Speech of

PROFESSOR SYDNEY BRENNER

Winner of the 1992 King Faisal International Prize

For SCIENCE (Biology)

Your Royal Highnesses,

Distinguished Guests,

Gentlemen,

I am most proud to have been awarded the 1992 King Faisal International Prize for Science and wish to express my deep appreciation of your generous recognition of my work in molecular genetics.

The pursuit of scientific research demands some talent and knowledge but the most important requirement is to be in the right place at the right time. I count myself as fortunate to have been born in 1927 so that when the structure of DNA was discovered by Watson and Crick in 1953 I was young enough to grasp its revolutionary content and yet old enough to do something about it. And when I came to Cambridge in 1956 to join Francis Crick in the MRC Unit at the Cavendish Laboratory, to begin our research in molecular genetics, we were able to add the significant biological component that ultimately linked the structure of the genetical material with its function in living systems. My scientific life has been contemporaneous with the great developments in molecular biology and genetics that have dominated the last half of this century and I have witnessed the growth of our science from its small beginnings into the large, pervasive discipline that it has become today.

The structure of DNA explained how it could replicate and mutate and it also generated what came to be called the Sequence Hypothesis. This stated that the linear sequence of nucleotides in DNA specifies the sequence of amino acids in proteins and that the comp1ex three dimensional structure of proteins, on which their function depends, is the product of the amino acid sequence and is not separately determined. This raised two questions: What is correspondence between nucleotides and amino acids? How does information get out of DNA into protein? The first was answered by the determination of the genetic code; the second was solved by the discovery of messenger RNA. Our work used a bacterial virus, phage T4; with it we proved by pure genetic experiments that the code was triplets code, and we exploited the biochemical properties of bacteriophage infected cells to demonstrate the existence of messenger RNA. We also discovered that certain mutations were "nonsense" because they terminated the growing polypeptide chain and we later worked out the structure of the three chain terminating triplets and showed that their suppressors were alterations in the anticodons of transfer RNAs.

In the early 1960s, impressed with the power of genetical analysis, I set out to develop a new experimental organism, the nematode, Caenohabditis elegans, as a model for the genetical study of development and behaviour. This is now a successful worldwide scientific enterprise. I worked out its genetics and isolated, mapped and characterized more than a thousand mutants and, with colleagues, began a lengthy project to define the entire cellular structure of the organism from serial section electron mierographs, so that today we know all of the cells, about a thousand, and the connections of all the neurons. Sulston's work established the cell lineage, that is, how the cells are uniquely generated during growth.

With the advent of methods of cloning and of sequencing DNA in the mid-1970s, it became clear that this offered a radically new approach to the study of genetics, and this field is now my main scientific interest. Classical experimental genetics depends totally on the breeding of organisms, but the new methods do not; they have liberated us from the tyranny of organismic life cycles and now we can study the genes of all organisms, including Man.

There is today an expanding international collaboration aiming to characterize the human genome, both far the knowledge it will be bring to the understanding of human disease, and also for the part it will play in understanding the evolution of biological complexity. The direct study of genes and genomes is a new science and differs from experimental physics. I have given it the name of genomy and, like astronomy, it relies largely on observation and measurement. In fact, the analogy is quite deep and the invention of sequency can be likened to the invention of the telescope by Galileo. Astronomers use powerful telescopes to look at distant objects and, the more distant the object, the further back in time they can see because it has taken the light that time to reach us. Detailed studies of genomic sequences of contemporary organisms also allow us to reconstruct the genes and genomes of long extinct organisms. It can be plausibly argued that the. genomes of higher organisms reflect the gene structure of very primitive microorganisms roughly because gene evolution became vastly slowed down as the complexity of biological organisation increased. It is fitting that I say these words here, because not only have ancient organisms left their residues in the form of oil, the wealth of your country, they have also left their genes, somewhat corroded by time, in our genomes, a legacy of knowledge of the past.

I thank you again for the Prize and for the invitation to come here to receive it.