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INTERNATIONAL CENTRE FOR GENETIC ENGINEERING AND BIOTECHNOLOGY

HELIX

THE ICGEB NEWSLETTER JUNE 1991

Biotechnology is a technology of great promise. It offers us an infinite number of ways of combating hunger, securing health and conserving our environment: concerns of crucial importance to the developing countries. UNIDO shares those concerns and is determined to harness the best resources to pave the way to sustainable development. Internationalization is a critical factor in that process. Centres, such as the International Centre for Genetic Engineering and Biotechnology, a major UNIDO project, provide an all-essential forum for effective international co-operation. They constitute an enabling scientific and educational environment for research and development into the pressing needs of developing countries. The Centre not only ensures access to state-of-the-art research and equipment, but it also disposes of a critical mass of scientific staff and can offer advanced training. By co-operating through the Centre with their counterparts in developed countries and engendering a sense of true partnership and dialogue, the scientists in developing countries not only remain at the cutting edge of a new technology, but they also help to keep it sharp and effective. The sense of community in the field of innovative research is heightened by the application of modern electronic communications, such as the Centre's computer information resource, ICGEBnet, and more recently its newsletter HELIX. A welcome addition to the services provided by the Centre, the newsletter aims at enhancing the dialogue among its large membership.

original contains color illustrations

Domingo L. Siazon Jr.
Director-General of UNIDO

Editorial

Biosafety is an emotionally charged term giving rise to fierce debate amongst scientists, policy makers and industry. In the West, safeguards demanded by environmentalists are often seen by industry as discrimination against biotechnology products, by subjecting them to extra levels of testing and regulation. In developing countries lack of safeguards or indeed of any regulatory framework is viewed with concern. It is often felt that deregulation will turn these countries into testing grounds for releases of transgenic organisms which would not be given test permits in the developed word. The testing of a rabies vaccine in Argentina in 1986 is often quoted as an example. On the other hand in the case of most developing countries, adoption of a regulatory framework, although legitimizing environmental releases, does not guarantee adequate monitoring of field tests due to lack of resources and expertise. In this sense, it is feared that regulation *per se* could be a more serious cause of relocation of potentially hazardous experiments to developing countries than lack of regulation itself. Some analysts argue that even if relocation is not on the cards, adoption of rigid regulations ridden with bureaucratic procedures is likely to be a serious impediment to technology transfer, limiting the availability of much needed products and processes to developing countries.

A number of initiatives is underway (see News), all trying to allay possible apprehensions over biotechnology applications, facilitate technology transfer and harmonize risk assessment methodologies.

But even if one denudes biosafety of all elements that tend to tint it politically, there remain questions to be answered before one takes a more relaxed attitude towards biological safety. True, a decade ago, a lot of the fears were originally generated by relative ignorance. Could genetic tampering through recombinant technologies lead to unpredicted genomic alterations? Is recombinant gene transfer through species barriers any different from that occurring in nature randomly through transduction and transformation? Most of these fears have been dispelled since. In fact the precision and

In the case of most developing countries, adoption of a regulatory framework, although legitimizing environmental releases, does not guarantee adequate monitoring of field tests due to lack of resources and expertise.

ICGEB: scientists and programmes

Francisco E. Baralle, born in Buenos Aires on 26 October 1943, graduated in medicine and chemistry at the University of Buenos Aires, Department of Organic Chemistry. After gaining his Ph.D. he transferred to the *Instituto de Investigaciones Bioquimicas Fundacion Campomar* directed by Prof. Luis F. Leloir. In 1974, he moved to the MRC Laboratory of Molecular Biology, Cambridge, UK, where he worked in the Division directed by Prof. Frederick Sanger. From 1980 to 1990 he was Professor of Pathology at Oxford University and Fellow of Magdalen College. He is a member of the European Molecular Biology Organization. He was appointed Head of the Trieste Component of ICGEB in September 1990.

