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CONTENTS

UNIDO's *Emerging Technology Series: Genetic Engineering and Biotechnology* is established as a mechanism of current awareness to monitor developments in the genetic engineering and biotechnology sector and inform governments, industry and academia, primarily in developing countries.

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TO OUR READERS

UNIDO has been the first among UN agencies to promote biotechnology and take active steps to strengthen the capability of developing countries in genetic technologies through the establishment of the International Centre for Genetic Engineering and Biotechnology (ICGEB), and more recently, we have been concentrating our work on aspects that influence the commercialization of biotechnology derived products. This work has culminated in the operation of the Biosafety Information Network and Advisory Service (BINAS), as well as in the establishment of close cooperation with the OECD aimed at addressing issues related to the international harmonization of regulatory oversight in biotechnology.

The successful establishment of ICGEB and its operation as an autonomous intergovernmental organization as of 1 January 1996, in accordance with its statutory provisions, is a landmark for UNIDO's biotechnology programme. At the same time it has signaled a new challenge, namely the need to re-focus UNIDO's biotechnology programme in a way that maintains its synergism with ICGEB, builds on the visibility of on-going activities and responds effectively to client needs. In this respect, it is anticipated bringing together the former members of the Panel of Scientific Advisors of ICGEB to discuss the redirection of UNIDO's biotechnology programme in their capacity as members of the Biotechnology Advisory Council. The outcome of the meeting will be instrumental in formulating the blueprint of the Organization's biotechnology programme for the biennium and will provide the occasion for officially launching UNIDO's Biotechnology Advisory Council.

Investment and technology now play a vital role in the industrial growth of developing countries, as well as in their gradual integration into the international economy. However, the changing national and international economic environments are prompting developing countries to take a fresh look at their efforts to secure and widen investment and technology flows.

Technology is now the core of competitive strategies of successful industrial firms. The new and rapidly evolving generic technologies, such as biotechnology, new materials and information technologies, offer many opportunities and challenges for broad competitive strategies. They engender entirely new products, services, markets and businesses. Their impact is trans-sectoral, radically improving the competitiveness of products, processes and services of firms in a large number of traditional industrial sub-sectors. For instance, biotechnologies save energy and raw materials inchemicals, pharmaceuticals and food processing; new materials improve product specifications and lower production costs in engineering and chemical industries; and information technologies allow companies in all industrial sectors to re-engineer critical processes, improve overall efficiency and raise productivity across functional areas. Access to information is now a key to competitiveness.

Through a new series of awareness publications, which combine the former *Industrial Technology Monitor Series* and the *Technology Trends Series* into the present *Emerging Technology Series*, UNIDO plans to sensitize industry and governments to the need for and requirements of technology monitoring and assessment in the areas of new and emerging technologies. This merging of the two former series will enable UNIDO to cover many more subjects in the ever widening field of advanced technology. We shall also focus more on UNIDO's activities in the subjects presented. What you now have before you is the first issue on the subject of genetic engineering and biotechnology, which will be followed by three more this year.

Managing Director
Investment and Technology Promotion Division

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A. SPECIAL ARTICLE

THE FERMENTED FOODS OF AFRICA: THEIR POTENTIAL

by

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1. Introduction

Bread, cheese, beer, wine and vinegar are fermented food products that have been studied since the days of Louis Pasteur. These products are not part of the new surge of interest in what has come to be known as indigenous or traditional fermented foods, which for all practical purposes began in the aftermath of World War II. The best-studied of these as a group are those of South-East Asia. The preponderance of literature on products such as soy sauce, tempeh, fish sauce and paste, etc., has left the impression in many minds that South-East Asia alone went away with the art of food fermentation.

None the less, the literature available to date on the fermented foods of Africa, albeit scanty, seems to indicate the presence in this "cradle of mankind" of numerous and varied kinds of both fermented products and methods of preparation. Very little of the knowledge encompassing these foods has been tapped to this day. The indigenous knowledge concerning these foods is found with elderly rural women. The depth of knowledge these women command cannot be readily appreciated until one actually delves deeply into it. To say the least, these women's knowledge is both amazing and overwhelming—an endless, ever-expanding universe of its own. Again, it is only when one has been subjected to an in-depth exposure to this world of information that the facts about it begin to dawn on one.

The bottom line is we do not know much about the methods of preparation and the extent of the dependence on food fermentation in the cottages of Africa's straggling villages. Time is not on our side; these foods and their methods of preparation must be documented. Urbanization, which has already taken its toll, continues to pose an impending danger on what remains of the indigenous knowledge concerning these foods. The unwritten, down-transfer of know-how from mother to daughter has been breached by urbanization, and knowledge is slipping away into the grave with the passing away of old memories. We need to have "food banks" of knowledge analogous to "gene banks".

Perhaps a word on the gathering of indigenous knowledge itself is in place at the end of this introduction. The securing of detailed and correct information from old rural women is not as easy as it might seem at first; it could be quite a tricky business. There is not much in the literature by way of offering useful guidance. The person gathering the information is largely on his or her own. The first steps are likely to stumble into puddles and potholes, but as experience is gained, things become better controlled. The duration of the time of gathering is perhaps the most important single factor in ensuring as accurate and thorough information as possible. Second to this perhaps, comes the building of the bridges of mutual confidence between the investigator and the source of information—the elderly rural women. Among male investigators, the best ones would be those sensitized towards the cause of women—those who know that women are technologically-minded too. This type of investigator would go to the villages to learn, not to teach.

As much as possible, information on indigenous foods should be taken from old women. Information taken from men of all ages and from young women should be considered with great caution. A man living 40 years with an expert woman in the same house would give extremely erroneous accounts of the food his wife has made for all those years!

The social aspect of information gathering is a complex one. For male investigators, the job might be tougher, perhaps calling for a certain degree of mettle. In Sudan, interest in food aspects of life means meddling into women's affairs—one of the seven shames. Beside the grinning and simpering of others, this author had to put up with the taunts of members of his own extended family who felt shamed.

Rural people tend to remain reticent about certain foods—the foods they know, from past experience, that townfolk (symbolized by the investigator) ridicule and belittle. In one such case, which the author came across, a young girl told of a food which turned out to be an interesting product. The child, however, was flogged by the family for revealing the food!

Finally, however detailed the verbal description of a food preparation method given by an experienced woman, it would not be complete. The investigator is advised to watch the process at work. He or she would more often than not discover some important nuance that was skipped during the verbal description.

2. Africa's fermented foods are ancient

Africa is believed by many experts to be the home of the origin of mankind (Clark, 1976; Lemonick, 1987; Birx, 1988). Should this be true, it would be very likely that the first person to consume a fermented food product lived in Africa. Many regions in the African savannah have been shown to have supported many human communities early in prehistory. Archaeological excavations revealed that human communities lived in the Central Nile Valley at the confluence of the Blue and White Niles some 9,000 years ago (Arkell, 1949). These people lived mainly on Nile fish and snails as food. Three thousand years later, that community was replaced by cattle-owning people who lived mainly on beef, but also gathered (Krzyzaniak, 1984), or even cultivated (Klichowska, 1984; Doggett, 1988) sorghum and millet.

Similar communities flourished elsewhere in Africa. Linguistic evidence, for instance, has suggested that

agriculture had been known for 7,000 years in Ethiopia and 6,000 years in the Lake Chad region where sorghum and millet were used as staples and animals were raised (Ehret, 1984).

It would be hard to believe that the communities discussed above did not know food fermentation. With such perishable foods as meat, fish, milk and moistened flour in a hot, humid environment, such as prevailed in savannah Africa, chances are very high that those people did practice some form of food fermentation. Evidence, however, is lacking.

Nevertheless, we do have concrete evidence that Africans did practice food fermentation in sub-Saharan zones even thousands of years ago. The Central Nile Valley, the Sudan today, was the seat of the rise and fall of perhaps the best-known ancient kingdoms of sub-Saharan Africa. These included Kerma (2,600 to 1,500 BC), Cush (1,500 to 690 BC) and the Kingdom of Meroe (690 to 325 AD). Of these, we know more about daily life in the latter kingdom, Meroe. The people of that kingdom, which thrived some 2,000 years ago, knew very well the art of food and beverage fermentation. Perhaps today, nothing epitomizes African fermentations better than sorghum beer. This beer was brewed and consumed by the Meroites. The Greek geographer, Strabo (7 BC), mentioned that the Ethiopians (Meroites) made a drink from sorghum. Shinnie (1967) equated this with the present-day sorghum beer of Sudan called *merissa*. Even more indicative is the impressive wall graffito left for us by the Meroites, which depicts two male figures sitting under a thatch in the act of drinking beer from an earthenware jar placed between them. One of the figures is shown holding a bamboo straw with which he is sipping a drink from the pot. The artist wanted to communicate to us the fact that the drink was inebriating, which he achieved by drawing lines radiating from the head of the drinker (Hintze, 1979). Exactly the same situation shown by the drawing can be seen today in parts of Sudan and in other African countries, like Uganda.

Wine-making was also widely known in Meroe. Wine presses and numerous wine jars have been uncovered by archaeologists (Adams, 1966). In addition, a drawing has been found on a Meroitic ceramic jar showing a procession of dancing men carrying ladles about to be dipped into wine jars (Woolley and Randall-McIver, 1910).

The people who built these kingdoms of Sudan were believed to be black Africans and so were the communities who lived much earlier at the confluence of the two Niles (Arkell, 1949; Shinnie, 1967). In fact, the drawings of men and women from the era of Meroe show clear African features, including frizzy hair and large facial features. These drawings can be found in Dirar (1993) and references therein.

The purpose behind the above discussion is to give the reader the necessary background against which to judge the importance of food fermentation in the life of the African.

3. Some selected foods and processes

Our discussion here will be confined largely to examples from the fermented foods of Sudan. In spite of the fact that the dominant culture in Sudan is Arabic and Islamic, about 90 per cent of the 90 or so fermented foods of the country are pure African foods not known in the Middle East. It is this fact that gives legitimacy to the title of this article. More detailed accounts can be found in Dirar (1993) and Dirar (1994).

African fermented foods can be broadly grouped into three functional groups: the staples, the relishes and sauces, and the beverages. In Sudan, the staple dishes are basically made from sorghum and to a lesser degree from pearl millet. These two cereals form the indigenous grains of Africa and people must have known how to process them for thousands of years. The introduction of cassava and corn following the European invasion of the Americas in the fifteenth century resulted in a recession in the use of the indigenous grains in many parts of the continent. Nevertheless, the sorghum-and-millet culture persisted in important regions. Cassava and corn (maize) did not find footing in Sudan, where the sorghum culture still figures prominently.

Sorghum fermented products in Sudan form not only the major and most important foods, but the most sophisticated, and the ones prepared through the most complicated procedures. It is noticed that practically all sorghum products of Sudan are fermented, while those from millet are not necessarily so. Research has shown that fermentation of sorghum raises the digestibility of its protein from a value as low as 45 per cent to as high as 86 per cent! (Axtell et al., 1982).

Some 30 important food products are made from sorghum in Sudan. These can be grouped into two: those made from ungerminated grain and those made from sorghum malt. The former are the more important, being the true staples that go with the various relishes and sauces, and the second group form the beverages and snacks.

3.1 Sorghum products from ungerminated grain

Aceda is the traditional stiff porridge of rural Sudan and which makes the staple dish. It is made from sour dough fermented by a spontaneous population of mixed lactic acid bacteria. It is generally consumed together with one of a variety of sauces, but it can also be slurried in water to give *moss*, which is used to fatten women.

Kissra is often described as the staple of Sudan, and although this is not entirely correct, it is still acceptable. *Kissra*, which is a paper-thin sheet of bread made from the same sour dough from which *aceda* is made, is replacing the latter in many parts of Sudan. It is probably more nutritious than *aceda*, as it contains about 50 per cent solid matter, whereas *aceda* has about 20 to 25 per cent. The thin wafer, which is baked by spreading a small portion of a thin batter on a large hotplate, takes only 17 seconds to bake.

Abreh is probably the finest sorghum food by all standards. It comes in smooth, almost transparent flakes of sheet-bread, much thinner than *kissra*. Its batter is obtained by prolonged souring of sorghum flour. It is usually prepared in the holy Muslim month of Ramadan, when people fast all day. It is supposed to serve as a thirst quencher.

Nasha is a sour thin porridge made from sorghum sour dough like that from which *aceda* and *kissra* are made. A quantity of the sour paste is mixed in a copious amount of water. After resting the suspension to settle the coarser particles, the supernatant is decanted and given another period of rest. It is again decanted and the process repeated until virtually no more precipitate is obtained. The liquid is then boiled to give *nasha*, a drink "as smooth as bone-marrow". It is especially given to malaria patients and to Ramadan fasters.

Jiriya is certainly the most refined of all the sorghum and millet porridges of Sudan. It is made from a starch preparation called *jir* (literally, lime). The porridge is prepared for dignitaries and always comes with the richest of sauces. It is a translucent, well-moulded mass that shakes like jelly. The procedure followed in the preparation

of *jir* is probably the most complicated of all African food preparation methods. The product, *jir*, is related to West Africa's *ogi*, although the starch of the latter is less refined and the procedure followed in its preparation much shorter (Bascom, 1951).

3.2 Sorghum products from sprouted grain

An aspect of special importance of the sorghum food culture is the extensive use of sprouted sorghum grain in Sudan. Commonly in Africa, germinated grains are used for the making of beer. While this is also true for Sudan, important non-alcoholic foods and beverages are also made in this country. The importance of sprouted grain has taken on new proportions in Africa in the last years, primarily in its capacity as a possible candidate for upgrading and developing baby and weaning foods. The initial step in this endeavour should be the documentation of the traditional malt products in Africa. Sudan has some seven solid food products that are traditionally produced from sorghum or millet, in addition to beer.

Hussuwa, for example, is one such product mostly given as a treat to children. It is mostly in the form of solid balls or mass and could be consumed as a solid, or slurried in water first. It is also consumed by adults, particularly as an energy-restoring food. The sweet-sour, brown product is often referred to as 'poor man's milk'. Its preparation methods take many forms. For instance, one could watch a woman in the village cook the three meals of the family out on an open fire daily for three months without having a hint that a few inches underneath that fire a large earthenware jar is buried which contains the fermenting *hussuwa* in warm incubation.

Hulu-mur or 'sweet-sour' comes in the form of scorched brownish flakes originally baked on a hotplate in large sheets. This is another of the fermented products prepared especially for Ramadan fasters. Its nutritional function is to replenish the blood sugar level. The flakes, which contain some 30 per cent sugar, are first soaked and the liquid consumed, while the solids are thrown away.

Assaliya is clear beer made from *assal* or syrup obtained through a tedious process of extraction of sorghum or millet malt. The procedure to obtain *assal* is again one of the most complicated in Africa. The related African clear beers, such as *otika* of Nigeria (Ogundiwin, 1977), *amgba* of Cameroon (Chevassus-Agnes et al., 1976), *chakpalo* of Benin (Mathurin, 1985) and *dolo* of Mali and Burkina Faso (Rooney et al., 1986) are prepared by simpler procedures. The *assal* (Arabic for honey) from which *assaliya* is made is sometimes given fresh to babies.

Khemiss-tweira is composed of five ingredients: grain flour, malt flour, roasted sesame seeds, salt and sugar. The food comes in the form of a granular meal. In its making, it goes through two stages of fermentation. *Khemiss tweira* is basically a traveller's food. It is consumed by adding water to the dry meal to make a paste or slurry. It is also given to schoolchildren staying in boarding-houses away from home. The product is probably a nutritionally balanced meal.

3.4 Fermented sauce ingredients

3.4.1. Meat products

Some 11 fermented meat products are made in the Sudan. The most important is a member of the jerky types. Strips of meat are either sun-dried or shade-dried to give the product. The other fermented meat products are a bit unorthodox. In *beirta*, for instance, the kidneys, spleen, liver, lungs, heart and caul fat are chopped and mixed with 2 kgs of chopped hindquarter muscle meat and placed in a pot. Then about half a litre of milk is added and the whole hodge-podge is allowed to undergo fermentation for four days. Then, the pot is opened and a little salt mixed in and a second stretch of fermentation is allowed for three days. The product is used to make sauce for *aceda* porridge.

Miriss is prepared by fermentation of the caul fat, i.e. the fat surrounding the stomach. The fat is kneaded with a quantity of an ash preparation, *combu*, and fermented for up to six days. The product is very white and extremely foul-smelling.

At least three fermented products are made from fresh bones (and their attendant meat scrapings). *Dodery*, for example, is prepared from the marrow-impregnated, meshy joint bone endings. These are chopped, sun-dried and pounded into a paste which is mixed with *combu* and fermented for up to five days.

3.4.2. Fish products

The Nile Valley probably has a greater variety of fermented fish products than other regions of Africa. The Sudan has at least four distinct such products. *Kejeik* represents the common, dry, split fish of Africa. *Fesseikh* is fermented whole fish made of a particular species and is known also in Egypt. However, *mindeshi*, a fish paste, and *terkin*, a fish sauce paste, appear not to be known in other parts of Africa.

Basing his judgement on indigenous knowledge only, Dirar (1993) wrote that "*terkin* seems to carry a tag of antiquity". Actual archaeological excavations supported this statement. Ahmed (1992) uncovered earthenware jars in northern Sudan in which he found fish bones which he identified as remains of *terkin*, perhaps 3,000 years old (Ahmed, personal communication).

3.4.3. Dairy products

The most important product here is *rob*, or buttermilk. Milk is soured overnight, churned to recover the butter and what is left is *rob*. It can be drunk as it is, turned into sauce for *aceda*, or wasted away as a by-product of butter production. Butter is boiled to give the highly valued *samin* or ghee.

Gariss is fermented camels' milk and is famous for having alcohol in it. It is basically the food of camel-herders, i.e., young men who spend months out with the camels away from home. *Gariss* is claimed to have medicinal value. It is consumed whole without churning.

Biruni is interesting because it may be fermented and aged for up to 10 years. It is mainly a food security product. At the time of milk abundance, villagers take surplus milk to the medicine man who keeps these milks fermented for years and other people may help themselves to this milk stock at times of dearth.

3.4.4. Plant products

The most important of these are meat substitutes and flavours. The fermentation takes a proteolytic course, giving a foul-smelling product, the flavour of which simulates, after cooking, that of fermented meat.

Kawal is made from the green leaves of a wild legume shrub, *Cassia obtusifolia*. The leaves are pounded, packed in a clay pot, which is then buried in a pit in the ground for two weeks. The fermented paste is then moulded in the form of small balls or discs and sun-dried.

Furundu is made from the pounded seeds of the minor cultivated crop *Hibiscus sabdariffa*, or roselle. The paste

made from the crushed seeds is mixed with *combu* before fermenting. The sun-dried fermented balls smell typically of slightly fermented meat products.

Sigda is made in a similar way as for *furundu*, but sesame seeds are used instead. The product is much richer in oil and may come as a soft paste or in the form of balls.

3.4.5. Unconventional products

These are made from raw materials that do not enter into the mainstream of what is normally considered food. In a way, these products are bizarre and no similar products have been reported in the literature.

Okah is cows' urine fermented in large earthenware pots for at least one year and may reach an age of 10 years. The urine must come from a heifer that is no longer suckling, but which has not yet reached adulthood, and it must be feeding, at the time of urine collection, on green pasture. The product, which becomes thick in the course of time, is highly esteemed and is used to prepare sauce for *aceda* porridge. It is claimed to be a cure for malaria.

Beiga is fermented caterpillars of a special kind recognized by the tree on which they feed. Live larvae are gathered in large numbers and placed live in a pot, which is covered for six days. During this period the caterpillars die and undergo fermentation. The mass of separate insects is sun-dried and used for sauce-making as required.

Duga is fermented locusts. Big, fat, egg-laden insects are placed in a pot and allowed to ferment for three to ten days. They are then sun-dried, pounded into a meal and kept in cloth bags for use in sauces.

Kesherneh is obtained by the fermentation of a certain kind of a jumping frog. The frogs are first boiled in water, sun-dried, pounded and fermented. The product may be sun-dried in the form of small balls.

4. Role of Africa's fermented foods in nutrition

The fermented foods of Africa have been developed in a hostile environment of food shortage, hunger, famine and drought. The fact that they prevail in abundance in the savannah and semi-desert zone of the continent attests to this and so does the fact that they are mostly prepared in seasons of plenty and kept for the seasons of scarcity. The fermentation and sun-drying as a double preservation method of such material as hides, skins, hooves, entrails, fat, insects, leaves, etc., all come in the context of food security.

While the evidence indicates that in savannah and semi-desert regions of the continent, calorie deficiency is the primary concern of man and animal (Guthrie, 1983), the need for protein follows closely behind. The deficiency in energy is made up by fermenting fat and malt-containing cereal products which have an abundance of sugar.

Protein shortage is tackled in a variety of ways. First, every part of the slaughtered animal that can be consumed is fermented, sun-dried and stored. Secondly, insects and other small animals which abound in the rainy season are collected, fermented, sun-dried and stored. Thirdly, plant protein sources are tapped and proteinaceous parts such as leaves and seeds are fermented, sun-dried and kept for later use.

But the major source of dietary protein in the sorghum-millet regions of Africa is the cereal itself, the staple. The more porridge one consumes, the more protein one gets. The fermented foods are mainly relish and sauce ingredients and they encourage the intake of more of the cereal.

It is not only the quantity of protein taken up that matters, but the quality of the protein itself. Experts believe that in Africa the most limiting amino acids are the sulphur-containing amino acids, although lysine is often quoted as the limiting one (Platt, 1964; Annegers, 1974). It is interesting that the three major meat substitutes of plant origin in Sudan, *kawal*, *furundu* and *sigda*, were found to be particularly rich in sulphur amino acids (Harper and Collins, 1992). *Kawal* is additionally rich in calcium and iron. The meat substitutes of plant origin make an important group of fermented foods in Africa and prevail across the continent from the Nile to West Africa. Those of West Africa perhaps include *dawadawa*, *ugba*, *ogiri* and *ogili-isi* (Ochinfa, 1986; Odunfa and Oyeyiola, 1985; Achinewhu, 1983; Raymond, 1961).

A major group of nutrients that the fermented foods furnish is the vitamin group. The provision of B vitamins by African beers, for instance, is well-documented (Platt, 1964; Chevassus-Agnes et al., 1976). The meat substitutes of plant origin have not been well-studied for their vitamin content, but it is highly likely that they are rich in this group of health-promoting nutrients. The frequent involvement of fermented foods in tribal religious rituals and the halo of sacredness that is sometimes attached to certain fermented foods seem to point towards their content of vitamins and amino acids. The symptoms of vitamin deficiency diseases are so strange that the rural African would easily refer their cause to higher powers and the foods that cure such diseases may well be considered sacred.

Fermented foods may help protect the consumers against disease by providing minute doses of antibiotics produced by the microorganisms effecting the fermentation. Al-Tunisi (1850) inquired about the reasons the foods of the people of Darfur, Sudan, were either sour or rotten and the inhabitants of the province told him that he who did not eat those foods would have to fear disease. Hesseltine and Wang (1980) mentioned that fermented foods of the orient contained antimicrobial substances that might give protection against infection to people consuming them.

5. Industrialization of Africa's fermented foods

5.1 Strategy

Obviously there is a political aspect to the industrialization of Africa's foods. A number of questions will have to be answered; a number of issues have to be resolved. Who would be the targeted consumer of the industrialized product? Who should collect the financial benefits? Who should own the industry? Where does the intellectual right lie? What level of technology should be applied? Which food should be given priority in industrialization?

The indigenous fermented foods of Africa have been developed and the technology of their production preserved through the millennia by poor rural women. These women depended on these foods to feed their families in a world of scanty provisions. Many of them sell these foods in the local markets as an income-generating activity which helps supply medicine and send children to school. Large-scale production of these foods would certainly put these women out of business and the damage incurred to their families, unless somehow checked, would be enormous.

5.2 Implementation

Documentation of the fermented foods of a country should be a good point to start an industrialization

programme. The gathering of detailed indigenous knowledge of various African countries about their foods and the dissemination of this knowledge across the continent and the resulting exchange of indigenous ideas and techniques should in itself help in the development of these foods. A good example is the special interest given by African scientists to the Sudanese sorghum product *abreh*. Researchers in West Africa are contemplating the idea of producing *gari* in the form of *abreh* flakes. In southern Africa, in Botswana in particular, researchers who are interested in non-alcoholic sour sorghum products, are thinking of producing the Sudanese product *abreh* in that part of the country. It is interesting to note that these researchers did not become interested in *abreh* because they read about it, but because they saw and touched samples of the product. International agencies who are interested in African fermented foods may need to try holding a collector's exhibition of these foods in place of the usual traditional conferences.

African food fermentations are rural women's biotechnology. These rural women actually deal with microbial starter cultures and with enzyme preparations. In one salient example in Sudan, women use a special starter culture for making a honey wine, *duma*. This is a lucrative business in the towns of southern Sudan. Each woman has her own starter strain or line, which she keeps as a secret not to be given to others. The starter strains consist of yeasts and bacteria in the form of tiny pellets called '*duma* grains'. Women have developed full knowledge of how to isolate this starter culture from nature through enrichment culture techniques, how to build up a large microbial biomass amounting to litres in size, how to use this biomass to produce the mead in a matter of hours and how to preserve the culture live for years.

Berbassa is a microbial culture used in the far north of the country to prepare a special kind of bread, *gergosh*. Again, an enrichment culture technique is followed. Milk is over-boiled and evaporated to a condensed state. A few legume beans are then thrown into it while it is still warm. The container is well closed and buried in a stack of grain for warmth. Within 24 hours a frothy preparation is obtained which constitutes the starter culture.

The most common enzyme preparation used in Sudan is sorghum malt. In the brewing of the popular opaque beer, *merissa*, only five per cent of sorghum malt is used. All evidence shows that this small amount of malt is used as an enzyme preparation. When for some reason this enzyme source is not wanted, women use barley and wheat enzyme sources (or ungerminated grain) to convert sorghum starch to sugars. They know that unsprouted sorghum grain has no amylase enzymes, whereas barley and wheat have. The technique is used in the north, where the last two cereals are grown.

Micro-organisms make the difference between the fermented food and the starting raw material. It is therefore imperative that research identifies the species used in a certain process and paves the way for the formulation of a starter culture for it. Selection of more effective strains would in itself raise the quality of the food. Later improvement of these strains through the conventional genetic techniques should lead to even better starter cultures. Theoretically, genetically engineered starter strains could be developed for specific situations, although this should not be an urgent matter. The genetics of microorganisms used in indigenous fermented foods will form a chapter in the second edition of the *Handbook of Indigenous Fermented Foods* (Steinkraus, personal communication).

Research should be carried out on the nutritional aspect of the food to be industrialized. Each food bridges a gap in the nutritional system. The role of the food in providing essential amino acids, vitamins and minerals should be well understood before committing the product to industrialization.

Admittedly, some cottage procedures of food preparation are tedious and time-consuming, since a great number of steps are involved. Technologists and food engineers tend to reduce this number of steps. It is understandable that sometimes economic considerations force us to do this, but if the deletion of a certain step in the process would be at the expense of the nutritive value or acceptability of the food, then industrialization has defeated its purpose. All the more often this situation happens when technological development outdistances research. Also, the phrase that "this step is superfluous" is often encountered in the literature of African foods. It is a fallacy that the African rural woman has any time to waste on a "superfluous step" in food preparation. The step might not be dispensable, but perhaps we have not discovered its essentiality. Therefore, no part of the indigenous procedure followed in food preparation should be omitted until its merits have been disproven.

A few of the indigenous fermented foods of Africa have already been industrialized (Steinkraus, 1989). The South African approach to the large-scale production of sorghum beer and of the sour pap *mahewu* is one of industrial affluence with facilities identical to any Western food production facility. This approach might not be suitable for most African countries, taking into consideration the rather austere economic conditions.

The Nigerian approach to the industrialization of *gari* and *ogi* has a greater degree of economization and dependence on local expertise and material in building the plants and equipment. There is much simplification here and the whole business looks like it could suit a number of other African countries.

In Sudan, *kissra* and *abreh*, the sorghum sheet-breads, have been produced industrially. A production line which can be packed all on to one truck has been invented by a non-specialist. The whole plant has been manufactured almost completely in Sudan and its use is spreading widely in the country. However, unlike the case of South Africa and Nigeria, this development in Sudan has not been backed by research. The whole thing is rather empirical, and microbial spoilage of the batter has often led to the wasting away of tons and tons of dough. There are attempts from some international agencies to spread the use of this machine to other sheet-bread producing countries like Ethiopia and India. *Kissra*, which is taking over rapidly from the porridge *aceda* in Sudan, has a great potential, if given the chance, to replace stiff porridges such as *ugali*, *ting*, *bogobe*, *to*, *dalaki*, *kenkey* and *tuo zaafi* of other African countries (Steinkraus, 1983; Campbell-Platt, 1987; Quin, 1964; Vogel and Graham, 1979).

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B. NEWS AND EVENTS

UNIDO News

ICGEB highlights progress

The International Centre for Genetic Engineering and Biotechnology (ICGEB), has recently reported several significant research findings.

HIV diagnostic test. An indigenous diagnostic test has been developed by selecting epitopes from the HIV envelope protein and synthesising those epitopes in a continuous sequence. An independent evaluation has shown that the sensitivity of the ICGEB kit is 100 per cent, specificity is 98.7 per cent and more importantly the kit does not give false negatives or false positives.

Human recombinant IFN-g. The IFN-g gene was synthesised and a recombinant vector was used to express the gene in *E coli*. The IFN-g can be produced at a level of 10 mg/1. The purity of the product meets international standards and the specific activity is more than 2x10 units/mg. The significance of the method lies in the extremely low production cost.

Studies in vaccine design. Research is primarily directed towards the design of epitope-based vaccines. Using the surface antigen (HBsAg) of the hepatitis B virus as the working system, a cysteine-rich peptide that spontaneously oligomerizes to reconstitute a conformational epitope presented by the native, homo-oligomeric protein has been generated. Its protective efficacy in chimpanzees is currently being evaluated in collaboration with Howard Fields of the US Center for Disease Control.

Cotton transformation programme. *Gossypium hirsutum* constitutes 85 per cent of the cotton market with a raw material value of $5 billion. Insects that attack the cotton plant at various stages of growth currently lead to major losses in annual yield.

The cotton programme aims to increase the level of insect resistance through a transgenic approach with *Bt* genes. A simple tissue culture protocol for multiple short differentiation from *apical meristem* has been developed. The procedure is genotype independent and has been tested on more than 10 commonly cultivated varieties of *gossypium hirsutum.*

Screening resistant plants against gall midge. A polymerase chain reaction (PCR)-based assay has been developed which could effectively reduce the time period required to screen and select for gall midge-resistant rice lines under field conditions.

As screening for resistance can now be conducted independently of the availability of insects, breeding of resistant varieties can be accelerated.

