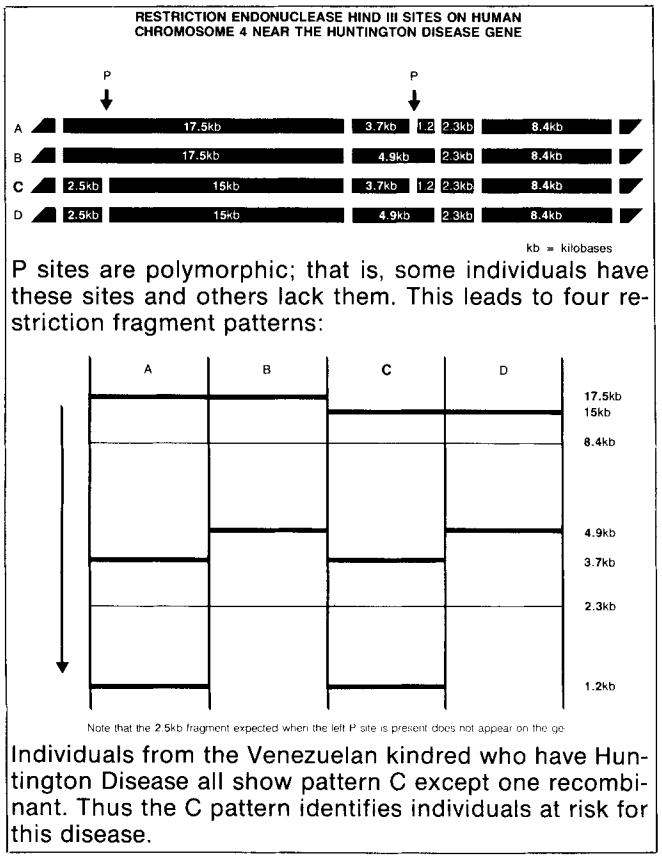

Figure 2. Molecular Genetics in the Detection of Huntington Disease. Fragments of DNA that are produced when DNA from different individuals is cleaved by the restriction endonuclease Hind III. Fragments are separated by size by electrophoresis on agarose gels. The arrow in the lower portion of the figure indicates the fragments' direction of movement. Differences in the fragments produced are inherited and show close linkage to the presence or absence of Huntington Disease in members of a large family studied in Venezuela. The association of pattern C with Huntington disease allows one to predict that individuals with this pattern will develop the disease.

very large family in Venezuela, almost 100 relatives suffer from Huntington Disease, and all except one show the same RFLP (Figure 2). The one exception is a recombinant, indicating the RFLP is not due to the altered gene causing Huntington Disease but rather is a nucleotide change that occurred nearby. Because of the association of the RFLP and Huntington Disease, it is now possible to identify those individuals in this family or in other groups who are likely to develop the disease. Other families in which Huntington Disease occurs are now being analyzed to determine if they will show a similar pattern (Youngman et al. 1986).

The search for associations between a particular RFLP and other inherited disorders is likely to be a fruitful area of investigation for years to come. It is likely that this sort of technology, once fully developed, will become extremely useful in diagnostic medicine.

Advances in Marine Biology

The many fields of marine biology have experienced rapid growth in the last five to 10 years. The task of choosing only a few accomplishments across all these fields was very difficult. We are basing this presentation on the criteria of originality of the advance in its particular field and its overall significance to marine science.

We introduce some of these new discoveries and provide pertinent references for further reading on the subjects. The topics included are:

- deep-sea hydrothermal vent and cold seep communities
- the 1982-83 El Nino event
- satellite technologies for studying the sea surface
- human impact on marine resources and the concomitant effect on marine ecosystems
- magnetic receptors in marine animals.

In 1977, a team of marine geologists studying the characteristics of the ocean floor around a tectonic spreading zone near the Galapagos Islands unwittingly made one of the most significant finds in the history of marine biology. They found an entirely new ecosystem based not on solar energy like other ecosystems on this planet, but rather on chemical energy. Since 1977, this new type of ecosystem, now known as the hydrothermal vent or deep-sea hot spring ecosystem, has been studied intensively by biologists.

Studies have shown that chemosynthetic bacteria form the base of the food chain using hydrogen sulfide as their primary energy source. When the H_2S is oxidized, energy is released which is then used to synthesize organic compounds via the Calvin-Benson cycle (Figure 3).

