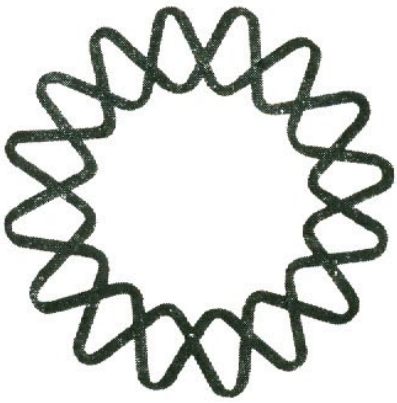
Centro de Investigación
sobre Ingeniería Genética
y Biotecnología.

Research Center for Genetic
Engineering and Biotechnology



Research Scientific Coordination
National Autonomus University of México

Coordinación de la Investigación Científica
Universidad Nacional Autónoma de México

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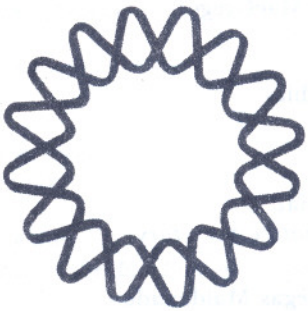

Research Scientific Coordination
National Autonomus University of México

Coordinación de la Investigación Científica
Universidad Nacional Autónoma de México

UNIVERSIDAD NACIONAL AUTONOMA DE MEXICO. (UNAM)

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RESEARCH CENTER FOR GENETIC ENGINEERING AND BIOTECHNOLOGY.

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Report Presentation

This document is a summary of the first six years of work at the Research Center for Genetic Engineering and Biotechnology (Centro de Investigación sobre Ingeniería Genética y Biotecnología (CIIGB) from the Universidad Nacional Autónoma de México (UNAM).

It presents different aspects of its organization, research lines, technology development, teaching and training of skilled staff.

The CIIGB was created in April 1982, as a decree by Dr. Octavio Rivero Serrano, Rector at that time of the Universidad Nacional Autónoma de México (UNAM). The construction of the physical facilities at Cuernavaca, Mor., were finished in December 1984 and the academic personal began working in January 1985. These facilities were officially inaugurated in August of the same year by the President of México, Miguel De la Madrid Hurtado, together with the Rector of UNAM, Dr. Jorge Carpizo MacGregor.

The first two and half years were dedicated to three main tasks: first, to define the main fields of research, technological development, teaching and training; second, to design the physical facilities at Cuernavaca and procure funds to equip them; third, to select new academic staff and to shape the graduate curricula in specific areas. The former activities were developed according to a Document written by the Internal Counsel of the Center. The written plan lays down the academic foundations of the Center for the short and long term.

The first year in Cuernavaca was dedicated to the instalation of the equipment, as well as to the initiation of academic work and hiring of academic staff. Academic work was in full swing by 1986.

CIIGB started activities with a Research Staff of nine. Today, in 1988 there are 24 reserches working in 14 researche groups. The Research Staff is assisted by 29 academic technicians adn 80 students (45 of them, postgraduates). This implies that the Center can still incorporate more Academic Staff since it has been planned for 200 individuals. The objetive in due time, is to duplicate the number of Research Staff.

According to studies made by a group of experts from the United Nations Industrial Development Program, the Research Center has adequate space to accomodate 35–40 researchers. There is confidence that this objetive will be achieved.

The academic endeavour of the Center has been developed according to the general objetives that made possible its creation, which are:

1. To gather fundamental knowledge in biology within the Center's fields of competence;
2. To create the needed mechanisms to apply fundamental knowledge in order to generate biotechnologies;
3. To foster a liason between the University and the country's private sector through proposals allowing the use of biological technologies;
4. To participate in the descentralization of research, higher education and training of specialized human resources.

Even though the CIIGB is a young Institution, it has made contributions in basic and applied research technological development as well in the areas of teaching and trining. However, we believe this is just the beginning, as the existing research groups are consolidated and new groups incorporated in selected fields, the contributions of the Center will be of a larger magnitude.

It is important to mention that the Center's main effort in the scope of basic and applied research lies in the study of specific projects, within disciplines such as molecular biology, biochemistry, microbiology and bioengineering.

The area of protein biotechnology is the central core for technological developlent. In fact, four out of six transfered tecnologies and seven out of eight patents registered or under review are protein biotechnology projects, including the production of unicellular protein, the use of enzymes in biocatalysis, the use of proteic components from scorpion venoms for selective labeling, the overproduction of specific proteins, etc.

Correspondingly, the incorporation of new research groups should contemplate this general scheme and incorporate new ideas in the study and handling of proteins without leaving out the effort in molecular genetics, microbiology, fermentation engineering, and development of bioprocesses.

Preface

Molecular Genetic Engineering and its Relationship with Biotechnology

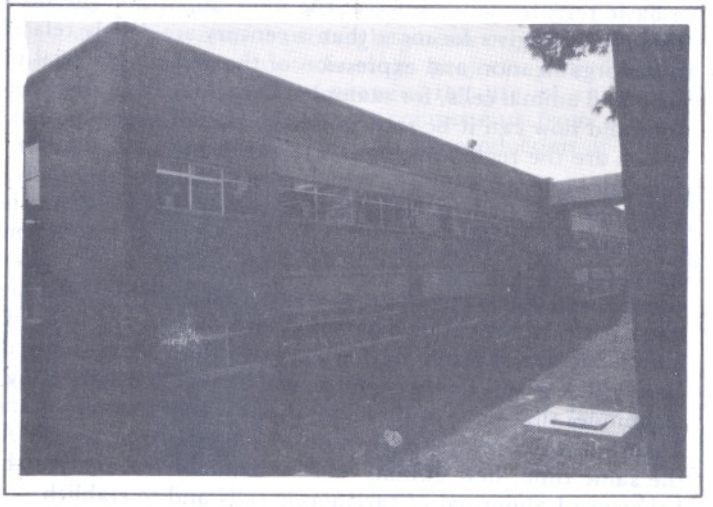
A turning point in the history of Biology was marked by the discovery of the structure of the genetic material in 1953, bringing to life a new field, Molecular Biology. Thereafter, a clearer and molecular image of the functioning of a living cell and specially of the structure of its genetic material, has emerged. The year 1970 marks an important period: the beginning of the enzymatic manipulation of the genetic material from living organisms and consequently the birth of Molecular Genetic Engineering. Today, with the use of recombinant DNA techniques, it is possible to isolate fragments of genetic material that carry specific genes. The possibility of studing these genes has permitted, among other things, a detailed biochemical and molecular analysis of the chromosomes that constitute the genetic material of living organisms.

The feasibility of this analysis is of fundamental importance in basic research since some of the most important questions raised by biologists for more than a century are deeply related to the organization and expression of the genetic material in plant and animal cells, for example : How does DNA duplicate itself and how can it be transmitted to posterior generations? Which are the regulatory signals in DNA and what kind of molecules interact with it? ; Which is the nature of the genetic programs that allow for cellular differentation? ; How has the structure of the genes and chromosomes changed throughout evolution? . The complexity of the chromosomes from higher animals and plants have kept man ignorant in these and many other basic biological phenomena. Nevertheless, the bulk of knowledge accumulated during the last fifteen years shows us clearly that it will be through the use of genetic engineering techniques that some of these questions will be answered, and a more distinct image of the normal cell will be acquired. At the same time, new options will be available to analyze the behavior of abnormal of carcinomic cells and to stablish

rational strategies for treatment of diseases with molecular basis.