Prof. Baralle was involved in the determination of the primary structure of eukaryotic mRNA. In 1977 he was the first to complete the sequence of the messenger of human beta-globin and, in 1979, to clone the gene of the beta-globin, a component of the human embryonic haemoglobin. He carried out research on thalassemia and is currently studying the genetic factors involved in the

susceptibility to atherosclerosis. In his laboratory he is developing projects on the study of the genes of apolipoprotein AI and AII components of the High Density Lipoproteins (HDL) involved in the reverse cholesterol transport. High plasma levels of HDL seem to be associated with a low incidence of coronary heart disease. The knowledge of the genetic mechanisms which regulate these levels can be not only of great scientific interest but also of great value in clinical practice. Another project focuses on the different coding genes for the extracellular matrix proteins such as fibronectin and tenascin, and the RNA alternative splicing mechanisms involved in the generation of isoforms of these proteins. In the field of hypertension, Prof. Baralle is interested in adducin, a cytoskeletal protein whose properties could influence arterial tension.

In collaboration with pharmaceutical companies he has initiated biotechnology projects aimed at producing polypeptides of pharmaceutical value such as erythroprotein, the coagulation in factor VIII and some lymphokines.

In his laboratory at ICGEB, apart from carrying out basic research in the above fields, an applied project has been initiated for the development of diagnostic kits, innovative vaccines and the production of recombinant monoclonal antibodies for immunodiagnostics and therapy. Particular attention is focused on Hepatitis B and C vaccines. They are being developed using a novel epitope presentation system based on the capsid of the Black Beetle Virus (BBV). This structure allows a considerable flexibility for the blending of foreign T and B cell epitopes in a strongly immunogenic context.

The virology group at ICGEB-New Delhi

Research activities, headed by Dr. Shahid Jameel, are currently directed towards studies, at the molecular level, of two types of viral hepatitis: hepatitis B and enteric non-A non-B hepatitis.

The Hepatitis B Programme

Hepatitis B is a major world health problem with an estimated 200 million carriers of this disease worldwide. The predominant mode of transmission is parenteral, where chronic carriers constitute the reservoir for spread of infection to other susceptible individuals, either horizontally or vertically. Severe chronic hepatitis B frequently leads to premature death from liver failure. Chronic hepatitis B is also associated with the development of primary hepatocellular carcinoma (PHC) with risk of PHC development being about 300-fold that of age matched non-carriers.

The aetiological agent for this disease, hepatitis B virus (HBV), is a small (42 nm), partially double-stranded DNA virus (Fig.1). The host range of HBV is narrow, to date productive infections have been established only in human beings and higher primates. In permissive hosts viral antigens and DNA are found primarily within liver cells, which harbour abundant quantities of replicative and assembly intermediates as well as mature virions. The genome of HBV is circular DNA of only 3.2 kilobases in length which encodes at least four viral antigens: DNA polymerase (P), Core (HBc), Surface (HBsAg) and X (HBX) proteins.

The hepatitis B programme is focussed on the following aspects:

1. Expression and characterization of functional domains of the X-protein (HBX).
2. Analysis of the enhancer element of HBV.
3. Novel approaches towards the design of a molecular vaccine for hepatitis B.
4. Lymphokine-derived immunostimulatory agents as potential adjuvants.

1. Hepatitis B virus X Protein

Of all the HBV-encoded proteins, X is the least understood. Recently, it has been shown to be capable of trans-activating a number of viral and cellular promoters or enhancers. Most significant in this respect is trans-activation of the long terminal repeat (HIV-LTR) of the human immunodeficiency virus (HIV) by X, as it is the first evidence of an interaction between HBV and HIV at the molecular level. This supports clinical observations that a majority of AIDS patients also test positive for hepatitis B. Does HBV infection in any way predispose towards HIV infection? With the HBV X protein trans-activating the HIV-LTR, it is possible that HBV infection may activate a latent form of HIV into full-blown AIDS.
Research is directed towards an understanding of the mechanism of this trans-activation. A simple-minded mechanism would involve binding of X to its target DNA sequence(s), just like a number of known transcription factors. Preliminary evidence rules this out because X does not seem to bind DNA, and no consensus nucleotide sequence can be localized on target DNA. Trans-acting factors that do not bind DNA generally act by interacting with or modifying other DNA-binding proteins.

This problem is being approached by generating a number of site-directed mutants of the X protein. The trans-activating properties of these mutants will define the functional domains of this protein. Simultaneously co-precipitation of X and other cellular proteins with anti-X antibodies is being pursued to define proteins capable of associating with X.