Further details of the ICGEB research programmes can be obtained from: The Director, ICGEB National Institute of Immunology Campus, S Jeet Singh Marg, New Delhi-110 067, India. Tel: 91 11 6862317 Fax: 91 11 6862316. (Source: *News Release*,1996)

UN and other organizations News

FAO and UNDP establish Mediterranean Aquaculture Project

FAO and UNDP established a Mediterranean Regional Aquaculture Project (MEDRAP) to provide advice and expertise on the region's aquaculture activities. One of the features of MEDRAP is an electronic information system, the System of Information for Promotion of Aquaculture in the Mediterranean (SIPAM), in which eight countries are currently participating in the experimental phase to select, store and retrieve data on a variety of topics and products of interest to aquaculturists. Networks have been established to foster cooperation among experts from Mediterranean countries on technical, scientific, social, economic, legal, and environmental aspects of aquaculture development in the region.

The value of biodiversity to areas such as the Mediterranean Sea is that they provide variety to those who enjoy and consume the resources, and a measure of stability and resilience to the natural or domesticated systems of which they are a part. New developments in fisheries management are incorporating genetic stock identification into traditional stock analysis. Thus, the breeding structure and genetic health of fish stocks can be more accurately assessed.

In aquaculture, genetic resources must be managed so that inbreeding is avoided and desirable culture characters can be improved through selective breeding programmes. Furthermore, it is the genetic diversity of organisms that will allow them to continue to evolve and adapt to the impacts that both humans and nature will inflict upon the worlds seas, lakes and rivers.

The utilization of the wide range of genetic diversity, the crucial building block of all biodiversity, is just now beginning in the aquatic sector of the Mediterranean. Thus we should look forward to further advances in both conservation and utilization. It is only through such conservation that fisheries and aquaculture can be sustainably productive.

For further information, contact: Dr. D.M.Bartley, Fisheries Department, FAO, Viale delle Terme di Caracalla, 00100 Rome, Italy. Tel: +39-6-5225-4376. Fax: +39-6-5225-3020. E-mail: devin.bartley@fao.org.

Other FAO contacts include: John Caddy, Technical Secretary of the General Fisheries Council for the Mediterranean, and Salvatore Coppola, Fisheries Resources Officer, for information and databases on the Mediterranean area, both at the above address. (Extracted from *Diversity*, Vol. 11, Nos. 1&2, 1995)

Balkan Plant Biotechnology Network set up

In July 1995, in Varna on the Black Sea coast of Bulgaria, a group of 20 or so Balkan plant scientists and biotechnologists agreed to establish the Balkan Plant Biotechnology Network (BPBN) as a mechanism for promoting technical collaboration in agricultural development in the region.

For Eastern Europe, however, it was clear that the region was too diverse—climatically, agronomically, and politically—and simply too large, to be encompassed sensibly within a single network. There were, therefore, to be three: Russia, the northern and central Eastern European States (the Baltic States, Poland, Hungary, Czech Republic, Slovak Republic, Ukraine, and Belarus), and the Balkan countries.

The initial participants in the Balkan network will be Albania, Bulgaria, former Yugoslav Republic of Macedonia, Greece, Romania, Turkey, and Yugoslavia, all of which were represented at the meeting. Slovenia and

Croatia, whose delegates were unable to attend, will also be invited to join. The stated overall objective of BPBN is "to establish free communication between plant scientists, in order to focus their expertise on the development and use of new technologies for agriculture, so as to improve the economies of the Balkan countries".

The network's coordinator will be Atanas Atanassov, head of the Institute for Genetic Engineering (IGE) in Kostinbrod, Bulgaria. IGE is one of the premier institutes for advanced biotechnology in the region and has managed to attract considerable external funding.

Among the aims of BPBN are identifying problems of mutual interest, making an inventory of resources, and establishing effective communication between research laboratories and the applied sector, including R&D companies. One of its general strengths is that many of the individuals involved have either worked in Western Europe or North America—and may therefore be more adept than their compatriots in attracting external finance. (Extracted from *Bio/Technology*, Vol. 13, August 1995)

ORSTOM's work on viruses, rodents and fevers

Haemorrhagic fevers are devastating illnesses that break out in sudden epidemics; new diseases (eg. Ebola fever) regularly emerge.

ORSTOM began to study haemorrhagic fevers, and the viruses that cause them, 15 years ago. Work has been carried out in tropical Africa, in Western high-security laboratories, and in the savannas of South America.

One family of viruses involved are the *Arenaviridae*. The main questions ORSTOM set out to answer were how these viruses survive in the wild and why they suddenly cause epidemics among humans.

Arena viruses nearly all have a limited geographical range. Apart from one found in bats, all prove to have a single rodent species as their vector and reservoir. One early ORSTOM finding, for example, was that Lassa fever virus is absent from the Central African Republic because its specific ecological niche is occupied by a related virus, harmless to humans.

From their research on the genetics of the viruses and the evolutionary history of rodents, ORSTOM's researchers now think that an ancestor of today's arena viruses infected the earliest rodents, some 40 million years ago. Then, as rodents spread around the world and speciation progressed, the viruses evolved in parallel. Later, climatic or other natural barriers kept rodent species in their respective ranges, and their viruses with them. Evolution and speciation continued. Although it leaves some puzzling questions, this picture fits well with the genetic relationships found among African arena viruses, and their very marked differences with the American viruses. As regards human health, it suggests that epidemics occur when human activity disrupts the equilibrium between a virus and its host species.

Besides its arena virus research, ORSTOM is studying the new, deadly Sabia virus from Brazil. Researchers have developed a reliable, sensitive diagnostic test and a drug which, though still at the research stage, successfully cured an ORSTOM researcher infected in the laboratory!

ORSTOM is also involved in the search for the animal reservoir of the Ebola virus, and is working on related filaviruses. Other targets are the bunyaviruses and hantaviruses. And work continues on yellow fever, which breaks out anew when vaccination efforts slacken. Dengue fever is extending its range, its epidemiology becoming more complex; ORSTOM researchers are studying Asian strains of this virus at Yale Arbovirus Research Unit. (Source: *ORSTOM Actualités*, 1995)

Biosafety

Call for International regulations on POPs

Toxic chemicals such as dioxins and polychlorinated biphenyls—now classified as persistent organic pollutants (POPs) because they are long-lived and concentrate as they climb the food chain—were in the international spotlight at a United Nations meeting in Washington to address land-based threats to the marine environment. Ministers from more than 100 countries appeared to support calls from the Nordic countries to begin developing a legally binding treaty on reduction or elimination of releases of POPs.

POPs are at the heart of regional water quality efforts, including the International Joint Commission's call to phase out the industrial use of chlorine, through different agencies have different names for POPs.

Whatever their name, they are increasingly being recognized as a global concern: experts now agree that most POPs enter bodies of water from the air and that some POPs can travel thousands of miles from the point of release. As a recent report in *Science* noted, POPs, are now found in the world's most remote spots. they can concentrate in the colder Arctic and Antarctic regions, where they are "distilled" out of the cold air. The concentration of one country's toxic compounds in another country's natural environment and food supply has created the pressure for international action.

While the study of bioaccumulation and transport of POPs is becoming more sophisticated, research is in the early stages on their impact on hormonal, immune, and developmental systems. To identify priorities for research, the US National Academy of Sciences formed a panel to conduct a two-year investigation with funding from the Environmental Protection Agency and other agencies. (Extracted from: *Chemical Week*, 11 October 1995)

Global biotechnology regulation?

This EBIS reports on the preparations for the second Conference of the Parties (COP) to the Convention on Biological Diversity (see EBIS 3.1, page 10). Among other things, this will consider "the need for and modalities of a protocol setting out appropriate procedures, including, in particular, advance informed agreement, in the field of the safe transfer, handling and use of any living modified organisms resulting from biotechnology that may have adverse effect on the conservation and sustainable use of biological diversity".

As with so many biotechnology issues, opposing points of view are being passionately promoted by the different protagonists. Environmental groups, such as the Friends of the Earth and Genetic Resources Action International (GRAIN), have called unequivocally for a binding regulatory mechanism to rule the testing, release and trade of GMOs. Several developing and developed countries share this point of view. They fear the unscrupulous operator unable to obtain permission to release in Europe or the US using the developing world as testing grounds for uncontrolled and risky experiments. On the other hand, the International Bio-Industry Forum (representing the major biotechnology industries world-wide) have issued a statement of principle indicating their support for the development of biosafety principles and guidelines at the national level. Where such national guidelines are not

in place they promise to adhere to generally accepted scientific standards of care as observed in their own countries.

Others have argued that a legally binding protocol might take considerable time to be agreed and enter into force between so many parties. In the meantime, the possible role of scientifically based technical guidelines might be seriously considered. These could be drawn up quickly and easily on the basis of world-wide experience to date. An appropriate biosafety instrument, whether legally binding or not, should be risk-based and should not lead to unnecessary stigmatization of a technology with potentially great benefits. Furthermore, it must not provide possibilities for a technical barrier to trade just at the time when the GATT and other agreements are working towards freer trade.

These debates take place at the same time that the US regulatory authorities are rapidly giving consent for the marketing of transgenic crops (some 15 agronomically improved crops will be planted widely in the USA in 1996). Presumably, these regulators believe that the risks to be addressed and the means to manage them in these new and improved crops do not differ significantly from those developed by more traditional means. The knowledge and experience gained from biosafety research is leading to increased confidence. This suggests that consideration should be given to whether existing sectoral provisions, including quarantine controls for seeds, plants, vaccines, foods, pesticides, etc., are not the most appropriate response to ensure the safety of biotechnology. This is the approach being taken in the European Union for medicinal products, additives in feeding stuffs, plant protection products, novel foods and seeds. (Source: *EBIS*, Vol. 5, No. 2, October 1995)

EU Parliament calls for UN biosafety protocol

The European Parliament has called for a legally binding protocol on biosafety—the safe handling, transfer, and use of organisms created by biotechnology—to be drawn up under the United Nations biodiversity convention as a matter of urgency. In a resolution, dated 14 July 1994, the Parliament called on the European Commission and the EU's Council of Ministers to support the protocol at the second conference of parties to the convention. The resolution noted that recent reports showed there is considerable international traffic in genetically modified organisms (GMOs) that is completely unregulated, and that deliberate releases of GMOs are being carried out in many developing countries that have no legislation or infrastructure to ensure their safe use. "This situation is putting the entire biosphere of the planet at risk," the Parliament said. It called for a moratorium on transfers of such organisms to and from countries with no biosafety legislation until the protocol comes into force. (Source: *Environment Watch: Western Europe*, 21 July 1995)

Findings of European biosafety experts visit to China

A party of seven scientists from five European countries visited China from 17 to 29 June 1995 to assess the situation with regard to large-scale release of plants transgenic in viral sequences and transgenic microbes. A major aim was to initiate contacts to develop monitoring techniques for farmer release of transgenic organisms.

The party had initial meetings with representatives of the China National Centre for Biotechnology Development (CNCBD) and from two research centres in Beijing to gain background briefing to the regulatory situation with regard to field releases. The party then split into two groups, one of four virologists and the other of three microbiologists to make field visits in various parts of China.

The virology group visited various sites in two regions, Lioning province in the north-east and Henan province in the centre of China. They saw experimental plots and farmers' fields of tobacco plants containing various viral transgenes. They were very impressed with the cleanliness of the crops in both areas. The overall impression was that farmers' release of transgenic tobacco posed no more risk than non-transgenic plants. This view was based on the care that farmers take of tobacco crops and that interactions of superinfecting viruses were no more threatening than joint natural infections.

The group of microbiologists visited sites in Jiaxing in the east and Guangzhou in the south of China. There they saw fields which had been inoculated over the past six to eight years with *Alcaligenes faecalis, Enterobacter cloacae and Klebsiella oxytoca* which had been modified to increase their nitrogen fixing capacity. These mutants were reported to give marked increases in yields of rice, wheat, barley and watermelons. The results of a range of tests, performed on both the sites in these fields and on the modified bacteria, indicated that the modified bacteria did not persist in the soils and that they had no animal or human toxicity.

After the field visits the two groups reassembled in Beijing and visited several research institutes involved in research on genetic modification of plants and microbes. These visits gave an important insight into the transgenic organisms which are "in the pipeline" for eventual field release. The party then had wind-up sessions with officials of the CNCBD and the EU.

The overall impression was that the current field releases are causing no apparent problems. However, the two main issues that emerged are:

(a) That there are many more genetically modified organisms that will reach the field release stage soon and there may be specific problems associated with these; and
(b) There is the concern that unpredicted problems may arise.

It was considered that the best approach to dealing with these issues would be to initiate collaborative research projects between Chinese and EU scientists to address specific aspects of the perceived problems and to develop monitoring techniques for farmer-scale releases.

The idea for this mission arose at the 3rd International Symposium on The Biosafety Results of Field Tests of Genetically Modified Plants and Microorganisms held in Monterrey, California, in November 1994. As at previous biosafety meetings, the reports on the large-scale field releases by Chinese scientists elicited great interest from participants from other countries. The Chinese scientists have accumulated several years of experience of farmer-scale releases of transgenic tobacco, a situation not yet achieved in other countries. Because of the differences in biosafety issues between small controlled releases and farmer-scale releases it was recognized that the Chinese experience would be of importance in effecting large-scale releases in other countries. The main biosafety issue is the monitoring of releases of transgenic organisms which are not under the close control of the scientists or regulatory authorities. It was recognized that the close contacts that the EU has with Chinese scientists through the China-EC Biotechnology Centre in Beijing could provide a means of

cooperatively expanding upon the experience of the Chinese. This mission dealt with two areas of science, transgenic protection of plants against virus infection and manipulation of microbes to enhance properties beneficial to agriculture.

General guidelines on "Safety Administration Regulations on Genetic Engineering" were published in December 1993 by a committee of the State Science and Technology Commission. The purpose of this legislation is:

- To promote research and agricultural and industrial activities;
- To protect public health and the environment;
- To accord with regulations in other countries.

The system of management is at four levels:

- The State Science and Technology Commission is in overall charge and is setting up a national biosafety committee which will include some scientists;
- The relevant administrative authorities, e.g. Ministry of Agriculture, Ministry of Public Health;
- Administrative authorities in major institutes;
- Local biosafety committees.

Four levels of genetic engineering work are suggested, each relating to one of the four above. Thus, permission for the lowest level will be from the local biosafety committee and that for the highest level from the national biosafety committee. Although the Regulations outline the four levels, we were unable to get guidance as to what type of releases would fall under what level.

Currently, the detailed specific subregulations are being drafted by committees under the various relevant ministries. Those under the Ministry of Agriculture are at the fourth draft and it is hoped to have them finished by the end of 1995.

Conclusions reached by the EU experts were that:

- It is clear the application of genetically modified bacteria to improve crop yields (mainly rice) has developed rapidly in China. A great thrust to this development was given by the need to apply new strategies including biotechnological means in order to feed a densely populated country.
- Biosafety regulations have not been in use in China so far. Hence, little attention has been paid by Chinese scientists to the issue of biosafety of the releases performed. However, a draft document describing guidelines has been obtained, which places major responsibility with the proposing scientist. It is unclear when these guidelines will be implemented.
- Without the pretention to be complete, a comprehensive picture has been obtained of two types of releases of genetically modified bacteria at two locations in China. This information is suitable, since it provides insight into previous releases, against a background of existing strict European regulations in this area.
- A spirit of openness about the issues raised was encountered amongst the Chinese colleagues visited. Moreover, they repeatedly expressed the desire to collaborate in future work on the biosafety of the releases.
- The samples obtained will allow the European side to apply their advanced monitoring techniques to obtain a preliminary picture of the fate of the inoculants.
- A project aimed at monitoring the releases in China at the two sites visited is a desirable outcome of these initial contacts.

(Extracted from *Report of the EU Biosafety Expert Mission to China*, June 1995)

Regulatory Issues

EU Directive covers national and international transport of genetically modified micro-organisms and biological agents

By 1 January 1997 member States must implement Council Directive 94/55/EC relating to the approximation of the laws of member States with regard to the transport of dangerous goods by road. This Directive lays down in its annexes specific requirements for the safe transport, national and international, of genetically modified micro-organisms and biological agents, which until now have only been recommended for international transport.

An equivalent proposal to cover the same goods in rail transport is under discussion. (Source: *EBIS*, Vol. 5, No. 2, 1995)

USDA proposes to virtually abandon oversight of field testing

In late August 1995, the US Department of Agriculture (USDA) issued a proposal to dramatically deregulate field testing of genetically engineered crops. The new rules, if adopted, would mean that virtually all field tests of genetically engineered crops in the United States would be exempt from risk assessments.

Among the changes proposed under the new rules, the Department would no longer evaluate the risks of gene flow from crops with wild relatives in this country or of viral genes added to crops for virus resistance. The Department even goes so far as to exempt viral genes not yet discovered or characterized. The USDA also proposes to no longer require companies to submit reports on completed field trials, effectively denying public access to data needed to assess the safety of field testing. In the area of commercialization, the proposal would expedite the approval of crop varieties that are "closely related" to previously commercialized varieties, potentially opening a huge loophole that may allow companies to avoid assessments of risky varieties. (Extracted from *The Gene Exchange*, December 1995)

General

Europe and Japan will form working group

Officials of the European Union (EU, Brussels) and of Japan's Ministry of International Trade and Industry (MITI, Tokyo) have agreed to establish a working group to exchange information about biotechnology policy. Stefano Micossi, the Director General for Industry of the EU's European Commission (EC), and Yoshihiro Sakamoto, MITI's Vice-Minister for International Affairs, decided to take on board a recommendation made last February by a round-table of top European and Japanese industrialists that biotechnology was an area that would benefit from closer cooperation between the two economic superpowers.

The working group will provide a forum to discuss such issues as the harmonization of rules covering health, safety, and the environment, as well as the mutual recognition of clinical-trial and field-test results.

Japanese industrialists, though, prefer to take a slow approach to harmonization and recognition. Since, in most instances, biotechnology is still a minor activity for most Japanese multinationals these firms have much to lose should public opinion suddenly turn against the technology

because of a worst-case scenario caused by a rashly introduced, faulty product. Nevertheless, once products have proven themselves in the US and Europe, Japanese companies will want to quickly introduce them in Japan. Thus, they are keen to have well-tried regulatory approaches already in place within their government agencies.

Indeed, Japanese public opinion greatly favours biotechnology, most likely because the Japanese are well known for their acceptance of science and technology and the benefits that it often bestows. Studies of Japanese public perception, in fact, indicate that 81 per cent of the Japanese people have no concerns or few concerns relating to biotechnology research. Moreover, a majority of the Japanese people say that they have few concerns or no concerns about using medicines, dairy products, vegetables, or meats that are produced through biotechnology processes. This compares starkly with some of the recent surveys of European public perception, in which generally 50 per cent or fewer Europeans voice such acceptance of biotechnology research and products.

Officials of MITI and the EC expect to meet in the coming months to develop a timetable and to consider how the working group should be constructed. (Extracted from *Biotechnology*, Vol. 13, August 1995)

Human genome programmes world-wide

A report by Bertrand R. Jordan, "An Assessment of Progress in Human Genome Programmes Worldwide", attempts to provide a first-hand yet synthetic and reasonably up-to-date picture of developments, trends and problems in the field of the human genome analysis programme. Based on a one-year survey of approximately one hundred genome research laboratories all over the world, the report compares fundings between the USA, Japan, the UK, France, Germany and Sweden. The research evaluation, which, it is stated, does not necessarily reflect the official position of the European Commission, notes that serious discussion about launching a human genome sequencing programme began in the USA in the mid-1980s. Other countries followed suit, notable Japan (with, however, four or five different programmes whose coordination took time to become effective) and the United Kingdom, with a well-integrated Human Genome Mapping Project. The Soviet Union started a project in 1989, although efforts were hampered by lack of hard currency, communication problems and by the subsequent disintegration of the Union. France has also been present in the field, with both an official genome programme and a very successful project run by non-governmental organizations. It appears that different indicators show that the USA has a clear lead. The United Kingdom is in a strong second place, and France is a more distant third, slightly ahead of Japan. On a continental basis, the European Community is almost equivalent to the US. Recent successes of the European Union Research Programmes (sequencing yeast chromosome III) are increasing the share of Europe in this field. (Source: *EBIS*, Vol. 5, No. 1, 1995)

Developing sustainable agricultural production systems for the 21st century

The biggest single challenge of the 21st century will be to further develop sustainable agricultural production systems that can meet the food and fibre needs of the world population without damaging the environment, according to Simon G. Best, managing director of Zenecca Plant Science (Wilmington, DE).

He calls his vision an optimistic one that is based on an objective assessment of the potential for new agricultural technologies to meet the following critical needs:

- For the developed world—better quality, healthier and better value food to ensure that the role of nutrition in disease prevention can be maximized to reduce the costs of therapeutic health care.
- For the developing world—dramatically increased availability of affordable basic food; primarily to meet population growth in Asian countries, many of which will be able to pay for imported food from strategic producers such as the USA, at unsubsidized world prices, even though these will gradually rise.
- Industry's projections concur with those from independent bodies such as the Worldwatch Institute that the supply/demand balance for all major food and feed grains and protein crops will become critical within 10 years.
- For the whole planet—increased sustainability and reduced environmental impact not only of agriculture, but also of many other basic industries such as pulp/paper, plastics and fuels to which renewable raw materials from biomass, which are designed for more efficient and cleaner processing, will make a critical contribution.

(Extracted from *Genetic Engineering News*, July 1995)

A million ECUs for biotechnology in public

The European Commission is spending one million ECUs over the next three years on advancing public awareness and understanding of biotechnology across Europe. A sum of 600,000 ECUs is going to the European Federation of Biotechnology Task Group on Public Perceptions of Biotechnology. A further 400,000 ECUs will coordinate international opinion research in association with the Task Group.

The European Federation of Biotechnology is the central, Europe-wide organization for biotechnology. It incorporates more than 80 biotechnology-related scientific societies. Established in 1991, its Task Group on Public Perceptions of Biotechnology has 50 leading members from Europe's biotechnology industry and research, communications and survey research, the media, and environmental, consumer and patients' organizations.

The overall aim of the Task Group is to promote greater public awareness and understanding of biotechnology and to encourage informed, open debate. It does this in a number of different ways:

- A series of widely distributed briefing papers on key issues in biotechnology for non-specialists;
- Details for the public on sources of information about biotechnology;
- Public conferences to advance the debates about the ethical, social and legal issues raised by biotechnology;
- Courses on communicating with the public for industrialists and researchers.

This money will enable the expansion of these activities and also new targeted activities for specific groups: industrialists, environmentalists, consumers etc. Key emphasis will be on the Task group's position as the independent intermediary for all the varied parties concerned with—and by—biotechnology.

Further information from: Prof. John Durant (Task Group chairman), Assistant Director, The Science Museum, Exhibition Road, London SW7 2DD, Great Britain. Tel:

+44 171 9388201; fax: +44 171 9388213, or Dr. David Bennett (Task Group secretary), Cambridge Biomedical Consultants, Schuytstraat 12, 2517 XE The Hague, Netherlands. Tel. and fax: +31 70 3653857, or Dr. Bernard Dixon (Task Group journalist member), 130 Cornwall Road, Ruislip Manor, Middlesex HA4 6AW, Great Britain. Tel: +44 1895 632390; fax: +44 1895 678645. (Source: *Press Release*, 1995)

IAEA Symposium to Assess Plant Breeding through Nuclear Energy

More than 175 experts from 46 countries gathered in Vienna last June to learn about the latest efforts to enhance the diversity of genetic materials for plant breeding through nuclear energy and related technology.

A key topic was the modification of genetic composition of plants through mutation induction by radiation and chemicals. A major concern was how induced changes in genetic composition may affect gene expression. Gene inactivation was discussed along with how such activities as pathogen resistance, chemical composition, and a variety of other functions may be influenced.

The Joint FAO/IAEA Division Section on Genetics and Plant Breeding has been a strong proponent on the use of mutation induction for developing new crop varieties since its inception in 1964. According to the database recording the numbers of mutant varieties released for agricultural usage, roughly 1,800 cultivars have been developed through mutant induction over 30 years of activity. In many instances this has had a major positive impact on crop productivity.

A major objective of the meeting was to strongly encourage interaction between investigators heavily involved with the development and use of sophisticated procedures for genetic mapping and other activities relating to plant genetics and other scientists who are concerned with practical plant breeding.

The growing movement towards utilization of mapping procedures to gain a better understanding of genetic manipulation was evident in the large segment of the meeting devoted to newly developed methodologies for chromosome mapping along with reference to the sequences of the genes involved. The results will increase genetic knowledge of existing germ-plasm collections. Projects with cereals, non-cereals, and vegetatively propagated species described progress utilizing molecular markers. Reports indicated that marker-assisted selection, gene introduction from wild species, and gene isolation would be very important future breeding applications of marker technology, although currently a number of genetic relationship and genetic diversity studies are under way.

Participants discussed in detail numerous specific areas that do or could advance plant breeding: plant pathogenesis; the process of apomixis involving production of progeny without fertilization; genetically controlled tolerance for stresses such as abundant aluminium; and the impact of methylation of various cell constituents on gene expression. There was a continued interest throughout the presentations in the features that influence plant growth and how plants react to genetic change and what is known about genetic control of such adaptations.

In addition to various discussions of advanced molecular technologies, many participants reported by lecture or poster on their particular plant breeding activities. The range of crops and specific breeding objectives was very large including grain crops, fruits, ornamental, vegetables including tubers, and tropical species.

The proceedings are expected to be published. To order a copy, contact: Publishing Section, International Atomic Energy Agency, P.O. Box 100, A-1400 Vienna, Austria. For additional information, contact: Dr. M. Maluszynski, Head, Plant Breeding and Genetics Section, Joint FAO/IAEA Division of Nuclear Techniques in Food and Agriculture, International Atomic Energy Agency, Wagramerstrasse 5, P.O. Box 100, A-1400 Vienna, Austria. Tel: +43-1-20602. Fax: +43-1-234564. (Source: *Diversity*, Vol. II, No. 3, 1995)

Crop productivity and sustainability—shaping the future

2nd International Crop Science Congress

Food, including safe drinking water, constitutes the first basic need of all human beings. Advances in crop sciences coupled with the hard work of farm families have helped to ensure adequate food supplies so far. In spite of the pivotal role of crop sciences in conquering food insecurity, it was only in 1992 that an International Crop Science Congress (ICSC) was held in Ames, Iowa. At that conference it was decided to accept the invitation of the National Academy of Agricultural Sciences of India to hold the second ICSC in New Delhi, India, from 17 to 23 November 1996.

The second International Crop Science Congress is being held at a time when several new challenges confront crop scientists. Increasing population and improved purchasing power will necessitate keeping the rate of growth in food production above population growth rates in the next millennium.

Diminishing per capita availability of arable land and irrigation water coupled with expanding biotic and abiotic stresses and land and forest degredation make attention to sustainable advances in the productivity, profitability and stability of major cropping systems essential. For safeguarding food and nutrition security at the household and individual levels, crop intensification and diversification will be needed in most developing countries but will have to be achieved on an ecologically sustainable basis.

New tools of molecular biology and an awakened consciousness relating to the conservation of plant genetic resources open up new opportunities for bringing about novel genetic combinations. Ecologically sustainable methods of pest and soil health management are spreading and both production and post-harvest technologies are showing continuous improvement. Symbiotic patterns of international collaboration are emerging to ensure that the fast spreading IPR environment does not harm global and national food security.

Contact: Prof. S.K. Sinha, Secretary-General, 2nd ICSC, National Academy of Agricultural Sciences, Indian Agricultural Research Institute, New Delhi-110 001, India. Fax: 91-11-332-4005; Tel: 91-11-3321623/3321822/33225106/3328616. (Source: *First Circular of the 2nd International Crop Science Congress)*

International Centre for Genetic Engineering and Biotechnology: meetings and courses, 1996

Meetings and Courses organized by ICGEB:

1-5 April Trieste, Italy	**Theoretical Course**: RNS Structure and Function

Organizer: Glauco Tocchini-Valentini
Requests for information and applications directly to: Ms. Elisabetta Lippolis, ICGEB, Padriciano 99, 34012 Trieste, Italy. Tel: +39-40-3757332; Fax: +39-40-226555; Tlx: 460396 icgebt i; E-mail: courses @icgeb.trieste.it

10-13 April, Trieste, Italy — **Symposium**: Gene Therapy of AIDS, Cancer and Genetic Disorders
Organizers: Mauro Giacca, Giorgio Palù, John Rossi, Nava Sarver
Requests for information and applications directly to: Ms. Elisabetta Lippolis, ICGEB, Padriciano 99, 34012 Trieste, Italy. Tel: +39-40-3757332; Fax: +39-40-226555; Tlx: 460396 icgebt i; E-mail: courses @icgeb.trieste.it

14-27 April, Enugu, Nigeria — **Workshop**: Gene Cloning
Organizer: Nduka Okafor
Requests for information and applications directly to: Prof. N. Okafor, Foundation for African Development through International Biotechnology (FADIB), P.O. Box 1457, Enugu, Nigeria. Tel: +234-42-459360; Fax: +234-42-453202, 250611; Tlx: 51445, 51300 sezen; 51208 trade.