The potential of genetic engineering is quite broad, and, together with the manipulation of the genetic material from living organisms emerges a new tecnology; new because it brings a different perpective to the empirical work of existing biological systems of wich very little is known and which implies the handling of many variables. Soon, a single microorganism or an existing biological system will not be sufficient to accomplish a process. Many of the present and future processes will be designed genetically, by exploiting the feasibility of manipulating genetic information from one organism and introducing it into another.

Cells specialized in the building of unimagined products have been made available by the manipulation of the genetic material. Until recently it was difficult to imagine that a microbe cell could build human proteins such as insulin or interferon. Today, there are not many products in nature that cannot be obtained thanks to the *in vitro* recombination of the genetic material from different microorganisms. Possibilities are such that the horizon is nounded only by man's imagination.



Man is living a new step in history. It is clear that great part of the future technology will be one that uses living systems, their products, or theirs parts. In other words, it will need to be biological technology or biotechnology. The reason is simple: an important part of man's problems are susceptible to treatment or manipulation with biological technologies: hunger, disease and at least part of the ecosystem's pollution and energy production. Important efforts have been made by the government and private sector from several countries channeling economic and human resources for the structuring and implementation of biotechnological development schemes.

UNAM Agreement to create the Center

Based on former considerations, and in view of the developing state of genetic engineering and biotechnology at the international level, and the potential of these methodologies and their participation in national priority areas, the Rector of the Universidad Nacional Autónoma de México, Dr. Octavio Rivero Serrano, founded in April 1982, the Research Center for Genetic Engineering and Biotechnology (Centro de Investigación sobre Ingeniería Genética y Biotecnología) as a subdependency of the Scientific Research Coordinating Board (Coordinación de la Investigación Científica).

GENERAL SECRETARY

AGREEMENT NUMBER 1

To the Directors of Schools, Faculties, Institutes and Centers, General Directors and Chiefs of Administrative Units.

Considering:

That different research groups of The UNAM are developing, on areas of Genetic Engineering and Botechnology, high quality projects guaranteeing their continuity and development.

That the UNAM is aware that it is crucial for México to participate in the ellaboration of its own technologies, based on fundamental knowledge, to solve specific problems of social significance in areas such as healh, food, energy and pollution.

That the development of biotechnology at the international level makes possible the participation of the Center, through the use of genetic engineering, in finding solutions to problems in those areas.

That the UNAM is interested in promoting the decentralization of Academic and Research programs and in fortifying the scientific pole being developed in the city of Cuernavaca, Morelos.

That the staff of the Molecular Biology Department and the Internal Council of Biomedical Research Institute (Instituto de Investigaciones Biomedicas), together with the Technical Council of Scientific Research and the Commitee of Academic Differentiation, have given their support.

With the agreement of the Rector, from this date, the Research Center for Genetic Engineering and Biotechnology is created.

1. The Center will relay on the Scientific Research Coordinating Board and there will be a Director in charge appointed by the Rector of the UNAM. It will have an Internal Council in accordance to the University Legislation. The Center will be localized in the city of Cuernavaca, in the State of Morelos. The Technical Council of Scientific Research will be its academic authority.

2. The Center will have a Technical Committee that will provide guidelines for collaboration with other University dependencies, will serve as consultant in the formulation of programs and their follow up, recommending masures to assure their progress. The Technical Committee will be integrated by the Coordinator of Scientific Research, who will preside it and by the Directors of the Faculties of Medicine, Veterinary Medicine and Zootechny, Chemistry and FES–Cuautitlán, the Directors of the Institutes of Biology and Biomedical Research, the Directors of the Research Center for Nitrogen Fixation and Cellular Physiology and by the Director of the Center.

3. The Center will have the following initial objetives and functions:

A) To perform basic research in the areas of:
   a) Molecular y biology, enzymology, biochemistry and chemical synthesis of nucleic acids.
   b) Biochemistry of proteins and peptides.
   c) Microbiology and genetic improvement of microorganisms of basic and industrial interest.
   d) Fermentation, scaling up and bioengineering processes.
   e) Enzymatic engineering.

B) Applied Research.
   Using the information and the fundamental knowledge generated by the basic research in the areas mentioned above, there will be development of biological technologies that could lead to the solution or to better alternatives for problems in the following areas of applied research: food, health, pollution and energy.

C) Coordinate the effort of UNAM's dependencies working in the described areas.

D) Participate with other UNAM's dependencies and with other institutions in the country or elsewhere, developing projects and research on their specific areas.

E) Contribute in the training of specialized staff in the mentioned disciplines.

F) Teaching in specific areas.

The Research Center for Genetic Engineering and Biotechnology will be integrated by staff working at the Department of Molecular Biology, Developmental Biology and Biotechnology of the Biomedical Research Institute. Its budget will be set by the University Board to support the programs of the groups collaborating with the Center under the responsibility of the research members. The Center will count with the human resources, material and equipment set by the Scientific Research Coordinating Board.

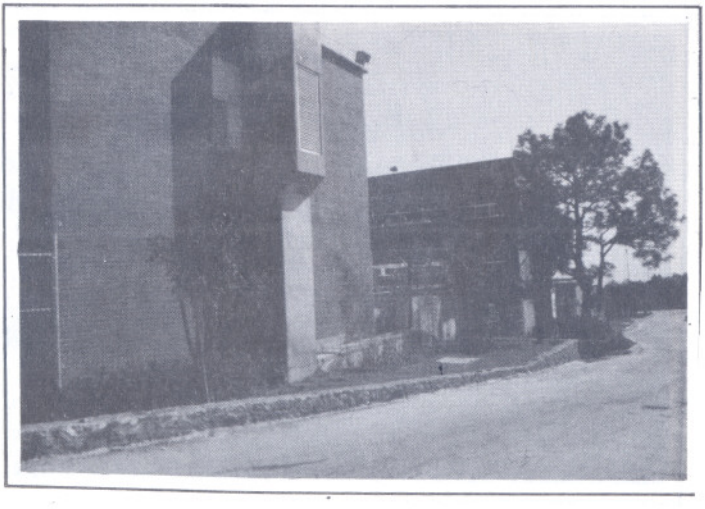
"Por mi Raza Hablará el Espíritu"
Cd. Universitaria, April 26, 1982.

General Secretary
Lic. Raúl Béjar Navarro.

Location

The physcial facilities for the Research Center for Genetic Engineering and Biotechnology are located in the city of Cuernavaca, in the State of Morelos. The Center occupies an area of approximately 25,000 square meters in a lot of land laned to the Universidad Nacional Autónoma de México (UNAM) by the Universidad Autónoma de Morelos (UAEM)

The proximity of the Research Center to other UNAM institutions is critical to the emergence of a scientific pole therefore allowing for planned interaction with existing and future-UNAM center in Cuernavaca.



