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NOTES

IMPRESSIONS FROM THE XVth INTERNATIONAL CONGRESS OF GENETICS, India, New Dehli. December 12 - 21, 1983.

The XVth International Congress of Genetics was held in New Delhi from December 12 to December 21, 1983. The meeting took place in the comfortable Ashok Hotel well equipped for this function. Perfect organization, friendly atmosphere and a mild climate (24°C - 25°C) were conducive to the proceedings. The Congress was the biggest event of this kind in the history of India; no wonder that it aroused the general interest of society, press, and television.

The solemn inauguration was honored by the participation of the Premier of India, Mrs. Indira Gandhi. The Minister of Agriculture, Mr. Rao Bindera Singh, was also present. The opening speech was delivered by Mrs. Gandhi. India is a little apprehensive about the technical abilities of genetic engineering and at the same ti me it is appreciative of the benefits brought about by the "green revolution". The introductio n of new varieties of cereals and rice, secured self-sufficiency for this country and averted the danger of famine. All these problems were reflected in Mrs. Gandhi's speech. Mrs. Gandhi regarding her country as the Third World's center of genetic engineering, at the same time cautioned the participants against dangerous, unpredicable consequences that might result from misuse of this fascinating method. Science, first of all, should serve as a means for creation of a better life. Mrs. Gandhi appealed to the scientists for an increased international cooperation in creation of plants with more efficient photosynthesis and the ability of atmospheric nitrogen fixation. Mrs. Gandhi also emphasized the achievements of her country in the introduction of new varieties of useful plants.

During the Congress, three plenary sessions were held: 1. Genetic Engineering, 2. Biotechnology and its Varied Applications, and 3. Genetics and Society. There were thirty-one symposium sessions, thirty-three communication sessions, thirty-three poster sessions, and two evening sessions. During one of these Dr. H. K. Jain (New Delhi) delivered a paper "Harnessing Genetics for Mankind's Increasing Food Needs". The other, was held as a part of the so-called Coromandel Lectures, during which Borlaug Awards are given (Norman Borlaug, born in Norway and presently working in Mexico was the winner of the Nobel Peace Prize in 1972, for research on the introduction of new cereal varieties. (In cooperation with Dr. Borlaug, initiated the green revolution in India). The winner of the Borlaug Award in 1982 was Dr. N. S. Subba Rao from the Institute of Agriculture in New Delhi. Splendor was added to the celebration by the beautiful paper full of humanistic significance. "Does Progress Have a Future?", delivered by John Maddox, chief editor of Nature.

There were also two social events, a banquet, and a theatrical evening during which Old--Hindu dances were presented. Thus, the program was varied and eventful; and the atmosphere of this mysterious country left unforgettable impressions.

During the Sessions all major subjects connected with genetic material — DNA were discussed: Replication (A. Sarasin, Villejuif, France; C. M. Radding, Connecticut, USA; F. W. Stahl, Oregon, USA), Repair (P. C. Hanawalt, Stanford, USA; M. Radman, Brussels, Belgium), Mutagenesis (F. Sobels, Leiden, Holland; S. Mitra and W. M. Generoso, Tennessee, USA; J. E. Trosco, Michigan, USA), Oncogenesis (D. V. Goeddel, San Francisco, USA), Transformation (R. D. Hotchiss, New York; H. O. Smith, Maryland; S. Lack, New York; S. H. Goodgal, Philadelphia — all from USA). The problems dealing with food providing for growing human population and improvement of living and health conditions were most frequently discussed in the local press. The main subjects dominating at the Congress were, without

any doubt, genetic engineering and biotechnology. These techniques infiltrate all fields of molecular biology, and the range of their application is constantly growing.

Undoubtedly, the biosynthesis of interferon and human insulin have been the most remarkable achievements of genetic engineering so far. The research on interferon was presented in the paper "Interferon Genes", delivered by Charles Weissmann from Zurich. Interferon is a protein produced by virus-infected cells which protects other animal cells against viral infections. Weissmann was the first to isolate a gene of human interferon. He placed it on a plasmid which was then introduced to *E. coli*, thus forcing bacterial cells to produce interferon. At present, it is known that interferon is not a homogeneous protein. Depending on the source of isolation and the method of induction, interferons have been classified as α (for leucocyte), β (for fibroblast), and γ (for immune). Dr. Weissmann is working on α interferon (IFN-α 2), its evolution, multiplication, transcription, and gene expression. It has been proved that in human cells there are thirteen discrete genes of α interferon. By removing gene fragments, scientists found that about seventy eight initial nucleotides are not important for the expression of protein with interferon activity. The expression of the human interferon gene was also obtained in mice, after the gene had been introduced into rabbit γ-globin plasmid.