2. HBV Enhancer

Enhancers are cis-acting DNA elements that are able to potentiate transcription from RNA polymerase II (B) transcribed promoters independent of orientation and distance. They also confer tissue specific gene expression and most interestingly, they are often found transposed to proto-oncogenes thereby inducing tumor formation.

A major HBV enhancer has been mapped to a region between the surface and X genes. This enhancer can transcriptionally regulate at least three HBV promoters -- the X and core promoters are located downstream while the surface antigen promoter is located upstream. It also binds several cellular proteins and exhibits liver specificity. A second liver specific enhancer has recently been identified adjacent to the core promoter of HBV. It may be developmentally regulated as excessive core gene expression is observed in advanced hepatocellular carcinoma when HBV replication is virtually absent.

The research programme includes a detailed mutational analysis of certain repeated sequence elements present within the major enhancer region of HBV. Cloning out enhancer binding factors from liver cDNA libraries using the "South Western" technique is also underway. These studies are likely to help in understanding

mechanism(s) of gene expression in cells infected with the virus, its role in pathogenesis of hepatitis and hepatocellular carcinoma and tracing the evolutionary origin of hepadnaviruses.

3. A Molecular Vaccine for Hepatitis B

The synthetic peptide methodology has proved immensely useful in mapping important domains within surface antigen proteins of a variety of pathogens. However, keeping the phenomena of MHC-restriction and antigenic variation in mind, it appears unlikely to us that a synthetic peptide vaccine will prove effective in a genetically outbred human population. A novel approach is being followed to overcome these problems. Proteins will be designed that code exclusively for a variety of selected immunologically and functionally relevant determinants of the hepatitis B surface antigen. The synthesis, assembly and expression of the gene for one such construct is currently underway. It is anticipated that studies of this nature will also help elucidate some basic principles applicable towards the design of molecular vaccines in general and in addition provide an excellent model system to study the mechanism of antigen processing and presentation.

As a corollary to these above described studies, synthetic peptides are used extensively to identify important and potentially useful regions of HBsAg. Recent efforts have also been focussed at reconstructing conformation-dependent antigenic determinants of HBsAg with synthetic peptides.

The development of a recombinant HBV vaccine is also planned. This will include sequences from the pre-S regions to improve the immunogenicity as compared to the vaccines currently available. Certain novel approaches aimed at maximizing HBsAg expression in cultured cells are currently being pursued to provide a cost-effective alternative to the presently available recombinant HBV vaccines.

4. Lymphokine-derived - Immunostimulatory Agents

Broadly speaking the approach here involves the use of synthetic peptides from lymphokine sequences that are capable of potentiating the immune response against a given immunogen. Our initial efforts are focussed on human interleukin-1β (IL-1β) since a nonapeptide derived from this protein with immunostimulatory activity has already been described. We have shown that coupling of this nonapeptide sequence to a given peptide immunogen can confer in-built adjuvanticity at least in the murine system. We are currently examining the potency of other IL-1 derived sequences and, in particular, peptides that combine various functional regions of the native IL-1 protein. It is expected that such 'bonsai' versions of IL-1 will find application as adjuvants in a variety of vaccine preparations including that for hepatitis B.

By enhancing immunogenicity of a given vaccine in such a manner, it should be possible to reduce the number of immunizations required to confer total protection. This would then make it more amenable to global immunization both by reducing cost and increasing efficacy in terms of lower drop-out rates and thereby be of particular benefit to the developing world.