6-10 May, Trieste, Italy — **Theoretical and Practical Course**: Human Immunoglobulin Genes: Repertoire Analysis and Expression of Recombinant Antibodies
Organizer: Oscar Burrone
Requests for information and applications directly to: Ms. Elisabetta Lippolis, ICGEB, Padriciano 99, 34012 Trieste, Italy. Tel: +39-40-3757332; Fax: +39-40-226555; Tlx: 460396 icgebt i; E-mail: courses @icgeb.trieste.it

2-14 June, Marrakech, Morocco — **Theoretical and Practical Course**: Biotechnology and Agriculture Improvement in Developing Countries
Organizers: Abdallah Oihabi and Abdelouahhab Zaid
Requests for information and applications directly to: Dr. A. Oihabi or Dr. A. Zaid, Department of Biology, Faculty of Sciences-Semlalia, B.P. S15, Marrakech, Morocco. Tel: +212-4-434649; Fax: +212-4-436769; Tlx: 74013m facsmar

17-20 June, San Luis, Argentina — **Theoretical Symposium**: Theoretical and Experimental Aspects of Protein Folding
Organizer: Jorge A. Vila
Requests for information and applications directly to: Dr. J.A. Vila, IMASL-Universidad Nacional de San Luis, Ejército de Los Andes 950, 5700 San Luis, Argentina. Tel: +54-652-22803; Fax: +54-652-30224, 35630; E-mail: jvila@unsl.edu.ar

1-5 July, Trieste, Italy — **Theoretical Course**: Transgenic Organisms: Biological Risk Assessment
Organizers: Gilbert Howe and George Tzotzos
Requests for information and applications directly to: Ms. Elisabetta Lippolis, ICGEB, Padriciano 99, 34012 Trieste, Italy. Tel: +39-40-3757332; Fax: +39-40-226555; Tlx: 460396 icgebt i; E-mail: courses @icgeb.trieste.it

2-7 September, Trieste, Italy — **Practical Course**: Bioinformatics: Computer Methods in Molecular Biology
Organizer: Sándor Pongor
Requests for information and applications directly to: Ms. Elisabetta Lippolis, ICGEB, Padriciano 99, 34012 Trieste, Italy. Tel: +39-40-3757332; Fax: +39-40-226555; Tlx: 460396 icgebt i; E-mail: courses @icgeb.trieste.it

16-28 September, Havana, Cuba — **Theoretical and Practical Course**: Molecular Basis for the Diagnosis of Viral Hepatitis
Organizers: Guillermo Padrón Gonzalez and Shahid Jameel
Requests for information and applications directly to: Dr. G. Padrón Gonzalez, Center for Genetic Engineering and Biotechnology (CIGB), P.O. Box 6162, Havana, Cuba. Tel: +53-7-218070; Fax: +53-7-218008; Tlx: 512330 ingen cu; E-mail: inmdiag@ingen.cigb.edu.cu

4-15 November, New Delhi, India — **Practical Course**: Plant Transformation
Organizer: V.S. Reddy
Requests for information and applications directly to: Mr. G. Chatterjee, ICGEB, NII Campus, Aruna Asaf Ali Marg, New Delhi 110067, India. Tel: +91-11-6867356; Fax: +91-11-6862316; Tlx: 3173286 icgeb in; E-mail: chatterj@icgeb.trieste.it

25 November - 6 December, New Delhi, India — **Practical Course**: Methods in Disease Diagnosis
Organizers: S. Jameel and K.V.S.Rao
Requests for information and applications directly to: Mr. G. Chatterjee, ICGEB, NII Campus, Aruna Asaf Ali Marg, New Delhi 110067, India. Tel: +91-11-6867356; Fax: +91-11-6862316; Tlx: 3173286 icgeb in; E-mail: chatterj@icgeb.trieste.it

Meetings and Courses Sponsored by ICGEB:

20-31 May, Trieste, Italy — **Workshop**: Biomass Production and Utilization
Organizers: Giuseppe Furlan (UTS-ICTP) and Carlo V. Bruschi (ICGEB)
Requests for information and applications directly to: Ms. Lisa Iannitti, Workshop on Biomass Production and Utilization, International Centre for Theoretical Physics (ICTP), P.O. Box 586, 34100 Trieste, Italy. Tel: +39-40-2240111; Fax: +39-40-224163; Tlx: 460392 ictp i; E-mail: smrxxx@ictp.trieste.it

25-28 September, Trieste, Italy — **Final Conference**: EU Yeast Genome Sequencing Network
Organizers: Carlo V. Bruschi (ICGEB) and André Goffeau (UCL)
Requests for information and applications directly to: Dr. C. Bruschi, Microbiology Group, ICGEB, Padriciano 99, 34012 Trieste, Italy. Tel: +39-40-3757304; Fax: +39-40-226555; Tlx: 460396 icgebt i; E-mail: bruschi@icgeb.trieste.it

Source: ICGEB, AREA Science Park, Padriciano 99, 34012 Trieste, Italy. Tel: +39-40-37571; Fax: +39-40-226555; Tlx: 460396 icgebt i

1996 ATCC workshops/conferences

1-5 April 1996
Recombinant DNA: Techniques & Applications

9-12 April 1996 and 19-22 November 1996
Polymerase Chain Reaction (PCR) Applications/Cycle DNA Sequencing

16-19 April 1996
Basic Techniques in Molecular Mycobacteriology

1-3 May 1996 and 11-13 September 1996
Cell Culture & Hybridomas: Quality Control & Cryopreservation Techniques

4-7 June 1996
In Vitro Toxicology: Techniques and Applications

18-20 September 1996
Downstream Processing, Recovery and Purification of Proteins

24-27 September 1996
Fermentation Microbiology

2-4 October 1996
Microscopy/Photomicrography

9-11 October 1996
Growth & Preservation of Animal Viruses

15-18 October 1996
Freezing & Freeze-Drying of Microorganisms

11-15 November 1996
Advanced Recombinant DNA Techniques & Applications

For information on ATCC Workshops contact:
ATCC, Workshop Coordinator, 12301 Parklawn Drive, Rockville, MD, USA 20852. Tel: (301) 231-5566; Fax: (301) 816-4364. ATCC Internet Address: http//www.atcc.org/workshops/workshop.html

International Society for Environmental Biotechnology
Boston 1996 Meeting

Meeting on: *Global Environmental Biotechnology Approaching the Year 2000*

This will be the third biennial meeting of the International Society for Environmental Biotechnology (ISEB) and will be held at the Northeastern University at Boston, USA, from 15 to 20 July 1996. Presentations of state-of-the-art technical papers will be integrated with tutorials and workshops by practising technologists in the broad field of environmental biotechnology. By having both selected presenters and experienced tutors, it is anticipated that all participants will benefit from this interactive symposium. The focused nature of this on-campus ISEB meeting will afford substantial directed time for professional interchange. A number of social events within Boston will further promote informal exchange of ideas, discussion of technical problems, and exploration of new applications. Workers with experience in one area of environmental biotechnology will learn from the wealth of established backgrounds of those in other areas. This meeting is designed to be, in every respect, truly global.

Programme outline: As with all meetings of the ISEB, papers are particularly invited for the following sessions, although the programme is not limited to these aspects of environmental biotechnology.

- Biomonitoring
- Bioprocessing
- Bioreactor design and operation
- Bioremediation
- Diagnostic systems
- Ecology
- Genetics
- Institutional and business issues
- International and government issues
- Metals and leachates
- Residue utilization
- Subsurface contaminant migration
- Water treatment
- Special topics

Further details from: Donald L. Wise, Ph.D., Cabot Professor of Chemical Engineering and Director, Center for Biotechnology Engineering, 342 Snell Engineering Center, Northeastern University, Boston, MA 02115, USA. Tel: (617) 373-2992 Fax: (617) 373-2784

Biosensors 96—the foremost conference in the field

Following the tremendous success of the third Biosensors conference held in New Orleans in 1994 involving over 300 submitted abstracts and participants from 30 countries, the Fourth World Congress on Biossensors will take place from 29 to 31 May 1996 in Bangkok, Thailand.

The conference, organised by Elsevier Advanced Technology, returns to the Far East in 1996 completing a six-year cycle of biannual meetings in strategic sectors of the globe.

Biosensors '96 is the principal conference in the field. The intense three-day event covers every facet of the science, application and commercial exploitation of biosensors and bioelectronics and will be attended by all the prime movers in the field.

For the first time in 1996, a symposium on bioelectronics will be dedicated to the more general exploitation of biochemicals in electronic devices. The plenary sessions in this year's event will emphasize new horizons, with critical appraisals of the opportunities offered by improved understanding of biophysical interactions at the molecular level.

The Biosensors congress is the forum for highly original communications and provides a comprehensive picture of recent developments and catalyzes interactions that mould the future directions of the area.

Format of the Congress: The congress will be structured as three symposia:

- Catalytic Biosensors
- Affinity Biosensors
- Bioelectronics

Contributions describing the industrial development of analytical instruments, as well as more fundamental aspects of the technology, will also be encouraged and supplemented by a display of commercial equipment.

Following the excellent response to the first exhibition held at Biosensors '94, there will be increased space allocated at the 1996 event for companies to display their commercial equipment.

For the first time the supporting journal for the conference, *Biosensors and Bioelectronics*, will sponsor an award for the most original oral and poster presentations, to be selected at the conference.

For further information please contact: Gill Spear, Biosensors '96, Elsevier Science Ltd, Conference Department, The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, UK. Fax: +44 (0) 1865 843958; Tel: +44 (0) 1865 843643; E-mail: g.spear@elsevier.co.uk. (Source: *Press Release*, January 1996)

The impact of AIDS in Asia

Contrary to popular belief, the AIDS epidemic has only slightly slowed the growth of per capita income in Asia, but by broader measures it seriously damages the quality of life.

"The epidemic is having a powerful and deleterious effect on human development," said Peter Godwin, regional HIV Project Chief for the United Nations Development Programme (UNDP). He added that recent research "makes clear, with hard evidence, just how vulnerable the region is".

Mr. Godwin addressed an international conference on AIDS in Asia, held in Chiang Mai, where AIDS illnesses and deaths have grown so dramatically due to prostitution and drug use that foreign workers must be imported for labour-short industries.

He said the Asia-Pacific region now has only 16 per cent of the world's HIV infections, but it was expected that the annual number of new infections in Asia would exceed those in Africa by 1997 and that Asia's global share would rise to nearly 25 per cent by the year 2000.

Mr. Godwin said India, Burma and Thailand will be especially vulnerable, but the epidemic will also be very severe in Cambodia, China, Laos, Nepal, Pakistan, Bangladesh, Indonesia, the Philippines, the South Pacific islands and Viet Nam.

To evaluate the effects on national economies, UNDP and the Asian Development Bank have supported research on eight Asian countries: China, India, Indonesia, South Korea, Burma, the Philippines, Sri Lanka and Thailand.

The "human development index" that UNDP has been using since 1990 takes into account life expectancy at birth; adult literacy rate; a measure of schooling enrolment, and real GDP per capita.

Mr. Godwin said a Columbia University research team hired by UNDP used data from nearly 60 countries and found that the more severe the AIDS epidemic in a country, the less the improvement in the human development index. (Extracted from: *International Herald Tribune*, 19 September 1995)

TB's global surge

Fifty years after tuberculosis became curable, a worldwide surge in drug-resistant strains of the disease is occurring, not just because of the limits of medical science, but also because of the profit motives of pharmaceutical companies, according to experts at an international meeting held in September 1995.

There are more cases of tuberculosis today than ever world-wide. At least two million people die from it each year, many from strains of the bacteria that have become resistant to the available drugs.

Yet, although new drugs have been developed and are ready for testing, pharmaceutical companies are unwilling to invest the money it would take to bring them to market.

Pharmaceutical companies have asserted that it can cost more than $200 million to bring a new drug to market.

Many participants also strongly criticized the World Health Organization, for spending minuscule amounts on tuberculosis after declaring it a "global health emergency."

The tuberculosis bacterium has infected 1.75 billion people world-wide. It makes eight million people sick each year and its death toll of two million, out of the 50 million people who die world-wide each year, makes it the leading killer among infectious diseases, the World Health Organization said.

An overwhelming majority of cases occur in developing countries; fewer than 10 per cent occur in developed countries. In the USA, for example, there were about 26,000 new cases of active tuberculosis reported last year. Participants at the conference said drug company officials had told them that the low number of cases in the United States represented too small a market to warrant large investments.

The resistance problem has also gained a foothold in third world countries, where its threat is even greater because it is less likely to be monitored and drugs are available without prescription, leading to overuse and misuse.

The worsening problem reflects a lack of political leadership in battling the disease, a soaring world population that lives under crowded conditions, and, to a lesser extent, its occurrence as a complication of AIDS, participants said. (Extracted from: *International Herald Tribune*, 19 September 1995)

Taking the middle ground from laboratory to plantation

There are two extreme views on the potential benefits of new biotechnology in plantation forestry. In the one view biotechnology is seen as a quick-fix substitute for the long-term grind of conventional tree breeding, and as promising a quantum leap in improving the quality of fibre available to the paper industry. In the other, investment in biotechnology R&D simply diverts limited resources and attention away from the important practical work of traditional tree breeding. As with all such contentious issues, there is a middle ground.

The new biotechnology is not a substitute for conventional breeding in either forestry or agriculture. It is simply an additional tool-kit breeders can use to achieve their objectives more rapidly and efficiently than is currently possible. Since we are only just beginning to domesticate tree species, it is easy to make substantial gains simply by selecting the best seed sources and identifying the best individuals for propagation or seed production. Until these basics are in place it does not make sense to apply expensive new technology—but development lead times are long and we need to invest in R&D now to give us practical options in the future. The funding requirements are complementary, not conflicting.

What can biotechnology offer? A tree breeding programme involves repeated cycles of screening a range of genetically variable families; selection of those which have the highest value according to the defined breeding objectives; and interbreeding these to produce a new set of trees from which to select ones with even higher value. At each generation the benefits of investment in breeding are captured by multiplying the selected trees for clonal plantations or using them to produce seed in orchards. All of these steps take time and cost money and biotechnology can help in the following ways:

- Gene mapping, and the identification of marker genes which are closely associated with those controlling commercial traits (Marker Assisted Selection), can reduce the need for field testing and allow seedlings to be screened for traits such as wood density—which are not expressed until the trees are mature. Accuracy of selection may also be increased. Scientists have demonstrated the potential of this technique, but laboratory costs and skill levels required have so far prevented use in any operational breeding programmes. Markers have other potential uses such as monitoring the genetic diversity in breeding populations.
- Breeding by normal sexual reproduction can only recombine the genes which already exist in the parents. The techniques of Genetic Modification (GM) now allow valuable genes to be transferred between species which are not sexually compatible. Because this is a high cost technology and the pay-back period is inevitably long, forestry has attracted little investment in GM R&D. Nevertheless, there have been a number of field trials of GM poplars and eucalyptus and we can confidently expect some commercial uptake within the next five years.
- Ideally foresters would like to exactly reproduce the very best selected trees on a plantation scale. This can be done with cuttings in species such as eucalyptus, poplars and willows, but not with most of the conifers. There has therefore been much R&D on tissue culture techniques which aim to rejuvenate trees or store samples of tissue taken at the juvenile stage, and then to regenerate large numbers of plants by micro-propagation or embryogenesis. Experience so far has been that while these techniques are useful in rapidly bulking up the numbers of copies of a selected genotype, the final commercial scale propagation is most economically carried out by macro-propagation (cuttings).

Eucalyptus for fibre production

Via joint ventures the Shell Group has established eucalyptus plantations for fibre production, primarily in South America (Chile and Uruguay). Each company manages its own breeding programme supported by a central forestry research unit in the UK. This unit is interested in all these areas of new technology but has identified GM as having the greatest long-term potential to enhance productivity. The first traits targeted for GM are: herbicide tolerance; lignin modification; and cold tolerance.

The concept of GM is simple, but successful implementation requires more than mastery of the science. Techniques must be made available at a cost which makes sense in the framework of forestry investment. Intellectual property issues have to be investigated and we must satisfy both government regulators and the general public that what we are doing is socially and environmentally responsible.

At present the cost of isolating genes *de novo*, or licensing them from the various agrochemical companies, is beyond the level at which any one plantation company with, say 40,000 ha of trees could make a reasonable return on their investment. A consortium approach to R&D presents a solution if it is possible to define equitable conditions for members to commercialize the products. It is also reasonable to invite the downstream users of fibre to share such up-front costs with the tree growers.

It is increasingly common for any development in molecular biology to be protected by patents. Even to make use of your own technological developments you will probably have to pay a variety of licence fees for enabling technology. This is familiar territory in some other industries, but is relatively new to foresters and tree breeders.

Finally, trees will be no exception to the rule that a comprehensive series of field evaluations and assessments will be required before approval to plant on a commercial scale. The general community has raised valid questions about the possible consequences of release of any GM organisms. While surveys indicate that there is relatively less concern about non-food plants, it will certainly be necessary to demonstrate that, for any combination of novel trait/species/growing environment, the risk of negative environmental impact is acceptably low. The chances of successfully managing the introduction of this new technology will increase if the industry is able to develop and support a unified view on responsible best practice.

There is an opportunity to produce an increasing proportion of the world's wood supply from plantations, but the necessary investment will only be made if these are financially viable projects capable of long-term sustainable management. Genetic improvement is one of the key means by which foresters can increase yield, quality and adaptation. Just as in agriculture, forest tree breeding will find ways to benefit from the new biotechnology. The question is not whether we should bother with biotechnology but, since we cannot afford to ignore the opportunities, how do we resource the R&D needed to make these tools widely available in the 21st century? (Extracted from an article by Dr. Rod Griffin in *PPI*, August 1995)

To test or not to test?

The international medical community is considering proposals which would only allow genetic testing of treatable diseases. They also seek to bar potential discrimination on the basis of genetic information.

The Belgian Medical Association presented a draft paper to the recent World Medical Association (WMA) annual council meeting in Bali. Because of the psychological risks, it recommends that genetic tests should only be provided for conditions that have "a therapeutic or prophylactic remedy", such as changing eating habits if at risk of heart disease; or if they could help an affected couple decide whether to have children or abort a diseased foetus.

Other recommendations say that genetic information should be kept strictly confidential, except when the predicted condition might cause danger to other people; and that psychological counselling should be offered before the test, when the results are given and for some time after.

WMA members will debate the Belgian paper over the coming months, and the council will vote on whether to adopt it as a declaration in April 1996. A spokesman stresses that the recommendations are likely to be altered substantially before being adopted.

The WMA represents 64 national medical associations with a total of three million members. Its declarations are not binding, but act as guidelines for doctors on ethical and other issues, and help the associations lobby Governments on changes to the law. (Source: *Chemistry & Industry*, 18 September 1995)

Cancer therapy to account for 90 per cent of the gene therapy market in 1997

Gene therapy is expected to enter the market by 1997, with 70 per cent of the market activity predicted to be in the USA, according to a *Scrip* report published in June 1995, *The Current Status and Future Potential of Gene Therapy.*

The report predicts that initially 90 per cent of the market will be composed of cancer gene therapy but forecasts that, by the year 2000, gene therapy for genetic disorders will constitute 32 per cent of the market with cancer accounting for approximately 48 per cent. It forecasts that therapies for viral/HIV indications will constitute approximately 8 per cent of the market by this time.

The report was compiled using more than 2,000 pieces of information and includes the current status and scope of gene therapy, its future potential, and company information. The ethical, social, and legal implications of gene therapy are also discussed.

For more information, contact Tom Horrocks, *Scrip Reports*, 18/20 Hill Rise, Richmond, Surrey TW10 6UA, UK. Tel. +44 181 332 8966; Fax +44 181 332 8992. (Source: *Microbiology Europe*, Vol. 3, No. 4, July/August 1995)

C. COUNTRY NEWS

Brazil

Bioremediation

Brazilian researchers are currently testing a bacterium developed to eliminate pesticides from soil contaminated over periods of more than 20 years. The project is being conducted by a group of scientists at the nuclear energy research centre (Centro de Pesquisa de Energia Nuclear de Piracicaba) at Piracicaba, Sao Paulo. Sample contaminated soils are genetically modified in laboratories to augment the velocity and intensity of elements that naturally destroy the pesticides over longer periods of time. The project was presented during the Second Latin American Biodegradation and Biodeterioration Symposium held in Gramado, Rio Grande do Sul in April. The symposium was co-ordinated by Dr. Christine Gaylarze, head of the soil department, Faculty of Agronomy, Federal University of Rio Grande do Sul. (Source: *Biotechnology Business News*, 4 August 1995)

Brazil to test transgenic bean

Cenargen (Centro Nacional de Pesquisa de Recursos Geniticos e Biotecnologia), part of the Brazilian Government's agricultural research organization, EMBRAPA, will carry out field tests on a transgenic bean it has developed.

The transgenic version of the bean, Brazil's staple diet, has had its proteins enhanced by the introduction of a gene from the Brazil nut capable of synthesizing methonine. Cenargen isolated the gene in the 1980s but only managed to introduce it into the bean by developing its own technology involving bombarding tungsten microparticles covered in DENA at speeds of over 1,000 miles an hour into the bean cell.

Three generations of bean have been produced so far, but field tests will only begin once Brazil's new law on bio-safety becomes operational. (Source: *Biotechnology Business News*, 4 August 1995)

Canada

NewLeaf potato approved for Canada

Seven genetically engineered foods have been approved for human consumption by Health Canada in the past year. Among them is Monsanto's NewLeaf potato, which has been altered to include pest-fighting genes from the bacterium *Bacillus Thuringiensis* (Bt). The genes protect the plant from the Colorado potato beetle, the potato crop's worst insect pest. Bt itself has been in use for over 30 years to control pests in gardens and by organic farmers.

Agriculture and Agri-Food Canada has also granted environmental safety approval for the NewLeaf, clearing the way for it to be the first genetically engineered whole food product available to the public in Canada. The initial NewLeaf line is a Russet Burbank potato developed by NatureMark Canada. (Source: *AgBiotech Bulletin*, February 1996)

Aquaculture on the rise

Aquaculture is a growing industry in Canada. In 1995, for example, the value of salmon farming in British Columbia was $167 million, compared to $70 million for the traditional commercial salmon catch. There are an estimated 80 active salmon farms in British Columbia, providing direct employment for 1,100 people and indirect employment for 1,000.

The growth in aquacultural enterprises has prompted the British Columbian Government to review the environmental impacts of the industry. The British Columbian review will consider the impact of escaped farm fish on the genetics, health and habitat of wild stock; diseases transferred into wild stock; fish farm wastes; and the effects of aquaculture on the adjacent marine environment. (Source: *AgBiotech Bulletin*, January 1996)

China

Collaboration agreement to develop leukaemia drug

Sang-A Pharmaceutical, a major South Korean drug company, has entered into a co-development agreement with the Pharmaceutical Research Institute of Beijing Graduate School of Pharmacy to investigate Homoharring Tonine (HHT), a new drug for the treatment of leukaemia.

A bioactive substance extracted from a yew tree, HHT selectively acts on G1 and G2, which contribute to cancer cell growth, and thus produces excellent anti-cancer effects, according to Sang-A. When used in combination with an established leukaemia drug, HHT exhibits no crossover resistance, which is why it has very few side-effects.

Currently, Sang-A is conducting last-minute clinical studies of HHT in conjunction with the National Cancer Institute of the United States. Commercial production of the new drug will begin in 1997. (Source: *McGraw Hill's Biotechnology Newswatch*, 18 September 1995)

Côte d'Ivoire

Catfish farming

Africa has no tradition of fish farming; the first such projects date back only 50 years. Early attempts largely failed, because they involved over-sophisticated methods and technology. But yearly fish imports into Côte d'Ivoire amount to approximately 200,000 tons, while domestic fish stocks are declining. In 1979, the Layo experimental aquaculture station was set up on the Ebrié lagoon at Abidjan, by ORSTOM and the Centre de Recherches Océanologiques, in a fresh attempt to develop intensive fish farming.

Research has involved several species, and one has now reached the commercial stage. This is *Chrysichthys nigrodigitatus*, a catfish greatly appreciated locally; demand far outstrips supply, and local wild stocks are in sharp decline. Essentially a bottom-dwelling species, it is also well suited to the slightly brackish lagoon environment of Ebrié.

Research began in a lagoon enclosure with wild stock, the first step being to master reproduction in captivity. By 1984, this was achieved and an initial breeding stock of 450,000 fry were hatched. Methods were gradually improved, and the reproduction rate is now 80 per cent (a female can produce a third of her own weight in eggs). The right conditions then had to be defined and established for each stage in the fishes' development. Then came trials

of commercial-scale production at the Jacqueville fish farm.

At the same time, the Layo centre was developing an artificial fish feed based on by-products from local industry: fish meal from a tuna cannery, cotton meal, broken rice and waste cassava meal.

Today, the Jacqueville farm is a fully independent private enterprise, turning out 200 to 300 tons a year, and a further 30 to 50 tons are produced by independent fish farmers. However, output cannot expand beyond 500-600 tons, since local supplies of raw material for the feed are limited.

Despite some teething trouble on the commercialization side of the project, there is now a network of sales outlets supplying Abidjan with this much-appreciated fish—and the local economy has received a welcome boost. (Source: *ORSTOM Actualities*, No. 48, 1995)

European Union

Demonstration projects in the biotechnology programme of the European Union

The new biotechnology programme includes for the first time support for demonstration projects. Up to 6 per cent of the total programme budget is earmarked for this activity. The intention is to provide an additional mechanism for the exploitation and dissemination of the technology. Indeed, since "seeing is believing", undertaking a demonstration project seems particularly appropriate when the uncertainties and risks associated with innovation might discourage potential users from adopting a newly developed technology. Such uncertainties might appear, for instance, when new biotechnologies have to substitute well-proven existing practices; when there is a need to show compliance with regulatory requirements and market standards; or when the negative public perception of biotechnologies is a deterrent for their application by users.

A general definition of demonstration states that its objective is "to prove the technical viability of a new technology, together with, as appropriate, its economic advantage". Thus a demonstration project is to verify, on a scale of operations representing reality, the different aspects of the new technology which might affect its implementation in the real world. Thus, proving the "technical viability" of a new technology might involve proving its superiority with respect to current practices, its ability to comply with regulations, its validity with respect to standards, its public acceptance, etc. In the context of the biotechnology programme, the second objective of a demonstration project, "proving the economic advantages of a new technology", firstly applies to increased profits for industry but can also be taken in a wider sense to include economic advantages in enhanced efficiency of public services who use the new technologies (e.g., food, health, environment, etc.), or even in a direct contribution of a particular project to improving the public perception of new biotechnologies.

The following characteristics must be evident in a demonstration project:

1. It must be precompetitive in nature.
2. It must show novelty in technological innovation.
3. It must be on the basis of established knowledge without a research component.
4. The partnerships established must include technology producers and users.
5. Proposals should indicate project deliverables and their exploitation, dissemination, etc.
6. Extended audiences of demonstration projects may include industrial platforms, consumer organizations, public authorities, etc.

(Source: *EBIS*, Vol. 5, No. 2, October 1995)

Summary of the EU 4th framework programme and in-vitro testing

The 4th framework programme runs from 1994 to 1998, with a total budget of 12,300 million ECU.

There are four areas of activities:

1. Specific programmes (including life sciences and technologies);
2. Interactions with third world countries;
3. Dissemination of results;
4. Training activities.

Activity 1 includes specific programmes, i.e. on life sciences and technologies. This area has been allocated a total budget of 1,572 million ECU, divided between biotechnology (552 million ECU), biomedicine and health (BIOMED) (336 million ECU) and agriculture and fisheries (684 million ECU).

In the biotechnology programme four areas are addressed:

1. Cell factories;
2. Genome analysis;
3. Plant and animal biotechnology;
4. Cell communication in neurosciences.

Four other areas address:

5. Immunology and transdisease vaccinology;
6. Structural biology;
7. Prenormative research, biodiversity and social acceptance;
8. Infrastructures.

In addition, there are horizontal activities (in areas requiring increased attention to the improvement of technology transfer) and participation in the human frontier science programme.

For full documentation on the 4th framework programme, please contact: CEC, DG XII-E1-SDME 2/3 Biotechnology, Dr. Line Matthiessen, 200 Rue de la Loi, B-1049 Brussels, Belgium. Tel.: 32 2 296 57 74; Fax: 32 2 295 53 65. (Source: *News Release*, November 1995)

EU structural biology activities to be reviewed

The European Commission, in association with the national authorities of Member States, is conducting a survey of structural biology R&D activities in Europe. It is hoped that the information on national programmes and activities will assist the development of further R&D collaboration between EU researchers. The survey results will be published in late 1996. It will include research activities in industry, research institutes and universities. The scope of activities to be included is:

1. Biomolecular folding, modelling and design;
2. Molecular recognition and signalling;
3. Biomolecules of special importance (biocatalysts, antibodies, binding molecules, storage molecules, etc.).

The 1996 report will provide a more comprehensive view of research activities in a wider area of structural biology. (Extracted from *Irish Biotech News*, January 1996)

France

New strategic research programme

The Ministry of Higher Education and Research in France has selected seven areas for life sciences. These areas comprise 14 concerted and coordinated actions for which 14 scientific and research technical committees will be set up. The seven areas are:

1. Genetics. Some of the main objectives in this area include elucidating the function of genomes; reducing the time needed to identify a gene and its function; identification of genes responsible for or predisposing to serious diseases; the mechanisms of the co-evolution of genomes and horizontal transfer of genetic information.
2. Biology of development, reproduction and ageing. Four areas will relate to: embryogenesis, morphogenesis and differentiation; intercellular communication and reproduction; molecular mechanisms; and cellular ageing.
3. Structural biology and pharmacochemistry. The present interface between chemistry, physics and biology should change direction from structural analysis of isolated molecules to molecular interactions and intercellular dynamics of macromolecular systems.
4. Cardiovascular physiopathology and pharmacology. Topics will include: physiopathological mechanisms and pharmacology, biopathology of prions, imagery and neuropathology, and multidisciplinary development of functional imagery.
5. Bioinformatics. The GIS INFOBIOGEN was recently installed in Villejuif and its functions include: development of transfer and service activities, training, coordinating the national network of bioinformatic activities, encouraging the valorization of biological software and data banks produced in France. Two major actions for 1995 are: additional actions within the national centre (INFOBIOGEN) to enhance the coordinated development of regional centres and a call for proposals to encourage the development of bioinformatics.
6. Biotechnology. In spite of prominent and competitive research programmes, biotechnology has not experienced success in France as it has in the United States, Japan, Germany or the United Kingdom. In order to remedy this situation, the Ministry has listed biotechnology as one of its priorities in terms of development and support. The year 1995 will concentrate on five areas: bioconversions, biomolecular engineering, biotechnology and the environment, biotechnology and agrofood, biotechnology and genetics.
7. Environmental science.

(Source: *EBIS*, Vol. 5, No. 1, 1995)

Germany

Centre for Environmental Biotechnology founded

The Ruhr University of Bochum (RUB) is currently establishing a centre for the application of biological methods.

The aim of this centre is to advance the use of biological methods to purify the soil, water and air, and the biological treatment of waste. The transfer centre will primarily advise interested users on application of biological methods in the environment. The new transfer centre at the RUB is one node in a network of four consulting facilities active throughout the country. Besides the RUB, there are Dechema (Frankfurt), TU Hamburg-Harburg Technologie GmbH (Hamburg) and the Environmental Research Centre (Leipzig). Additional nodes are planned for Stuttgart and Greifswald. (Source: *Handelsblatt*, 14 June 1995)

Firms receive award to develop monoclonal-based cancer therapy

Two companies in Munich, Germany, are working together to develop a new monoclonal antibody (Mab)-based therapy for minimal residual disease, which often remains after surgical treatment of solid tumours. The goal is to prevent metastases in cancer patients without using conventional—and highly toxic—chemotherapy.

Mab therapy showed some promise in this area in a five-year survival trial. As a result, the Research Foundation of Bavaria recently awarded almost $3 million to MorphoSys GmbH and Micromet GmbH for their joint programme.

The participants in the collaboration are each developing one aspect of the therapeutic approach. MorphoSys is using its proprietary technologies to develop a panel of optimized human antibody-based therapeutic candidate molecules directed against selected tumour-associated antigens. Micromet, meanwhile, is developing a non-toxic effector mechanism designed to elicit an immune response against targeted cells.

The candidate molecules will be developed consecutively. Clinical trials are expected in the second quarter of 1996. Development of the remaining therapeutic candidates will start in the second quarter of 1996.