These chemosynthetic bacteria occur both solitarily and in symbiotic relationships with some major vent animals such as the giant tube worms, giant clams and crabs. In the solitary form, these bacteria are subject to grazing by some vent residents. In the symbiotic form, the bacteria act essentially like chloroplasts in plants providing organic compounds for their hosts, while receiving protection and H_2S from the host and vents. The presence of H_2S rather than heat seems to be the most important factor in determining the presence of "vent" faunae since the heat dissipates very rapidly in 2 degree Celcius water, leaving no noticeable effects a few meters away. Cold seep areas, particularly around Florida, have a similar fauna with the same biochemistry.

Since the early finds at the Galapagos rift, 10 additional hydrothermal vent areas have been discovered throughout the eastern Pacific. It appears that this "new" ecosystem is widely distributed and may even

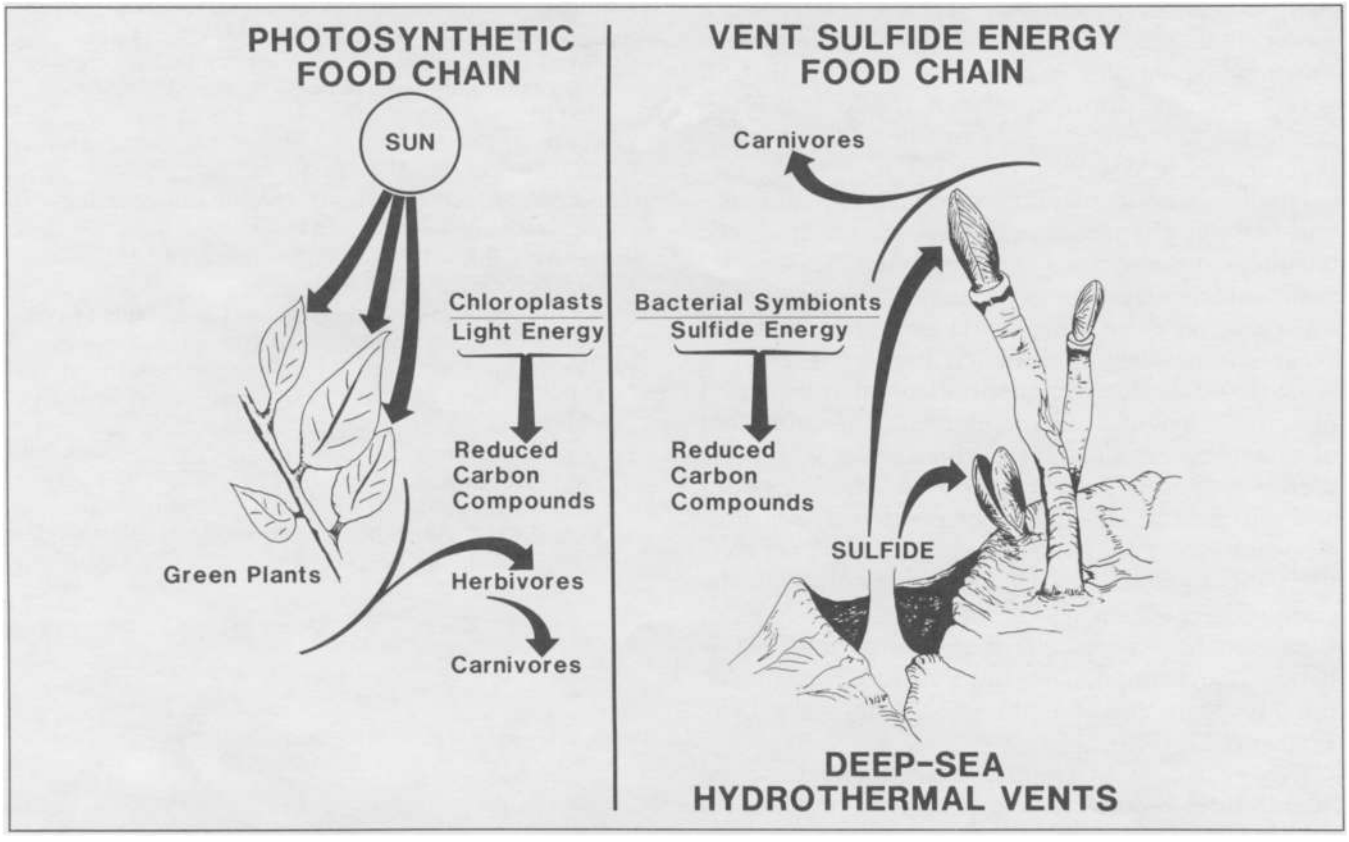

Figure 3. A Comparison of Sunlight-Driven versus Sulfide-Driven (in Deep-Sea Hydrothermal Vent Communities) Food Chains. In photosynthetic chains sunlight is used in the chloroplasts to drive CO_2 fixation via the Calvin-Benson cycle. In the vent tube worm and clam, energy released from sulfide oxidation by bacterial symbionts is used to power the Calvin-Benson cycle for synthesis of reduced carbon compounds (after Jannasch 1984).

be found world-wide (Somero 1984; Jannasch 1984).

In recent years, the single most important phenomenon in the field of marine science was an eastern Pacific warming trend called the El Nino-Southern Oscillation event of 1982-83. This El Nino is significant because of its far reaching effects on world weather, oceanic conditions and populations of marine organisms. El Nino-type events are not rare and occur at fairly regular intervals of about five to 10 years. However, the 1982-83 event was the most severe in recent years and was studied intensively.

El Nino-Southern Oscillations involve changes in atmospheric conditions over the equatorial Pacific Ocean and have a long-range, profound impact on global weather patterns. Results include large-scale changes in climate, such as droughts in normally productive areas and heavy rainfall in normally dry regions.

The 1982-83 El Nino event's impact on the marine environment of the eastern Pacific was equally as profound. A decrease in easterly winds during this period increased the eastward flow of the equatorial counter-current (among others) "piling-up" warm water in the eastern Pacific. This caused reduced upwelling, due to lessened easterly winds, and ocean warming which decreased primary productivity in the eastern Pacific. The lower production had a dramatic impact on marine organisms, with lower population levels resulting in most. The 1982-83 El Nino event also widened the distribution of many marine species into higher latitudes with elevated sea surface temperatures (Canby 1984; Rasmussen 1985).