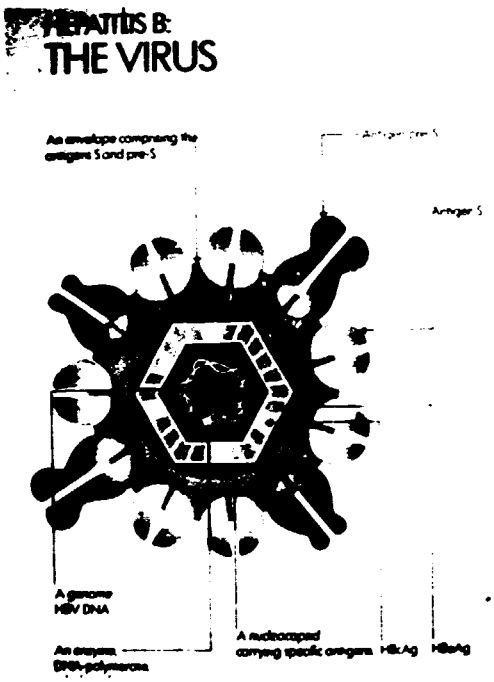


Figure 1

The Enteric Non-A Non-B Hepatitis Programme

The development of diagnostic tests for viral hepatitis A and B has led to the realization that another form of viral hepatitis exists. The diagnosis of this Non-A, Non-B (NANB) hepatitis is currently one of exclusion. Two major forms of NANB hepatitis are recognized worldwide.

Of these, enteric NANB hepatitis follows a faecal-oral transmission, with contaminated drinking water as the major source of infection. This form of hepatitis is endemic to the Indian subcontinent and a number of major epidemics have been reported in the last few years. A seroepidemiologically similar disease has also been reported from Southeast and Central Asia, parts of Africa, the Middle East, the Soviet Union, as well as parts of North and Central Americas. Current estimates project that with the availability of definitive diagnostic protocols, this form of hepatitis may exceed hepatitis B as the world's most common form of hepatitis.

The candidate aetiological agent has been identified as a 27-34 nm viral particle in the stools of patients (Fig. 2). Initial efforts con-

cerning enteric NANB hepatitis are aimed at cloning the genome of this virus. To this end, an animal model system has been set up involving transmission of the disease from human patients to rhesus monkeys by inoculation of infectious stool suspensions. Subtractive cDNA libraries from animal materials in bacteriophage lambda are currently in preparation. These libraries will be screened with convalescent sera to identify specific clones. Regions of the viral genome once cloned will provide the basis for developing definitive diagnostic reagents, and later on, a recombinant vaccine. Based on minimal nucleotide sequence information available, polymerase chain reaction (PCR) based strategies are also being pursued for developing a confirmatory diagnostic test for enteric NANB hepatitis.

The Virology research group at ICGEB has ready access to a protein sequencer, automated peptide and oligonucleotide synthesizers and an animal house.

Figure 2

Published work from the Virology group at ICGEB — New Delhi

1. S. Jameel, A. Siddiqui, H.E. McGuire and K.V.S. Rao (1990). *Hepatitis B virus X protein produced in* Escherichia coli *is biologically functional.* J. Virol. 64:3963.

2. K.V.S. Rao and A.R. Nayak (1990). *Enhanced immunogenicity of a sequence derived from hepatitis B virus surface antigen in a composite peptide that includes the immunostimulatory region from human interleukin 1.* Proc. Natl. Acad. Sci. U.S.A. 87:5519.

3. S. Dash, K.V.S. Rao, B. Joshi, N.C. Nayak and S.K. Panda (1990). *Significance of natural polymerized albumin and [illegible] receptor in hepatitis B infection of hepatocytes.* Hepatology (in press).

Profile of research staff

Vidhu Jain (Laboratory Technician, M.Sc., Jawajarlal Nehru University, 1989). Purification of peptides by h.p.l.c. Purification of oligonucleotides and assembling synthetic genes.

Shahid Jameel (Assistant Scientist, Ph.D., Washington State University, Pullman, USA, 1984). Expression of HBV genes in heterologous systems. Molecular cloning and PCR analysis of the ET-NANB genome.

Ravinder Kumar (Laboratory Technical Assistant, B.Sc., University of Delhi, 1984). Maintenance of eukaryotic cell lines, preparation of media and care of P3 lab. Serodiagnosis of hepatitis markers in patient sera.

Vijay Kumar (Research Scientist, Ph.D., All India Institute of Medical Sciences, New Delhi, 1984). Characterization of the enhancer element of HBV. Structure-function analysis of HBX and gene expression.

Venkatasamy Manivel (Senior Research Fellow, Ph.D., Indian Institute of Science, Bangalore, 1983). Characterization of immunomodulators and peptide antigens derived from HBsAg.

Kanury V. S. Rao (Research Scientist, Ph.D., M.S. University of Baroda, 1983). Designing a molecular vaccine against HBV by recombinant DNA and synthetic peptide techniques. Characterization of immunomodulators and immunologically relevant determinants of HBsAg.