The pre-clinical development and the early clinical phases will be conducted by Micromet, in conjunction with the Institute for Immunology at the Ludwig-Maximilian University at Munich. For the later clinical phases, the companies plan to collaborate with partners in the pharmaceutical industry. (Extracted from *Genetic Engineering News*, 15 May 1995)

India

IRRI returns rice germplasm

The International Rice Research Institute (IRRI) has restored to India 5,311 accessions of rice germplasm of traditional rice cultivars from Assam and neighbouring areas of northern India. These cultivars also include valuable genes for insect pest resistance. The original seed was deposited in IRRI 30 years ago by the Assam Rice Collection whose collection has since deteriorated or been lost. For additional information, contact: IRRI-India Liaison Office, C-18, Friends Colony (East), New Delhi, India. Fax: +91-11-692-3122. (Source: *Diversity*, Vol. II, No. 4, 1995)

Biologicals joint venture

Biosys of Palo Alto, California, has signed a memorandum of understanding to set up a manufacturing joint venture in India to export biological insecticide products to Europe. The US company plans to form a 50:50 joint venture with Indofils Chemicals, a member of the KK Modi group. The venture will operate under the

name Modi Biosys India with products marketed by Indofil Chemicals and 50 per cent destined for Europe. (Source: *European Chemical News*, 21 August to 3 September 1995)

Italy

Italian cancer research institute offers catalogue of cell lines collected from all over Europe

A series of databases of biomedical interest, such as human and animal cell lines, human B lymphoblastoid cell lines and synthetic oligonucleotides, has been set up by the National Institute for Cancer Research of Genoa, Italy, together with the Advanced Biotechnology Centre. This latter is an interdisciplinary group of researchers, including medical doctors, biologists and electronic engineers.

The information has been collected from Italian and European laboratories and cell banks. The databases are available on-line, and catalogues have also been produced, available as a printed record and as an electronic catalogue for PCs (IBM compatible).

One of the databases, called Cell Line Data Base (CLDB), contains detailed information on the origin, function, optimal culture methods, availability in cell banks and laboratories of human and animal cell lines. The catalogue contains complete information on 2,650 cell lines, including the cell lines collected in the two main European banks, the European Collection of Animal Cell Cultures (Porton Down, UK) and the DSM Collection of Human Cell Lines (Braunschweig, Germany), and other important collections mainly related to inherited diseases. More than two thirds of the Cell Lines are said not to be described in other commercial catalogues.

Hybridomas and other immunoclones are not described in the CLDB because information in this field is widely available in Europe through the ImmunoClone Data Base. This project, coordinated by the Centre Européen de Recherches Documentaires sur les Immunoclones (CERDIC, c/o CICA, 2229 route des Crêtes, Sophia Antipolis, F-06560, Valbonne, France) and funded by the European Community, involves seven European partners.

Details: Dott.ssa Tiziana Ruzzon, IST, Istituto scientifico per lo studio e la cura dei tumori, Viale Benedetto XV, n. 10, I-16132 Genoa. Tel.: (39) 10 35341; Fax: (39) 10 352999. (Source: *EBIS*, Vol. 5, No. 2, October 1995)

Japan

DNA Industry Forum formed

The Ministry of International Trade and Industry (MITI) has formed a DNA Industrial Forum to prepare measures to promote the industry through the collaboration of academic, industrial and communication sectors. The Forum will promote research efforts and create guidelines for the application of research achievements for industrial purposes. MITI, through studies, will establish a "Future Outlook for the DNA Industry".

The Forum will create policy guidelines for the application of useful biological functions to industrial purposes. The subjects for study include:

1. Research infrastructure such as collection of DNA analysis data;
2. R&D on biosystem analysis and protein structural analysis;
3. Support systems for venture business;
4. Ethics and safety issue.

An interim report of the results of the study will be presented, while the future outlook of the DNA industry will be included in the final report. (Source: *Kagaku Kogyo Nippo*, 4 August 1995)

Japan Energy starts trials with KNI-272

The Japan Energy Corporation announced that it plans to start clinical trials of KNI-272, a new AIDS drug, by the end of this year.

KNI-272 is a protease inhibitor belonging to a new class of anti-AIDS drugs and is expected to be useful as a second-generation anti-AIDS drug. In Japan, it was designated as an orphan drug and is in the pre-clinical stage.

The timing of clinical trials in Japan will be determined depending on the outcome of Phase I and II trials in the United States in 1995.

For marketing in countries other than Japan, the Corporation intends to select marketing partners that boast a strong sales network in each country or region. (Source: *McGraw Hill's Biotechnology Newswatch*, 18 September 1995)

Kazakstan

National Biotechnology Centre attracts international investment

The Government of Kazakstan has recently launched a national scientific programme aimed at the "Utilization of biotechnological and genetic engineering methods in medicine, agriculture and industry". To coordinate the R&D, production and training elements of this programme and to provide a new vehicle for additional funding, a National Centre for Biotechnology, or NTsB, has been created. NTsB is made up of a number of important R&D institutes belonging to the National Academy of Sciences (NAN), the Ministry of Agriculture and major production facilities belonging to the Kazak Ministry of Health (see table). The new Centre received a major boost in April 1995 when the United States announced that it was investing US$ 5.6 million to set up antibiotics, vitamins and pharmaceutical production at a plant belonging to NTsB. Additional substantial investment from other Western countries is in the pipeline.

Kazakstan's biotechnology programme incorporates more than 200 individual scientific projects being conducted at 25 R&D facilities. Its aims include:

- The determination of priorities for R&D and production within the bioindustry;
- The provision of support for fundamental research;
- The conversion of the country's military microbiological facilities;
- The construction of modern GMP-standard biotechnology production facilities;
- The development of international ties;
- The initiation of training schemes to provide a new generation of specialists for the industry.

Kazakstan has succeeded in formulating a well-thought-out national programme for the development of a modern, profitable bioindustry. The country is fortunate to possess some of the most advanced facilities for the manufacture of genetically engineered products in the former Soviet Union, a highly qualified workforce, easy access to the Baikonur Cosmodrome, and a substantial R&D base. In addition, a stable political situation and the presence of proven oil and mineral resources are providing

Table: Facilities within the National Centre for Biotechnology (NTsB), Kazakstan

National Academy of Sciences
- M.A. Aitkhozhin Institute of Molecular Biology & Biochemistry, Almaty

Ministry of Health of Kazakstan
- Science Production Complex *Biomedpreparat*, Stepnogorsk (Akmola *oblast'*)

Ministry of Agriculture of Kazakstan
- Science Research Agricultural Institute, Gvardeiskii

Unknown subordination
- Biocombine, Almaty
- Institute of Pharmaceutical Biotechnology, Almaty a nd Stepnogorsk
- Institute of Physiology, Genetics and Bioengineering of Plants, Almaty
- Medicobiological Institute, Stepnogorsk
- Production Association *Progress*, Stepnogorsk (Akm ola *oblast'*)

The director of the Centre is Murat K. Gilmanov, who can be contacted at Abaya 38, Almaty, Kazakstan. Tel./Fax: +7 3272 670 367.

a solid basis for Western inward investment. Against this background, the prognosis for the successful implementation of Kazakstan's biotechnology programme appears t o be very good indeed. (Extracted from *Microbiology Europe*, Vol. 3, No. 4, July/August 1995)

The Netherlands

Transgenic animals

The Dutch Secretary of State for Agriculture has started a consultation procedure on a draft proposal for rules applying to genetic modification of animals. The draft proposal bans modifications in the hereditary structure of animals unless a permit is provided by the Minister of Agriculture, Fisheries and Nature Management. Scientists working at universities and companies would require such a permit. A committee is intended to deliver an opinion as to whether or not unacceptable health problems or suffering is caused to animals and as to whether ethical standards are exceeded in the case of experiments.

Modifications for which a licence is required are modifications in the DNA structure of an animal or an embryo; the "unnatural" fusion of cells and the transplantation of cell nuclei. No permit is needed for test-tube fertilization, embryo transplantation and embryo-cloning. The draft does not ban the transport of genetically modified animals nor the import of meat of such animals. The draft proposes to leave genetically modified insects used as biological pesticides outside its scope.

Details: Ministry of Agriculture, Fisheries and Nature Management, Direction MKG, dep. Gen W, PO Box 20401, 2500 EK The Hague. Tel.: (31) 70-3793066; Fax: (31) 70-3477552. (Source: *EBIS*, Vol. 5, No. 1, 1995)

TNO develops biofilter using moulds

TNO's (Netherlands Organization for Applied Scientific Research) Department of Environmental Technology has developed a new biofilter that can remove styrene and other harmful hydrocarbons from waste air. The researchers cultivated moulds in a compressed bed with ceramic material. This produced a biofilter which appears to work much better than conventional biofilters with bacteria and compost.

The plastics industry has devoted much attention in recent years to suppressing styrene emissions. Styrene is released primarily during the manufacture of glass fibre reinforced plastic products. The industry has a choice of a number of options to reduce these styrene emissions.

The TNO Department of Environmental Technology has developed a new biological filtering technique that offers a number of advantages over existing bioprocesses. Using this technique, ISEPCo (Inert Support Extreme Physiological Conditions), the moulds grow on an inert ceramic carrier.

One of the advantages is that the moulds are much stronger. For example, they are more resistant to an acidic environment and dehydration. Project leader Dr. J. van Groenestijn believes that the stability of the ISEPCo filter is particularly important. Conventional compost filters usually cease to be effective after three months, for reasons which are not yet entirely clear. However, laboratory experiments have shown that TNO's new mould filter still works perfectly after one year.

One other advantage is the formation of an air mycelium, a network of wafer-thin wires. This creates an extremely large exchange surface area. Furthermore, the decomposition environment using the ISEPCo filter is "dryer" than with a compost filter, which means that hydrophobic substances can reach the active mould more easily. According to Groenestijn, this makes the process highly suited to the decomposition of other substances that dissolve poorly in water, such as benzene, toluene and xylene.

According to TNO researchers, using this method up to 50-80 grams of styrene per cube (filter content) can be removed per hour, with a yield of 90-99 per cent, depending on the process conditions.

TNO is now working on commercializing the filter technique. (Source: *Technisch Weekblad*, 14 June 1995)

Niger

Multidisciplinary millet research in Niger

Millet, an essential food in Niger, provides 73 per cent of the country's grain output. It is an undemanding crop that can thrive with a short rainy season, but yields are low and very variable. In recent years, Niger has suffered severe food shortages due to drought, and ORSTOM has set out to improve yield and drought resistance in millet.

Along with field research, the programme involves ORSTOM's high-technology laboratories in Montpellier, and the Niamey Plant Genetics Laboratory in Niger. It involves collaboration with international and Niger organizations and also provides training internships.

A first step, with funding from FAO, IBPGR and ICRISAT, was to collect samples of the huge number of wild and cultivated West African millets that constitute the crop's gene pool. Three thousand samples are now conserved at ORSTOM's Montpellier centre.

There are three elements to the work:
- Genetic studies, to make maximum use of available diversity in terms of drought resistance, phenology, etc.;
- Morphophysiological study of the millet plant, to discover how it reacts to drought at different stages of development;
- Other factors governing yield in field conditions, with emphasis on husbandry methods, e.g. the timing of cultural tasks, length of fallow periods, planning density, associated crops, use of organic manure from stock grazed on the stubble.

Among the findings so far:
- When drought sets in at the flowering and grain formation stage, millet slows down flower production and concentrates on filling out the most developed ears. This is why, in drought years, varieties that produce few ears give a reliable yield while potentially high-yield varieties underperform.
- Animal droppings, because they roughen the soil surface, reduce capping and wind erosion and help infiltration and water retention in the arable layer.
- Some wild millets are apomictic; it may be possible to transfer this trait to cultivars, while some naturally apomictic species could prove especially useful as forage crops.

The researchers have also developed a computer program called Milstress, which models whole-plant reactions to drought, day by day, according to moisture balance. Though it has yet to be validated in field conditions, Milstress will be useful in comparing cultivars with different morphological and phenological traits. (Source: *ORSTOM Actualities*, 1995)

Russia

From SCP to mycoprotein. Is biotechnology set to feed the Russians?

Russian biotechnologists have announced plans to begin production of microbial protein for direct human consumption. Initially, two major facilities belonging to the bioindustry will have newly developed technologies installed and are expected to begin production of the protein biomass soon. If this pilot project is successful, additional plants will subsequently be switched over to production of microbial protein. The eventual aim is to produce 2 million tons per annum of the new product. If these plans are fully realized, biotechnology may make a significant contribution to eliminating protein deficiencies in Russian diets. (Extracted from *Microbiology Europe*, Vol. 3, No. 5, September/October 1995)

Sweden

International institute established to offer evaluations in biotechnology

The Stockholm Environment Institute has established an international Biotechnology Advisory Commission (BAC). On request, this group will provide national authorities with impartial advice to evaluate the applicability and safety of biotechnologies. Members of the BAC are based in 11 different countries, both developing and industrialized, with many years of experience on scientific, economic and legal issues regarding biotechnology research and development. The members have been drawn from the public and private sectors and provide expertise in the fields of applied ecology, ecological genetics, microbial ecology, microbial biochemistry, molecular biology of plants and micro-organisms, molecular genetics, entomology, genetics, marine biotechnology, plant breeding, plant pathology, international environmental and regulatory law, and economics.

The BAC is prepared to assist with the risk and benefit analyses of proposed specific introductions of GMOs, through independent reviews.

Details from: Stockholm Environment Institute, Lilla Nygatan 1, Box 2142, Stockholm, Sweden. Tel.: (46) 8 723 02 60; Fax: (46) 8 723 03 48. (Source: *EBIS*, Vol. 5, No. 1, 1995)

United Kingdom

UK needs new monitoring body

British members of parliament are calling for a special commission to monitor developments in genetics and biotechnology, and to oversee how they are applied. The ethical and political implications of genetics should not be entrusted wholly to industry, insurers and local authorities, they say.

The House of Commons Science and Technology Committee is worried about the "patchiness" of regulations covering the use of genetics in medicine and insurance. An independent Human Genetics Commission (HGC) would plug many of the gaps, it says in its new report.* This would absorb the Gene Therapy Advisory Committee, currently attached to the Department of Health, which approves gene therapies and screening techniques, and advises local health authorities on ethical issues.

The HGC would control whether companies offering genetic screening are providing the appropriate services to the right people. "There is a very real danger that unscrupulous companies may prey on the public's fear of disease and genetic disorders and offer inappropriate tests", the report warns. The HGC would also act as a central body to ensure that all the regional authorities of the National Health Service can provide genetic services.

The Committee is also concerned about privacy issues raised by genetic testing. Insurers and employers might use genetic profiles to deny insurance policies or jobs to people who are likely to suffer ill-health, it says. The report argues that a person's genetic code is their property: no one should be forced to disclose such information, and it should not be grounds for discrimination.

Patents represent another thorny issue. The Committee thinks that human genes and gene fragments should only be patentable if the application includes a new, industrial use. However, it adds, the HGC should have the power to decide which applications are patentable by monitoring developments world-wide. It also recommends that the European Patent Convention should be redrafted so that genetics patents can be challenged if their claims are too broad. (Source: *Chemistry & Industry*, 7 August 1995)

Agreement with Argentina to implement UN programme

Argentina and the United Kingdom have signed an agreement to implement the UN Programme for the Environment (PNUMA) on biotechnological security rules and regulations that has yet to be approved internationally.

* "Human genetics: the science and its consequences". HMSO.

As these guidelines are already a part of a project, the two Governments decided to implement them "bilaterally" and promised to "encourage other countries to adopt similar measures". Consequently, "activities that involve new organisms (that have been created in a biotechnological form) in the two countries will be developed in accordance with general principles of evaluation and the control of risks as established" in the PNUMA project.

Argentina and the United Kingdom will "quickly" establish "voluntary mechanisms through which any transfer of new organisms from one country to another will be accompanied by information about its characteristics or behaviour".

The agreement states: "In some cases a prior agreement can be a precondition established by the receiving country before making the transfer" in order to prevent major risks.

These rules and regulations were implemented in October 1995, and at the beginning of 1996 a joint regional seminar will be held to exchange "experience and information" on biotechnology. (Source: *TELAM*, 8 September 1995)

United States of America

Application for release of transgenic arthropod

The first application to release a transgenic arthropod has been submitted by a University of Florida scientist to the USDA. It is an engineered mite that feeds on other mites. USDA action on this application will set the precedent for oversight of this new group of engineered organisms. The Union of Concerned Scientists is urging the Agriculture Department to delay any decision on the mite for 90 days to allow more scientific input and public participation in the decision process. For additional information, contact: Rich Hayes, Union of Concerned Scientists, Washington Office, 1616 P St., NW, Suite 310, Washington, DC, 20036, USA. Tel.: +1-202-332-0900. Fax: +1-202-332-0905. (Source: *Diversity*, Vol. II, No. 4, 1995)

National Academy of Sciences panels find dramatic decline in marine life—call for a 10-year biodiversity research programme

The National Research Council (NRC) of the US National Academy of Sciences has called for a 10-year research programme on marine biodiversity which, if financed, could provide policy makers with crucial information on the seriously threatened diversity of marine life and how best to conserve it. Such new information could lead to enhanced and sustained use of marine organisms for food, mineral resources and biomedical products, while at the same time preserving the diversity and functions of the sea.

Knowledge about marine genetic resources would also be greatly enriched if the programme is successful. Such knowledge, biological scientists assert, is urgently needed because of the dramatic decline in marine life. They point to a 1994 report by the Food and Agriculture Organization of the United Nations (FAO) warning that fishing stocks around the world are facing depletion.

Social unrest is already evident in communities wherever the fishing industry has been destroyed. The depletion of fishing stocks, the destruction of coral reefs, the pollution of wetlands and the erosion of shorelines are also disturbing the balance of life within the sea's 70 per cent of Earth's surface.

"Critically inadequate knowledge"

Even basic descriptions of marine biodiversity lag far behind those for the terrestrial species. The report, prepared by a group of 11 marine scientists, stresses "the critically inadequate knowledge of the patterns and the basic processes that control the diversity of life in the sea".

Marine scientists are regularly discovering vast numbers of previously undescribed species in familiar oceanic habitats such as coral reefs, bays and estuaries. At the same time, however, they are also witnessing the disappearance of species discovered only a few years ago.

The NRC report outlines a revolutionary research agenda that "proposes a fundamental change in the approach by which biodiversity is measured and studied in the ocean". The research challenges would be addressed by both large and small groups financed through peer-reviewed grants from various agencies. The ambitious programme will require major new funding that will have to be assured over 10 years, according to the report, and would supplement existing programmes and resources from federal, state and private sources.

An essential component of the programme relies on the role of taxonomists. As the report acknowledges, this could prove the Achilles' heel of the total programme.

To compensate for the dearth of taxonomists, the report suggests developing a cadre of parataxonomists, such as those who work on identifying plants at INBio in Costa Rica. (Extracted from *Diversity*, Vol. 11, No. 4, 1995)

Field testing following notification

In August, the Animal and Plant Health Inspection Service of the US Department of Agriculture (APHIS, Washington, DC) announced proposals that would allow field testing of most genetically engineered plants to occur following notification, rather than after the granting of a permit. According to APHIS estimates, this would save applicants approximately 95 per cent of their administrative costs. Furthermore, the proposals would reduce the reporting requirements for field trials conducted under notification.

Currently, the regulations require that introductions of most plant species be done under permit from APHIS, with applications for permits evaluated on a case-by-case basis. Since 1987, APHIS has issued over 560 release permits and over 1,280 movement permits, most of them for plants.

APHIS plans to extend the notification procedure to most other plants. The main exclusions from the procedure will be plants listed as weeds or parasitic plants. In addition, there will be some restrictions on the type of plant virus sequences that can be included in any constructs administered under the notification scheme. To ensure that introduced genetic sequences do not pose a significant risk of the creation of any new plant virus, plant virus-derived sequences must be non-coding regulatory sequences of known function. Alternatively, they can be antigen genetic constructs—derived from plant virus genes that are prevalent and endemic in the area where the introduction will occur—that infect plants of the same host species and that do not encode any functional noncapsid gene product responsible for cell-to-cell movement of the virus.

Based on trials to date, APHIS estimates that about 99 per cent of all field trials could now be conducted under notification procedures if its current proposals are accepted. (Source: *Bio/Technology*, Vol. 13, October 1995)

TECHNOLOGY AND INVESTMENT OPPORTUNITIES

TECHNOLOGY OFFERS

"SIMBIONT" PREPARATION

Biological mycorrhizal formula using fungi. Ecologically clean plant growth stimulator.
Techno-economic advantages: Increases yield capacity of crops by 30 per cent, enlarges leaf surface by up to 25 per cent (e.g. tea and tobacco) and root system by 100 to 200 per cent.
Application areas (uses): Agriculture (seeds, grain, vegetables and fruit).
Environmental aspects: Increases humus content of soil, strengthens disease resistance and is 100 per cent ecologically safe.
Degree of development: Patented: Patent No. 370932 of 6 December 1972 in Russia. Produced under laboratory conditions on an experimental scale. Small lot sale is organized.
Production capacity: Recommended economic scale: 300 litres per year. Unit market price in Russia US$5 per 1 ml.
Inputs: Raw material, utilities, etc.: 3 cubic m of water per 24 hrs. and 350 kwt power per 24 hrs.
Land/building (sq.metres) Indoor: 1,000 Manpower: 15 skilled, 15 unskilled
Project cost (in US$, excluding land, building and labour): US$ 2,000,000 Equipment/Machinery (FOB): US$ 550,000
Terms of Transfer: Joint venture

(For further information, please contact: Mr. Vitaly Koleshnikov, Executive Director, International Foundation of Science, Culture, Economics, 13/7 Prechistenka Street, 119034 Moscow, Russia.)

ASSAY KITS FOR WATER, FOOD, FISH AND SHELLFISH

Two licensable technologies are offered: (1) A portable and user-friendly immunoassay kit to detect cancer-causing toxins (microcystins) in water, fish and algae-based health foods. (2) A patented US Patent No. 5-180665, Canadian Patent No. 2055935) rapid and highly sensitive enzyme assay for diarrhetic shellfish poisoning toxins and microcystins.
Main use: Analysis of drinking and recreational water, food, fish and shellfish for the presence of microcystins and diarrhetic shellfish poisoning toxins.
Main advantages: Rapid, sensitive and cost-effective
Degree of Development: Laboratory or prototype
Know-how available: Yes
Technology is available for license but is covered by patent protection

(For further information contact: Dr. Ram Mehta, President, Prairie Biological Research Ltd., 4290-91A Street Block C, Edmonton AB, T6E 5V2 Canada, Tel: 403-450-3957; Fax: 403-450-3960)

FUEL PRODUCTION BY IMPROVED BIOCONVERSION PROCESSES

Global depletion of oil reserves leads to examination of the technoeconomics of biomass as a renewable energy source. Sugars, starches and cellulosics, especially agricultural and forestry waste residues (straw, manure, sawdust, paper sludge) are potentially viable sources. At present, the two promising conversion routes are by fermentation to produce ethanol or methane.
Main use: (1) Ethanol process by packed bed reactor technology. Yeasts which are used to continuously ferment carbohydrate solutions to ethanol. (2) Methane process by two-stage anaerobic codigestion. The production of methane from carbon substrates (waste carbohydrates in general) is maximised by optimisation of one or two factors.
Degree of Development: Laboratory or prototype
Technology available for license

(For further information, please contact: Dr. M. Moo-Young, Department of Chemical Engineering, University of Waterloo, Technology Transfer and Licensing Office, Needles Hall, Room 3005, Waterloo ON, N2L 3G1 Canada; Tel: 519-888-4058 Telex: 069-55259; Fax: 519-746-3575)

BIOMASS CONVERSION BY WATERLOO FAST PYROLYSIS PROCESS (WFPP)

A fast flash pyrolysis process using fluidised bed reactors has been developed which can convert organic waste such as forest wood waste, agricultural waste and minicipal waste into pyrolysis fuel oils. The WFP process gives very high liquid yields compared to other methods and can use the gases generated to sustain the conversion process after initial start up. Further refinement steps can be carried out on the pyrolysis oils to produce specialty chemicals, ethanols and fermentation sugars.
Main use: Conversion of forest wood waste into liquids. Agricultural waste (such as corn stocks and bagasse) into liquids. Conversion of rummer and other organic industrial/minicipal waste, including sludge into liquids.
Main advantages: A process demonstration unit has been built and tested to convert peat into activated carbon. Laboratory scale units are operational and tests can be carried out on samples. Liquid yields and liquid composition analysis reports for a fee.
Degree of Development: Laboratory or prototype
Preliminary information only.

(For further information, please contact: TheDirector, University of Waterloo, Technology Transfer and Licensing Office, Needles Hall, Room 3005, Waterloo ON, N2L 3G1 Canada; Tel: 519-888-4058 Telex: 069-55259)

DIAGNOSTIC KIT FOR BRUCELLOSIS

A product/process technology to diagnose brucellosis infection in humans and cattle. Defined monoclonal antibodies applied in Enzyme Linked Immunoabsorbent Assay (ELISA) will discriminate between Brucella A and M antigens and will identify reactive bacteria, including E.coli 0157, Salmonella N (0:30). and *Yersinia enterocolitica* (0:9). The technology incorporates proprietary molecular knowledge of Brucella systems recorded in 25 NRC publications.

Main use: Biotechnology firms, pharmaceutical companies and manufacturers of human and veterinary diagnostic equipment will be interested in this opportunity.

Main advantage: Competitive techniques use inferior polyclonal approaches incorporating poorly defined antibodies.

Degree of development: Laboratory or prototype

Know-how available: Yes

Available for license

(For further information, please contact: Mr. Arvind Chhatbar, Licensing Advisory Officer, National Research Council, Intellectual Property Services, Office Building M-58, Montreal Road, Ottawa ON, K1A 0R6 Canada; Tel: 613-990-9550; Fax: 613-952-6082)

DEVELOPMENT OF ALFALFA VARIETIES WITH HIGH WINTER HARDINESS

Development and implementation of selection and bioengineering to increase winter hardiness in alfalfa (*Medicago sativa*). The process calls for the use of new technologies in molecular biology and of biotechnologies whereby hardiness genes are inserted directly into poorly cold resistant plants that have otherwise interesting agronomic characteristics.

Main use: Development and implementation of selection and bioengineering to increase winter hardiness in alfalfa.

Main advantages: Growers, dealers, distributors and trades people in the seed business.

Degree of Development: Laboratory or prototype

Technology available for license

(For further information, please contact: Mr. Michel Germain, Soils and Crops Research Development Centre, Agriculture and Agri-Food Canada, 2560 Hochelaga Boulevard, Sainte-Foy PQ, G1V 2J3 Canada; Tel: 418-657-7980; Fax: 418-648-723;1 E-mail: germainm@em.agr.ca)

PROCESS FOR LONG-TERM STORAGE OF JERUSALEM ARTICHOKE TUBERS

The Canadian Department of Agriculture has developed a process for 12 months storage of Jerusalem artichoke tubers. The details of this low-cost know-how process will be revealed to those companies requesting and signing a confidential disclosure agreement.

Degree of Development: Laboratory or prototype

Know-how available: Yes

Technology available for license

(For further information contact: Mr. F. Yassa, Assistant Director, Agriculture Canada, Industrial Relations Office, Research Branch, Building 60, Central Experimental Farm, Ottawa ON, K1A 0C6 Canada; Tel: 613-759-1000; Fax: 613-759-7768)

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ATCC Workshops and Conferences

The American Type Culture Collection (ATCC, which is a non-profit organization set up as an international repository for biological cultures, provides education in the field of microbiology as part of its mandate. The ATCC's Laboratory Workshop Programme offers "hand-on" training programmes, with at least 50 per cent of each workshop involving hands-on training, and the remainder devoted to lectures. The following is a selection of the workshops offered by the ATCC. Those readers interested in more information on these workshops may apply to the contact address given below.

- Downstream Processing, Recovery and Purification of Proteins
  (18-20 September 1996)
- Fermentation Microbiology
  (24-27 September 1996)
- Microscopy/photomicrography
  (2-4 October 1996)
- Growth of Animal Viruses
  (9-11 October 1996)
- Freezing and Freeze Drying of Microorganisms
  (15-18 October 1996)
- Hybridoma Technology and Monoclonal Antibody Product Development
  (4-7 November 1996)
- Advanced Recombinant DNA Techniques and Application
  (11-15 November 1996)
- Polymerase Chain Reaction (PCR) Applications/Cycle DNA Sequencing
  (19-22 November 1996)
- In Vitro Toxicology: Techniques and Applications
  (3-6 June 1997)

For information of ATCC workshops contact:

ATCC
Workshop Coordinator
12301 Parklawn Drive
Rockville, MD 20852, USA

Tel.: (800) 359-7370 or (301) 231-5566
Fax: (301) 816-4364
ACTT Internet address: http://www.atcc.org/workshops/workshop.html

D. RESEARCH

Research of human genes

Transgenic mouse produces monoclonal antibodies

The joint research team of Olympus Optical Co. Ltd., the International Medical Centre, and the Tokyo University's Medical Science Research Institute (MSRI), have successfully developed a method for the production by mice of a monoclonal antibody with which the "HLA types", the types of human leucocytes, could be determined. The HLA type determination is indispensable for transplant treatment.

At present, antibodies must be taken from the blood of pregnant women, a considerably involved and tedious way to collect antibodies. With the development of the new production method for uniform monoclonal antibodies that would permit the distinction between minutely different HLA types, the HLA type determination should soon be automated for assuring quick results.

Human cells, such as leucocytes, have on their surfaces a protein named HLA which assumes different types specific to individuals. For the transplant of bone marrow or an organ, it is crucial that the HLA type of a patient, or a donee, exactly matches with that of a donor. The research team tried to mass-produce the antibody associated with a specific type of HLA. First, a mouse's egg was fertilized by *in vitro* fertilization and a certain HLA type-producing gene was inserted into the egg. The egg was transplanted into the uterus of a temporary mother which eventually gave birth to a transgenic mouse carrying the human HLA. This mouse was then injected with a cell that could produce HLA of another type. Because the previously inserted HLA and the later injected HLA were of different types, the transgenic mouse would recognize the second HLA as a foreign object and begin to produce an antibody against the second HLA. The research team removed cells of this mouse's spleen where the antibody was produced. The monoclonal antibody that would tie up HLA of a specific type was produced through the cultivation of these cells. The group was able to produce more than 10 kinds of these antibodies by changing the type of the injected HLA. There are so many types of HLA that the probability of two individuals, except when the two are siblings, having a complete match for their HLA types is one out of several tens of thousands.

For the determination of the HLA type of a patient, antibodies that work against known types of HLA are used to see which antibody will bond with the patient's blood cells. Today, these antibodies are made with blood taken from pregnant women. However, because these antibodies are mixtures, it requires training and experience to make judgement on the HLA type. In addition, it takes several hours before one obtains the result, so that it is difficult to use these antibodies before dealing with an emergency transplant case. In contrast, monoclonal antibodies are uniform and pure, so that they can be easily used for HLA type determination. The research team also test-produced an automatic HLA analyser with the new monoclonal antibody, and confirmed that determinations can be made in approximately 10 minutes.

