

S2DTimes

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News

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TREATMENT OF GENETIC DISEASES WITH ESSENCE (Exon-Specific Splicing Enhancement by small Chimeric Effectors)

Scientists at Cold Spring Harbor Laboratory have devised a mechanism to correct RNA splicing defects that are implicated in diseases such as breast cancer, muscular dystrophy, and cystic fibrosis. Adrian Krainer and colleague Luca Cartegni looked at natural proteins that guide which segments of the pre-mRNA are included in the new truncated mRNA. One end of the natural protein binds to the pre-mRNA, while the other end recruits enzymes that cut and paste the transcript. The scientists attached the recruiting portion of the protein to a synthetic molecule that can be programmed to any piece of RNA according to its sequence. They designed molecules corresponding to a mutant form of the BRCA1 gene linked to breast cancer. The molecule triggered the splicing machinery to add the missing piece of BRCA1 mRNA that is usually skipped in the mutant gene. By correcting the splicing error, a normal mRNA was made from a faulty pre-mRNA transcript.

In addition, Krainer and Cartegni used their technology on a defective form of the SMN2 gene, which is associated with the neurodegenerative disease spinal muscular atrophy (SMA). The designer molecules improved the production of correctly spliced SMN2 RNA, which are usually produced in only small amounts in SMA disease.

The scientists named the new method ESSENCE (Exon-Specific Splicing Enhancement by small Chimeric Effectors). They plan to create ESSENCE designer splicing molecules that can easily enter cells and target specific splicing sites. The development of such molecules may eventually help in treating many diseases that are caused by splicing defects.

Biographies of the Notables in Science

In this newsletter, we will feature the notable Paul **Berg**



Paul Berg (1926 – Present)

Dr. Paul Berg, a molecular biologist, who, in 1972, created the first recombinant DNA molecule, which led to the conception of the field of genetic engineering.

Dr. Berg was born in New York in 1926. In 1948, he received his B.S. from Pennsylvania State University and then earned a Ph.D. from Western Reserve University in 1952. He joined the faculty at Stanford University and became a professor in 1959.

Berg's interest in science was sparked, when as a youth in Brooklyn, New York, he read "Arrowsmith" by Sinclair Lewis and "Microbe Hunters" by Paul de Kruif. A great influence in Berg's love for science was Miss Sophie Wolfe who organized a science club and ran the demonstration lab in his high school. According to Dr. Berg, "Miss Sophie Wolfe made science fun, she made us share ideas, and the better you did, the more you were praised." Over the years, Miss Wolfe had influenced three Nobel Laureates: Arthur Kornberg, Jerome Karl, and Berg.

Dr. Berg received the Nobel Prize in chemistry in 1980 for his work on recombinant DNA technology. In one of his experiments, he removed DNA from an animal virus called SV40, and inserted it into a circular DNA called a plasmid which is found in bacteria. The recombinant plasmid was introduced into the bacteria to reproduce many copies of the inserted SV40 virus. Because of his work, he was one of the leaders in the scientific community in setting up guidelines for the safe, responsible use of recombinant DNA technology.

Besides, the Nobel Prize, Dr. Paul was the recipient of the prestigious Albert Lasker Medical Research Award in 1981.

In advising young people who are interested in science, Dr. Berg says, "great scientists, like great athletes, have to have a passion, to be driven to discover and solve problems. Given that there are often long periods between meaningful experiments, successful scientists have to be resilient in confronting failure ... It is disappointing to encounter students who have all the right skills and intelligence but lack the drive. By contrast, there are students with less innate aptitude, but who possess the passion to succeed and most often do. Drive is not something you can teach. Our task is to try to get people excited and to experience the special feeling of success."

Dr. Berg is currently Willson Professor of Biochemistry at the Stanford University. During his free time, he plays tennis and collects contemporary American sculpture and paintings. He and his wife, Millie, are married for 50 years, and have one son, John, who is a musician and a graphic designer.

Hands-on Activity

First Activity- Level: Easy

Inherited Trait: Understanding genotypes and recessive versus dominant genes

What is your genotype for attached/free earlobe trait?

Background: The free earlobe trait is dominant over attached earlobe. Let us designate the gene for free earlobe, F, and for attached earlobe, f. Since we all inherit an allele from each parent, a dominant trait will have the genotype of either FF or Ff. Recessive trait will always have the genotype ff.

To find out their genotypes for earlobe trait, students will check their earlobe trait, their parents' earlobe trait, record their observations, and then deduce the genotypes using The Punnett Square.

For example: If you have free earlobes- your genotype is either FF or Ff. Your dad's earlobes are also free- genotype is either FF or Ff. Your mom's earlobes are attached- genotype ff.

If Dad's genotype is FF, then Punnett Square is:

If Dad's genotype is FF, then Punnett Square is:

	F	F
f	Ff	Ff
f	Ff	Ff

All offspring have free earlobes. Examine your siblings' (if you have them) earlobes.

If Dad's genotype is Ff, then Punnett Square is:

	F	f
f	Ff	ff
f	Ff	ff

50% offspring have free earlobes and 50% have attached earlobes.

The following site will give examples of other traits to test:

<http://k12science.ati.stevens-tech.edu/curriculum/genproj/traits.html>

Suggestion: Encourage students to write a report on their findings using a model of a scientific plan (aim, significance, background information, method, results and conclusion).

Second Activity- Level: Advance

Sickle Cell Anemia: Diagnosis Using Simulated Restriction Analysis of DNA.

This is a great activity for students to understand the principle of restriction enzymes and their application in RFLP (restriction fragment length polymorphism). Students will also learn about the effect of point mutations in disease at the DNA level.

DNA from normal homozygous individuals (genotype AA), heterozygous carriers of the trait (genotype AS), and homozygous sickle cell patients (genotype SS) produces different sizes of restriction fragments when cut with the restriction enzyme *Mst* II. In Southern blot analysis, these RFLPs are detected as characteristic banding patterns, using a radioactive β globin gene probe. β globin gene is defective in sickle cell anemia.

The web site for this activity is found at:

<http://genetics-education-partnership.mbt.washington.edu/class/activities/HS/sickle-DNA-TOC.htm>

Suggestion: Check the kits we offer - Cancer Gene Detection and Genetically Inherited Disease Detection at:

<http://www.science2discover.com/diagnostics.htm>.

Note: If you have any trouble with this activity or you have any questions, please e-mail us at: activityquestions@science2discover.com or call us at: 888-359-6075.

Humor

<http://home.attbi.com/~wildlifebio/Jokes.htm#JOKES%20LIST>

Two biologists are in the field following the tracks of a radio-collared grizzly bear. All of a sudden, the bear appears out of the brush and runs toward them. The biologists scramble up the nearest tree, but the bear also climbs up the tree after them. The first biologist starts taking off his heavy leather hiking boots and pulls a pair of running shoes from his backpack. The second biologist gives him a puzzled look and says, "What in the world are you doing?"

He replies, "I figure when the bear gets close to us, we'll jump down and make a run for it."

The second guy says, "Are you crazy? We both know you can't outrun a full-grown grizzly bear."

The first guy says, "I don't have to outrun the bear, I only have to outrun you!"

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