Girish C. Shukla (Laboratory Technical Assistant, B.Sc., University of Delhi, 1983) Routine DNA cloning, plasmid isolation, gene expression and preparation of laboratory reagents.

ICGEB: affiliated centres

BIOTECHNOLOGY OF MINING — BACTERIAL LEACHING OF MINERALS IN CHILE

by **Jorge E. Allende** *President of the National Committee of Biotechnology of Chile*
The Chilean National Committee for Biotechnology is part of CONICYT the Government's National Council for Research in Science and Technology. The National Committee for Biotechnology coordinates the activities of ICGEB affiliated laboratories in Chile.

Chile, like many other developing countries, is highly dependent on mining. Copper exports account for nearly 50% of the foreign currency that the country receives annually. It is not surprising, therefore, that one of the priority areas of the National Committee for Biotechnology of Chile is the bacterial leaching of minerals.

As the grade of the existing copper ores becomes lower and lower through continuous exploitation bacterial leaching and hydrometallurgy become more important in the mining business. Some experts have estimated that 20% of all the copper presently extracted in the U.S. is produced through processes involving bacterial leaching. The commercial feasibility of the bacterial leaching process depends a lot on the type of copper ore involved.

High grade sulfide copper ores (above 0.5%) are extracted through the classical pyrolytic process, which is faster and more economical but which has serious problems due to atmospheric contamination. Oxide ores of copper can be chemically leached with concentrated sulfuric acid treatment of the minerals in heaps or piles. The most abundant copper ores, however, are chalcopyrites which are mixed cuprous and ferrous sulfides. These sulfide ores are quite recalcitrant to chemical leaching and can only be leached effectively through the action of bacteria. The bacteria that can carry out this process are very peculiar micro-organisms since they require a very acid environment (below pH 3.0) to grow and derive their energy from ion oxidations. There are a number of microorganisms that can participate in the leaching process including bacteria from the genera *Thiobacillus*, *Leptospirilli* and *Sulfolobus*. Some of these bacteria are shown in figure 1. However, the best known and most abundantly found is *Thiobacillus ferrooxidans*. This gram negative bacterium can fix atmospheric CO_2 and N_2 to obtain carbon and nitrogen compounds for its metabolism and uses atmospheric O_2 to oxidize ferrous to ferric ions and sulfides to sulfate. These oxidations are its sources of energy.

Figure 2 shows that *T. ferrooxidans* can attack chalcopyrite directly to solubilize ferric and sulfate ions. The ferric ion can in turn oxidize the cuprous ion of the chalcopyrite to cupric ions that go into solution.

Empirically the action of these bacteria can be observed in a situation when a heap of ore containing copper oxides and chalcopyrites is irrigated with dilute sulfuric acid as shown in the experimental heap presented in Fig. 3.