In order for this device to be used for actual HLA type analysis, at least approximately 60 antibodies need to be prepared. Therefore, the group must try to produce more monoclonal antibodies to be able to deal with many different HLA types. (Source: *Nikon Keizai Shimbun*, 8 May 1995)

Scientists close in on cause and possible treatment for Alzheimer's

Researchers world-wide may finally be homing in on the cause—and therefore the treatment—of Alzheimer's disease. The still mysterious malady is now the third largest medical problem in the United States alone, afflicting some four million people at an annual cost of more than $50 billion.

The only definitive diagnosis of the disorder is available at autopsy, when plaque containing abnormal β-amyloid protein is found wrapped around brain cells. Since it is now widely recognized that amyloid deposits are involved in the development of the dementia characteristic of the disease, much current research aims at understanding amyloid formation and trying to inhibit it.

The latest data was provided by a British team led by Dr. Mark Pepys, professor of immunology at the Royal Postgraduate Medical School in London. They recently described the function of an associated protein, called serum amyloid P component (SAP). Long ignored by other scientists, SAP apparently is intimately bound to β-amyloid in amyloid deposits and protects it from attack.

Based on many *in vitro* experiments, the British researchers hypothesize that normal SAP protects the abnormal amyloid fibrils from the body's natural tendency to get rid of them—but they claim that SAP can be removed.

Toward this end, the British team is now working with Hoffmann-LaRoche (Basel, Switzerland), screening the company's entire library of 125,000 compounds. This research will be followed, they hope, by drug discovery and development.

Studies by Picower Institute for Medical Research (Manhasset, NY) researchers show that a common reaction product between proteins and sugars occurs in higher amounts in the brains of Alzheimer's patients. These sugar-derived end products can accelerate the formation of amyloid fibres, which, in the test tube, closely resemble the amyloid plaque found in such patients' brains. The researchers are working on substances to prevent the formation of the fibres in the first place and at the same time seeking pharmacologic ways to induce the removal of the material once it is formed.

Most important, perhaps, is understanding the normal waste-removal process that enables most people to get rid of amyloid protein in the brain. Studies at Gliatech (Cleveland, OH) show that amyloid normally can be destroyed by enzymes and certain cells. When proteoglycans bind to the protein, however, the resulting complex becomes resistant to enzymatic breakdown as well as to destruction by the scavenger cells.

The researchers theorize that what triggers Alzheimer's disease is as follows: the levels of the key protein within the brain are determined by the rates of both the formation and removal of the protein. A change in this balance can lead to an accumulation of amyloid plaque, which is eventually transformed into the dense senile

plaques found associated with dying neurons in Alzheimer's disease. Central to the process is the activation of the glial cells, which causes a release of a variety of molecules, including proteoglycans. They believe these proteoglycans bind the nearby amyloid protein and keep it from being broken down—leading to senile plaque formation. But, goes the theory, the proteoglycan binding to amyloid can be reduced "allowing for degradation of the amyloid peptide and slowing of the disease process".

Researchers are taking a variety of approaches to attacking the Alzheimer's disease process, but most are in some way linked to the apo E polymorphism. In one of the latest research advances, a team led by Judes Poirier at McGill University found that Alzheimer's patients who did not carry the apo E4 allele, the so-called "bad" form of the protein, responded dramatically to Cognex, a medication that increases the amount of the nerve messenger acetylcholine in the brain. Neurons producing the brain chemical degenerate in Alzheimer's patients and the chemical is crucial to learning and memory.

Another retrospective study by Martin Farlow at the University of Indiana found the same correlation between the apo E genotype and the response to Cognex. The exact role of apo E itself is still not understood, but the protein is made mainly in the liver and it shuttles cholesterol among the body's cells. It is also produced in the brain, and there it has been linked to regeneration and repair of neurons, among other possible roles. Recently, for example, Alan Roses' group at Duke University found the protein in the post-mortem brain tissues of normal non-demented individuals as well as in the tissues of Alzheimer's patients. Apo E has also been found in the amyloid plaques of the disease, and the protein has been implicated in the formation of tangles in the brain that are composed of a mutated form of a common protein called tau.

Two years ago the Duke University group reported a link between apo E and Alzheimer's disease and since then many studies have verified the original finding. The three forms of apo E, 2, 3, and 4, are now linked to different probabilities of getting the disease: in the worst case two doses of apo E4 are associated with the highest risk. Yet the picture is complicated. Because there are three alleles of the same gene, there are six possible combinations of apo E, and form number two may even protect against the disease. Furthermore, some ten per cent of individuals with two doses of apo E4 will not get the disease.

Some experts estimate that roughly 40 to 60 per cent of Alzheimer's disease patients are apo E4 carriers: and 80 per cent may carry at least one dose of E3.

Other groups are devising ways to prevent the deposition of the small protein called AB peptide that is the main component of the amyloid plaques of Alzheimer's. And still other groups are testing new compounds that increase the production of acetylcholine or corticotropin releasing factor in the brain, or regulate calcium in neurons.

Possibly a definitive treatment for Alzheimer's may require several approaches, mirroring the disease itself. (Extracted from *Genetic Engineering News*, 1 June 1995 and *McGraw Hill's Biotechnology Newswatch*, 1 January 1996)

Songbirds hold a clue to memory loss

Bird brains could prove to be a most unlikely source of information about Alzheimer's disease. A protein that may help songbirds learn to sing is similar to the protein found in plaques in the brains of Alzheimer's sufferers, report US researchers.

Male zebra finches are taught how to sing by a tutor, usually their father, when they are about a month old. It takes about two months of learning and rehearsing before the finch is up to scratch.

During this tuition period, the University of Illinois researchers found abundant amounts of a particular protein in the parts of the birds' brains that control song. After the bird becomes fluent, the gene that controls expression of the protein is abruptly switched off and the levels of protein decline, remaining constant into adulthood. Team leader David Clayton calls the protein synelfin.

Significantly, synelfin has a human analogue; it is one of the two intrinsic components of the characteristic plaques that accumulate in the brains of Alzheimer's disease patients. The other is amyloid precursor protein.

Clayton has also highlighted another link between synelfin and Alzheimer's. Synelfin bears a strong resemblance to a group of proteins called apoliproteins. These are carriers of fatty substances, such as cholesterol. One version of the gene that expresses one apoliprotein has recently been shown to predispose its bearers to develop late-onset Alzheimer's.

Clayton's team is now testing different versions of synelfin on transgenic mice to see the effects on memory and learning. (Source: *Chemistry & Industry*, 21 August 1995)

Kyoto University develops early diagnosis method for dementia identifying DNA defect

Assistant Professor Yasuhisa Fujibayashi's research group at the Faculty of Pharmacy, Kyoto University, developed a new method that could derive an early diagnostic method for dementia which could not be detected unless it was in its advanced stage. According to the new method, a patient's DNA (deoxyribonucleic acid) in mitochondrion, a small energy-generating organ in a cell, is examined. If it is found that the DNA is full of defects, then the patient is diagnosed to be soon suffering from dementia. The group confirmed the effectiveness of this method with mice. Assistant Professor Fujibayashi says "The same method may be applied to humans."

The research group had raised a group of mice in such a way that they would age faster than normal mice and show signs of memory impediment. The brains of these mice as well as the brains of normal mice were removed from the animals, and DNAs in mitochondria from the brains were examined. As a result, the group found that the DNA defect rate for the aged mice was 0.092 per cent, which was more than three times greater than the rate of 0.027 per cent for the normal mice.

Mitochondrion, a small organ existing in a cell, is responsible for oxygen breathing. This organ is considered to be a separate life-sustaining body that happened to settle within a cell in the process of evolution. Mitochondrion has its own DNA, different from cellular DNA. Mitochondrion's DNA is prone to damage, and it is suspected that damaged genes produce strong toxins, such as oxygen radicals, to cause senility and dementia.

It has not yet been conclusively determined that the defects in the DNAs of mitochondria from cranial nerve cells are the cause or the effect of dementia. However, Assistant Professor Fujibayashi speculates "Since it is certain that dementia is somehow associated with the DNA's defects, I wonder if the presence of the DNA's

defect or the oxygen radical may be used as a marker for diagnosis." (Source: *Nikkei Sangyo Shimbun*, 17 April 1995)

Geron reports first cloning of human telomerase

Geron Corporation of Menlo Park, CA, has reported the first cloning of the RNA component of human telomerase, demonstrating that telomerase inhibition leads to cancer cell death.

In collaborative research carried out by scientists at Geron and Cold Spring Harbor Laboratory, the human telomerase RNA (hTR) was successfully cloned using immortalized kidney cells. It was subsequently found that these cells contained elevated hTR levels.

When the cloned gene was used to inhibit telomerase, proliferation of human cancer cells was also inhibited after a short period of growth and tumour cell death resulted.

The Geron and Cold Spring Harbor Laboratory research teams have also cloned and characterized the mouse telomerase gene, which will provide a key experimental tool for further research. (Source: *Biotechnology Business News*, 1 September 1995)

Genetics holds out hope for obesity

A storm of publicity has accompanied research showing that fat mice get thinner when injected with genetically-engineered protein. The biotechnology company Amgen has enjoyed healthy share gains ever since it made the work public, while hundreds of overweight people have been offering themselves as human guinea pigs.

The market potential is huge. In the US, a third of the population is obese. In the UK, this figure is about one in 20. The dieting industry is worth millions of dollars. The company says that clinical tests could start in a year; a marketable product could follow in up to five years.

Amgen has paid the Rockefeller University in New York for an exclusive licence to the so-called obesity (ob) gene. The agreement allows the company to develop and sell products based on the gene. The Rockefeller team have shown that the protein expressed by the ob gene is present in the blood of mice and humans, but is missing from mice with a mutated ob gene. These animals are very overweight, diabetic and inactive, with low metabolic rates and body temperatures. The team calls the protein leptin, from the Greek word *leptos* meaning thin.

The New York scientists reported that ob mice lose 30 per cent of their bodyweight, mostly in body fat, after two weeks of daily injections of recombinant leptin into the brain. Twice-daily injections in normal mice resulted in a 12 per cent weight loss, decreased food intake and a 16 per cent reduction in body fat.

The researchers concluded that leptin acts like a hormone in regulating body fat stores and body weight. They believe that leptin signals to the body that there is too much fat. The body responds by eating less and speeding up energy consumption. Both mouse and human leptin gave the same results.

An independent Amgen team injected obese and lean mice daily for 28 days with leptin. They reported that the obese mice lost body fat, ate less and took in less glucose and insulin, and their body temperature, metabolic rate and activity increased. The lean mice showed a smaller weight loss and no change in metabolic rate.

The teams' next goal is to track down the target sites for leptin in the brain. (Source: *Chemistry & Industry*, 3 July 1995)

Research on animal genes

RLGS-based positional cloning method

Y. Hayashizaki and his research team of Riken Tsukuba Life Science Centre (The Institute of Physical and Chemical Research; Riken) have succeeded in identifying the *reeler* gene that is responsible for the phenomenon in which non-differentiated nerve cells move to specific positions, differentiating, and forming brain layer structures, in the process of three-dimensional structural formation of the brain of higher animals.

This *reeler* gene is the causative gene of the mouse *Reeler* mutant, in which the regular brain layer structures are perturbed. The brain is formed through the process of undifferentiated brain cells migrating to their prescribed positions and becoming the various functional nerve cells. A group of cells known as pioneer neurons among the non-differentiated cells move to the brain surface (pia matter), and non-differentiated cells follow these cell groups and undergo differentiation. The non-differentiated cells, which move later, continue to migrate to the cortex by crossing over the cells which have already differentiated, terminate movements, and develop in the required positions. Therefore, in the brain of higher animals, the brain layer structure is formed by nerve cell orientation.

The *reeler* mouse mutant is the phenotype in which the migration of these non-differentiated cells has been disturbed. This mutant mouse brain lacks movement of these non-differentiated cells, so the brain layer structure is not formed and diverse nervous disorders become apparent such as the loss of muscular coordination.

The cloning of the *reeler* gene that is responsible for this physical disorder had been regarded as an indispensable step to the clarification of the mechanism of shift and differentiation of non-differentiated cells.

The research institute has been engaged in research to develop a restriction landmark genomic scanning (RLGS) technique to scan genomes and pinpoint restriction enzyme cutting parts on genomes as a landmark. The deduced amino acid sequence of the *reeler* gene product isolated in this research indicates that the *reeler* gene product is an extra-cellular matrix protein with epidermal growth factor (EGF) type motif manifested by pioneer neurons. Expressing this molecule determines the direction of migration of the non-differentiated nerve cells to enable the formation of the layer structures of normal brains. The base sequences identified to the 5,000 base pair parts at the lower-stream side of the total length of 12,000 base pairs, and is usable for function clarification.

Isolating and identifying the *reeler* gene has clarified that the protein generated by the gene prescribes the direction of movement of non-differentiated nerve cells and creates normal brain layer structures, and may resolve the mechanism of generation of the three-dimensional layer structures of the brain.

Further details from Tsukuba Life Science Centre, Genome Science Laboratory, 3-1-1, Takano-dai, Tsukuba City, Ibaraki, Pref. 305, Tel.: +81-298-36-9145, Fax: +81-298-36-9098. (Source: *Jetro,* August 1995)

Scorpions provide protein scaffold

Natural selection has made scorpion venom protein into an ideal platform for engineering new proteins, according to scientists from Commissariat à l'Energie Atomique in Paris.

Scorpions have evolved many different toxins, but they are all based on a 37 amino acid peptide called

charybdotoxin. This contains all the commonest structural features found in proteins, and is locked into shape by three sulphur-sulphur bonds, buried inside the core. These properties make charybdotoxin such a perfect scaffold, explains team leader Claudio Vita. If the vital bonds are not disturbed, the rest of the molecule can be altered by attaching side chains or switching amino acid sequences, without changing the peptide's basic shape.

The team doctored a section of the peptide so that it had the same side chains, in the same configuration, as carbonic anhydrase, an enzyme which binds zinc ions. They only had to make eight changes to the charybdotoxin, but the resulting peptide mimicked carbonic anhydrase's properties almost perfectly. Vita is currently using the technique to make proteins which might have medical applications; for example, he has made one which blocks the receptor sites for the neurotransmitter acetylcholine, which could be useful in anaesthetics. At the moment, the team is only trying to mimic existing proteins, but Vita believes that synthetic, tailormade proteins could also be possible. (Source: *Chemistry & Industry*, 17 July 1995)

Antisense protects tumour-prone mice from Burkitt's lymphoma

Antisense compounds injected into tumour-prone mice protected 75 per cent of the animals, keeping them from developing Burkitt's lymphoma, according to a new study.

Researchers led by Eric Wickstrom, professor of pharmacology at Jefferson Medical College in Philadelphia, were able to demonstrate that an antisense construct could survive in the bloodstream long enough to find the target gene—the pro-carcinogen c-myc gene, then bind with the gene and cut off expression of the lymphoma-causing protein. The treatment also appears to have long-lasting effects.

Three groups of 12 tumour-free mice were given placebo, an infusion of scrambled DNA or the 15-nucleotide antisense strand.

In a control group of mice observed from birth, 95 per cent developed tumours. Nine of the mice in each of the control groups developed tumours. But only three in the antisense group developed tumours. These mice were observed for 48 weeks without developing tumours, even though the treatment ended after six weeks.

In his protocol for clinical testing, Wickstrom will attempt to find patients who have a genetic predisposition to developing lymphoma, and infuse them with the anti-sense DNA therapy in hopes of preventing the development of cancer.

In another part of the study, he will infuse the antisense therapy into patients already suffering from cancer in hopes of slowing or curing the disease.

Wickstrom said the long-lasting effects in mice of the antisense strand, which is metabolized or secreted from the body after a short period of time, remains a mystery. (Extracted from *McGraw Hill's Biotechnology Newswatch*, 18 September 1995)

Research on plant genes

Redemption for tobacco

Virginian biotechnologists have altered the tobacco plant's genes so that it produces an enzyme used to treat Gaucher's disease, a rare genetic disorder. Carole Kramer and colleagues at CropTech Development, a spin-off firm from the Virginia Polytechnic Institute, inserted a stretch of DNA encoding an enzyme called glucocerebrosidase (GCR) into the genome of a bacterium that attacks the tobacco plant. They spotted the bacteria onto small pieces of tobacco leaves, and grew these leaf sections into whole plants which produced GCR in their leaves.

The Virginian team inserted GCR to show that they could engineer plants to produce complex enzymes. GCR breaks down the lipids and fats produced as by-products in the metabolism of macrophages—immune cells found in the spleen, liver and bone marrow.

Gaucher's disease sufferers, of whom there are only 5,000 world-wide, cannot make their own GCR; their macrophages swell with accumulated fats and die. This leads to bone disorders and severe anaemia, and can be fatal.

Kramer's team claims that each tobacco plant can produce one dose of GCR. This would last a Gaucher's disease sufferer about a fortnight. The team hopes to begin clinical trials of the tobacco-produced GCR in three to five years.

As there is no regulatory framework for therapeutic proteins derived from plants, CropTech's GCR may have to undergo lengthy and expensive clinical trials with no guarantee of approval. (Extracted from *Chemistry & Industry*, 16 October 1995)

Japan Tobacco develops gene insertion method using Agrobacterium

Japan Tobacco Industries (JT) has recently developed a gene insertion method for corn using Agrobacterium. Until now, the practical application in monocotyledonous plants such as corn was not possible. However this gene insertion method, which uses Agrobacterium, is both simple and efficient. Last year at the same laboratory, Japan Tobacco was successful with this application to rice, which is a monocotyledonous plant. By expanding the range of application to corn, the possibility of application to a wide variety of monocotyledonous plants has been increased.

Using Agrobacterium has many advantage points, including efficiency. However, until now, practical applications were only possible in dicotyledonous plants which are in the host range of this same bacterium. With monocotyledonous plants, which include important grains such as rice, direct gene insertion is accomplished through electropolation of protoplast and particle guns.

The method developed uses immature embryos adapted to infections of Agrobacterium with high splitting activity. Cell structures induced from immature embryos have the merit of a high capacity for plant regeneration. Also, the bacterium has an independently developed plasmid called a super binary vector. Through this vector, the transition of genes into plant structures is reinforced, and with corn which formerly had a low effectiveness, gene insertion with 17 per cent effectiveness is now possible.

With this method, genes inserted into corn are at present transmitted smoothly up to three generations, and the stability of the insertion has been verified.

Presently, Japan Tobacco is progressing with the development of tobacco and tomatoes which have resistance to the cucumber mosaic virus using gene recombination. (Source: *Kagaku Kogyo Nippo*, 10 July 1995)

Plants that glow in the dark

Crops that glow in the dark could give farmers early warning of disease and damage, according to UK researchers. This would open the way for the most effective, minimal use of pesticides and fungicides.

The jellyfish *Aequorea victoria* glows with blue light when under stress. Anthony Trewavas of Edinburgh University and colleagues from Oxford University have inserted the jellyfish gene that codes for luminescence into tobacco plants and mosses. When a plant is 'stressed', either by wounding or pest attack, it luminesces.

At the moment, the light produced by the plant is not visible; Trewavas uses a luminometer or a special camera that can image luminescence to detect the light. Because organisms read genetic codes differently, he will have to 'resynthesize' the gene before it will give off visible light like the jellyfish.

The key is the plant's 'cellular alarm', says Trewavas, which is based on the flow of calcium ions. Cells prevent calcium from entering but when a plant experiences an external stimulation, channels in the cell membrane open and let the calcium through. The jellyfish protein detects the change in calcium levels and responds by luminescing, he explains.

The response can occur weeks before the plant develops a disease, especially with fungal enemies, reports Trewavas. "Such plants could be distributed as one in a thousand seeds which could be easily monitored and identified." More romantic applications include roses containing the gene that glow when touched by the hot breath or hands of lovers. Commercialization is likely to take three years. (Source: *Chemistry & Industry*, 2 October 1995)

Plantibodies: an alternative approach to endow plants with new properties

The expression of antibodies in plants can provide an alternative approach in engineering resistance against many plant pathogens. An EU-funded biotechnology project aims to improve the basic technology to express and target antibody molecules in plants. They are termed "plantibodies", and offer an alternative to antisense technology. These plantibodies have potential applications in engineering disease resistance, altering metabolic routes (catalytic antibodies), and in modifying plant growth.

Recently this project demonstrated the feasibility of antibody mediated resistance by expressing antibodies that interfered with infection of artichoke mottled crinkle virus (AMCV) in the cytoplasm of *Nicotiana benthamiana.*

The variable domains of antibodies carrying the antigen-binding loops (V_H and V_L domains) were used. They can be used separately from the constant domains of antibodies without the loss of affinity. The researchers focused on the expression and targeting of functional 'single chain' variable fragments (scFv) of antibody molecules in plants.

Monoclonal antibodies (MAbs) interfering in the assembly of artichoke mottled crinkle virus (AMCV) were selected. Cytoplasmic expression of anti-AMCV scFv resulted in reduction of infection incidence and delay in symptom development in *Nicotiana benthamiana.* Optimization of expression and subcellular targeting were also studied using model antibodies. Initial results show that functional scFvs can be expressed in the cytoplasm, endoplasmic reticulum and extracellular compartments of plant cells. However, optimal inhibition is achieved with cytoplasmic expression of scFvs.

Similar results have been achieved, using extracellular full size antibodies, with tobacco mosaic virus in tobacco, *N. tabacum.* The strategy is also applicable to other pathogens and is likely to result in resistance against sedentary plant parasitic nematodes *(Heterodera, Globodera* and *Meloidogyne sp.)* and phytopathogenic bacteria.

It is as yet unknown how the intracellular plantibody confers resistance. Regardless of the mechanism this approach is of great value in conferring new plant defences in addition to broadening our understanding of virus-plant interactions.

The expression of antibodies in plants is a promising approach in obtaining disease resistance. This work will be of interest to plant breeding companies seeking to exploit new strategies in their product development programmes. European organizations interested in establishing links in order to benefit from this initiative should send initial enquiries to: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel: +353 1 8370177; Fax: +353 1 8370176. (Source: *News Release,* 19 September 1995)

Research on viral genes

AIDS experts see hope in gene link

Australian scientists have discovered a rare strain of the AIDS virus with an unexpected chink in its genetic armour. Their subjects are a small cluster of people in Australia who are infected with the strain and share a remarkable property—none have developed AIDS, despite having carried the virus for about 14 years.

The finding suggests new opportunities for developing vaccines and drugs on the basis of the newly recognized genetic defect. Researchers cautioned, however, that much more work needed to be done.

In their efforts to develop a vaccine, scientists have been trying for years to attenuate the AIDS virus experimentally. It now turns out that nature has done so, yet this rare strain might never have come to light but for the persistent efforts of a social worker and administrator at the Sydney Red Cross Blood Transfusion Service.

The AIDS virus has nine genes, one of which is called nef for "negative factor", because originally it seemed to retard the virus's replication. The Australian virus has three small segments of genetic material that are missing from its nef gene, and two that are absent from a genetic segment known as the long terminal repeat.

These defects are apparently the reason for the virus's relative lack of virulence. Although biologists are still not sure how nef works, they suspect that the defective form of nef inhibits progression of HIV infection by slowing replication of the virus and reducing the amount of virus in the body. (Extracted from *International Herald Tribune,* 11-2 November 1995)

'Molecular scalpel' induces cell suicide

Researchers at the University of Michigan Medical School have developed a 'molecular scalpel' that exploits a protein which orders tumour cells to kill themselves.

Most living cells are programmed to self-destruct — a process called apoptosis. Cancer cells are exceptional because they live as long as their host lives. Recently, scientists from the University of Chicago found that all tumour cells express a protein known as Bcl-2, which suppresses apoptosis and can even render chemo- and radiotherapy ineffective. The Michigan researchers were studying a protein called Bcl-x_s. This appeared to have no function in the body (although it is made by a gene that also encodes a protein similar to Bcl-2). However, in

cultured cells, the team found that Bcl-x_s enhanced apoptosis.

The scientists engineered a virus to contain the gene encoding Bcl-x_s and then infected tumour cells with it. They found that every type of tumour cell they infected quickly withered and died. These included cells from breast, colon and stomach tumours, and from a childhood tumour called neuroblastoma.

Initially team leader Michael Clarke had thought that the protein might enhance the activity of p53, an enzyme that is known to suppress tumours, but some of the tumours under study did not contain p53. Clarke now thinks that the Bcl-2 protein slows down all the processes that lead to apoptosis, while the Bcl-x_s neutralizes the effects of Bcl-2 and reinstates the normal self-destruct order. Significantly, the modified virus did not affect the bone marrow cells that generate blood, which are often damaged by other cancer therapies.

Clarke has not done *in vivo* tests with the virus. Another team, some of whom were involved in Clarke's research, has started animal trials; these will take several years.

However, trials involving the virus in chemotherapy treatment could begin within a year, Clarke predicts. Chemotherapy drugs can destroy a lot of the patient's bone marrow, so some cells are removed before treatment and used to top up the bone marrow afterwards. Unfortunately, the removed marrow often contains cancer cells. A small amount of the modified virus could instruct the cancer cells in the bone marrow samples to destroy themselves, leaving the healthy marrow unscathed.

The University of Michigan has applied to patent the Bcl-x_s gene sequence and its use in the modified virus. (Source: *Chemistry & Industry*, 4 December 1995)

Research on bacterial genes

Antibiotic resistance

American researchers claim to have found the strongest evidence yet that antibiotic resistance can be passed from animals to humans.

Drug resistant strains of bacteria emerge when a few bacteria survive exposure to an antibiotic by mutating and then reproduce, passing on their resistance. Clay Walker at the University of Florida detected the bacterial gene that gives resistance to the antibiotic tetracycline in both livestock and people.

If these preliminary findings are backed up, then the current practice of treating cattle with antibiotics may increase the incidence of drug-resistant bacteria in humans, he adds.

Walker studied 42 people suffering from gum disease. He found that 31 had a bacterial gene called tet (Q) in their mouths. This gene is also found in the intestines of cattle.

The bacterial genes found in the cow were 99 per cent similar to those in the patients, reports Walker. That is, one of every 100 nucleotide bases—the smallest unit in the DNA chain—was different. Tet (Q) consists of 1,500-2,000 nucleotide bases.

This high similarity suggests that the gene was transferred recently from one species to the other, explains Walker. "If the genes in each species had developed through natural selection, the percentage of similarity would have been much lower, around 80 per cent, or one nucleotide different out of every 10."

The US Center of Disease Control and Prevention has reported a sharp increase in antibiotic-resistant strains of bacteria that cause pneumonia and meningitis. It blames excessive and inappropriate use of antibiotics. (Source: *Chemistry & Industry*, 4 September 1995)

New plastic-degrading bacteria discovered

A group from the Ecological Chemistry Research Institute headed by Yutaka Joban of the National Institute of Bioscience and Human Technology, the Agency of Industrial Science and Technology (AIST), has discovered a pair of bacteria that decompose plastics. Bacteria that degrades polyvinyl alcohol (PVA) was discovered in cooperation with Rakuto Kasei Industrial Co. (President, Hiroshi Asada, Otsu City, Shiga Prefecture), a chemical products manufacturer. The other, discovered jointly with Tsukuba University, breaks down polylactic acid. The low degradability of both plastics has had a negative impact on the environment to date. The researchers believe the new bacteria can be practically applied to better treat these plastics.

PVA is used in textile mills to prevent fibres from fraying. Since it is a water-soluble plastic, it can be easily washed away once manufacturing is completed. However, because the plastic does not naturally decompose, critics have argued that it should be prevented from polluting the environment. The group has speculated that the decomposing capability of the PVA decomposing bacteria was reduced by the presence of hydrogen peroxide generated in the process of decomposition. Therefore, the group first cultured the bacteria collected near the Research Institute in a medium containing PVA. Then they added an enzyme that decomposed hydrogen peroxide to finally isolate the bacteria. As a result, the newly discovered bacteria nearly completely decomposed PVA in concentrations of 0.2 per cent in four days.

The other plastic, polylactic acid, is synthesized using the by-products of starch production and is processed into films and fibres for use in such things as food containers and clothing. Polylactic acid is not completely unfriendly to the environment, but before it can be decomposed by bacteria in a natural setting it must be hydrolyzed into lower molecular-weight molecules.

The group mixed the bacteria collected from the soil with emulsified polylactic acid with a molecular-weight of 190,000. When emulsified, only the decomposed portion of the polymers turned transparent, making it possible to find the decomposing bacteria immediately. After searching 43 samples, a transparent crater indicating decomposition was obtained from one of the samples. It decomposed 30 per cent of the polylactic acid in two weeks.

Neither one of these bacteria is present in the environment in large quantities. However, by culturing them under conditions that boost their capacity to decompose substances, such as in compost or activated sludge, the researchers believe the bacteria can be used on a practical scale to treat these two plastics. (Source: *Nikkei Sangyo Shimbun*, 8 August 1995)

Microorganisms that reproduce in organic solvent developed

Japan's National Institute of Bioscience and Human Technology (NIBH), Agency of Industrial Science and Technology, jointly with Tonen Sekiyu Kagaku K.K. (Tonen), have developed a technology for artificially creating a microorganism that would have no problem in reproducing in an organic solvent. A microorganism which normally had no such capability was subjected to the action of ultraviolet light and chemicals, and it gradually evolved

to organisms which were quite stable in an organic solvent. The joint R&D group also confirmed that a radical change had taken place in the fatty acid components of the cell wall of the original microorganism. The group is hoping that the technology will be a valuable step towards the introduction of biotechnology into petroleum chemical processes.

The group selected an agro-bacterium in the *pseudomonas* genus from which the evolution produced three different stocks of organisms capable of surviving in an organic solvent. Although most microorganisms need water for survival, the newly evolved organisms are able to propagate in an alcohol (heptanol).

The evolution of the bacterial organism was artificially caused by irradiation with ultraviolet light and the action of a chemical (ethyl methane sulphonate). After a series of certain treatments, the group tested a micro-organism with the alcohol to check its resistance against the organic solvent. If no resistance was shown, the organism was further subjected to the treatments. After nearly six months of repeated treatments, the organic solvent-resistant organism was born.

The group examined the structure of the alcohol-resistant bacterium, and found the cell wall to have drastically changed from that of the original bacterium. The overwhelming majority of fatty acids that were in the original bacterium's cell wall were fatty acids with an even number of carbon atoms in their chains. In contrast, fatty acids in the cell wall of the alcohol-resistant stocks were found to be different from the original ones:

(1) More fatty acids had an odd number of carbon atoms;
(2) Fatty acids were branched rather than straight chains; and
(3) More unsaturated fatty acids were present.

According to reports, although microorganisms that can reproduce in an organic solvent have been in existence in nature, it has been essentially unknown what part of these bacteria has actually been contributing to the resistance.

Today's chemical industrial processes are being operated at the expense of enormous energy. Less energy-consuming processes that would emit less by-products are desired for the next generation's processes. One type of these processes may be the bio-processes using micro-organisms, in particular, microorganisms capable of multiplying in oil. (Source: *Nihon Kogyo Shimbun*, 11 April 1995)

Research Instrumentation

Researchers develop advanced nucleic acid amplification technology

Researchers from Vienna, Austria, have developed a method for the exponential amplification of nucleic acids at one temperature. The ISO-CR method uses specially designed and easily manufactured oligonucleotides, and only one enzyme.