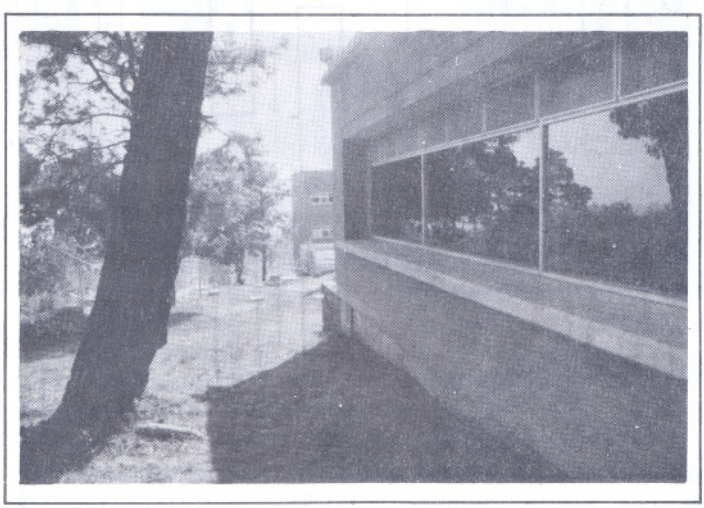
Likewise, the location of relible entities with broad academic future out of México City contribute effectively to the descentralization of research and higher education.

Through collaborations with the UAEM, the Center will contribute to the academic enrichement and maintenance of higher education standards in the State of Morelos.

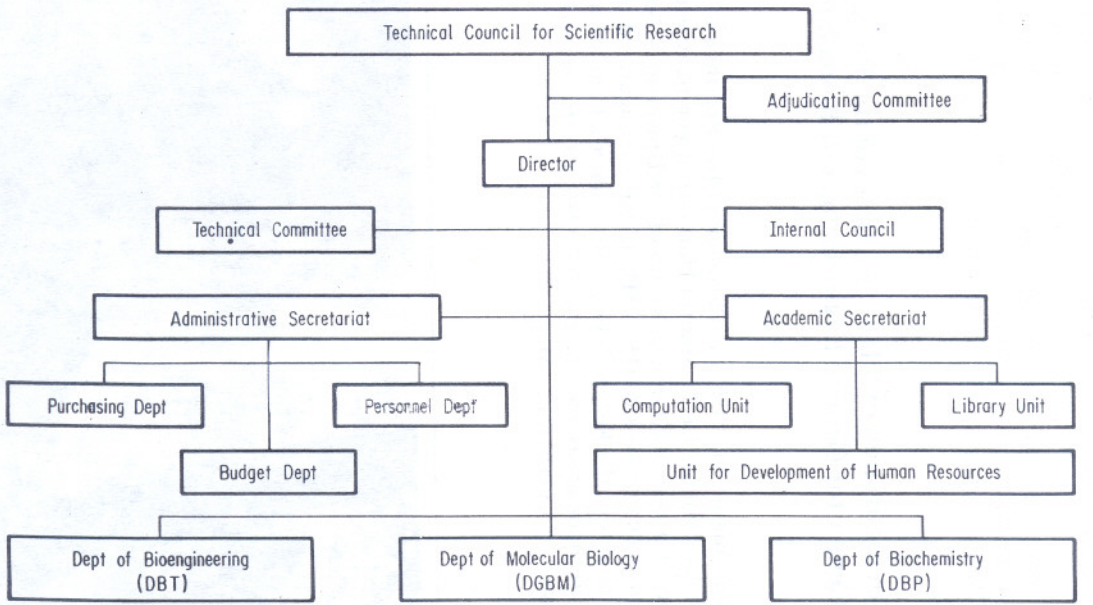
The Research Center is actively seeking mechanisms to facilitate exchanges between the UNAM and the Goverment agencies and the private sector for the development of biotechnologies.

Inauguration of Plant Facilities of the Research Center for Genetic Engineering and Biotechnology

On August 16, 1985, the President of the Republic of México, Lic. Miguel De la Madrid Hurtado in company with Dr. Jorge Carpizo MacGregor, Rector of the Universidad Nacional Autónoma de México (UNAM) officially inaugurated the installations of the Research Center for Genetic Engineering and Biotechnology as part of the UNAM's city for scientific research in Cuernavaca, Mor.

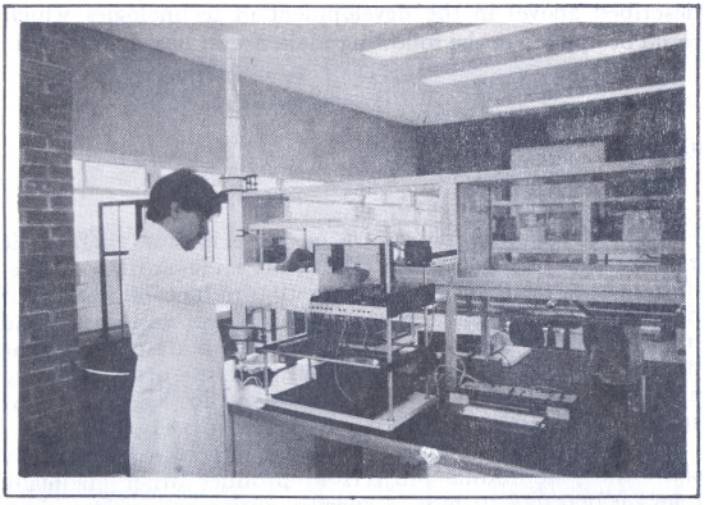


ORGANIGRAM


Technical Council for Scientific Research
Adjudicating Committee
Director
Technical Committee
Internal Council
Administrative Secretariat
Academic Secretariat
Purchasing Dept
Personnel Dept
Computation Unit
Library Unit
Budget Dept
Unit for Development of Human Resources
Dept of Bioengineering (DBT)
Dept of Molecular Biology (DGBM)
Dept of Biochemistry (DBP)

Objetives

1. To gain basic knowledge in Biology within the Center's areas of competence.
2. To construct the framework needed for the basic knowledge that will help generate biotechnologies.
3. To encourage the establishment of a link between the University and the private sector through mechanisms that foster the use of biotechnologies.
4. To participate in the decentralization of research and higher education and in the training of specialized staff.



Areas of Research

1. Basic Research.

The Center conducts basic research that will help generate understanding in the following areas:

i) Molecular Biology of Nucleic Acids (organization, control and manipulation of specific regions of the genome, genetic enginnering, DNA replication and chemical synthesis of DNA).

ii) Biochemistry of proteins and peptides (development of purification methods for proteins and peptides; biochemistry, molecular biology and physiology of neuropeptides, isolation of antigens and production of antibodies; characterization of venom, from poisonous animals).

iii) Genetic microbiology and genetic improvement of -- strains from organisms of basic and industrial interest (E.*coli*, X. *campestris, K. lactis, S. thypi, S. Streptomyces* sp., *Pseudomonas* sp., etc.).

iv) Fermentation, scaling up and bioengineering of processes (development of biological tecnhiques at a level of pilot plant, basic studies on fermentation, kinetics, separation, etc.

v) Enzymatic engineering (development of a basic methodology in the use of immovilized enzymes in different reactors).

2. Applied Research.

It is our objetive to utilize existing knowledge as well as new information generated through basic research (in the areas described above) in the development of technologies which could be applied to the following main areas: health and food.

i) Health

By exploiting the power of novel techniques in genetic engineering, the scientists at CIIGB are endeavoring to develop strains from microorganisms to produce molecules of medical interest such as, human insulin, over production and modification of antibiotics, like penicillin amidase, and in the design of microbiological electrodes. The use of monoclonal antibodies and specific DNA fragments for the design of specific diagnostic systems, are also been developed.