Research is also being carried out on the improvement of the technology of interferon production. At present, interferon is produced in *E. coli* carrying a defined plasmid with the interferon gene. Interferon protein is purified after the disruption of the bacterial cell walls. Weissmann, together with his Finnish collegues, used as a vector for interferon an α-amylase secretion plasmid of *B. subtilis*, which induces production of α-amylase and its release to the medium. The whole sequence coding for mature human interferon IFN-α2 was linked to this plasmid, by a signal peptide for α-amylase secretion. Cells of *B. subtilis*, transformed by such a plasmid, release into the medium a hybrid protein which is cleaved after the last peptide signal and released into the medium in the amount of 0.5 — 1.0 mg per liter. It is hoped that this yield can be increased ten times.

The state of research on the synthesis of human insulin was reported by Saran Narang (Ottawa, Canada) in the paper "Total Synthesis and Expression of Human Preproinsulin Gene". To obtain the sequence of 258 basic pairs coding for human proinsulin, 41 deoxyribonucleotide fragments, 11 - 15 long nucleotides were synthesized and then ligated by T4 phage ligase. Such a 258 base-pair-fragment was ligated to a pBR321 plasmid. The coding sequence was preceded by ATG start signal and ended in TGA stop signal, and the whole gene was terminated in sequences recognized by EcoRI and BamH1 enzymes. The plasmid was then cloned in *E. coli* and isolated. The gene coding for preinsulin was cleaved by restriction enzymes and ligated to 74 base-pair fragment which included sequences preceding human preinsulin and was flanked on each side by loci recognized by EcoRI enzyme. The whole lot was cloned on *E. coli* M13mp8 vector. Site-specific mutagenesis was applied to remove the EcoRI site which was located between the pre- and proinsulin. To test the expression of proinsulin a 25 base-pair leading sequence was added to the other EcoRI site. By this procedure the preproinsulin gene was located in a proper reading frame with N-terminal sequence of β-galactosidase and its expression was placed under the control of *lac* promoter.

The expression of proinsulin was also obtained in yeast *Saccharomyces cerevisiae*. Proinsulin gene was linked to the promoter and leading sequence of GAL1 gene on the plasmid for yeast and *E. coli* PYT6710.

According to Narang, who developed the phosphotriester method of nucleotide synthesis and who has been constantly improving it, chemical synthesis of a gene at present is much more simplier; what once required half a year of hard work, now may be obtained in 10 - 24 hours.

During the biotechnology session, prof. Louis Chedid, from the Pasteur Institute (Paris), delivered a brilliant speech on synthetic vaccines. Conventional vaccines, the injection of attenuated or inactivated viruses, are not completely safe. An attenuated virus may undergo mutation and inactivation may not be complete. Sometimes the source of natural antigens is dangerous (Hepatitis B, HBs antigens), or the antigens cannot be obtained in a sufficient amount (malaria sporozoites). However, it is known that not all the proteins of the virus coat, but only

its short protein chain which determines its antigenic properties is necessary to obtain virus resistance. This is the basis for obtaining synthetic vaccines. Synthetic vaccines peptides, which constitute antigenic determinants of the virus coat, result in production of specific antibodies inactivating the virus, and protect the host cells against virus infections. At present, the chemical synthesis of peptides presents no difficulties. Protein determinants of vaccines which are localized on a virus surface and are accesible to antibodies can be identified by computer graphic methods.

Another problem concerning the application of synthetic vaccines, as well as highly purified antigens or inactivated viruses is the duration of immunity induced in an organism. The duration of vaccines depends greatly on auxiliary substances — adjuvants. Those used before consisted usually of inactivated *Mycobacteria* (not admistered to humans) in water-oil emulsion, alum or aluminium hydroxide. Professor Chedid was a member of the group that synthesized and characterised chemical adjuvants. These are simple peptides of muramyl dipeptide type (MDP). Recently several hundreds of MDP analogues have been synthesized and characterised. One of them, murabidide, is undergoing clinical tests. These peptides are often directly coupled to polypeptides of synthetic vaccines. In this way synthetic vaccines were obtained against diphteria toxin, influenza, *Streptococus* infection, *E. coli* heat-stable toxin, and virus-induced foot and mouth disease. Synthetic vaccines against hepatitis-B (presumably commercially available within a year) and polio virus are being developed. According to professor Chedid, there are great prospects for synthetic vaccines, which may be useful in curing cancer.

The problem of synthetic vaccines was also discussed by Dr. G. P. Talwar (New Delhi) in the paper "Hybridomas — a new dimension for immunodiagnostics and immunotherapy". This new sensational technique refers to the production of monoclonal antibodies. The essential point of this technique, developed in 1975, is hybridization of cells producing specific antibody with myeloma tumor cells in order to assure unlimited multiplication of hybridoma cells. Theoretically, any gene, synthetic or natural, can be cloned in this way, and specific pure antibodies can be produced in large quantities. Using this method Dr. Talwar succeed in obtaining antibodies against "zona pellucida", the envelope of mammalian ovum, thus preventing fetal development. One injection is sufficient to provide several months of protection against pregnancy. Attempts have been made to immunize women, but the technique still requires some improvement. Antibodies administered to rodents and primates at the beginning of pregnancy result in natural abortion.