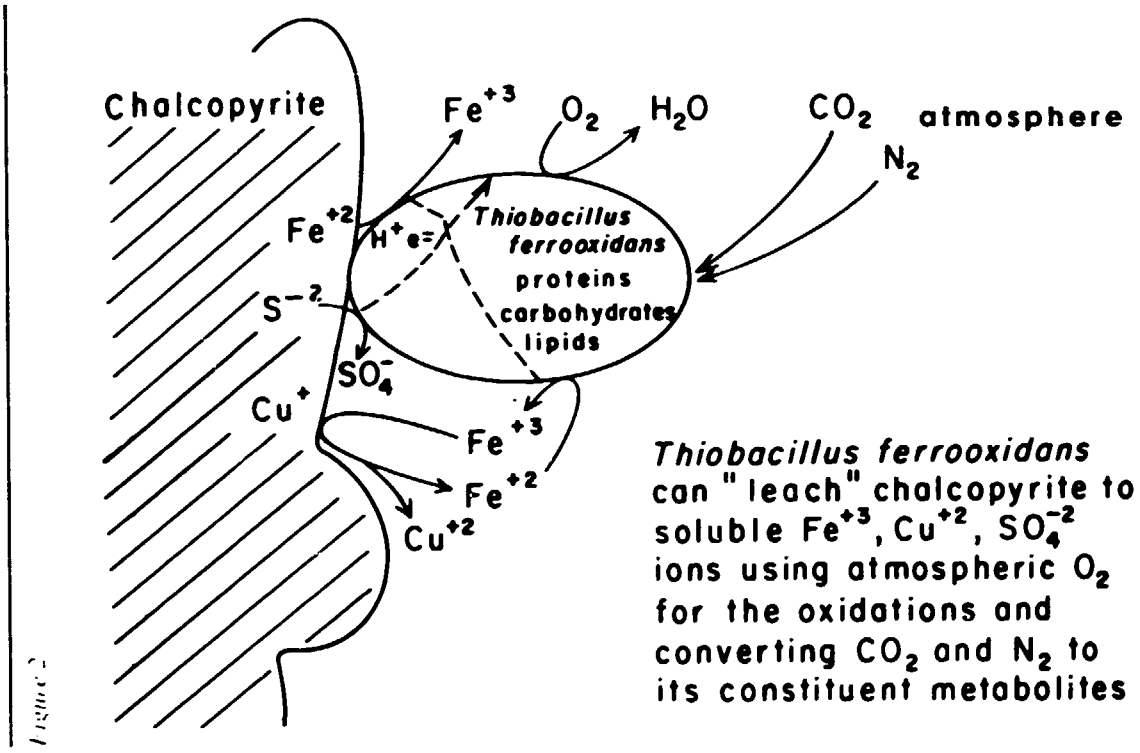
Analysis of the effluents emerging from such a heap reveals that there is an initial yield of solubilized copper due to the fraction of copper oxides present in that ore. After a variable period of several weeks, during which the heap has been intermittently irrigated with the acid solution, the effluent again contains soluble copper in appre-

Figure 1

ciable amounts and also shows the presence of leaching bacteria in numbers that normally range from 10^{8} — 10^{10} bacteria/ml. The extraction of copper by this method is very slow since it may take several months to achieve a commercially significant percent of the copper sulfide in the ore. Very often, however, the low grade ore that can be treated in this way has already been withdrawn from the mine together with richer ores and dumped due to the process. Copper recovery from these ores, therefore, constitutes a welcome bonus for the mining operation.

How can biotechnology help such a process? The reply of the mining engineers and executives is to ask the bio-scientists to try to accelerate the process. From laboratory experiments performed with columns packed with typical ores, it can be demonstrated that growth of the bacteria in the ore is intimately related to the yield of copper leached from the mineral. However, there are a large number of other factors such as the granulometry of the ore being treated, the fluid dynamics within the heap of ore, the composition of the ore, the temperature outside and inside the pile, the partial pressure of the atmospheric gases required by the bacteria. For this reason, a biotechnology project that deals with improving the bacterial leaching of copper ores requires a large transdisciplinary team of researchers that ranges from basic bacteriologists and molecular biologists to mining engineers, geologists and electrochemists.

In 1985, a group belonging to the Chilean National Committee for Biotechnology, won the approval of the Chilean government, the United Nations Development Programme (UNDP) and the United Nations Industrial Development Organization (UNIDO) for a project to carry out research in the bacterial leaching of Chilean copper ores. This project had a first stage covering 1985-1987 and second stage 1988-1990. It has involved six institutions: the University of Valparaiso, the Technological Institute of Chile, the Centre for Mining and Metallurgy and the Chilean Copper Corporation (CODELCO). CODELCO is one of the largest copper mining companies in the world since it controls all the state owned mines of Chile. There are more than 50 researchers who have actively participated in this project which has had a direct budget of approximately US$2 million and in addition much larger resources, when in-kind contributions are considered. This major project has been divided into three subprojects dealing with the biological, the engineering and the mining aspects. Table 1 shows some of the research topics that have been investigated by these three different groups.



After five years' time, considerable progress has been achieved in understanding the biochemistry and physiology of the bacteria, in determining some of the key parameters that limit leaching in heaps and piles, in designing the bio-leaching operations and in monitoring the progress of a leaching process. From a level of practically zero knowledge about the process, Chilean researchers now constitute a group with expertise that is recognized internationally. A large number of publications and two patent applications have resulted from the work carried out. More important, however, a large number of young researchers have been trained in advanced biotechnological techniques and have been infused with the philosophy of working on top

research of high relevance to the country and of participating in large inter disciplinary teams.