There is the possibility of initiating, within a relatively short time, additional projects to produce other medically relevant peptides such as, a specific antiserum against viral, parasities, and enterobacteria antigens. Another aspect of the work being carried out is the characterization and fractionation of venoms from poisonous animals and insects.

ii) *Food*

Scientists at CIIGB work on different areas of unconventional food such as: production of unicellular protein

from methanol and milk serum. An additional line of research applies enzymatic engineering to the food industy. There is on going work on designing systems of immobilized enzymes which are relevant to the food industry, such as lactase.

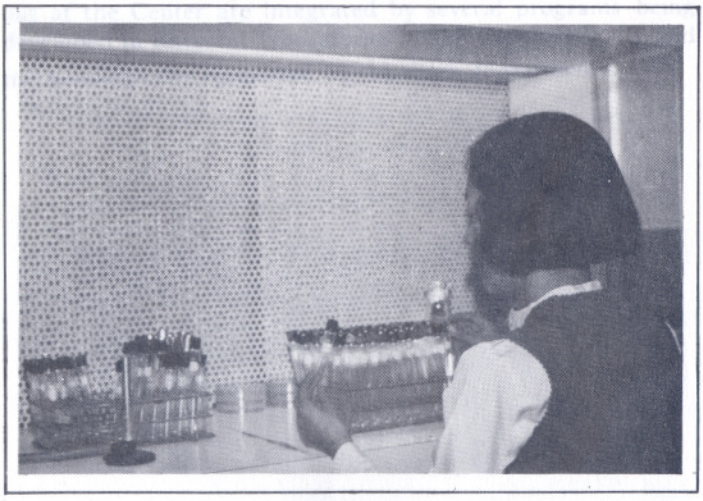
In the area of microbiological electrodes, technologies to immovilize viable cells and enzymes in different supports, have been developed.

Electrode prototypes, which detect glucose and lactose and which also determine the biochemical demand of oxygen and the concentration of antibiotics, have been designed.

Another dimension of the research being done is the production of other types of biomolecules of interest to the oil and food industries such as the polysarcharide xantan.

3. Teaching and Development of Human Resources

The academic staff actively participates in the formation of students who are attending the School of Science and Humanities of the UNAM and who are enrolled in one of the two following programs: bachelor, master and doctorate in Biomedical Research and specialization, master and doctorate in Biotechnology.



Finally, the academic staff and students have organized a serie of ongoing conferences in the areas of Molecular Biology and Medicine which take place at the Medical School of the Universidad Autónoma del Estado de Morelos (UAEM).

Research lines, programs and projects

The Center´s research lines, programs, projects and technological advancements are in different stages of development and in several cases represent "models" of applied basic knowledge in Biology. Most of them are multidisciplinary and imply the participation of several members of the academic staff from different departments.

Several projects are part of one program. A line of research is integrated by one or more programs with the exception of research, line number 8 which is constituted by in progress technological developments. Each of the research lines carried out at the Center are integrated by several programs being developed in different laboratories which are technically and methodologically supported by the three departments.

At the end of each project we indicate the following:
The starting year; if it is an initial stage (I), if it is in process (P), or if it has ended (T). Furthermore we also indicate if the project is related to health (S), food (A), or polution (C), finally we indicate the Departments in which it takes place.

Research line No. 1

Biochemistry and molecular biology of enteric bacteria

Programs

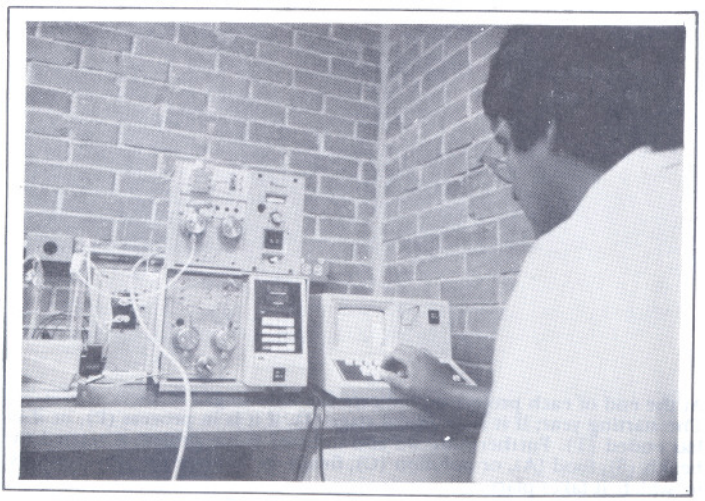
1.1 Isolation, characterization, manipulation and regulation of genes which control nitrogen metabolism in *E. coli* and other microorganisms.

1.2 Isolation and characterization of the gene coding for *E. coli* penicillin acylase.

1.3 Isolation characterization and manipulation of the genes that code for the outer membrane proteins of gram negative pathogenic bacteria.

1.4 Dissection and characterization of molecular elements involved in the replication of cloning vectors.

1.5 Genetics of bacterial enterotoxins.



Program 1.1 Isolation, characterization, manipulation and regulation of genes which control nitrogen fixation in *E. coli* and other microorganisms.

As a model for this research study we have selected the structural genes from the following enzymes: glutamine synthetase, glutamate dehydrogenase and glutamate synthase; since they code for key enzymes in nitrogen metabolism.

Our main approach has been the analysis of the expression of the structural genes for these enzymes by studying different growth conditions and the influence of various mutations in gnes involved in their regulation.

On the other hand, the characterization at a molecular level, of how the activation and/or repression of genes take place, has been one of the appoaches towards an undertanding of the functional and structural features of the elements which control nitrogen assimilation in enterobacteria.

Likewise, by manipulating physiological variables, and by the isolation and genetic characterization of mutations in structural and regulatory genes (and their control regions), we want to acquire an improved perspective of the regulatory mechanisms of nitrogen metabolism.

Specific projects

Physiological and genetic parameters which affect *E. coli's* sensitivity to methylammonium.
O. Santana and L. Servín
1985/T/S/DGBM

Isolation and characterization of *E. coli* mutant strains hypersensible to methylammonium.
T.C. Olamendi and L. Servín
1985/T/S/DGBM

Isolation and characterization of the genes that code for glutamate synthase of *E. coli* K–12.
G. Gosset, B. Becerril, G. Oliver and F. Bolívar
1982/P/DGBM

Isolation and characterization of the gene that codes for glutamic acid dehydrogenase from *E. coli* K–12.
B. Becerril, F. Valle, L. Riba, E. Merino and F. Bolívar
1982/P/DGBM

Isolation and characterization of the genes that code for glutamate synthase and glutamate dehydrogenase from *S. typhy*.
B. Becerril, J.L. Puente, M. Fernández, E. Calva and F. Bolívar
1986/I/DGBM

Program 1.2 Isolation and characterization of the gene coding for *E. coli* penicillin acylase.

Penicillin acylase is used in the conversion of the antibiotic penicillin to 6-aminopenicillanic acid. This product is subsequently used in the synthesis of semisynthetic penicillins. Our objetive is to characterize and manipulate this gene. So far we have isolated it from the genome of *E. coli* strain ATCC 11105 and we have determined the gene´s nucleotide sequence.