In contrast to well-known processes, such as the polymerase chain reaction and ligase chain reaction that use thermal cycles, the ISO-CR method can be performed in water baths, and is easily automated. Whilst other isothermal processes need at least two enzymes, the ISO-CR is performed with one enzyme which is polymerase or ligase.

The method is reportedly extremely specific and sensitive, and can form the basis of simple and reliable diagnostic and screening methods. It may also have possible antiviral and anticancer applications. A patent application has been filed.

To fully exploit the new proprietary method, the inventors are seeking partners to develop and market ISO-CR-based products.

For more information, contact Dr. Thomas Schlederer, Dragonerweg 21, 1220-Vienna, Austria, Tel.:+431 369 292 4447, Fax: +431 369 292 4457 or Tel./Fax: +431 280 4950. (Source: *Microbiology Europe*, July/August 1995, Vol. 3 No. 4)

Improved fermentation process

Researchers at the University of Illinois (Champaign) have implanted eyes and a brain into the fermentation process. In a prototype system designed to produce a natural insecticide from bacteria, agricultural engineers have reported faster cell-growth rates and higher product yields than those achieved in traditional bioprocessing.

The prototype—a machine vision/neural network supervisory control system—lets users see online what is happening at the cellular level during bioprocessing by drawing and analyzing samples, and then making necessary corrections to assure quality control. The system also compiles data during processing. Depending on a producer's needs, the central controller's supervisory function can be trained by developing software based on data taken over time and under varying conditions in fermentation.

To help account for uncertainties that occur, researchers included fuzzy logic technology. A neural network compensates for changing conditions, allowing each batch of cells to be treated the same during processing. (Source: *Genetic Engineering News*, 15 April 1995)

Scientists one step closer to understanding how proteins fold

Dr. George Rose of the US National Institute of General Medical Sciences and Rajgopal Srinivasan at the Johns Hopkins University (Baltimore, MD) have developed a method that promises to come closer to cracking the protein-folding code. Their computer program, LINUS, is based on the following assumptions: no two atoms are allowed to be in the same space at the same time; amino acids are encouraged to be in the conformations most commonly seen in proteins; and hydrophobic or "water-fearing" amino acids are encouraged to cluster in the protected centre of the protein.

LINUS replaces each amino acid side chain—which can range from 1 to 18 atoms—with a single sphere that varies in size depending on the type of amino acid. The program divides the protein sequence into overlapping pieces. Starting with pieces only six amino acids long, LINUS randomly twists the amino acids into any of four possible localized structures: helix, sheet, turn or coil. The process repeats 5,000 times, with each trial conformation ranked according to how energetically favourable it is. If a conformation is ranked as favourable in more than 70 per cent of the trial structures, and it enables interaction between some amino acids, it is frozen in position, creating a starting point for the next cycle.

LINUS then starts another cycle by extracting larger overlapping pieces and twisting them into 5,000 new conformations. The process continues, with LINUS taking ever-larger bites of the protein each round. The final structure is made up of the conformations that are most

favoured in the last cycle. (Source: *Genetic Engineering News*, July 1995)

General

Unlocking the secrets of unusual enzymes

Scientists at the Medical Research Council Laboratory of Molecular Biology in Cambridge, UK, have uncovered the 3D structure of a very unusual enzyme made from RNA. This enzyme is used by viruses during replication to chop up long strands of genetic material into "virus-sized" pieces. The findings help explain how the enzyme works and may give scientists new leads in tackling human genetic diseases such as leukaemia and in combating viral infections.

The enzyme that William Scott, John Finch and Aaron Klug studied is known as a "hammerhead" RNA after the shape in which its chemical sequence has traditionally been represented in diagrams. Using X-ray crystallography, the researchers have shown that the actual shape of the molecule resembles the lower-case Greek letter gamma (γ).

Determining this enzyme's structure will help scientists develop new tailor-made ribozymes for use in biotechnology and medicine. Ribozymes are under study in other laboratories as a means of destroying RNA produced during viral infections such as HIV.

For more information, contact Professor Aaron Klug, MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK, Tel: +44 1223 248 011, Fax:+44 1223 213 556. (Source: *Microbiology Europe*, Vol. 3 No. 4, July/August 1995)

New clue to malaria

Grim as the clinical status of malaria may be, scientists have lately made spectacular progress in deciphering a central component of the parasite's power. They have discovered how *Plasmodium falciparum* manages to evade a person's immune system, even while it makes its presence in infected red blood cells flagrantly obvious.

In three papers that appeared in the journal *Cell*, and a fourth in *The Proceedings of the National Academy of Sciences*, an international group of researchers described how the parasite changes proteins to stay one step ahead of the host antibodies, a process called antigenic variation.

They have identified a huge family of genes, called the var genes, for variability, that the parasite can mix and match to generate millions of antigenic proteins.

These antigenic proteins are extraordinary molecules, serving at once as the parasite's dagger and its cloak. When *Plasmodium falciparum*, a single-celled protozoan parasite, invades a person's red blood cell, the better to feast on the haemoglobin within, the parasite damages the host blood cell and makes it vulnerable to the clean-up mechanism that transports injured blood cells to the spleen for destruction.

That fate would also kill the parasite embedded inside. To prevent splenic death, the parasite sends out proteins to the surface of the red blood cell to form knobs, latching the cells to the inner surface of the blood vessels and keeping them from being washed into the spleen.

By putting its personal plug on the exterior of the red blood cell, however, the parasite risks alerting the body's immune system. This is where the var genes come into play. They allow the parasite to vary its anchoring knob proteins just enough to elude the immune system's sentinels while still keeping its own co-opted home fastened to the blood vessels and allowing the protozoan to happily feed and breed within.

As soon as the immune system figures out the hallmark of the parasite's presence and moves in for the kill, the parasite switches its var genes, creating new protective proteins to which the immune system is temporarily blind.

Scientists have long suspected that the parasite varies parts of itself as its core defense strategy, but the isolation of these genes has proved elusive until now.

With the large gene family identified, researchers can begin to trace just how the parasite changes its genes around and can seek ways to prevent it from doing so, thereby giving the body a chance to recognize infested blood cells and act. (Extracted from *International Herald Tribune*, 24 August 1995)

ERATO synthesizes super molecule bonding

The research group in charge of the Nagayama Protein Integration Project (Coordinator: Professor Kuniaki Nagayama, Tokyo University) sponsored by the Exploratory Research for Advanced Technology Organization (ERATO), successfully synthesized a gigantic "protein super-molecule" by combining three proteins. The group was able to combine the proteins to a trident-shaped synthetic compound by genetic engineering and organic synthetic chemistry. It is rare that different proteins are combined to a super-molecule without losing each unit's functions. This synthesis is regarded to be a significant step forward in developing the potential of protein engineering for its application in the fields of electronics and medicine by combining different protein molecules.

The synthesized super-molecule consists of three protein molecules of ribonuclease connected radially to another compound. Ribonuclease by itself can break down ribonucleic acid (RNA). The group confirmed that the synthesized super-molecule was also capable of breaking down RNA. The first task for the group was to synthesize the "connector" molecule for the three protein molecules. This connector was of a three-pronged shape with sulphur attached to the terminal of each prong, so that one of the cysteine molecules on the surface of ribonuclease could be easily bonded to the connector via the sulphur. Since ribonuclease had three cysteine molecules on its surface, there was a total of nine cysteine molecules available for bonding with three sulphur atoms. The design of the super-molecule was such that the only cysteine molecule at a certain position of ribonuclease had to combine with the sulphur atom. In order to achieve this design, the group modified ribonuclease by a genetic engineering technique.

The group used *Escherichia coli* to produce "altered ribonuclease" that lost all three cysteine molecules, but had one of them inserted back in at the desired position. Thus, the group was able to synthesize the super-molecule by connecting the trident-shaped material with the three altered ribonuclease molecules under specific conditions. The group used two trident-shaped materials: one with longer arms, and the other with shorter arms. Both of these materials were able to combine with the three altered ribonuclease molecules to form two super-molecules, large and small. These super-molecules are said to be heat resistant. In the future, the group plans to synthesize all types of super-molecules from different proteins. One of the advantages of synthesizing protein super-molecules is the ability to easily make protein crystals.

In developing biological chips using proteins, it is mandatory to have stable protein crystals by combining proteins together into a super-molecule without losing each protein's own functions. Thus, the super-molecule synthesis should spur new applications of proteins. (Extracted from *Nikkei Sangyo Shimbun*, 10 April 1995).

Escaped protein dissolves bone

A protein found in every living cell could have a secret Jekyll-and-Hyde existence, according to British researchers. When safely locked inside cells it performs a vital function, but if it escapes, it may dissolve bone. The team from the Eastman Dental Hospital in London, is investigating the cause of gingivitis, or gum disease, which eats away the bones in which teeth are embedded. The team noticed that the surface of one bacteria that causes gum disease, *Actinobacillus actinomyctemcomitans* was covered in a protein coat. They removed this by washing the bacteria in saline and adding the extract to cultured bone cells. To their surprise, the cells dissolved. The protein responsible seems to be chaperonin—previously only found inside cells.

Chaperonins are complex multiple proteins. Normally they have two functions: they "massage" newly-synthesized proteins, so that they take up their characteristic folded structures, and they ferry other proteins through cell membranes. But no-one ever suspected their darker side. This effect is not confined to tooth bacteria. The team extracted the chaperonins from *Escherechia coli* and found that they were also extremely active bone dissolvers. This could explain why sufferers of inflammatory bowel diseases caused by *E. coli* often contract bone diseases such as osteoporosis. (Source: *Chemistry & Industry* 18 September 1995)

Development of non-disruptive biomarkers for genetically modified microorganisms

Deliberate release of Genetically Modified Microorganisms (GMOs) for environmental purposes is frequently hampered by public concern over their ecological impact on native systems. The possibility of uncontrolled genetic exchange between the introduced GMOs and the native bacterial population, which could generate undesirable genetic combinations is the major cause of potential hazards.

However, the integrated work of five European laboratories has brought into reality the possibility of monitoring GMO performance *in situ* by the development of genetic and biochemical biomarkers.

The development of at least three surface reporters was established in the first year of the project. These are proteins that become exposed on the surface of the GMO and can be tracked immunologically after introduction into the environment.

Various biomarkers have been integrated into regulatory circuits of *Pseudomonas sp.* and employed to monitor non-disruptively the degradation of polychlorobiphenyls (PCBs), halo/alkyl benzoates in soil and rhizosphere microcosms.

These markers have either enzymatic, antigenic, or physical properties which permit qualitative measurement of GMO activity in terms of natural transfer, stability and growth phase.

There is considerable scope for the use of GMOs in both agricultural and environmental research. Further development within this EU-funded project will allow for the effective monitoring of GMOs while enhancing our understanding of their performance in nature. For details contact: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel: +353 1 8370177; Fax: +353 1 8370177. (Source: *News Release*, 19 September 1995)

Roll-your-own RNA

A team from the University of Rochester in New York has developed a nanoscale version of an old photocopier. The device, which produces many copies of a DNA sequence along a single chain of RNA, could be used in genetic research and eventually gene therapy. The technique employs a tiny ring of DNA, containing 34 base pairs and 30Å across. According to team leader Eric Kool, RNA polymerase—the enzyme which transcribes DNA into RNA, the first step in protein synthesis—runs around the circle, producing multiple copies of the sequence joined end-to-end. One unusual aspect of this discovery is that the circle does not contain a short sequence of bases known as a promoter, which normally tells the RNA polymerase where to start reading the DNA. Kool thinks that the circular shape itself might act as a promoter.

In Kool's experiments, the enzyme rolled around the circle 260 times, making an RNA strand 9,000 bases long. Such molecules could be useful in laboratory genetic research, especially if the team can figure out how to cut the long strands up into the individual sequences. For example, the strands could be spliced together with other RNA sequences to make hybrid RNA.

The team is also working on rolling circle DNA synthesis, which works the same way as the RNA technique, but uses different enzymes and building blocks and requires a 'primer' section of DNA to bind onto the ring and trigger the synthesis. (Source: *Chemistry & Industry*, 7 August 1995)

Enzyme speeds up sequencing

Researchers in the US have developed a new enzyme which, they claim, makes DNA sequencing faster and more accurate. Dubbed *Thermo Sequenase*, the enzyme is heat resistant, so it can be used in automated sequencing machines.

Stanley Tabor and Charles Richardson, of Harvard Medical School, have already made a mark in the field of gene sequencing by developing *Sequenase*, the market-leading DNA polymerase enzyme produced by Amersham International. DNA polymerases add chain-terminating 'caps' to the fragments of DNA produced by the gene sequencing process.

Some of these caps are fluorescent, so that when the DNA fragments are separated, they form bands on a sequencing chart. But with current heat-stable enzymes, the bands can vary in intensity making them hard to read and reducing the accuracy.

Sequenase, unlike other polymerases, is able to select mainly the fluorescent caps, so all the bands on the chart are of equal intensity. *Sequenase* is 2,000 times more selective than current enzymes, but is unstable under heat. This means that it cannot be used in automatic sequencing machines, which heat and cool samples many times.

The researchers identified the portion of *Sequenase* that allows it to select the fluorescent caps. Then they grafted this section into a heat-stable polymerase—obtained for a bacterium which lives in hot springs—to make their new *Thermo Sequenase* enzyme. (Source: *Chemistry & Industry*, 17 July 1995)

E. APPLICATIONS

Pharmaceutical and medical applications

Cancer drugs benefit parasitic diseases

Two anti-cancer agents extracted from the yew tree—paclitaxel from the trunk and docetaxel, a synthetic analogue—could have applications in the treatment of parasitic diseases caused by unicellular protozoan parasites.

The potential has been shown by work carried out by researchers at the joint CNRS/National Museum of Natural History in Paris and at the Chemical Institute for Natural Substances of Gif-sur-Yvett's CNRS unit near Paris.

They have demonstrated that docetaxel can block the development of the malaria agent *Plasmodium falciparum* at the blood infection stage.

Effective dose levels would be lower than those needed for anti-tumour action of the drugs. (Source: *European Chemical News*, 23-29 September 1995)

Malaria vaccine setback

Efforts to produce a vaccine against malaria have received a serious setback, with the results of the latest clinical trial in Africa showing that the synthetic vaccine SPf66 failed to protect children against the first attacks of the disease.

Researchers vaccinated 630 children in The Gambia aged between six and 11 months with the SPf66 vaccine—a polypeptide made up of three blood-stage antigens of *Plasmodium falciparum* developed by the Colombian scientist Manuel Pattaroyo.

When the vaccine was tested last year in southern Tanzania, it was found to be 31 per cent effective in protecting children against malarial infection. However, those results received a cautious welcome from specialists. It now seems they were right to be circumspect. In this latest trial, researchers reported an overall protective efficacy against the disease of only 3 per cent. (Source: *Microbiology Europe*, Vol. 3, No. 5, September/October 1995)

Bacteria blocker eases ulcers

Although antibiotics can provide relief from ulcers caused by *Heliobacter pylori* bacteria, they do not prevent infection. A US biotechnology company believes its new vaccine could solve the problem.

It is the first oral vaccine to use a protein rather than a complete virus or bacterial cell to stimulate the immune system, says Thomas Monath, vice-president for research at OraVax in Cambridge, Massachusetts. OraVax opted for a protein because whole, dead or deactivated cells could increase inflammation of the mucous membranes in the stomach, worsen ulcers, or even cause cancer.

An oral vaccine was necessary, Monath explains, because *H. pylori* lodges in the mucous lining of the gastro-intestinal tract, out of reach of the main immune system, which is the target of injected vaccines. The mucosal immune system, which normally fights pathogens in and around the mucous membranes, fails to combat *H. pylori* by itself, says Monath.

The OraVax vaccine stimulates the mucosal immune system into action, protecting the stomach lining from getting infected with *H. pylori* and killing any bacteria already present. The vaccine is a urease enzyme which joins up with and sits prominently on the surface of the bacterium in the stomach, where it is exposed to attack from the immune system. The enzyme resists digestion by stomach acids and forms large protein particles that elicit the mucosal immune response.

In pre-clinical trials in mice, the vaccine gave full protection for more than six months, reports Monath. Four weekly doses of the vaccine cured existing *H. pylori* infections in 75 per cent of animals. Moreover, there is evidence that immunity may be long-lasting, said Monath. Phase I clinical trials have been completed; further trials are planned. (Source: *Chemistry & Industry*, 4 September 1995)

Whooping cough vaccine looks promising

SmithKline Beecham's vaccine programme has received an important boost, with encouraging results from a clinical trial of its new agent against whooping cough. The new vaccine appears to be more effective and safer than current products.

The product, *Infanrix*, is a combination vaccine designed to protect against whooping cough (pertussis), diphtheria and tetanus. The whooping cough component consists of three purified proteins from the pertussis bacterium; pertussis toxoid, a weakened version of the bacterial product which attacks cells inside the throat; filamentous haemagglutinin, a sticky substance which binds the bacteria onto the throat lining; and pertactin, part of the bacteria's outer membrane. This type of vaccine is known as "acellular"; in contrast, the current whooping cough vaccine contains whole, dead bacteria.

The US National Institute of Allergy and Infectious Diseases has just completed two clinical trials of *Infanrix*, involving more than 25,000 children in Sweden and Italy. It tested five diphtheria-tetanus-whooping cough vaccines: three acellular, two of which, including *Infanrix*, contained pertactin; one whole-cell; and a control. This provided the first major comparison of the safety and efficacy of acellular and whole-cell vaccines, says SmithKline-Beecham.

The acellular vaccines with pertactin provided 84-85 per cent protection against whooping cough, compared with 36-48 per cent for the whole-cell versions. The vaccine without pertactin only provided 58 per cent protection. Moreover, the acellular vaccines did not cause any of the side-effects associated with whole-cell whooping cough vaccines, such as fever, allergic reactions at the injection site and seizures.

Infanrix is on sale in Germany, both as a vaccine to immunize babies against whooping cough, diphtheria and tetanus, and in a weaker form as a booster. (Extracted from *Chemistry & Industry*, 7 August 1995)

Anti-tumour trees

Tropical plants have yielded many important and powerful drugs. A molecule discovered by researchers from Terumo KK in Tokyo may become the basis for a new class of anti-cancer agents. The molecule tackles cancers by blocking the genetic processes that can send cells haywire.

The compound, found by screening many plant extracts for anti-tumour activity, comes from the leaves of *Ervatomia microphylla*, a tree which grows in South-East

Asia. It works by suppressing the action of the proteins encoded by two oncogenes known as *ras* and *scr*. These are stretches of DNA which have been altered by processes like point mutation; instead of doing their normal jobs, they trigger rapid multiplication of cells, leading to tumour formation. The *ras* oncogene is present in about a fifth of all human tumour cells.

The protein encoded by the *ras* oncogene is thought to interfere with the cells' signalling systems, the team explains. It makes the cells change shape, divide rapidly and pile up on top of each other. Currently, there is no way to prevent this, they add; all the compounds that suppress the protein are so toxic they are useless as drugs.

The team hopes this new compound might be different. In *in vitro* tests, it returned cells containing *ras* and *scr* genes to their normal functions, slowing the rapid division and correcting the abnormal shape. It seems to work by a "very different" mechanism to other growth inhibitors, they add. (Source: *Chemistry & Industry*, 17 July 1995)

Enrich/purge technique boosts effectiveness of cancer treatment

A new technique for enriching progenitor blood cells and purging tumour cells before reinfusing blood cells into cancer patients offers significant advantages over bone marrow transplantation has been reported by researchers at the Stanford University Medical Center. Cancer patients who receive the enriched and purged blood cells recover from the procedure significantly faster and require fewer blood cell transfusions than patients who undergo bone marrow transplantation.

By creating a high concentration of the desired progenitor cells, the enrich/purge technique replaces the several-hour transfusion of unprocessed blood progenitor cells with a 15-minute procedure to transfuse the processed cells. The new technique refines an existing method in which blood progenitor cell (or stem cell) transplants are substituted for autologous bone marrow transplants. In a clinical trial using autologous blood stem-cell transplants in 21 patients with non-Hodgkin's lymphoma, the Stanford team used a technique for separating high- and low-density portions of the blood to maximize the number of stem cells. Stem cells are of low density, so the high-density portion is discarded. Then, using antibodies to target the tumour cells, the low-density mixture is purged of malignant cells. (Source: *Genetic Engineering News*, July 1995)

Melanoma vaccine trial begins

University of Pittsburgh Cancer Institute (UPCI) investigators are vaccinating people with advanced cases of melanoma using molecules that are over-expressed in melanoma cells. "This trial differs from the vast majority of vaccine trials for melanoma because we are vaccinating individuals with part of a specific melanoma protein, or peptide, rather than with whole melanoma cells", said John Kirkwood, MD, a clinical co-principal investigator of the study.

The peptides being evaluated are Melan-A and gp 100, whose functions are unknown, and tyrosinase, an enzyme involved with pigment formation. All three molecules are normally found in melanocytes but their production is greatly increased in melanoma. The two-month trial involves 36 patients divided into three groups of 12. Each group will receive four weekly injections of either Melan-A, gp 100 or tyrosinase, along with an immune stimulant called MF-59.

At the end of the sixth week, the investigators will assess the immunologic effect of the vaccine by determining whether treated patients develop a skin reaction to the peptide against which they were vaccinated. Also the researchers will withdraw patient blood to test immune cells for reactivity against the peptides. At the clinical level, the investigators will measure the cancer's response to treatment and will track disease progression, as well as overall long-term survival. (Source: *Genetic Engineering News*, July 1995)

Wider access offered to new AIDS drugs

Two drug companies have announced they will offer broader access to experimental AIDS drugs that have shown promising results in human trials.

The new actions mean the number of people receiving the drugs under special, early-access programmes will nearly double, to more than 7,000.

Hoffmann-La Roche Inc. of Nutley, New Jersey, said it would make its drug available by lottery to about 2,000 more people. That is in addition to a lottery in July in which 2,280 people were selected.

Another company, Abbott Laboratories of Abbott Park, Illinois, said it would offer its experimental drug to at least 1,400 people by early next year.

The drugs belong to a new class of compounds, the protease inhibitors, that have shown considerable promise in human testing. The drugs dramatically decrease the amount of human immunodeficiency virus circulating in a person's blood and elevate the number of CD4 cells, critical immune cells that are depleted by the virus.

The long-term benefits of the drugs are uncertain, but tests suggest that they may be more effective than older AIDS drugs.

Besides Abbott and Hoffmann-La Roche, a third company, Merck & Co. of Whitehouse Station, New Jersey, has moved into advanced testing of a protease inhibitor. About 1,400 people have been selected by lottery to receive the Merck drug this autumn.

The announcements this week mean that 3,500 new patients can receive the drugs under "compassionate use" programmes. Several thousand people are receiving the drugs as part of more formal clinical trials. (Source: *International Herald Tribune*, 22 September 1995)

Takeda synthesizes rDNA osteoporosis drug

Takeda Chemical Industries has successfully synthesized a human cathepsin L inhibitor using recombinant DNA technology for the first time.

Cathepsin L is an enzyme that plays a major role in bone matrix degradation. A cathepsin L inhibitor for animals has already been synthesized, but the human inhibitor had not been made available.

A group including Tsuneo Yasuma of Takeda Pharmaceutical Research Division reported that this inhibitor, TAK-726 (tryptophanal derivative), is highly selective for cathepsin L, and bone resorption is excellent according to the experimental results.

The company expects that this agent will become a new drug for the treatment of osteoporosis. (Source: *McGraw Hill's Biotechnology Newswatch*, 2 October 1995)

New drug fights infectious diseases

A new drug that boosts the immune system could prove useful against chronic infections without encouraging the emergence of drug-resistant disease strains.

Therapies involving cytokines, the hormones that coordinate immune responses, have been considered for several diseases including tuberculosis, cancer and AIDS. But their use as drugs has several drawbacks: they are toxic, are broken down rapidly in the body, and are not delivered effectively to the immune system's important sites, such as the spleen and lymph nodes. Cytokines have to be injected in very high doses and at frequent intervals to produce an effect.

John Rhodes and his colleagues at Wellcome Research in Beckenham, Kent, think they may have overcome these hurdles by using a molecule called tucaresol to produce cytokines within the body at the right places. This potential new drug can be taken orally and, because it is not prematurely broken down in the body, it can be given in small, infrequent doses.

Tucaresol, a substituted benzaldehyde, is effective against viruses and tumour growth in mice, the team reports (*Nature*, 1995, **377**, 71). The Wellcome scientists believe that it is unique in providing an oral treatment to stimulate the immune system and offers a new therapeutic approach to treating chronic infectious diseases. However, clinical trials are still several months away. (Extracted from *Chemistry & Industry*, 18 September 1995)

Discovery of MAS compounds could lead to infertility treatment

Researchers at Rigshospitalet (University Hospital of Copenhagen, Denmark), in collaboration with Novo Nordisk (Bagsvaerd, Denmark), have discovered a group of compounds that could lead to a treatment for infertility problems and, paradoxically, provide hormone-free contraception for women and men. The compounds, dubbed MAS (meiosis-activating sterols) are present in ovaries and testes. Under normal circumstances they induce the egg cell to complete meiosis and stimulate the formation of sperm cells in males.

Infertility may be due either to the failure of the egg to divide, or to failing sperm cell formation. Since MAS works on both sexes, it offers promise as a supplement to hormone therapy for infertile couples. Because MAS acts only on human egg cells and sperm cells, it is believed to have few or no side-effects.

Moreover, in the longer term it may be possible to block MAS, thereby preventing unwanted pregnancy. Potentially, the discovery could lead to a hormone-free contraceptive pill that can be used by both men and women. (Source: *Genetic Engineering News*, 15 April 1995)

CDP 571 beneficial in ulcerative colitis

Clinical investigators reported at the European Gastroenterology Week in Berlin the first results of a Phase II clinical trial in ulcerative colitis with Celltech's novel drug CDP 571, a genetically engineered human antibody. A consistent reduction in disease activity was seen in most patients in the trial and the treatment was well tolerated.

CDP 571 is a genetically engineered human antibody that blocks the action of an important mediator of inflammation, tumour necrosis factor (TNF), which has been developed by Celltech and is licensed to Bayer AG. During 1995 CDP 571 has been tested for clinical efficacy in two forms of inflammatory bowel disease, ulcerative colitis and Crohn's disease, at six leading UK hospitals. The first results were reported by Professor Rhodes and his colleagues of the Royal Liverpool University Hospital. Fifteen patients with mild to moderate ulcerative colitis who were in relapse or were unresponsive to steroid treatment were injected with a single dose (5 mg/kg of CDP 571) and their disease was followed for the next eight weeks.

A clear reduction in disease activity was seen in 10 out of the 15 patients, as demonstrated by a number of markers of disease activity and blood markers of inflammation. The results for all 15 patients after treatment included: a 27 per cent reduction in the disease activity score after one week; a 48 per cent reduction in the disease severity score as assessed by sigmoidoscopy after two weeks; and a 55 per cent reduction in the mean blood level of C-reactive protein (an inflammation marker) after one week.

It is of particular interest that these effects were observed in patients unresponsive to steroid treatment, as well as those in relapse. Improvement was maximal by two weeks with some disease markers remaining reduced at eight weeks. The treatment was well tolerated, and no significant side-effects were noted.

Celltech expects to announce the result of a 30-patient placebo-controlled study in Crohn's disease in the fourth quarter of 1995. A new treatment for Crohn's disease would be particularly beneficial because this disease is not well treated currently and many patients have to be treated by surgical removal of the inflamed bowel. It is estimated that about 300,000 people in Europe and the United States have this serious disorder.

CDP 571 is in full clinical development for the treatment of rheumatoid arthritis. Bayer are beginning Phase II studies in the United States, having obtained FDA approval. This follows very encouraging results in an initial Phase II trial in rheumatoid arthritis carried out in the United Kingdom. (Source: *News Release*, 18 September 1995)

Researchers discover new approach to diabetes

Pfizer (Groton, CT) scientists have discovered a genetic technique that may guide approaches to the prevention of Type II, or "adult-onset" diabetes. Their work is published in the April 1995 issue of *The Journal of Clinical Investigation.*

Patients with Type II diabetes have insufficient levels of a key cell protein, called "GLUT4", on their cell surfaces. The protein is crucial to the absorption of glucose. GLUT4 captures sugar and carries it into the cell's interior for conversion into energy.

Pfizer scientists reported that, using gene therapy, they boosted levels of GLUT4 in diabetic mice, both inside the cell and at the cell's surface. As a result, the test mice, though genetically susceptible to diabetes, developed with normal blood-glucose levels and insulin responsiveness. Furthermore, the mice displayed few symptoms of the disease as they aged.

After producing the human GLUT4 gene and injecting it into diabetic mice embryos, the researchers observed that these mice resisted the onset and effects of diabetes. The scientists further noted that the function of the pancreas did not diminish with age in the treated mice. Type II diabetes typically places a greater demand on the pancreas, leading to the organ's premature failure. Patients at this stage of the disease require insulin injections. (Extracted from *Genetic Engineering News*, 15 April 1995)

Skinethic Laboratory perfects human epidermal cell culture technique

A one-man start-up firm in central Nice has perfected a sophisticated technique for producing standardized human epidermal cell culture. Skinethic Laboratory is gradually finding a market among European firms phasing out testing on animals due to a European directive.

The artificial skin technique developed and patented by Dr. Martin Rosdy involves culturing a donor's epidermal cells in a serum-free cell culture environment. He says the skin cultures have all the characteristics of the human epidermis. They express all known markers of epidermal differentiation and behave like *in vivo* epidermis when treated with an active or irritant cosmetic product.

The defined environment permits detection of infinitely small quantities of mediators or factors secreted by the epidermis in response to application of toxic substances. The reconstituted epidermis is standardized in terms of thickness, number of cell layers, culture time and sensitivity to known chemical irritants. Production and test procedures follow international GMP and GLP standards.

The Skinethic Laboratory epidermis is reconstituted using an original cell-culture procedure developed by Dr. Rosdy when he worked in fundamental scientific research in Sophia Antipolis, a research and technology park located between Nice and Cannes, between 1983 and 1989. The human epidermis is produced routinely *in vitro* by culturing normal adult keratinocytes in supplemented chemically defined medium on inert polycarbonate filter substrates at the air-liquid interface for 14 days.

Vertical sections stained for histology and indirect immunofluorescence studies display a correct stratification and expression of major differentiation and basement membrane markets. The thickness and number of cell layers are directly controlled by the concentration of epidermal growth factor.

As a general rule, a 1 cm^2 skin piece produces 1 cm^2 of skin in three weeks. Starting from a 4 cm^2 skin piece, Dr. Rosdy is able to obtain as much as four billion proliferative epidermal cells, which can be used to produce a total of 4 m^2 of epidermis.