Although the UNDP sponsored project came to an end in December of 1990, the researchers involved in this project will continue to work in this area with funds from the Chilean National Fund for Science and Technology and from international sources. Prof. Carlos Jerez of the Department of Biochemistry of the Faculty of Medicine of the University of Chile has just won an ICGEB Collaborative Research Project to work on "Studies of the stress response in biomining microorganisms". Possible implications in the improvement of bioleaching process which he will carry out in collaboration with the laboratory of Dr. Hector Torres of Argentina.

Mining biotechnology is still in its infancy and certainly much work has yet to be done to achieve large breakthroughs in increased productivity. However this is clearly an area in which the developing countries must keep alert and which can be used to establish research teams and to link scientists to the problems of their societies.

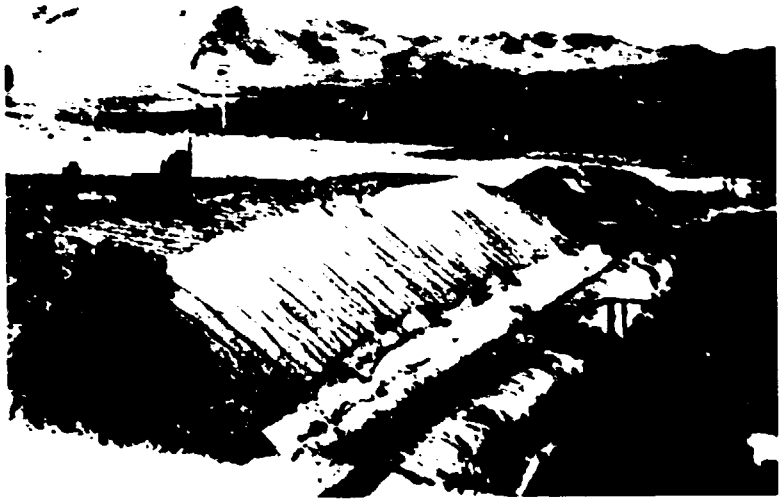


Figure 3

TABLE 1

Scientific Research Activities of the Three Subprojects of the Bacterial Leaching of Minerals

Biological Subproject

1. Study of the *Thiobacillus* proteins and enzymes involved involved in the ferrous ion oxidation
2. Biochemistry and genetics of CO_2 fixation in these bacteria
3. Chemotaxis of bacterial attachment to minerals
4. Strain identification by DNA probes and specific antibodies
5. Genetic manipulation of *Thiobacilli*
6. Selection of resistant strains to toxic metals
7. Lipopolysaccharides and proteins involved in attachment of bacteria to mineral surfaces

Engineering Subproject

1. Computer models on the leaching process in experimental columns
2. Ideal conditions for the leaching of concentrates in shaker tanks
3. Monitoring of CO_2, O_2, pH and other parameters under experimental conditions
4. Fluid dynamics of different kinds of piles and heaps
5. Design of inoculating methodology

Mining Operations Subproject

1. Pilot mineral leaching pile for demonstration of the process for potential users
2. Monitoring of various parameters including flora of micro organisms in actual mining operation that involve leaching
3. Design of piles and dump for biohydrometallurgy

NEWS

ICGEB coming of age

ICGEB, currently operating under the auspices of UNIDO, is expected to become an autonomous intergovernmental organization as soon as its statutes are ratified by 24 member countries. With the number of ratifications nearly reached, 23 of the required 24, ICGEB is about to enter into a period of transition. The Preparatory Committee for the establishment of ICGEB in its 16th session of 13—15 May 1991, asked the UNIDO Secretariat to prepare draft rules of procedure for the Board of Governors of the Centre. The next session of the Preparatory Committee is scheduled to take place in Vienna 22—24 October 1991.

ICGEB publications

"Activity Report 1990" is now available and can be obtained from the Director's office. It gives full details of the research programmes of ICGEB, as well as its training activities and services.

The Proceedings of the Colloquium on "Lignin Biodegradation and Practical Utilization", held at ICGEB-Trieste 27—30 June 1990, will be published in the fourth quarter of 1991 as a Special Issue of the Journal of Biotechnology. They will include some 21 papers dealing with various aspects of molecular biology and genetics of lignin biodegradation.