Furtermore, we work on aspects related to the processing of the enzyme´s precursor. The enzyme is composed of two polypeptides that originate from a common precursor.

Specific projects

Determination of the nucleotide sequence of the structural gene for *E. coli* penicillin acylase.
G. Oliver, F. Valle, G. Gosset and F. Bolívar
1984/T/S/DGBM

Localization and characterization of a regulatory region of the *E. coli* penicillin acylase gene.
F.Valle, G. Gosset and F. Bolívar
1985/P/S/DGBM

Program 1.3 Isolation, characterization and manipulation of genes that code for the outher membrane proteins of gram negative pathogenic bacteria.

Our aim is to acquire a better understanding of the structure of the outer membrane of *S. typhi*, the agent resposible for typhoid fever. The incidence of this disease in México is high, and since *S. typhy* is higly invasive, it presents serious health risks. We are interested in finding out which major proteins of the outer membrane correspond to those described for *E. coli* and which are particular to *S. typhi*. In the future we will look for relationships between altered proteins and chages in invasivenes, resistance to phagocytosis, and adherence.

Therefore, we are studying the main outer membrane proteins through the isolation and characterization of their respective genes. The nucleotide sequence of each gene will help us in deciphering which are the regulatory regions, as well as the primary structure of the corresponding protein. We are interested in characterizing the *S. typhi*-specific exposed epitopes. The isolated genes will allow for polypeptide overproduction. Consequently, the immunogenic properties of each protein could be tested, in conjunction with, or in the absence of, polysaccharides. Furthermore, specific antibodies could be generated, allowing us to correlate specific genes with proteins in an electrophoretic pattern.

Specific projects

Isolation and characterization of genes coding for outher membrane proteins of *S. typhi* by hybridization with the following *E. coli* genes: *omp*F, *omp*C, and *pho*E; and also with the *S. typhimirium omp*A gene.
J.L. Puente, V. Flores, A. Hernández, M. Fernández, Y. Fuchs and E. Calva.
1985/P/S/DGBM

Isolation of genes for *S. typhi* outher membrane proteins by immunodetection with serum from patients with thipoid fever.
J.L. Puente, M. Fernández, Y. Fuchs and E.Calva
1985/P/S/DGBM

Program 1.4 Dissection and characterization of molecular elements involved in the DNA replication of cloning vectors.

Our goal is to generate knowledge on the molecular mechanisms that underline and regulate DNA replication in well

characterized systems. Techniques for fine manipulation of nucleic acids (genetic engineering), and classic genetic methods are employed. General knowledge has been applied in the designs and development of improved cloning vectors.

Specific projects

Studies on transcription in *E. coli* at the origin of the plasmid pBR322.
M. Zurita, H. Lomelí, J. Osuna and X. Soberón.
1983/T/DGBM/USQM

Isolation of a minimum substrate for RNAse H, with efficient replication on *Col*E1 type plasmids.
J. Cruz and X. Soberón.
1984/T/DGBM/USQM

Program 1.5 Genetics of enterotoxins.

Campylobacter jejuni is a microorganism largely responsible for a major portion of enteritis in underdeveloped and developed countries. Due to difficulties in growing this microorganism in the laboratory, its pathogenicity was only recognized during this past ten years. It has been determined that *C. jejuni* synthesizes an enterotoxin similar to *E. coli's* heat labile enterotoxin (LT) and the CT enterotoxin from *Vibrio cholera*. On the other hand it has also been postulated that *S. typhi's*, the causal agent for typhoid fever, has an enterotoxin similar to CT, although neither its structure nor its function have been characterized. Our objective is to find out in which genetic elements are the coding genes for *C. jejuni* and *S. typhi* enterotoxins. It is possible that a specific regulatory gene exists in addition to the structural gene.

The characterization of the genes for these enterotoxins will help us understand their similarity with the *E. coli* and *V. cholera* genes. Likewise, we will obtain information about codon usage and the characteristics of the regulatory regions. In terms of biotechnological development, this information

could be utilized for designing specific DNA detectors for each enteropathogenic microorganism.

Specific projects

The characterization of plasmids and phages in *C. jejuni*. toxigenic and non-toxigenic strains.
M. Vázquez and E. Calva
1985/P/S/DGBM

Genomic cloning of *C. jejuni* toxigenic strains; search for the enterotoxin gene by immunodetection or by nucleic acid hybridization.
M. Vázquez and E. Calva
1985/P/S/DGBM

Characterization of the enterotoxin of *Salmonella typhi*.
M. Fernández, M. Vázquez and E. Calva
1986/I/S/DGBM

Research line No. 2

Biochemistry and molecular biology of parasites

Programs:

2.1 Characterization and purification of hydrolytic enzymes from *Entamoeba histolytica*.

2.2 Research studies on the genetic organization of *Entamoeba histolytica*.

2.3 Research studies on repetitive DNA from *T. cruzi* and *Plasmodium* sp.

Program 2.1 Characterization and purification of hydrolytic enzymes from *Entamoeba histolytica*.

We are presently working with proteolytic and phospholipasic enzymes from *Entaboeba histolytica* because of their possible participation in the invasivity and cytopathic effect of this protozoan. We are characterizing factors which affect the expression of these enzymes on cultivated amoebas.

The massive culture of entamoebas will provide us with the necessary biomass for the purification by affinity chromatography of the above mentioned enzymes, which will also be useful for future biochemical and immunological studies. Our research group also plans to study other aspects of cell biology and genetics of *Entamoeba* in collaboration with other scientists from México and the United States of América.

Specific projects

Characterization of a fibrinolytic activity from *Entamoeba histolytica*.

I. Cervantes, A. Alagón and R. López-Revilla
1983/P/A/DEP

Mass production of *Entamoeba* in PEHPS-1 media.
J. Vargas, S. Saíd-Fernández and A. Alagón
1983/P/S/DEP

Purification and characterization of a phospholipase from *Entamoeba histolytica*.
J. Vargas, A. Alagón and S. Saíd-Fernández
1985/P/S/DEP

Characterization of a hialuronidase from *Entamoeba histolytica*.
M.A. Torti and A. Alagón.
1985/P/S/DBP

Program 2.2 Studies on the genetic organization of *Entamoeba histolytica*.

Scientifc interest on the protozoan *Entamoeba histolytica* is due to two factors: first, *Entamoeba* is the agent responsible for amoebic dysentery and second, it has interesting biological properties. It shows great polymorphism both at the morphological and at the biochemical level; one can find variations in the levels of specific enzymes in different cultures of the same

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strain. We are interested in studying this organism's genome with the objective of describing some of its properties at the level of genetic expression.

The new techniques on separation of high molecular weigth DNA by pulse field gradient electrophoresis should allow the mapping of some *Entamoeba* genes at the level of chromosomes and should also allow the investigation of possible rearrangements of the genome which have already been observed in other protozoa. For this purpose we plan to clone some genes of interest, such as those which code for phospholipase, fibrinolysine or some abundant membrane proteins. We are also interested in cloning repetitive DNA elements of unknown function that colud provide useful markers for regions with potential instability in the chromosome. In order to obtain these clones we are constructing genomic and cDNA libraries of *Entamoeba* in collaboration with the Instituto Poliécnico Nacional (National Polytechnical Institute from México). In the long run we are interested in the possibility of genetic manipulation of amoebas through exogen DNA transformation. It is our belief that these techniques will allow us to better comprehend the phenomena of phenotype variability in amoebas.