Dr. Rosdy believes the epidermal cell culture technique is promising for reconstituting the autologous epidermis for patients with severe burn injury. "It is suitable for grafting because of its enhanced strength and the ability to be simply detached from the culture substrate without any enzyme treatment", he said. He is also redefining the product to include precise quantities of lipids for toxicology tests. (Extracted from *Genetic Engineering News*, 15 April 1995)

Genzyme Transgenics manufactures monoclonal antibody in goats' milk

Officials at Genzyme Transgenics Corp. (Framingham, MA) say they have achieved expression of a monoclonal antibody (Mab) in the milk of a production animal. The company also signed three new contracts for antibody production.

According to Genzyme Transgenics, the goats have produced a Mab at the level of more than four grammes per litre of milk. Similar work the company has done with recombinant proteins has shown that 10 goats have the potential to replace the bulk production capacity of a large biomanufacturing plant.

Under an agreement with Bristol-Myers Squibb, Genzyme Transgenics will develop transgenic goats expressing BR96, the pharmaceutical company's proprietary antibody. BR96-doxorubicin, a conjugation of the BR96 Mab with the anti-cancer drug doxorubicin, is being developed for potential cancer therapies and is currently in phase II clinical trials using material produced from mammalian cell culture.

The achievement of antibody expression came as a part of Genzyme Transgenics' work with a Japanese pharmaceutical company on a potential colon cancer treatment. The proprietary monoclonal antibody was expressed in goats and was conducted in collaboration with Tufts University School of Veterinary Medicine (North Grafton, MA). The work follows the expression of this antibody in mice, announced in December 1993, a process which is also the subject of pending patent protection. (Extracted from *Genetic Engineering News*, 1 June 1995)

Allelix announces partnership with Ontario Government

Allelix Biopharmaceuticals Inc. has announced the formation of a public-private sector partnership under the Government of Ontario's Industry Research Program ("IRP"). The partnership will provide funding allowing Allelix to accelerate work on a number of existing neuroscience projects.

This work includes a co-development and licensing agreement with researchers from the Playfair Neurosciences Unit of the Toronto Hospital on compounds patented by Playfair which protect the brain from neuronal damage caused by stroke, head and spinal injury. Stroke, along with traumatic head injuries, can cause irreversible damage to the brain through an overload of calcium. The compounds licensed from Playfair act through a novel mechanism which increases the cell's capacity to lower the excessive calcium. Allelix expects to begin pre-clinical trials with a lead compound in 1996.

Allelix Biopharmaceuticals Inc. is engaged in the discovery, development and subsequent commercialization of innovative pharmaceutical products. These products are developed by applying chemical approaches to disease targets identified and defined through advanced biological techniques. Allelix currently has two products in clinical trials: the anti-viral agent ALX40-4C for the treatment of HIV, and ALX1-11 for the treatment of osteoporosis. Allelix's research programmes focus on the discovery of central nervous system, anti-virals and anti-inflammatory therapeutic agents. (Source *News Release*, May 1995)

Livestock applications

Epicin inhibits bacteria deadly to shrimps

Epicore Networks Inc. (Calgary, Canada) reports that its Epicin aquaculture product can inhibit the growth of bacteria that plague cultured shrimp. Previous studies have already shown that Epicin, which is a biological complex of genetically selected micro-organisms, can improve water quality in intensive and semi-intensive shrimp farms.

Results of research conducted at the Institute of Aquaculture, University of Stirling, Scotland, have demonstrated that Epicin inhibits the growth of a wide range of vibrio bacteria. The infection (vibriosis) can cause devastation to shrimp farms. Recent collapses of the shrimp industry in Viet Nam, India, Bangladesh, the Philippines and China have been partly attributed to an increase in the incidence of vibriosis. The industry has also been seriously affected by the emergence of a number of pathogenic viruses, notably the Yellow-head baculovirus.

Epicore's laboratory research, which is being conducted by Dr. James Turnbull at the Institute of Aquaculture at the University of Stirling, is part of a programme that focuses on a number of the problems of the shrimp farming industry. Other facets include the bioremediation of pond sludge and improving the quality of shrimp feed through the addition of encapsulated broad-spectrum enzymes and microbial cultures.

Shrimp farming is undertaken in more than 50 countries and in 1993 generated world-wide revenues estimated at $5.5 billion. Thailand, the world's biggest producer, exports more than a billion dollars' worth of shrimp a year, 90 per cent of it farm-raised. In 1994, Ecuador produced an estimated 68 per cent of the farm-raised shrimp in the western hemisphere—100,000 metric tons valued at $500 million. (Extracted from *Genetic Engineering News*, 15 May 1995)

Chemical applications

How to churn out cheap proteins

Researchers at SmithKline Beecham say they have developed a new way to manufacture biological proteins in large quantities at low cost.

The technique has produced $5 million worth of an immune-boosting protein, M-CSF, in three weeks compared with a year for other techniques, reported Martin Rosenberg, the company's director of biopharmaceutical R&D. Production levels can exceed 20 mg of protein for every litre of cell culture. It can also produce receptor molecules, viral antigens, monoclonal antibodies and immune system compounds quickly and copiously.

The protein factory consists of embryonic blood cells of the fruit fly. These insect cells have several key advantages over bacterial and mammalian cell cultures. Around 500-1,000 copies of a single gene can be inserted into the insect cells, whereas it takes many months to clone similar quantities of genes into mammalian cells, and as copy number rises control declines.

Unlike bacterially-produced proteins, proteins cloned in the insect cells can readily be used in animal studies of new drugs. Proteins from bacterial clones do not fold properly and lack certain carbohydrate appendages that a mammalian cell needs to function; an expensive chemical processing step is needed to rectify this.

Normally, horse or bovine serum is added to cell cultures to supply growth factors, adding an expensive purification step to get at the protein. The insect cells avoid this completely because they can be modified to grow in serum-free media. "It is a biologist's dream", Rosenberg said.

Besides protein factories, the insect cell systems can be used for testing interactions between drugs and receptor molecules and to model the channels that transport ions across mammalian cell membranes. (Source: *Chemistry & Industry*, 4 September 1995)

Enzyme destroys pesticides

Research into developing high performance enzyme catalysts to detoxify nerve agents may also have major environmental applications converting organophosphorus compounds in pesticides and various pollutants into benign substances for disposal.

Organophosphorus compounds are used in chemical weapons and insecticides such as paraoxon, parathion and coumaphos. The current method of disposal is to incinerate the toxic material, then pass the remaining waste gas through carbon filters to absorb the residual nerve agent. This process, which generates hazardous waste, is inherently dangerous and costly. The alternative use of micro-organisms to destroy pesticide wastes is very slow.

The enzyme organophosphorus hydrolase, from *Pseudomonas diminata*, can detoxify organophosphorus agents, but in conventional form cannot be used in the field. The task given to Altus Biologics is to design a Clec organophosphorus hydrolase catalyst that retains high enzymatic activity when used in organic solvents and in a high temperature continuous gas-phase reaction. If successful, the market for disposing of the US chemical weapons stockpile could amount to $12 billion, according to US Army sources.

Altus claims its Clec process is very simple. A crude protein is crystallized in a batch reactor and then chemically cross-linked to give a heterogeneous catalyst which is very pure, much more stable and retains its activity. In addition, its productivity is high, reducing the overall cost of the process.

Altus says the process is very broad and has been applied to more than 20 enzymes. It has introduced six commercial catalysts containing Clec products with the main applications in pharmaceuticals and fine chemicals. (Source: *European Chemical News*, 5-11 February 1996)

Food production and processing

Saponins

Sugar substitutes may be sweet, but they do not taste quite like sucrose. Douglas Kinghorn, a professor of pharmacognosy at the University of Illinois, claims he has found a family of sweeteners that match sugar's taste profile better than other sweeteners.

The sweet compounds, a type of saponin called abrusides, are found in a weedy tropical vine, *Abrus precatorius* (rosary pea), grown in Indonesia and used to sweeten betel quid and also to treat a gastrointestinal disease called sprue. The plant is also found in Florida, where it is considered a weed.

Kinghorn says the abrusides are about as sweet as glycyrrhizin, a similar natural sweetener used in Japan. The compounds are also stable to heat and soluble in water. He thinks there could be a niche market for their use in health foods.

Japanese scientists have also identified saponins as the active ingredients in some Chinese herbal medicines claimed to prevent hangovers. Masayuki Yoshikawa of the Kyoto Pharmaceutical University and Johji Yamahara of the Research Institute for Production Development, have identified oleanene-type triterpene oligoclycosides in the angelica tree bark, soapnut tree pericarps, horse-chestnut tree seeds and camellia seeds. When given to rats an hour before a drink of ethanol, the saponins kept the animals' blood-alcohol levels down. (Source: *Chemistry & Industry*, 18 September 1995)

Removing cassava's deadly poison

Cassava is one of the developing world's most important crops but it contains a poison that threatens those that eat it. Scientists at Newcastle University now believe they can solve this problem by transferring part of the plant's own detoxification process into bacteria used in cassava fermentation.

Cassava is the third most important crop in the tropics after rice and maize, but the plant gives off hydrogen

cyanide when crushed; this can be as much as 1 g per kg of leaf. Traditional processing methods do not always remove all the cyanide, leaving the people open to chronic poisoning. Healthy humans can "detoxify" about 100 mg, but those on a poor diet cannot.

The gas is produced when two enzymes, ß-glucosidase and α-hydroxynitrilase, degrade the cyanoglucoside, which is stored in the plant cell vacuoles (fluid-filled cavities in the cytoplasm of the cell). The first enzyme converts cyanoglucoside into cyanohydrin and glucose, and then the second acts on cyanohydrin to produce HCN.

The plant chromosomes contain a number of copies of the genes encoding each of these enzymes; each gene gives rise to a slightly different form of the protein. The team has cloned the genes for the two enzymes and expressed them in bacteria.

The gene for α-hydroxynitrilase is expressed at much higher levels than β-glucosidase which needs some manipulation to make it fold properly, but one enzyme should be enough to improve detoxification, say the scientists.

Introducing a culture containing these genetically modified bacteria into cassava processing should allow the enzymes to convert the cyanoglucoside in the plants into HCN gas. In this way, the plant's toxic stores of HCN will be released before eating.

The most common fermentation process in Africa uses lactic acid bacteria.

Because cassava gives off HCN to ward off predators, the scientists are not attempting to develop a non-cyanide version of the plant. However, in the long term, they hope to be able to produce cyanide in the parts of the plant that people do not eat. At the moment scientists cannot introduce foreign genes into cassava. (Source: *Chemistry & Industry*, 2 October 1995)

Industrial microbiology

Luciferase for microbial quality analysis

Rapid testing kits that use the firefly enzyme luciferase are being used in microbiology quality assurance laboratories to detect microbial contamination.

The Cambridge, UK, company Celsis International has launched an initiative with the UK's Department of Trade and Industry and the Biotechnology and Biological Sciences Research Council (BBSRC) to help companies get to grips with this new technology.

Microbial contamination is currently measured in industry by plating out samples on agar plates and incubating them for between two and seven days.

The new rapid testing kits use firefly enzyme to measure adenosine triphosphate (ATP), a ubiquitous molecule in nature which is often regarded as the energy molecule of living systems. Any detection of ATP will, therefore, indicate the presence of living cells. In the same way that firefly tails glow, the test kit produces light which can be measured to show the presence of microbial contaminants.

The kits are extremely sensitive, and it is claimed they can detect one single cell in a sample. This is important as it might be necessary to detect only a few cells in a sample for quality control. The kits can produce results in only a few minutes holding out the prospect of almost real-time analysis.

There is a huge potential market for these rapid test kits. According to the market research organization Frost & Sullivan, there were 2.5 billion such tests performed last year. The rapid testing methods account for only 2.5 per cent of the total. Only a few firms other than Celsis produce the kits, including Amersham and Biotrace in the United Kingdom, and Lumac in the Netherlands. Although the technology has been around for a long time it is only now its potential in microbiological quality assurance is being realized. (Source: *European Chemical News*, 23-29 October 1995)

Microbes produce raw materials for plastic

Daicel Chemical Industries, Ltd. and Osaka Municipal Technical Research Institute have discovered two new microbes—*Alcaligenes xylosoxydans* and *Rhizobium meliloti*—acting to decompose cellulose acetate, material for biodegradable plastic.

The research team involved will continue to examine the microbes for the development and application of new biodegradable plastics. (Source: *McGraw Hill's Biotechnology Newswatch*, 2 October 1995)

Biodegradable aliphatic polyester copolymer

Mitsui Toatsu Chemicals, Inc. has succeeded in establishing technology to manufacture biodegradable aliphatic polyester copolymer by applying the direct polymerization process, allowing synthesis of an aliphatic polyester copolymer consisting of hydroxycarboxylic acid, diol and dicarboxylic acid, which is difficult by the ring-opening polymerization process.

The aliphatic polyester copolymer manufactured by the direct polymerization process features an excellent flexibility like polyethylene with an elongation of 100-500 per cent. The flexibility can be controlled without using a plasticizer. The degradability can also be controlled. As with polylactic acid, it is stable in ordinary working environments, does not harbour moulds, and can therefore be used to produce food wrapping and packaging materials.

Further details from Mitsui Toatsu Chemicals, Inc., Lace Business Development Dept., 3-2-5, Kasumigaseki, Chiyoda-ku, Tokyo 100. Tel.: +81-3-3592-4105; Fax: +81-3-3592-4271. (Extracted from *JETRO*, August 1995)

Genencor targets biomass process

Genencor and Eastman Chemical plan to commercialize new chemical processes based on the biocatalytic conversion of biomass. These processes are to be developed during a five-year research programme. A grant for the project has been awarded by the US National Institute of Standards and Technology (NIST) to Genencor and four joint venture partners. They are Eastman Chemical, Electrosynthesis, Argonne National Laboratory and Micro-Genomics, a specialist in metabolic engineering.

The research project will develop continuous processes to manufacture a wide range of chemicals using feedstocks such as corn syrup and soya.

It is hoped that new micro-organism technology with improved biocatalyst and enzyme systems will be developed and will include the downstream recovery and purification of products.

One project goal is to cut the development time of biocatalytic processes in half from the present 15-20 years.

Genencor says the processes will benefit sectors such as pharmaceuticals, cosmetics, health care and food additives. (Extracted from *European Chemical News*, 11-17 September 1995)

Living life to the extreme!

"Biotechnology of Extremophiles" is a major project funded by the EU Biotechnology Programme. The project integrates the work of 39 laboratories in 12 European countries and takes a multidisciplinary approach which includes the isolation, taxonomy, physiology, biochemistry and the genetics of extremophiles.

These investigations will develop our understanding of how extremophiles are able to sustain life in extreme biotopes, with particular interest to extremes of temperature, pH and high salt concentrations.

The potential of the biological and industrial capabilities of extremophiles may provide new opportunities for the development of biocatalysts and biomolecules of industrial interest.

Isolation and taxomony: A number of new screening and cultural techniques for the isolation and characterization of extremophiles have been developed.

Fermentation technology: Extracellular enzymes of industrial interest including amylases, proteinases and xylanases have been purified and characterized. Some of these exhibit extraordinary properties including the ability to function at temperatures of 50° C-120° C, within a pH range of 2-11, and are even detectable in the presence of high concentrations of detergents and organic solvents.

Expression of genes in extremophiles: More than 10 genes from extremophiles encoding extremely stable enzymes (including extracellular and intracellular enzymes) were cloned and expressed in mesophilic hosts.

The unique properties of extremophiles, particularly the extracellular enzymes produced, make them important candidates for various biotechnological applications with potential for the food, detergent, paper, pulp and pharmaceutical industries. For information contact: Phil O'Leary, BioResearch Ireland, Forbait, Glasnevin, Dublin 9, Ireland. Tel.: +353 1 8370177; Fax: +353 1 8370176. (Source: *News Release*, 19 September 1995)

Energy and environmental applications

Microbial cleansing agents in sewage treatment practices

Sewage is usually treated by the activated sludge process involving a complex mix of micro-organisms feeding off the pollutants in the waste water. The micro-organisms, collectively known as sludge, must later be freed from the effluent before it is discharged into lakes, rivers and oceans.

Scientists from two Australian universities, namely the University of Queensland (Centre for Bacterial Diversity and Identification) and La Trobe University, Melbourne, have discovered a genetic signature for a troublesome bacterium in a joint project, a discovery which would cut plant operating costs and improve the purity of effluent outflows.

This discovery has enabled the scientists to develop a DNA probe as a test unit to predict if the bacterium posed a threat in a sewage plant. If this was likely, operators could then take remedial action before a bacterial "explosion" led to a breakdown in the sewage process.

According to Dr. Linda Blackall of the University of Queensland, this discovery is likely to have a big impact in waste water treatment throughout the world. It will help avoid the environmental damage caused by unseparated sludge being pumped into oceans and rivers.

For more information contact: Dr. Linda Blackall, Centre for Bacterial Diversity, University of Queensland, Brisbane, QLD 4072, Australia. Tel.: 61-7-3653367. (Source: *Australia Science and Technology Newsletter*, 1995)

Thin-film membranes for large-scale fuel production and environmental clean-up

University of Colorado at Boulder researchers have developed a new type of thin-film membrane capable of withstanding high temperatures and harsh environments that could be used for jobs ranging from large-scale fuel production to environmental clean-up. The membranes are made of zeolite, a crystalline substance commonly used in industry as a detergent builder and purifier, said Richard Noble, co-director of CU-Boulder's Center for Separations Using Thin Films. The CU group has developed a method of growing ultra-thin layers of zeolite crystals on the interior walls of small ceramic and stainless-steel tubes, paving the way for their manufacture and use on an industrial scale.

Zeolite crystals harbour tiny, uniform-sized pores about the size of a small molecule. Gas and vapour molecules are "cued up" by the zeolite membranes, which reject the larger molecules and allow smaller ones targeted for removal to pass through the pores. The CU-Boulder group has received a patent on the membrane technology and is working with the Chevron Research and Technology Co. (Richmond, CA) and Golden Technologies (Golden, CO) to commercialize the process. (Source: *Genetic Engineering News*, July 1995)

Cleaning up chlorine

Takeshi Imamura of Canon in Tokyo has found a way to use agricultural wastes to help decompose chlorinated organic compounds that often contaminate the land around paper and pulp works.

The bleaching process, in which chlorine and its compounds are used to break down the lignin in pulp, produces a huge variety of chlorinated organic by-products. Some of these can be extremely hazardous. They are often water soluble and very stable in the environment, so if they get into the soil they can spread out, poisoning groundwater and eventually finding their way into drinking water.

Imamura's method involves bacteria that can decompose chlorinated organics. There are several of these, he notes, including methane-eating bacteria, such as *Methylocystes* and those that prefer aromatics, like *Pseudomonas putida* and *cepacia*. Many of these are used at clean-up sites. However, one drawback is that they have to be "induced" into degrading the compounds. This involves exposing them to another, often expensive, organic compound, usually an aromatic amino acid. This makes the bacteria produce oxygenase enzymes, which are vital for breaking down the offending bleaches.

Imamura has come up with a cheaper alternative. He has found that a water-soluble extract of lignacellulose-containing plants activates the microbes just as well as the amino aromatics. The beauty of this is that agricultural waste products can be used. The most useful are the wrung-out remains of cane sugar after processing and the tops of the canes, currently only used as fuel or animal fodder. An alternative is *p*-coumaric acid, a constituent of the plants' basic lignin skeleton, which is also cheaper than the aromatic amino acid. (Source: *Chemistry & Industry*, 1995)

Plants used to concentrate toxics

Phytoremediation, the use of plants to clean up contaminated soils, is gaining favour as a remediation technology, according to a recent article in *Science* (Vol. 269, 21 July 1995).

Metal-contaminated soil is a major environmental problem, and a high cost clean-up headache. Cleaning a hectare of land to a depth of one metre using conventional excavation/reburial methods can cost over $3 million, and is consequently limited to small areas.

Metal-scavenging plants are cheap to grow, meaning that they can be used on large areas. It may also be possible to extract the metals from the plants for re-use.

One plant being used for cleaning selenium-laden fields is the tropical mustard variety *Brassica juncea*. Field tests demonstrate that the plant reduced selenium levels in a contaminated field by 50 per cent over several years. The same plant has been shown to concentrate lead, chromium, cadmium, nickel, zinc and copper.

Scientists are also trying to identify the genes that code for the biochemical machinery that enables hyper-accumulators to take up large quantities of metals. It may then be possible to transfer these genes to faster growing plants that would be more effective accumulators.

One promising effort involves the transfer of a bacterial gene that detoxifies mercury into a plant, which was then able to grow in a solution containing mercuric chloride at levels toxic to control plants. The bioengineered plant survived by converting the mercury to an elemental form and slowly releasing it into the air (in amounts considered to be safe). (Source: *AgBiotech Bulletin*, October 1995)

Bioprocess for desulphurizing flue-gas wastes

Lone Peak Engineering, a Utah-based engineering company, has developed a bacterial method of converting sulphate and sulphite wastes from flue-gas desulphurization units into a high-quality sulphur.

The process employs a two-stage, bacterial reactor and a final filter process. If successful on a large scale, the waste destruction technology could reduce waste disposal cost, and produce saleable sulphur. Sulphur currently sells at US$ 125 per ton. (Source: *AgBiotech Bulletin*, October 1995)

Bioremediation activity set to expand

Bioremediation, the use of biological clean-up and recycling methods for combating environmental contaminants, which could possibly become the largest domain of biotechnology, is the subject of a study from the OECD (Organisation for Economic Co-operation and Development). After health care and agro-food production, so far the two main areas of application, the protection and restoration of the environment is becoming a priority goal of the life sciences and technologies.

Environmental biotechnology is becoming more popular, as biological clean-up and recycling methods are relatively cost-efficient when compared to the more traditional physical and chemical ones. The market potential for the new domain of biotechnology is considered to be vast, and is expected to grow from $40 billion in the early 1990s to some $75 billion by the year 2000. (Source: *EBIS*, Vol. 5, No. 1, 1995)

Treatment of waterway marine organisms by biotechnology

Environmental Projects Co. Ltd. of Japan, a manufacturer of waste water treatment facilities, has developed a system of applying biotechnology to remove shellfish and algae adhering to the waterways of power-stations adjacent to coastal regions.

Power companies are presently combusting and disposing of these shellfish and algae by burying them inside power-station compounds, or consigning the work to specialized industrial waste treatment enterprises, but the new system utilizes the anaerobic nature of microbes and reduces the treatment cost to less than one half compared to the combustion method.

Thermal power plants and nuclear power plants use sea water as cooling water, but barnacles and other shellfish, as well as algae, adhere on the waterways for sea-water intake, requiring cleaning up to four times a year with the volume of wastes treated each time running up to about 500 tons on average. Combusting these shellfish and algae requires the use of a large furnace, but salt action rapidly causes damage, and offensive odours are generated when the disposal work is consigned to specialized waste treatment enterprises.

With the new system, the shellfish and algae removed from the waterways and dumped on the ground are fed into an anaerobic bioreactor and hermetically sealed. The bioreactor contains microbes cultured beforehand, which open these shellfish in two days and completely dissociate the shells and soft tissues within five days. The soft tissues are then decomposed. The inside parts, which normally generate offensive odours, are liquefied within one month by microbe action, and converted into methane or carbon dioxide gas in two to three months, with the methane gas utilized to maintain the bioreactor at a fixed temperature (35° C).

The larger portion of the organic substances are decomposed in the preliminary stage of aerobic treatment, but must be reduced to discharge standards, so further treatment is performed in the latter stage with aerobic microbes. The ultimate treatment water that is given aerobic treatment is recycled and used for shell washing. The shells are washed and utilized as a source of calcium.

A system capable of treating roughly 500 tons of shellfish and algae is marketed at a domestic price of ¥500-600 million.

Further details from Environmental Projects Co. Ltd., 2-9-1, Omorihoncho, Ota-ku, Tokyo 143. Tel.: +81-3-3763-2393; Fax: +81-3-3763-2009. (Source: *JETRO*, August 1995)

F. PATENTS AND INTELLECTUAL PROPERTY RIGHTS

Neem patent challenged

Environmentalists are challenging the validity of a US patent on a natural pesticide, a move they hope will eventually make it impossible to patent biological resources and the way they are used.

In a petition filed with the US Patent Office, the activists assert that W.R. Grace & Co. obtained its 1992 patent by copying and claiming as its own procedures that farmers in India had developed over centuries.

At issue is a method Grace says it developed for extracting and preserving azadirachtin, the primary active chemical produced by seeds of the neem tree, universally cultivated and exploited in India.

The petition relies partly on the principle of "prior art", a concept that denies a patent to a process that would be obvious to a person with ordinary skills in an art—in this case, extraction of neem oil.

"Although W.R. Grace's processes are more technical, they are mere extensions of the same processes that Indian villagers have been using for hundreds of years", the petition states. "Patents cannot be granted for trivial changes to known products and processes."

W.R. Grace contends its patent is legitimate in that it is for a process, not a substance. The patent's focus is on a formula that extends shelf-life and effectiveness of the neem-based pesticide and applies neither to extraction or processing of neem extract.

Further, the company says the patent in no way provides exclusive use of neem seed, extract or pesticide. (Source: *Chemical Marketing Reporter*, 18 September 1995)

Resolution for changing legal framework on genetic engineering

A set of guidelines for use when changing the legal framework concerned with genetic engineering has been drawn up by the European Science Foundation, based in Strasbourg.

Points include:

- The legal framework for the contained use of genetically modified microorganisms should differentiate the relevant procedures more effectively in accordance with their risk potential;
- The definition of criteria for operations with such microorganisms would benefit from a new and workable risk assessment-based approach which should be developed in consultation with academic and industrial research scientists.

The regulations concerning field trials with genetically modified organisms should be simplified. The European Science Foundation, which represents 55 member research councils, academies and institutions devoted to basic scientific research in 20 European countries, underlines that the amendments that they propose in the resolution do not create any unacceptable increase in risk to human health and the environment.

The Foundation urges the European Commission to provide for an amendment of the legal framework on genetic engineering. It calls for adaptation of the directives to reflect the state-of-the-art in research and technology reached since the promulgation of the two Council Directives (90/219/EEC and 90/220/EEC) which could effectively improve the conditions for research and industry in the field of strategic importance for Europe.

Further information from: European Science Foundation, 1 quai Lezay-Marmésia, F-67080 Strasbourg Cédex; Tel.: (33) 88.76.71.17, Fax: (33) 88.76.71.17. (Source: *EBIS*, Vol. 5, No. 2, 1995)

European Patent Office costs under review

A survey published in May 1995 by the European Patent Office suggests that high official fees and translation costs are deterring European companies, especially small and medium-sized firms from filing patent applications through the European Patent Office. The survey was prompted by ongoing complaints from industry that European Patent Office costs were much higher than those in the United States Patent and Trademark Office, the Japanese Patent Office or national patent offices in European countries. The European Patent Office surveyed national patent offices, patent attorneys and companies with in-house patent departments about their patent experiences during 1992. Because costs arise from official fees, patent attorneys' service charges and applicants' own costs, the true costs can be difficult to calculate; this is complicated by differences in patent procedure from country to country.

However, the results of the survey indicated that the average cost of filing a patent application in the United States or Japan is approximately 20 per cent cheaper than in the European Patent Office, largely because the official fees are three times higher in the European Patent Office; the much lower attorney fees in Europe did not compensate for this. However, it is still marginally cheaper to lodge a patent application designated Great Britain, Germany and France via the European Patent Office than to file separately in these three countries, because only a single set of attorney fees is required.

The major problem with the European patent system is that once the patent is granted by the European Patent Office following initial filing and prosecution in one of the three official languages, English, French or German, the claims must be translated into the other two languages, and the patent must be registered in each designated country where the patent is to be maintained in force; this requires translation of the whole specification and claims into an official language of each of the designated countries. The cost can be very high indeed; for registration in the eight most popular member States, the total cost is an average US$32,500, of which translation costs one third of the total.

The Administrative Council of the European Patent Office has issued a discussion document listing suggestions for cost saving, and has invited comments from the research and industrial communities. Unfortunately most of the proposals, such as giving responsibility for searching to the major national offices, centralizing translation, or reducing duplication of work between the European Patent Office and national patent offices are politically sensitive. Therefore it is unlikely that any major reform will ensue in the short term. (Source: *Australasian Biotechnology*, Vol.5, No. 4, August 1995)

US Coalition Challenges Patents on Life

Acting in the wake of recent successful challenges to life patents, a broad coalition of indigenous, consumer, environmental and development non-governmental organizations from the United States, Canada and other countries met in early June 1995 to plan strategies to oppose the patenting, commercialization and expropriation of human, animal and plant genetic materials. After addressing major concerns such as the ongoing Human Genome Diversity Project—an attempt to take samples of human genetic material from indigenous communities around the world—the participants concluded that "the patenting of life is morally unacceptable, fundamentally inequitable and technically unworkable". We reproduce the final declaration that came out of the gathering:

* * * * *

Blue Mountain Declaration

The humans, animals, micro-organisms and plants comprising life on earth are part of the natural world into which we all were born. The conversion of these life forms, their molecules or parts into corporate property through patent monopolies is counter to the interests of the peoples of the world.

No individual, institution, or corporation should be able to claim ownership over species or varieties of living organisms. Nor should they be able to hold patents on organs, cells, genes or proteins, whether naturally occurring, genetically altered or otherwise modified.

Indigenous peoples, their knowledge and resources are the primary target for the commodification of genetic resources. We call upon all individuals and organizations to recognize these peoples' sovereign rights to self-determination and territorial rights, and to support their efforts to protect themselves, their lands and genetic resources from commodification and manipulation.

Life patents are not necessary for the conduct of science and technology, and may in fact retard or limit any benefits which could result from new information, treatments or products. Recent developments emphasise the importance of our common position:

- *The European Parliament in March 1995 soundly rejected a bill to authorize patents on life in the European Union;*
- *Three weeks later, the Indian Parliament refused a similar bill on life patents;*
- *In May 1995, a large coalition of religious leaders in the United States openly opposed patents on humans and animal life;*
- *A recent attempt by the US Department of Commerce to patent a human cell line from an indigenous Guaymi woman from Panama was opposed by a coalition of activists and withdrawn;*
- *Following protests by citizen groups, scientists and Governments, W.R. Grace's controversial patent covering all genetically engineered cotton has been revoked in both the United States and India;*
- *In May 1995 the indigenous peoples organizations of the South Pacific began drafting a treaty to declare the region a life form patent-free zone; other indigenous peoples are working to enact similar treaties in their territories;*
- *In the last two years, the European Parliament decided to stop all public European Union funding for research associated with the Human Genome Diversity Project. Additionally, the European Parliament legislated that publicly funded research should not give rise to privately held patents.*

As part of a world movement to protect our common living heritage, we call upon the world and the Congress of the United States to enact legislation to exclude living organisms and their component parts from the patent system. We encourage all peoples to oppose this attack on the value of life.

3 June 1995.

* * * * *

(Source: *Seedling*, July 1995)

International research planned for bio-patents

The patent offices of Japan, the United States and Europe are scheduled to inaugurate a cooperative research project aimed at their patenting practices for new biotechnology inventions, including genetic engineering.

