MODIFYING THE BIOLOGICAL WORLD FOR HUMAN BENEFIT 1. BIOTECHNOLOGY

Introduction

Man has co-existed with his environment that contains other living organisms - bacteria, plants and animals, since the beginning. There has been an obligatory inter-dependence between man and other forms of life eg. for food. Occasionally there have traumatic inbalance eg. famine due to crop failures; epidemics caused by organisms infectious to man. There has been a constant attempt by man to stabilise, and perhaps improve, the term of his relationship. He has for example developed better yielding, more drought resistant crops over many thousand of years; utilised products of plants and lower animals to improve the quality of his life eg. cotton and silk. With the rapid advancement of science and scientific techniques our knowledge of the biological world has improved tremendously in the last century. Indeed the growth in scientific knowledge has been an exponential one. We are therefore now able to use much more sophisticated methods in our attempts to manipulate other living organisms. The utilisation of other living organisms to obtain desired products on a large scale has been termed "Biotechnology". In a sense the dairy farming and sericulture are also forms of biotechnology. However, we will consider the more modern aspects, involving the latest scientific techniques, in the present series of lectures.

Biotechnology in relation to Health

Infections are a major cause of human and animal (domestic) sickness and death in tropical countries. Poverty, under nutrition, illiteracy, lack of medical care and poor hygiene contribute to the spread of infectious organisms which include viruses, bacteria, protozoans and worms. Immunisation remains the principle method of preventing specific diseases and has been successful in eradicating the dreaded disease smallpox from the earth. The development of synthetic vaccines using the techniques of genetic engineering offers great promise.

Essentially this technique involves the introduction by 'cloning' of a gene for a target pathogen antigen, into the DNA of a vector which is then used to synthesis large quantities of the recombinant protein in organisms such as bacteria, yeast or ever insect cell lines. The purified recombinant protein can then be used for mass immunisation.

The use of the pure protein rather than whole organisms has the advantage that deleterious side effects, which can cause death, are avoided.

Monoclonal Antibodies

Antibodies are protein molecules produced by white blood cells that are a basic part of the immune system. In 1975 a new era in immunology was launched by the discovery of the hybridoma technique, a method for creating pure and uniform antibodies against a specific target. Such antibodies are now widely used to measure hormone levels, to identify pathogens and in research.

Plant cell and tissue culture

Research efforts in plant cell and tissue culture have increased dramatically in recent years. Plant propagation using shoot tip culture is the most advanced area and is currently being used to propagate elite genotypes of several plant species in a number of countries. Propagation through tissue culture can also be used to select more desirable variants. It also important in developing genetically engineered plants, where genes for desirable traits are introduced into the plant cells, by recombination.

Animal production

Manipulation of genetic material and its exchange among countries has become an important means of upgrading animal production. Important developments here are in cryopreservation of germ material and the devleopment of simple techniques for identifying markers associated with desirable traits.

Industrial Biotechnology

The production of ethanol by the yeast induced fermentation of sugar is an age old biotechnological process. However this has now been extended to the production of chemicals such as acetic acid, amino acids, fructose, antibiotics etc. Enzymatic processes are being developed for the economical conversion of woody material and other agricultural byproducts into useful substances such as sugars. Enzymes are also beginning to find use as probes to detect

concentrations of chemicals including oxygen ie. as "biosensors".

Malaria

Malaria is one of the most important infectious diseases in the world. In Sri Lanka, we spend 15% of our health budget on malaria control and there are more than 350,000 cases of malaria detected annually (1988 figures). The development of a vaccine against the disease will contribute significantly to the eradication of the disease.

Major advances were made against malaria in the 1950s and 1960s as a result of the widespread use of insecticides and inexpensive as well as effective antimalaria drugs. However, the global malaria situation has deteriorated since then. This can be attributed to two major causes. These are (1) the failure or inability to continue with effective mosquito control measures in the face of rising costs and the development of insecticide resistance in mosquitoes and (2) the increasing incidence of drug resistance in the parasites. Other factors such as more rapid migration of people have also contributed to the increase in malaria transmission. The World Health Organization estimates that there are currently 210-220 million cases of malaria every year worldwide of which 85% are caused by Plasmodium falciparaum, the most dangerous of the malarial parasites (WHO, 1983). P. falciparum is responsible for about one million deaths annually, particularly in Africa, among infants and young children. Of great concern is the appearance of strains of P. falciparum that are resistant to the most widely used and potent anti-malarial drug, chloroquine. Chloroquine resistant P. falciparum was first observed in Thailand in 1959 and in 1960 in Colombia. Since then resistant strains of parasites have spread to large areas of South America, East Asia and East Africa and is now a problem also for the subcontinent. Resistance of P. falciparum to the alternative drug combination Sulphadoxine/Pyrimethamine has also been reported since the mid 1970s. Consequently there are now multiple resistant strains of P. falciparum, particularly in Thailand, that have to be treated with a combination of quinine and tetracycline as a last resort. Although a new blood schizonticide, mefloquine has recently been introduced, in general, the development of new drugs to combat malaria has been slow.

The drawbacks faced in controlling mosquitoes with insecticides and in drug treatment of malaria have been some of the reasons that have led to a consideration of an immunological approach to the control of malaria.

Encouragement for this venture comes from the considerable success of vaccines against many bacterial and viral diseases. However, the development of a successful vaccine depends on the presence of protective antigens that are shared between different strains of a given malaria parasite. Hopefully antigens that are shared between different Plasmodium species can also be indentified. Should extensive antigenic variation, as is observed with African trypanosomes, be a feature of Plasmodia, then the usefulness of vaccines is likely to be severely limited. While antigenic variation does occur in some Plasmodium proteins, the extent of this phenomenon among many potentially useful antigens has been shown to be limited.

Research at the IFS is focussed on identifying parts of the antigens of the parasite responsible for protection and then synthesising such portions for testing as vaccines.