Specific projects

Cloning of repetitive DNA elements and ribosomal genes from *Entamoeba histolytica*.
J. Cruz, A. Alagón and P. M Lizardi
1986/I/S/DBP

Isolation and characterization of chromosomes from *Entamoeba histolytica*.
J. Cruz, M. Reyes, M.L. Villarreal, A. Alagón and P.M. Lizardi
1986/I/S/DBP

Cloning of important structural genes in *Entamoeba histolytica*.
P.M. Lizardi, A. Alagón and I. Meza
1986/I/S/DBP

Program 2.3 Studies on the repetitive DNA of *T. cruzi* and *Plasmodium*.

It is known that in the genome of various parasite species repetitive DNA sequences are found which represent a large percentage of total nuclear DNA. Usually repetitive DNA sequences are species-specific, therefore making possible the taxonomic identification of the organism. Recently the detection of ten to thirty cells from *T. cruzi*, by means of hybridization methods, has been demonstrated (González et al., 1984). In collaboration with Dr. Nadia Nogueira and Dr. Antonio González in New York University Medical School we continue some studies on *T. cruzi's* repetitive genes.

In a project initiated by Dr. Lizardi at the Rockefeller University, four *P. falciparum* repetitive DNA elements were sequenced. These sequences showed specific hybridation for the species, in other words, the elements did not form hybrids with DNA from other *Plasmodium* species, such as *P. vivax* and *P. malarie*. The usefulness of these repetitive DNA clones in malaria diagnostic assays has been demonstrated in hybridization tests with monkey's blood infected with the parasite. This research project continues at CIIGB and besides, we have initiated a parallel project with the objetive of isolating and characterizing repetitive DNA clones from *P. vivax*, which is the most prevalent *Plasmodium* species of malarial infection in México. We also expect to obtain, from this parasite, clones of species–specific repetitive sequences, with similar potential application in diagnostic assays.

Specific projects

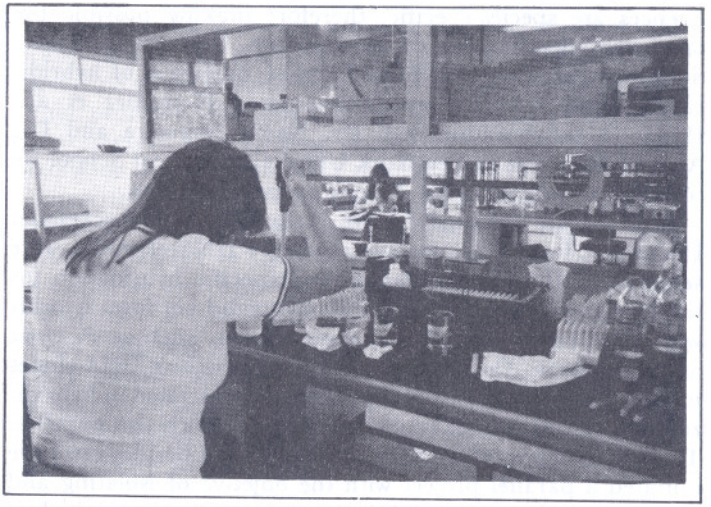
Structure and sequence of some repetitive genes in *T. cruzi*.
P.M. Lizardi, A. González and N. Nogueira
1983/P/S/DBP

Sequence and chromosomic localization of *P. falciparum* repetitive DNA elements.
M.T. Tusie, A. González and P.M. Lizardi
1986/P/S/DBP

Cloning of DNA repetitive elements from *P. vivax* and P. *P. malarie*.

I. Tusie, A. Alagón and P.M. Lizardi

1986/P/S/DBP



Research line No. 3

Biochemistry and molecular biology of viruses

Programs

3.1 Etiology and epidemiology of viral gastroenteritis.

3.2 Studies on the structure and function of rotavirus genome and the encoded polypeptides

3.3 Molecular biology for the control of the diarrhea caused by rotavirus.

Program 3.1 Etiology and epidemiology of viral gastroenteritis.

Diarrheal diseases are one of the leading causes of morbidity and mortality in children under five years of age in developing countries.

From the early 1970s it become clear that a large proportion of the diarrheic episodes in infants and young children are of viral etiology, with rotavirus being probably the single most important cause of acute gastroenteritis. In addition, several other viruses have also been associated with diarrhea, including pararotavirus, adenovirus and small round viruses.

We are interested in studying the incidence of these viruses in mexican children, and in understanding their epidemiologic characteristics as well as their association with diarrheic and healthy children.

In the case of rotaviruses, four serotypes have been defined, and our aim is to understand the epidemiology of the different serotypes, which in association with the study of the immune response of the host, will help clarify the role of serotypic diversity in rotavirus clinical immunity, a central issue for the development of control measures.

Specific projects

Identification by electron microscopy and characterization of small round viruses in stools from diarrheic and healthy children.
C.F. Arias, P. Romero, H.B. Greenberg and S. López
1987/I/DGBM

Serotyping of human rotavirus by ELISA.
L. Padilla, F. Puerto, A. Zamora and C.F. Arias
1987/I/S/DGBM

Characterization of rotavirus and pararotavirus isolated from symptomatic and asymptomatic children, by electropherotyping and northern blot hybridization
S. López and C.F. Arias
1987/I/S/DGBM

Serotype-specific seroconversion in mexican children infected with rotavirus.
F. Puerto, L. Padilla, A. Zamora and C.F. Arias
1986/P/S/DGBM

Program 3.2 Studies on the structure and function of the rotavirus genome and the encoded polypeptides.

Rotaviruses are composed of an RNA genome and a double layered caspid. The genome (about 20,000 bp) is made up of 11 segments of double stranded RNA, raging in size from about 660 to 3,700 bp. The caspid is composed of at least five protein classes; three of which compose in the inner caspid - (VP1, VP2 and VP6) while two (VP3 and VP7) form the surface layer of the virion. In addition to the structural proteins, the rotaviral genome codes for six non-structural polypeptides of unknown function, but probably involved in the replication and morphogenesis of the virus particles.

We intent to learn about the structure and function of the different polypeptides, through the structural analysis of the genome and the expession of wild type and mutagenized cDNA copies of selected genes in eukaryotic cells.

The information thus obtained, on the elements involved in the replication and assembly of the different viral particles.

should help in the understanding of the pathogenesis of infection as well as in the possible design of antiviral drugs.

Specific projects

Construction of a cDNA library of the pig rotavirus YM– genome.
I. López and C.F. Arias
1985/T/S/DGBM

Insolation of a pig rotavirus and determination of the primary structure of the gene that codes the VP7 glycoprotein
A. Ruíz, I. López, R. Espejo and C.F. Arias
1985/P/S/DGBM/USQM

Primary structure of the VP3 protein of pig rotavirus YM as deduced from cDNA secquence.
I. López, S. López and C.F. Arias
1986/P/S/DGBM/USQM

Construction of a full length cDNA clone of the *SA*11 rotavirus VP3 gene, and expression in vaccinia virus.
S. López and C.F. Arias
1987/I/S/DGBM/USQM

Nucleotide sequence determination of the rotavirus YM genes that encode the viral RNA polymerase.
L. Almanza, C.F. Arias and S. López
1987/I/S/DGBM

Isolation and molecular characterization of genomic rearrengements of the YM and Wa rotavirus.
E. Méndez, C.F. Arias and S. López
1986/P/S/DGBM

Generation of rotavirus reassortants by transfection of rotavirus infected cells with mRNAs transcribed *in vitro*.
C. Contreras, S. López and C.F. Arias
1987/I/S/DGBM

Program 3.3 Molecular biology for the control of the diarrhea caused by rotaviruses.