The use of satellite technology to study the oceans is a recent, promising development. Satellite systems such as Coastal Zone Color Scanner (CZCS) on the Nimbus-7 satellite and Seasat uses absorption-spectral analysis to measure primary production in the sea while infrared imagery can identify sea surface temperatures (to 0.1 degree celcius gradients) for the identification of convergences and fronts (Feldman et al. 1984). The latter has been used to detect concentrations of albacore tuna in the eastern Pacific.

Investigations of human impact on marine resources are not new. Only in recent years, however, has the full impact of one particular human-based overexploitation been realized. Specifically, intensive whaling in the southern oceans near Antarctica has had a dramatic effect on the Antarctic ecosystem. Depletion of baleen whale populations has prevented approximately 150 million tons of krill from being consumed per year. This excess has led to substantial increases in the numbers of seals and espe-

cially penguins, which seem to have established a new equilibrium with the available food resources. This new equilibrium is now threatened by plans of several nations, principally Japan and Russia, to increase the harvesting of krill in the southern ocean (Beddington & May 1982; Laws 1985).

Finally, an understanding of orientation, migration and homing phenomena can be related to magnetic receptors in many types of marine animals. Geomagnetic guidance systems are thought to exist in such diverse forms as bacteria, sharks, rays, tuna and porpoises. It has been postulated that some animals which contain ferromagnetic material (magnetite) may use a magnetic dipole moment (the equivalent of a compass needle) to orient themselves within the earth's magnetic field. In addition, sharks, skates and rays may be able to use their extremely sensitive electroreceptors to detect the weak, directional electric fields induced by currents flowing through the earth's magnetic field. Recently, live strandings of Cetaceans have been related to geomagnetic disturbances. Such impressive finds were unimaginable only 10 years ago (Kalmijn 1982; Klinowska 1986; Walker et al. 1984).

Other topics of interest that could not be discussed in this brief report include: persistent problems of marine pollution, status of world mariculture, community structure of coral reefs, diving physiology of marine mammals and the mechanism involved in the schooling behavior of fish.

A set of full-page size copies of the figures presented in this article, which can be used for overhead projection in the classroom, will be provided at no cost by contacting Oppenheimer.

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