The Proceedings of the research colloquium on "Diagnostic Approaches to Schistosomiasis", held in Shanghai, 15—17 November 1990, are expected to be published in July 1991. The colloquium was jointly organised with the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR). The proceedings, which include papers on state-of-the art serological and molecular methods of diagnosis, will be co-published by UNIDO and a major commercial publisher.

Biotechnology laboratory network planned

CIB, the Inter-University Biotechnology Consortium, which includes 15 Italian universities, and has its operational and administrative headquarters in Trieste, plans to set-up a laboratory network to carry out applied research and develop marketable products of industrial interest. The first laboratory of the network will be

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tion of commercialization of biotechnology through cooperation. The role of ICGEB in this regard will be considered.

Biosafety Code of Conduct

UNIDO is developing an international voluntary Code of Conduct (CofC) for the release of GMOs to the environment. The Code attempts to strike a balance between the need to protect public interest and the desire to attract investment in biotechnology applications. A first draft of the CofC was prepared by the UNIDO Secretariat based on the inputs of some 15 experts in the field, as well as the work of other international organizations. It includes a section on the operational modalities of an international mechanism which, upon request, could provide transparent and scientifically sound advice to national authorities on how to implement the Code. UNIDO is working on the CofC in close cooperation with the other members of the UNIDO/UNEP/WHO/FAO informal working group on biosafety. It is expected to finalize the draft in meeting convened by UNIDO 8—10 July 1991 in Trieste. The conference facilities will be provided by ICGEB.

Information Resource for the Release of Organisms into the Environment

The United Nations Environment Programme and the Microbial Strain Data Network (MSDN) organized a workshop that took place at UNIDO Headquarters in Vienna, 11—13 March 1991, with a view to consider the needs of establishing such an information resource as well as its operative modalities. The workshop was sponsored by UNIDO and was attended by ICGEB staff. Its proceedings are expected later in the year as a UNEP publication.

In the meantime, the Environment Directorate of OECD has developed an information pointer system (BIOTRACK) on field releases of modified organisms. BIOTRACK, restricted at present, contains some 300 entries. It is planned to be made available to a large number of users within 1991.

ICGEB keeps a close watch on regulatory issues in its member countries and is building a database of information based on the responses to a questonnaire, distributed earlier on this year, requesting information on biosafety regulations adopted in its member countries. Mechanisms of facilitating information exchange between ICGEB and the different database hosts and or accessing other information resources such as BIOTRACK are being examined. It is anticipated to provide the ICGEB user community with on-line access to such databases, resources through ICGEBnet.

Assessing Biotechnology Risks

An *ad hoc* Workshop of Senior Experts on International Procedures for Assessing Biotechnology Risks is to be held in London, 17—19 June 1991. The Workshop is organized by the United Nations Conference on Environment and Development (UNCED) and is being hosted by the Government of the United Kingdom. The major purpose of the Workshop will be to consider a draft document on international procedures for assessing biotechnology risks, for subsequent presentation to the Third Session of the UNCED Preparatory Committee.

Calendar June - December 1991

International Symposium
PSEUDOMONAS BIOLOGY AND BIOTECHNOLOGY
ICGEB-Trieste, 16—20 June

Theoretical Course
GENETICALLY MODIFIED ORGANISMS: SAFETY IN THE LABORATORY AND THE ENVIRONMENT
ICGEB-Trieste, 1—3 July

Conference
GENETICALLY MODIFIED ORGANISMS FOR THE 1990s
ICGEB-Trieste, 3—5 July

Practical Course
COMPUTER APPLICATIONS IN MOLECULAR BIOLOGY
ICGEB-Trieste, 22 July—2 August

Practical Course
PLANT TRANSFORMATION
ICGEB-N. Delhi, 15 July—3 August

Practical Course
NUCLEIC ACID SYNTHESIS AND GENE ASSEMBLY
ICGEB-N. Delhi, 2—21 September

Practical Course
TECHNIQUES IN GENOME RESEARCH
ICGEB-Trieste, 22—27 September

Theoretical Course
MARINE MICROBIOLOGY AND BIOCHEMISTRY
ICGEB-Trieste, 16—20 December

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