BREAKTHROUGH IN GENE THERAPY

Patrick Auburgh, a pediatric neurologist in Paris and his colleagues have recently made history by treating 2 patients of X- linked adrenoleukodystrophy (ALD) with gene therapy.

Currently the only therapy in ALD is bone marrow transplant. However, these two patients had no compatible donors. Hematopoetic stem cells were extracted from the patients. The normal gene which produces the ALD protein was inserted into these cells using an HIV derived lentivirus. Meanwhile the patients received chemotherapy to ablate their bone marrow to stop producing stem cells. Then they were infused with the treated stem cells. Beginning 14 to 16 months after infusion of the genetically corrected cells, progressive cerebral demyelination in the two patients stopped.

Viruses have been used for several years to deliver genetic material into actively dividing cells. This is a problem when using stem cells since they divide slowly. This was overcome by using the lentivirus like HIV which can integrate into a cells genome even when it is not actively replicating. To overcome activating oncogenes, Aurberg used a modified lentivirus which would not activate any close by genes. *(Science 6 November 2009:326; 818 – 823*)

THE NOBEL PRIZE FOR PHYSIOLOGY, 2009

The Nobel Prize for Physiology goes to 3 scientists who have solved a big question in biology - How DNA is copied in its entirety during cell division and how progressive degradation inside the cell is prevented? The answer lies at the end of the chromosome – the telomere and the enzyme that forms it – the telomerase.

When Elizabeth Blackburn (University of California) was working on the DNA sequence of a uniciliate organism called *Tetrahymena* she found that the ends of the DNA had a repetitive sequence CCCCAA. Around the same time Jack Szostak (Massachusetts General Hospital, Boston) found that when a minichromosome was introduced into a cell, it soon got degraded. The 2 scientists got together and added the CCCCAA sequence to the end of the minichromosome. Surprisingly, it prevented the degradation of the chromosome in an entirely different organism like the yeast. Soon it became clear that telomere DNA is present in all living creatures. Subsequently Elizabeth's graduate student, Carol Greider discovered the telomerase enzyme that extends telomere DNA without missing the very end portion.

Ongoing work has shown that if the telomere or telomerase is ineffective, the cell undergoes premature senescence. Hence there was initially great excitement that the secret of aging lies in the telomere. However the mechanism of aging is now considered to be much more complex. But several other genetic disorders including congenital aplastic anemias have been shown to be due to defective telomerase. The reverse is also true. For example, cancer cells often have overactive telomerase. Many clinical trials are now underway on a vaccine againt cells with overactive telomerase. (*Scientific American, 5 October 2009*).

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