Rotaviruses are the single most important cause of acute viral gastroenteritis in the young of a number of mammalian and avian species, including man, and as such they are of mayor medical and veterinary importance. Therefore, one of the high priority research aims in this field has been the development of control measures.

These viruses are composed of a genome made up 11 RNA segments, surrounded by a double layer capsid. The surface layer is formed by two proteins, VP3 and VP7, both of which induce neutralizing antiboidies to the virus. In addition, VP3 is also responsible for the enhanced infectivity observed in rotaviruses when the virions are treated with trypsin.

The advances in the understanding, at the molecular level, of some of the first interactions of the virus with its host cell have opened new perspectives for the production of a vaccine through the use of recombinant DNA techniques and synthetic peptides.

An attractive approach is to construct recombinant, attenuated enteric bacteria (e.g. *E. coli, S. typhi*), expressing the genes encoding the surface proteins of rotaviruses, to be used as live vaccines.

Furthermore, the use of synthetic peptides for disecting the first events of virus infection, i.e., adsorption and penetration, and to finely map the epitopes that induce neutralizing antibodies, should help in the development of rational preventive and therapeutic measures.

Specific projects

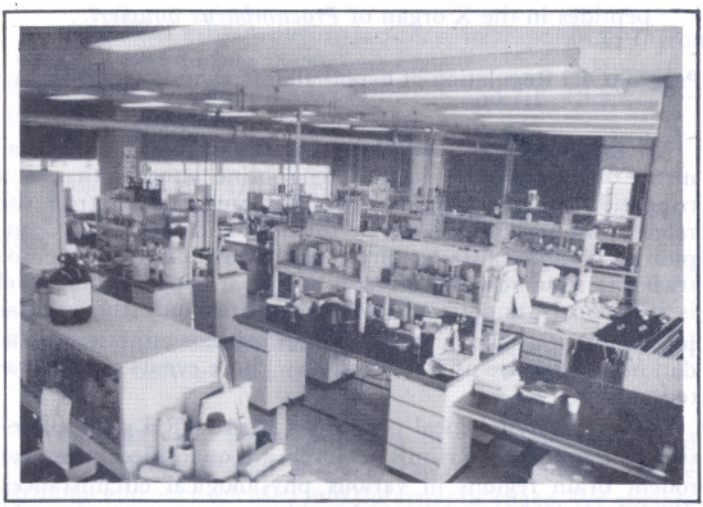
Chemical synthesis by the solid-phase method of peptides corresponding to some regions of the rotavirus proteins VP3 and VP7.
A. Espinoza, C.F. Arias and S. López
1985/P/S/DGBM

Mapping of rotavirus neutralizing epitopes with synthetic peptides.
G. García, S. López and C.F. Arias
1985/P/S/DGBM

Synthesis in *E. coli* of different regions of the SA11 virus VP3 protein.
M. Lizano and C.F. Arias
1985/P/S/DGBM

Immunological characterization of the *E. coli*-produced surface polypeptides of rotavirus SA11.
M. Lizano, M. Plebañski and C.F. Arias
1986/P/S/DGBM

Effect on the infectivity of rotaviruses of synthetic peptides that mimic the trypsin cleavage sites.
S. López and R. Espejo
1985/P/DGBM



Research line No. 4

Cellular biochemistry of peptidergic neurons

Programs

4.1 Regulation of hypothalamic peptide metabolism.

4.2 Release and inactivation mechanisms of TRH in rodent's nervous system.

4.3 Studies on the expression of genes which code for neuropeptides in the X organ of *Procambarus bouvieri*.

Program 4.1 Regulation of hypothalamic peptide metabolism.

We are interested in undersanding the intracellular mechanisms that participate in neuroendocrine integration. As a tripeptide released from the hypothalamus that controls the release and biosynthesis of Thyrotropin and Prolactin. Complex regulation exists by target tissue hormones and neurotrasmitters but how this effect is exered at hypothalamic level is still poorly understood. We therefore study the cellular biochemistry of the peptidergic neuron: biosynthesis, degradation and release of TRH and how these events are regulated.

To search physiological conditions where TRH gene expression is modified, TRH mRNA levels are quantified in several rodent brain regions in various physiological circunstances which include: hypo or hyperthyroid state, estrous cycle, cold exposure and lactation. In order to identify the responsible effectors, whether neural or hormonal, a hypothalamic cell dispersed culture system is being developed where the effects on biosynthesis will be studied (by measuring mRNA levels and 3H-Pro incorporation into TRH).

TRH inactivation is also studied in diverse paradigms. Results demonstrate regulation of some TRH peptidases by thyroid hormones in a tissue specific manner suggesting their involvement on feedback events.

These findings will be compared with TRH tissue levels and release in order to fully determine the intracellular steps which are under regulation.

Specific projects

Studies on TRH and SRIF biosynthesis and regulation in cell culture.
C. Cruz, M.L. Covarrubias, J.L. Charli and P. Joseph
1985/P/S/DBP/UB

Ontogenesis of TRH mRNA circadian rhythms in rats.
L. Covarrubias, R.M. Uribe, J.L. Charli and P. Joseph
1986/I/S/DBP/UB

Level of TRH mRNA during lactancy, in response to thyroid hormones and durling the estrous cycle.
R.M. Uribe, L. Covarrubias, P. Joseph and J.L. Charli
1986/I/S/DBP/UB

Phylogeny of the TRH gene.
L. Covarrubias, M. Rodríguez, J.L. Charli and P. Joseph
1987/I/S/DBP

Program 4.2 Release and inactivation mechanisms of TRH in rodent's nervous system.

In this regard our research focuses on the processes involved in TRH release as well as its inactivation inside the nerve terminal and once released into the synaptic space. We explore three possible inactivating mechanisms: uptake, degradation due to soluble soluble or membrane-bound peptidases and modification. Once these phenomena are characterized, we will try to define their physiological relevance.

We have been able to: 1) demonstrate the presence of an accumulation process for TRH in brain; 2) characterize a membrane peptidase (pyroglutamate aminopeptidase II, - PGAII) with high specificity for TRH which is localized in the external site of the synaptosomal plasma membrane and has heterogeneus regional distribution in brain. We are

currently trying to determinate if this enzyme is the principal agent responsible for TRH inactivation in the synaptic cleft. We are also pursing studies on its cellular localization, regional and organ distribution and developmental control. The process of intracellular TRH degradation and the role of soluble enzymes is being studied with the use of specific inhibitors of these enzymes.