The Japanese side will propose a prospective theme at a tripartite meeting. The research results will be compiled as a report and officially approved at a tripartite expert meeting to be held in spring 1996 at the European Patent Office (EPO).

The Japanese authorities expect to utilize the research results as a guideline for assessing patent applications. The index for the number of patent applications in Japan covering microorganisms and genetic engineering stood at 573 (1975 taken as 100) in 1993.

The envisioned research project will be related to, for example, (1) items included in a specification containing a claim and a detailed explanation of the invention in question, and (2) the patentability (uniqueness, inventive step and industrial potentialities) of an invention based on genetic engineering. (Source: *McGraw Hill's Biotechnology Newswatch*, 18 September 1995)

Patents fail to promote UK technology transfer

Patenting discoveries from research conducted in the UK's public sector does not foster technology transfer to industry, according to a new report. Most UK academics are concerned that industry will poach their ideas.

Scientists tend to file for patents too early, because they want to protect their inventions before asking companies for funding, finds a report by Andrew Webster of Anglia Polytechnic University. But they end up compromising the commercial potential of their work. "Patents filed early on in a research project may be underdeveloped, or inadequately supported by experimental evidence, to cover possible variations on the initial invention that could be taken up by competitors" says Webster.

Sometimes scientists delay or reduce their disclosures, out of the same fear of losing out. But this means that companies, government organizations and public interest groups have access to less information.

In 1985, the Government removed the monopoly held by British Technology Group on intellectual property rights from public-sector research. The Government expected this to trigger a change in culture, but this has not happened. Universities still hold relatively few patents despite having the opportunity and responsibility for making applications.

Many companies think that universities should get out of patenting completely, Webster reports. Industry should

consider if its informal links with universities, and its ability to patent at the right time, are both in jeopardy.

The best way to transfer technology from the public sector to industry is through informal contracts, Webster concludes. Industry should take a more active role, and universities and research funders should not judge the technology transfer activities of academics by the number of patents filed, he adds.

UK universities held 572 patents in 1994. Contrary to expectations, institutions with many patents did not necessarily reap a healthy financial reward from licenses. (Source: *Chemistry and Industry*, 3 July 1995)

Patent rights can get lost in cyberspace

The Internet offers the researcher a wealth of resources. For example, it both affords access to numerous scientific databases and supplies an efficient means for communicating the results of research to colleagues. In fact, researchers routinely use Internet as a medium for transmitting electronic copies of manuscripts and exchanging ideas and research findings in long-distance collaborations.

Yet this electronic communication may be placing a researcher's patent rights at risk by creating "prior art" or by unintentionally informing a third party about a new invention.

In patent law, prior art is the information that is used to judge whether an invention is both novel and non-obvious. In other words, prior art provides a standard to determine if an invention meets the legal requirements of a *patentable invention.* The underlying policy of the prior-art concept is that an inventor receives the patent grant in exchange for providing something new to the public. Accordingly, an invention is not patentable in the US if it was placed in the public domain before a "critical date" (i.e. the date of invention under 35 U.S.C. §102[a] or one year prior to the patent application filing date under 35 U.S.C. §102[b]).

Consider the situation in which a researcher publishes an article in an electronic journal on the Internet or posts a notice for a newsgroup discussion. Both forms of electronic publication are intentional, public disclosures of information. But can electronic communication be considered as prior art?

Although this issue has not been examined in the courtroom, current US case-law indicates that courts should have little difficulty in applying traditional patent law to an electronic publication. Indeed, courts routinely decide whether a new form of information is prior art. (A more detailed discussion of this topic is available from the Biotechnology Law Web Server at: http://biotechlaw.ari.net".)

Accordingly, a US patent application should be filed within one year of any electronic publication that describes subject matter that the researcher hopes to patent. Otherwise, all patent rights to the disclosed subject-matter may be lost in the US.

What happens to foreign patent rights when an invention is disclosed in an electronic publication prior to filing a patent application? In contrast to US patent rights, foreign patents can be lost as soon as the information is published. This is so because the one-year "grace period" for publication is unique to US patent practice.

In sum, the disclosure of an invention in an electronic journal or in a newsgroup presents a risk to patent rights because an electronic publication is analagous to a traditional paper publication. In both cases, a description of an invention is placed in the public domain.

Certainly, exchanging information via electronic mail cannot affect patent rights because this form of communication is private—or is it? The very act of sending E-mail can require repeated copying of the message. (Extracted from *Genetic Engineering News*, 15 May 1995)

G. BOOK/JOURNAL REVIEWS AND BIOINFORMATICS

Book/Journal Reviews

Applications to developing countries' food supply uncertain

The potential contribution of biotechnology to increasing food security or to more sustainable agriculture production in developing countries is uncertain, according to a technical paper from the OECD Development Centre. Many products emerging in OECD member countries (for example, herbicide-tolerant rapeseed, long shelf-life tomato) are not necessarily relevant to the problems confronting developing country agriculture, it is stated in the preface of *International Initiatives in Biotechnology for Developing Country Agriculture: Promises and Problems.*

The paper, by Carliene Brenner and John Komen, covers subjects including bilateral aid programmes, public/private initiatives and intellectual property rights, international initiatives in perspective, and the implications for planning and policy.

The report is available from OECD, rue André-Pascal, F-75775, Paris Cedex 16, France.

Food biotechnology: microorganisms

Industry and academia have a valuable new resource with the recent release of *Food Biotechnology: Microorganisms*. The 1,000-page compendium includes submissions from 47 distinguished scientists from nine different countries. It covers three broad areas: principles of food biotechnology, with examples of general applications; production of enzymes and food ingredients; and the manufacture of fermented foods.

Dr. George Khachatourians, professor of Applied Microbiology and Food Science at the University of Saskatchewan, co-edited the book with Dr.Y.H. Hui, head of the American Food and Nutrition Centre in California. Khachatourians describes the book as "the bible for looking at micro-organisms", giving both the state of the art in the field as well as future trends as seen by a wide range of experts.

Contact: Available from VCH Publishers Inc. of New York, 220 East 23rd Street, New York, NY, USA 10010. (Source: *AgBiotech*, November 1995)

People, Plants and Patents

People, Plants and Patents: The impact of intellectual property on trade, plant biodiversity, and rural society is a "non-consensus document" that identifies trends, concerns, and opportunities on intellectual property issues relevant to plant breeding and plant genetic resources.

The document was produced by the Crucible Group, and published by the International Development Research Centre. The members of the Crucible Group represent the widest cross-section of sociopolitical perspectives and agricultural experience on the topic, from outright opponents to all forms of intellectual property protection over life forms to key proponents of life patents—as well as those with views somewhere between these poles.

Their report identifies key issues and choices related to genetic patents and describes the broader context in which decisions are being made. The report also contains 28 consensus recommendations for policy makers.

Contact: The International Development Research Centre , PO Box 8500, Ottawa, ON, Canada KIG 3H9 (Source: *AgBiotech*, November 1995)

Bacterial mineral leaching

A summary on the subject of the use of bacteria to oxidize mineral sulphides for the release of metals from ores, concentrates or waste materials has been published by the OECD. The author, Paul Norris, of the University of Warwick, UK, notes that control over the composition of the active bacterial population is limited. This is because the systems are, in all practical senses, open to the environment. He says that dumps, heaps and *in situ* operations rely on natural populations of indigenous organisms, which proliferate whenever and wherever mineral sulphides are exposed to water and air. Paul Norris continues that naturally occurring populations of bacteria are to be found at mine sites, coal spoil sites where the coal contains pyrite, and in acidic hot springs and other geothermal areas.

It is likely that steps taken to optimize conditions for the growth of bacteria, that is by regulating the Ph and by adding nutrients, would ensure denser and more active populations than those naturally developing. However, in general, the microflora found in natural circumstances are potentially as active for the purpose of mineral sulphide degradation as any "laboratory strains".

This report is available from: OECD, rue André-Pascal, F-75775 Paris Cedex 16, Tel: (33) 1 45 24 82 00, Fax: (33) 1 45 24 97 67.

Biotech business CD-ROM launched

BioCommerce Data demonstrated its biotechnology business news CD-ROM, *Biocommerce Abstracts*, at the 9th Annual Biotechnology Industry Organization Meeting, which took place in San Francisco (California, USA) from 21 to 24 May 1995. The first issue of this quarterly service covers material from January 1981 to 3 April 1995. The CD-ROM is designed for users with no previous experience of information retrieval tools and provides summaries of more than 300,000 news articles. It operates either under Microsoft Windows or DOS.

Biocommerce Abstracts summarizes articles in all major biotechnology newsletters; certain US, Canadian, and UK newspapers and industry-specific magazines; and selected scientific journals. Indexed by every organization mentioned in the original articles, it provides access by company name, subject, and date with full Boolean logic search features. Users can print search results to a printer or file as well as display them on screen.

Information about strategic alliances, financing, management changes, product development, legislation, patents, licensing, mergers and acquisitions, and litigation is included. Both specific news reports and review articles describing specific technologies, markets, or companies are covered.

BioCommerce Data also publishes *Biotech Knowledge Sources* (a monthly listing of forthcoming conferences and books) and the *U.K. Biotechnology Handbook* (a directory of British organizations), and distributes *Nordic Companies*

in Biotechnology (a directory of Scandinavian companies published by Bioprint).

For more information, contact BioCommerce Data Ltd, 95 High Street, Slough, Berks. SL1 1DH, UK, Tel: +44 1753 511 777, or Fax:+44 1753 512 239.

New ATCC Yeast Reference Guide 1995

American Type Tissue Culture Collection (ATCC) announces availability of the ATCC Yeast References Guide. This book contains 254 pages of information and detailed descriptions of 4,714 strains representing 606 named species and varieties. All culture descriptions include their current nomenclature, sources of isolation, literature citations to their biological or taxonomic significance, and formulations for their maintenance media. Additionally, a separate listing of all ATCC registered yeast type strains and a cross-index of other laboratory strain designations that appear in the literature to the corresponding ATCC number are provided in separate sections.

The reference guide price, which includes shipping, is $35.00 for North American locations and $47.00 for overseas locations.

Information and requests should be directed to: ATCC Sales, 12301 Parklawn Drive, Rockville, MD 20852, USA, Tel: 301-881-2600; Fax: 301-816-4361

Bioprocess Engineering Principles

Pauline M. Doran, 1995 Academic Press
439 pages, distributed by Harcourt Brace & Company, softcover $65.95, hardcover $312.95

This is an excellent textbook. As the author states in the preface, its "its primary aim is to present the principles of bioprocess engineering in a way that is accessible to biological scientists". In this, the author succeeds admirably. Unlike many other chemical engineering texts, this book focuses solely on bioprocesses, and does not assume the reader already possesses a high degree of competency in engineering principles and mathematics. In every chapter the reader is first introduced to the basic concepts before being exposed to more complex operations. Extensive use of appropriate bioprocessing examples aids the reader's understanding and appreciation of the concepts being discussed. The book is very well structured. It covers basic engineering calculations; presentation and analysis of data; material and energy balances; heat and mass transfer; fluid flow and mixing; reaction kinetics; and reactor design and control. Problems are included at the end of each chapter as a teaching aid. This book is recommended to those teaching bioprocess engineering to biotechnology students, and to practising biological scientists who desire knowledge in this area.

The Lancet now online

The world's oldest and most prestigious medical weekly is available in full text on DataStar.

The Lancet (LANC), currently in its 172nd year of publication, is read and respected throughout the world as an authoritative periodical for the dissemination of high quality news, research and opinion.

It is the organ whose peer review procedure makes it the publication of choice for all wishing to achieve credible exposure for their research results. In a single year *The Lancet* receives 5,000 articles for publication and a similar number of letters. Of these up to 90 per cent will be rejected ensuring that the articles are of the highest calibre, rich in facts and highly topical. Letters form important content in their own right continuing themes from earlier issues and adding new bibliographies.

A publication whose pedigree is unmatched was further enhanced following its acquisition in 1991 by leading science publisher Elsevier (now Reed-Elsevier). Since then Dr. Richard Horton, at 33 *The Lancet*'s youngest editor since its founder Richard Wakley, has been appointed and a New York editorial office opened. Now the full text of this vital journal is available in electronic form via DataStar.

LANC is updated each week and coverage is from January 1995 onwards. The text of the original publication is given in full, excluding advertisement and situations vacant. *The Lancet* will also be made available on DIALOG at a later stage.

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per hour	87.00	60.00
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Biomaterials (incorporating Clinical Materials)

At the beginning of 1995, Butterworth-Heinemann Journals were integrated into Elsevier Science, giving the opportunity for rationalization of the biomaterials journal programme. As a result of this exercise, *Clinical Materials* will cease publication as an independent journal from the end of the 1994 subscription. From 1996 *Clinical Materials* will be incorporated into the journal *Biomaterials.*

Biomaterials is an international journal covering the science and application of biomaterials and associated medical devices. It covers the basic science and engineering aspects of biomaterials, including their mechanical, physical, chemical and biological properties, relevant design and production characteristics of devices constructed of these materials, and their clinical performance. In this context, biomaterials are defined as all those materials used in medical devices in which contact with the tissues of the patient is an important and guiding feature of their use and performance.

ISSN 0142-9612 (03004) ELSEVIER: Oxford; gopher: gopher.elsevier.nl WWW:http://www.elsevier.nl

New Agbiotech booklets available

Two new public information booklets funded by Ag-West Biotech and the Canadian Institute of Biotechnology and published by Westcross House Publications are now available.

Biotechnology, Agriculture and Your Food—An Introduction to the Benefits of Biotechnology in Agriculture is designed to provide the general public with basic information about the positive impacts of biotechnology on agriculture and food.

From Field to Plate—A Discussion of the Issues Surrounding Biotechnology in Agriculture provides consumers with information on the pros and cons of agricultural biotechnology.

Contact: Ag-West Biotech Inc., 230-111 Research Dr., Saskatoon, SK, S7N 3R2. Tel: 306/975-1939; Fax 306/975-1966,
E-mail: agwest@innovplace.saskatoon.sk.ca
A handling charge may apply for multiple copy orders.

The Citizen's Guide to Biotechnology

The Canadian Institute for Environmental Law & Policy has recently published *The Citizen's Guide to Biotechnology* by Burkhard Mausberg and Maureen Pressmerkur. The report, which explores ethical, environmental and social concerns arising from the commercialization of biotechnology products, is available for $19.99 from CIELP, 517 College Street, Suite 400, Toronto, Ontario M6G 4A2 (Voice 416-923-3529; Fax 416-923-5949).

Biotechnology in Latin America: Politics, Impacts, and Risks, edited by N. Patrick Peritore and Ana Karina Glave-Peritore, is a collection of articles by political scientists, biologists, sociologists, and other experts on the implications of biotechnology for developing countries. The essays explore how Latin American countries can benefit from biotechnology and avoid exploitation by first-world developers of the technology. Available for $16.95 (paper) or $45 (cloth) from SR Books, 104 Greenhill Ave., Wilmington, DE 19805-1897 (Voice 800-772-8937; Fax 302-654-3871)

Experiments in Plant Tissue Culture

Third edition–John H. Dodds, Michigan State University, and Lorin W. Roberts, University of Idaho, with a foreword by J. Heslop-Harrison.

This comprehensive text takes the reader through a graded series of experimental protocols and also provides a preliminary view of each topic. After an historical introduction, there are discussions of a plant tissue culture laboratory, aseptic techniques, and nutritional components of media. Subsequent chapters are devoted to callus induction, organ formation, cell suspensions, somatic embryogenesis, root cultures, micropropagation, anther and pollen cultures, xylem cell differentiation, isolation and fusion of protoplasts, storage of genetic resources, secondary metabolite production and quantitation of procedures.

A glossary of terms, a list of commercial sources of supplies, and a table of media formulations are included. This new edition has been completely revised and updated. The organization has been improved, and new illustrations have been added, together with new experiments on such topics as potato callus formation, and embryo culture.

Prices:

Hardback 0-521-47313-6, $59.95, £35.00;
Paperback 0-521-47892-8, $24.95, £13.95;
Cambridge University Press, 40 West 20th Street, New York, NY 10011-4211; international orders call 914-937-9600; call toll-free from within the US 1-800-872-7423

Molecular Biology and Biotechnology

This single-volume reference is the resource for any questions relating to molecular biology, biotechnology, or molecular medicine. This work, drawing upon the leading experts in the field, provides an invaluable 'reference source' for this task. Each subject is presented on a first-principles basis, including appropriate mathematics and extensive illustrations and references.

Molecular Biology and Biotechnology, edited by Robert A. Meyers is available for DM89.00 in the soft-cover version and therefore within reach of everyone who is interested in the subject.

This book may be obtained from: VCH, International Sales, PO Box 10 11 61, D-69451 Weinheim, Germany; Fax: 06201 606 184.

Canadian Biotechnology Handbook '95

Canadian Biotech News, in association with Ernst and Young, has announced the forthcoming publication of the *Canadian Biotechnology Handbook '95*. The handbook produces a comprehensive summary of the industry. Circulation is guaranteed to reach potential investors and alliance partners. The handbook will also be distributed internationally to biotech and pharmaceutical companies, Canadian consulates, venture capital companies and at selected trade shows.

For information contact: Dr. Maura Campbell, CMG Marketing Group, 463 Cambridge Street South, Suite 202, Ottawa, Ontario, KIS 5G3; Tel: 613/567-9406 or Fax: 613/567-9170.

Bio Computing

New BIN21 Node

BINAS, UNIDO's Biosafety Information Network and Advisory Service has just joined BIN21. BINAS has accepted to coordinate the theme "biosafety" within the BIN21 network acting as a focal point for this theme.

BIN21 nodes page can be found at: http://www.bdt.org.br/bin21/nodes.html and BINAS' web page is located at: http://binas.unido.org/binas/binas.html.

For additional information please contact: web master@binas.unido.org

US Patent and Trademark Office Web Site

The US Patent and Trademark Office has a very informative home page. For those who are interested in checking it out, use http://www.uspto.gov

Sources of gene patents

Full-text gene patents and other biotech-related patents are available at http://www.inform.umd.edu:8080/EdRes/Topic/AgrEnv/Biotech/Biotech nology_Patents-full_text

Patents for traditionally-bred organisms are available at gopher://gopher.nalusda.gov/11/infocntr/pltgen/germplasm/Patents

HyperSearch: keyword search for HyperCLDB

This is to announce availability of HyperSearch, the brand new search engine that allows for keywords searches within HyperCLDB, the hypertextual version of the Cell Line Data Base, available by the Advanced Biotechnology Centre WWW server (URL: http://www.ist.unige.it).

HyperSearch will allow you to carry out keywords searches in the descriptions of all cell lines included in HyperCLDB and, after retrieval, you will be able to continue navigation through usual links.

HyperCLDB has also been updated. Current release is version September 1995 and includes detailed descriptions of 3,124 cell lines available in European culture collections and laboratories (ca. 26 Mbytes of data). Among others are the European Collection of Animal Cell Cultures (ECACC, Salisbury, UK), the German Collection of Microorganisms and Cell Cultures (DSM, Braunschweig, DE), the German Cancer Research Centre (DKFZ, Heidelberg, DE), the Interlab Cell Line Collection (ICLC, Genoa, IT), the Russian Cell Culture Collections (St. Petersburg) and various other Italian collections of primary and continuous cell lines.

You are warmly invited to try HyperSearch and navigate HyperCLDB starting at http://www.ist.unige.it/tab/HyperSearch.html or at http://www.ist.unige.it/cldb/

indexes.html and send your comments to paulo@riscl.ist.unige.it.
(from Paulo Romano, Biotechnology Department of the National Institute for Cancer Research, Genoa, Italy).

Online buyer's guide for research products and services

Cold Spring Harbor Lab. Press introduces BIOSUPPLYNET—an online directory of biotech research products and services. This new WWW site offers free searching in the CSH Lab Manual Source Book database of 15,000 laboratory products and 1,400 suppliers. BIOSUPPLYNET features "Interactive Product Listings" (IPLs), which provide users with instant access to details on many of the products contained within its extensive database.

BIOSUPPLYNET is updated weekly and provides:
(1) Information on new products and special offers;
(2) Access to 15,000 laboratory product listings from over 1,400 suppliers;
(3) An opportunity for users to share expertise through product user groups;
(4) Immediate access to suppliers via email for technical queries and other information;
(5) Links to more than 100 biology-relevant Web servers.

BSN is accessible at: http://www.biosupplynet.com/bsn/

A free copy of the CSH Lab Manual Source Book can be obtained through Cold Spring Harbor Web Site, CLIO, http://www.cshl.org/

Public perceptions of genetic engineering

The report of the survey "Public Perceptions of Genetic Engineering: Australia 1994", by Dr Jonathon Kelley, International Social Science Survey/Australia, is now on the Web. The survey was commissioned by the Department of Industry, Science and Technology (DIST). The report, including questions, data and analysis, is located on DIST's home page at: http://www.das.gov.au/~dist/home.html

Hard copies of the survey can be obtained from: Mary Argall, Biotechnology Section, DIST, GPO Box 9839, Canberra, ACT 2601 (E-mail MArgall@dit.gov.au)

DNA vaccines

New on the Internet! Visit the DNA Vaccine Web at http://www.genweb.com/Dnavax/dnavax.html

Internet resources for the environmental industry

http://www.enviroindustry.com/resources/html

A well-maintained list of Internet resources relevant to the environmental industry, including general starting points, design for environment, government agencies, ISO 14000, law/regulation/policy, pollution prevention, recycling and waste water. Sponsored by the Environmental Industry Web Site http://www.enviroindustry.com/

InfoBiotech Canada

http://www.ibc.nrc.ca/ibc/

InfoBiotech Canada is a partnership of government, private and academic sectors with the goal of providing central, enhanced access to information on biotechnology in Canada and world-wide. Canada has a strong biotechnology research base and an emerging industry focused on applications of biotechnology in health care, agriculture, environment, aquaculture, forestry, mining and other sectors. We believe that encouraging the exchange of information on biotechnology will lead to economic and social benefits both nationally and internationally.

In addition to providing a capability for rapid keyword-based searches, the site allows one to browse a wide variety of sources such as:

- Hundreds of complete listings of biotech information providers
- Research and development information in Canada, the US and other countries
- Regulations and regulating bodies in Canada, the US and other countries
- Internet addresses of biotech-related companies
- A new products and techniques showcase
- Investment opportunities and technology transfer offices.

InfoBiotech Canada is an initiative of the National Biotechnology Strategy, instituted by the federal Government in 1983 to develop a strong national capability in biotechnology. Fourteen federal departments participate in coordinating activities to provide an appropriate infrastructure for the commercial development of biotechnology.

The InfoBiotech Canada server is maintained and developed by the Canada Institute for Scientific and Technical Information, part of the National Research Council of Canada.

For more information, contact Dr. Gordon Wood, National Research Council Canada at (613) 993 3294 or gordon.wood@nrc.ca

Biotechnology for the 21st Century: New Horizons

At a media event announcing regulatory reforms at the Food and Drug Administration impacting biotechnology drug development, Vice President Al Gore and the President's Science Advisor, Dr. Jack Gibbons, announced the release of the above-named report.

The 90-page report was prepared by the National Science and Technology Council's Biotechnology Research Subcommittee and describes the federal investment in biotechnology and identifies research priorities and opportunities for the future. To reach as broad an audience as possible, in addition to the print format, the report is available via the WWW at: http://www.nalusda.gov/bic/bio21/ or alternatively via the NSTC home page at: http://www.whitehouse.gov/White_House/EOP/OSTP/NSTC/html/NSTC_Home.html

In discussing the new report the Vice President stated "this report, a product of planning and coordination through the National Science and Technology Council, lays out priorities for future investment in research to enable the contributions of biotechnology in emerging areas beyond health—in agriculture, environmental remediation, bio-processing approaches to manufacturing, and in applications of biotechnology to preserve and utilize marine resources". Dr. Gibbons added "the collection of techniques that have come to be known as biotechnology—the use of restriction enzymes to cut and splice DNA and RNA, early sequencing technology, and regulation of gene expression—are largely the result of research in fundamental biology that was supported by the federal Government. The research at the very beginning of the product development pipeline, with broad utility across the entire spectrum of biotechnology applications, remains well within the domain of programmes supported by 13 Executive branch agencies." "Under the purview of the National Science and

Technology Council, these agencies conducted an extensive 18-month examination of their biotechnology research portfolios. Today, I am pleased to present the product of their efforts, Biotechnology for the 21st Century: New Horizons. This report identifies the leading priorities for federal investment in biotechnology research beyond health, and describes a number of specific scientific opportunities. The areas that were examined are: agriculture, environment, manufacturing and bioprocessing, and marine biotechnology and aquaculture."

BioResearch Ireland now on the Internet

BioResearch Ireland, Ireland's biotechnology contact research and product development organization is now accessible on the Internet. The home page address is: Http://www.forbairt.ie/BIORESEARCH.HTML

Information is available on each of the five research centres which comprise BioResearch Ireland, including research programmes and contact research services. Also outlined are products developed, i.e. diagnostic assays, cell culture products and reagents. Publications such as the quarterly newsletter "*Irish Biotech News*" are also shown, this highlights technology licensing opportunities, and available products. This is constantly updated to show the current edition.

Further information on BioResearch Ireland can be obtained from: Phil O'Leary, BioResearch Ireland, Forbairt, Glasnevin, Dublin 9, Ireland. Tel: +353 1 837 0177; Fax +353 1 837 0176.

Academy of Science

The Australian Academy of Science has just launched a WEB site.
http://www.asap.unimelb.edu.au/aas/aashome.html

It is gaining a reputation as a very useful site containing science policy reports in full, awards and grants information, publication details, and lots of information on science in Canberra.

Biosafety journal is online

Brian Kirsop, editor, Biosafety

BioSafety is a new online-only, peer-reviewed journal which publishes papers and reviews about biological safety, its assessment and its control. It specializes in studies targeting the release of genetically modified and wild-type organisms into ecosystems, monitoring of releases and biosafety regulations.

Publication in Biosafety is rapid. Papers are published individually and are online immediately after approval by referees; abstracts are freely available to all Internet users and copyright remains with the authors.

Contributions are invited; notes for contributors and subscription information may be obtained from biosafe@biostrat.demon.co.uk or online from the WWW. The URL is http://www.ftpt.br/cgi-bin/bioline/by

Patent database available on Internet

A patent database developed by CHI Research Inc. is now available on the Internet. The database provides key information for 1.7 million US patents issued since 1975, and tracks how each patent is cited in other patents. Some 10 million patent citations are included.

Contact: Charles Wise, Community of Science. Tel: 410 563 5382; E-mail cw3@bestpl.hcf.jhn.edu (Source: *AgBiotech Bulletin*, January 1996)

Patent information on Internet

Agricultural patent notices and cutting edge technology information are available through the USDA's National Agricultural Library.

Contact: Internet: at gopher.nalusda.gov70 and select NAL Information Centres and Technology Transfer Information Center. (Source: *AgBiotech Bulletin*, October 1995)

Bioethics resources available

The Iowa State University's Bioethics Programme is publishing a biannual newsletter of interest to Extension professionals, teachers, and others interested in the ethical issues associated with biotechnology.

The *Ag Bioethics Forum* is now available on the Web. It contains philosophical debates by experts on such questions as "Can ethical theory resolve disagreements about ag biotech?" However, you can still get it the old-fashioned way.

Contact: Gary Comstock, Program Coordinator, 413 Ross Hall, Iowa State University, Ames, Iowa, USA 50011-2063. Locate the Ag Bioethics Forum at http://www.public.iastate.edu/~grad_college/bioethics/
(Source: *Agbiotech Bulletin*, January 1996)

Panna online resources

PANUPS: PANNA Update Service (PANUPS) is a weekly news service featuring articles on pesticide use and sustainable agriculture from around the world, as well as action alerts and conference reports. PANUPS also includes a weekly online resource pointer which lists information about the latest books, reports, articles and other resources related to pesticides and sustainable agriculture. To subscribe, send E-mail to majordomo@igc.apc.org with the message: "subscribe panups".

PESTIS: Pesticide Information Service (PESTIS) is an online database containing pesticide reform-related material generated by NGOs, including articles, newsletters, reports and action alerts, all of which can be full-text searched. PANNA is developing PESTIS in collaboration with other groups including:

- Community Alliance with Family Farmers (CAFF);
- Institute for Agriculture and Trade Policy (IATP);
- Northwest Coalition for Alternatives to Pesticides (NCAP);
- The Pesticides Trust (UK);
- RAPALMIRA (PAN Latin America Regional Center).

For EcoNet users, PESTIS is available in the online databases section (in the main menu) under News Services. PESTIS is also available on the Internet via the EcoNet Gopher.

ECONET GOPHER: If you have access to a gopher client on your computer network, you can reach EcoNet's gopher by using the gopher address: gopher.econet.apc.org. The Pesticides and Sustainable Agriculture section of EcoNet's gopher contains PANNA reports and news items, the PESTIS database, articles and information that other groups and individuals have contributed, and pointers to other related Internet resources. Many of PANNA's reports are also available on the gopher.

PANNA'S WORLD-WIDE WEBPAGE: PANNA's Webpage (http://www.panna.org/panna/)offers a graphical interface with all of our existing online services such as PANUPS and PESTIS, and includes pointers to many other pesticide and sustainable agriculture-related information onthe Web and the Internet.

New genetic database launched world-wide

The Institute of Genomic Research Human cDNA Database (TIGR HCD) has been made available to academic researchers world-wide.

TIGR HCD, which is one of the largest databases of human genetic data yet constructed, forms the basis of the most extensive study of human genes, their expression and diversity.

The sequencing was carried out at The Institute of Genomic Research and Human Genome Sciences (London, UK). Smithkline Beecham, which collaborates with TIGR and HGS in their DNA research programme, has invested £5 million in academic researchers and non-profit organizations.

TIGR HCD currently contains 375,000 expressed sequence tags (ESTs) of genes and is being added to daily.

Some 50-60 per cent of the TIGR HCD database consists of "black-box genes", which no one as yet really understands. (Extracted from *Biotechnology Business News*, 4 October 1995)

TANZANIA INTERNATIONAL INVESTORS FORUM

DAR ES SALAAM

5-8 November 1996

A UNIQUE OPPORTUNITY FOR INVESTMENT AND TECHNOLOGY

Investent in Tanzania has been on the upward trend with the backing of the Government, particularly in the private sector. To capitalize on the positive trend of the Tanzanian economy and the renewed interest of foreign investors towards business opportunities in the country, the Ministry of Industries and Trade, the United Nations Industrial Development Organization (UNIDO) and the United Nations Development Programme (UNDP) are organizing an international investment and technology forum to bring together Tanzanian entrepreneurs with foreign partners from all over the world to discuss, develop and conclude business partnership agreements. The projects presented at the forum will cover:

* Manufacturing
* Tourism
* Mining
* Infrastructure (BOT)

To enhance the transfer of technology, especially for small- and medium-scale enterprises, stands and booths are available to display products/samples and provide information to technology seekers. Investment support organizations and banks will also be represented.

For further information, please contact:

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