

Nobel Prize in Medicines 1975



David Baltimore



Renato Dulbecco



Howard Martin Temin

The Nobel Prize in Physiology or Medicine 1975 was awarded jointly to David Baltimore, Renato Dulbecco and Howard Martin Temin "for their discoveries concerning the interaction between tumour viruses and the genetic material of the cell"

The fact that the viruses can cause tumours was shown already more than 60 years ago by Rous in studies of sarcomas and leukemias in chickens. However this observation was for a long time regarded as a biological curiosity and not until during the 1950ies was it shown that under certain conditions viruses could cause leukemias and other tumours also in other animals, e.g. mice. Studies of virus-induced changes of the growth characteristics of a normal cell to that of tumour cells - a phenomenon referred to as transformation - was facilitated during this decade due to the availability of methods for cultivating cells under laboratory conditions. This technique combined with the discovery of several viruses which could cause transformation in animals and in cell cultures provided facilities for studies of the role of the virus in this process. It was found that both viruses which contain genetic material of the same type as that present in chromosomes of

cells i.e. deoxyribonucleic acid (DNA) and also viruses containing a different type of genetic material, ribonucleic acid (RNA) could cause transformation.

Renato Dulbecco selected to study the effect of a relatively simply built DNA tumour virus on cells cultivated under laboratory conditions. He found that virus replication either led to a destruction of cells concomitant with a release of newly produced virus particles, or a transformation of cells. No production of virus particles by the transformed cells could be observed. The question was then raised whether the virus caused a transformation of cells and then disappeared or whether genetic material of the virus remain in the transformed cells. The discovery of certain foot-prints of the virus suggested that the latter alternative was the most likely one. This was finally conclusively proven by Dulbecco and coworkers who by the use of molecular biology techniques could show that the genetic material of the virus was built into the genetic material of the transformed cells. Hereby cells acquired hereditary properties which derived from the infecting virus.

The genetic material of the DNA viruses used in these studies only contains information for the production of about 7 different proteins. It has later been shown by others that only a fraction of the whole virus genetic material is needed to cause a transformation of cells and that this amount of genetic information only can account for the production of 1 to 2 proteins. The nature of these proteins are currently subjected to studies which may lead to a detailed insight into the mechanism of transformation.

Howard Temin was since the end of the 1950ies concerned with studies of tumour viruses which contain the alternative type of genetic material, i.e. RNA. He noticed that certain characteristics of tumour cells arising after infection with this type of virus suggested a possible persistence of virus genetic material in them. It was very difficult however to understand how the genetic information of viruses containing RNA could form a part of the hereditary material of the tumour cells. In order to explain this Temin postulated that the genetic information of an RNA virus capable of giving transformation could be copied into DNA, and that this DNA in a manner similar to that described for a DNA tumour virus could become integrated into the genetic material of cells. This proposal

by the overall majority of scientists was considered as heresy since it was in conflict with the central dogma accepted in the field of molecular biology in those days. This dogma implied that information transfer in nature occurred only from DNA to RNA and not in the other direction. Temin accumulated certain indirect evidences supporting his theory but the major breakthrough occurred in 1970 when simultaneously Temin and also David Baltimore showed the occurrence of a specific enzyme in RNA tumour virus particles which could make a DNA copy from RNA. This enzyme was called reverse transcriptase. Baltimore had previously been studying other virus-specific enzymes which copy RNA from RNA. By application of molecular techniques similar to those used in these studies Baltimore in parallel with Temin could show that the replication of RNA tumour viruses most likely involves an information transfer via DNA. The final proof of the occurrence of RNA tumour viruses in the form of a DNA copy integrated into the genetic material of transformed cells was provided by experiments by others showing that purified DNA from a transformed cell when introduced into normal cells caused the production of new RNA tumour virus particles.

Since 1970 there has been an explosive development of our knowledge concerning the occurrence of genetic material of the type found in RNA tumour viruses in nature. Somewhat unexpected it has been found that virus material of this kind can be found in all cells examined but that the amount of genetic material and its biological activity is highly variable. Provided certain conditions are fulfilled this genetic material can cause a change of the growth characteristics of cells and give rise to the appearance of tumours. Further it has been found that in case of RNA tumour viruses the genetic information which is responsible for cell transformation can be eliminated without impairing the capacity of these viruses to multiply and produce new virus particles. Today it therefore appears most likely that transformation induced by an RNA tumour virus is based on the presence of genetic material which this virus has picked up in connection with some kind of interaction with cells.

The finding of a general prevalence in cells of genetic material of a type corresponding to that found in RNA tumour viruses indicates that this material may play some as yet undefined role in the expression of the genetic material of cells.

Viruses causing tumours in man have not been demonstrated except in the case of wart virus. The type of tumours caused by this virus are of a benign nature. It appears likely however that viruses will be found to be involved in the appearance of at least certain tumours of a more serious nature in man. Technology to study such a possible relationship is available today and the conceptual foundation for an examination of this problem has been provided by the discoveries made by the Nobel Prize winners in physiology or medicine of 1975.

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