Monoclonal antibodies are useful in a number of other fields, e.g. identification of cells and enzyme proteins, in diagnostics, and in protein purification. Moreover, they can be applied as drug carriers, supplying specific tissues or organs with medicine. Antibody technique enabled Dr. Talwar to develop a simple test which allows for the detection of pregnancy without specific laboratory equipment. He also developed a useful test for diagnosis of leprosy which is still a great problem in India; 25% cases of this disease in the world are found in India.

The technique of monoclonal antibodies was also applied by Dr. Benzer and his coworkers (Pasadena, USA) in their studies on nervous systems. Seymour Benzer in his paper entitled "Monoclonal Antibody studies on the *Drosophila* and Human Nervous Systems" presented extensive experiments on identification of neural molecules. After the injection of *Drosophila* brain into mice, the spleen cells are isolated and hybridized with myeloma cells. This allows for obtaining a number of various hybridomas producing specific antibodies. The antibodies are used in the study of the architecture of nervous systems, development of retina, and the chemical basis of smell and taste. The search for antigenic homologies between human and *Drosophila* retinas and nervous systems proved that there is cross reaction of antibodies which points out to a high degree of homology of neural molecules and evolutionary conservatism.

In the paper "Application of Plant Tissue Culture in Agriculture and Forestry" Dr. V. Jaganathan presented the achievements in plant biotechnology. Recently, it has been possible to obtain a tissue culture from any part of a plant and such an explant subsequently grows to become a plant or a tree. Tissue cultures are applied in growing ornamental plants, vegetables, and recently — forest and fruit trees. Trees grown from tissue culture are then transplanted into

the ground. A thousand of teak trees (*Tectora grandis*) obtained by this technique are growing now in Chandrapur (India). Trees grown from tissue cultures are characterized by faster growth and earlier fructification and are free from viruses. By this technique virus-free banana plants and also virus-free potato and sugar cane were obtained. It is considered that cultivation of teak trees can satisfy the growing demands for fuel. The problem of cultivating trees for fire-wood is very important. Dr. M. S. Swaminathan (the Chairman of the Congress director of the International Rice Institute in Manila, and a talented and outstanding organizer) pointed out in his paper that out of 10 million hectares of forests which are being annually destroyed in the tropics of south America, Africa and Asia, only one-tenth is being reforested. Moreover, we do not know what trees or bushes we lose since only one species out of six has been classified. Dr. Jaganathan also reminded the Congress of haploid plants — growing from anther cultures — an achievement of Hindu Science. This method, intensively applied in China, brought about good results in plant breeding and in the production of new varieties of cereals. Cell cultures, owing to the economy of place, time and work, are useful in selection of mutants and production of plant hybrids for genetic engineering.

The papers presented at the Congress to point out to a great progress in construction of vectors allowing for introduction of foreign genes into man (R. S. Kucherlapati, Chicago, USA). It brings nearer the time when the curing of inborn defects by genetic engineering will be possible. On the other hand, still too little attention was paid to the protection of the environment from polutants. Dr. L. Fishbein (Jefferson, USA) pointed out to the enormous production of chemicals amounting to hundreds of billions of pounds. It is estimated that thousands of various chemicals are in every-day use in the United States. It is impossible to test all of them, but sample tests show that about 2% are carcinogenic. A number of compounds which are potential mutagens can be found in edible plants or in moulds infecting such plants. Exposure of human beings to carcinogenic compounds is harmful not only to them, but also to their offsprings. The correlation between the frequency of lung cancer and smoking is commonly known. Clinical experiments presented by H. J. Evans from Edinburgh (Great Britain) point out that smokers have an increased percentage of chromosomal aberrations, and, moreover, their children fall ill of leukemia and other diseases twice as often as than do children of nonsmokers. It is a sufficient reason to devote more attention to problems concerning environmental protection.

The Congress gathered about 2.500 people; 800 were from outside India (9 from Poland). Among the participants were three Nobel laureates in medicine: Har Gobin Khorana of Hindu origin and always surrounded by Hindu students (Massachusetts, USA) in 1968 for chemical synthesis of polyrybo- and polydeoxyribonucleotides: David Baltimore (Cambridge, USA) in 1975, for the discovery of reverse transcriptase (RNA dependent DNA polymerase); and Hamilton O. Smith (Baltimore, USA) in 1978 for the discovery and isolation of restriction enzymes.

The next Congress will be held in five years in Toronto (Canada). Prof. V. L. Chopra (New Delhi) was appointed Chairman of the International Genetics Federation for this period.

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