Specific projects

Distribution of the PGA-II in rat brain, spinal chord and peripheral organs.
M.A. Vargas, M. Cisneros, M. Méndez, P. Joseph and J.L. Charli
1984/P/S/DBP/UB

TRH degradation in slices of rat brain: effects of its inhibition on TRH release.
M. Méndez, M.A. Vargas, M. Cisneros P. Joseph and J.L. Charli
1984/P/S/DBP/UB/URIA

Effect of endocrine feedback on TRH degradation.
G. Ponce, J.L. Charli, J. Pastén, F. Mena, M.A. Vargas, C. Valverde and P. Joseph
1986/I/S/DBP/UB

Cellular localization of TRH degrading enzymes in cell culture.
C.Cruz, M.A. Vargas, J.L. Charli and P. Joseph
1986/I/S/DBP/UB

Program 4.3. Studies on the expression of genes which code for neuropetides in the X organ of *Procambarus bouvieri*.

The crustacean's X organ contains a series of neurosecretory cells which secrete various neuropeptides with hormonal function. Two of these are the pigment concentrating hormone (PCH) and the pigment dispersing hormone (PDH) which together control pigment concentration in the chromatophores. PCH and PDH molecular structures are known in some species, as well as some of their functions and part of their regulation. Therefore, because of the simplicity of crustacean nervous system, and the minimal interactions, they are being used as a model for answering the following question: Does nervous transmission participate and how in neuropeptide biosynthesis regulation?. The research strategy involves the isolation of the cDNA to their messenger RNAs and their use *in vivo* in various paradigms in order to delineate the regulatory events.

Specific projects

Search for the PCH gene through synthetic oligonucleotides.
Y. Fuchs, E. Calva, L. Covarrubias, P. Joseph and J.L. Charli.
1985/P/DBP/DGBM

Characterization of the gene and cDNA which code for DPLH.
L. Covarrubias, J. Santaolalla, H. Aréchiga and P. Joseph
1986/I/DBP/USQM

Research line No. 5

Structure, function and manipulation of peptides and proteins

Programs

5.1 Chemical and kinetic characterization of proteases of high specificity from the venom of mexican reptiles.

5.2 Purification and chemical characterization of toxins from scorpion venom.

5.3 Isolation and characterization of specific receptors through the utilization of peptidic toxins.

5.4 Functional characterization of toxins peptides.

5.5 Purification and characterization of the plasminogen activator from the saliva of hematophage bats.

5.6 Development and optimization of proteins and peptides purification methods.

5.7 Production of monoclonal antiboides against peptides and proteins .

5.8 Protein engineering.

Program 5.1 Chemical and kinetic characterization of proteases of high specificity from the venom of mexican reptiles.

The venoms from poisonous saurian and ophidian of México are highly rich in proteolytic enzymes, although they are poorly studied, so far.

Through the use of affinity chromatography and conventional purification methods, a kallikrein and two plasminogen activators from saurian *Heloderma horridum* venom have

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been obtained in homogenous form. Their characterization helps us explain at a molecular level the phylogenic relations between *Heloderma* and other organisms, and its participation in the intoxication physiopathology of this animal's bite.

We are performing a screeening study to detect these and other proteolytic activies in the venom of about twenty vipers, endemic in México. We explore their potential in basic research and the application of these highly selective tools. We have discovered a new type of toxin in the *Heloderma horridum* venom.

Specific projects

Sequencing of helodermatine, a new kallikrein present in *Heloderma horridum*'s venom.
A. Alagón, L.D. Possani and W.D. Schleuning
1985/P/S/DBP

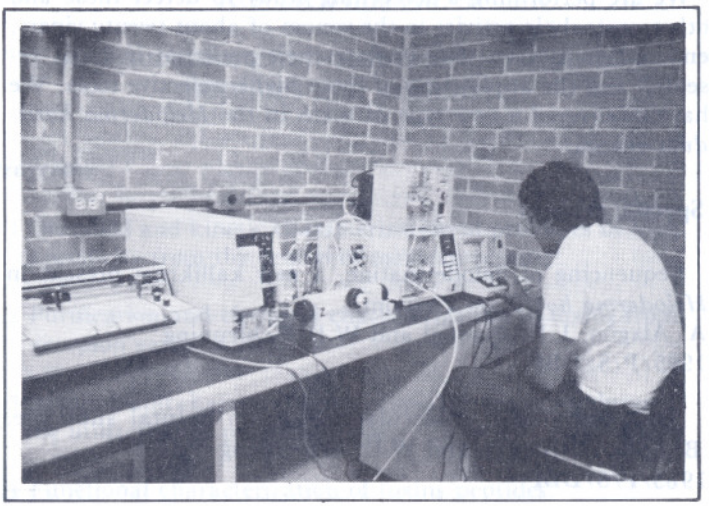
Helodermatine's molecular action on natural substrate.
B. Sosa, A. Alagón and W.D. Schleuning
1985/P/S/DBP

Purification and characterization of a toxin responsible for hypothermia from the venom of *Heloderma horridum horridum*.
J.M. Mochca, B.M. Martín and L.D. Possani
1981/P/S/DBP/UB

Program 5.2 Purification and chemical characterization of toxins from scorpion venom.

The venoms from many scorpion species contain polypeptides and proteins highly toxic to humans. The isolation and chemical characterization of these toxic components have permitted the discovery of their molecular mechanisms of action. Among the animals whose venoms have been studied extensively, are the snakes and scorpions. The use of chromatographic and electrokinetic techniques has made possible the separation of a large number of polypeptides and neurotoxic proteins. Many of them effect the acetylcholine receptor, ionic channels (Na^+, K^+, Ca^{++}) or participate in a series of important physiological functions like pancreatic secretion, hypothermia, and liberation of neurotransmitters.

The toxins have been purified to homogeneity; their amino-acids composition and primary sequences have been or are on the way of being determined.



Specific projects

Isolation and chemical characterization of toxins from *Centruroides noxius* Hoffmann scorpion venom.
A.N. Ramírez, B.M. Martín, G.B. Gurrola and L.D. Possani
1984/P/S/DBP

Isolation and characterization of two toxins from the mexican scorpion *Centruroides limpidus* Karsch.
A. Alagón, H.S. Guzmán, B.M. Martín, A.N. Ramírez, E. Carbone and L.D. Possani
1983/T/S/DBP

Total aminoacid sequence of aminoacids from a toxin isolated from *Centruroides limpidus tecomanus* Hoffmann scorpion venom.
A.N. Ramírez, B.M. Martín, G.B. Gurrola and L.D. Possani
1984/P/S/DBP

Isolation and characterization of toxins from *Centruroides infamatus infamatus* scorpion venom.
M.D. Dehesa, B.M. Brian and L.D. Possani
1985/P/S/DEBP/UB

Primary structure of toxins from the scorpion *Tityus serrulatus* Lutz and Mello.
L.D. Possani, B.M. Martín, M. Fletcher and P.L. Fletcher.
1981/P/S/DBP/UB

Purification and characterization of taicatoxin; a new and selective blocking peptide for the calcium channel.
L.D. Possani, B.M. Martín, A. Yatani, F.Z. Zamudio, J.M. Mochca and A.M. Brown.
1985/P/S/DBP/UB

Program 5.3 Isolation and characterizarion of specific receptors through the use of peptidic toxins.

The peptidic toxins purified to homogeneity, up to date, are components that recognize in a specific way some membrane receptors. For this reason, they have been transformed into useful tools for the isolation and functional characterization of receptor molecules. The alpha-toxin of elapides (*Naja naja siamesis*) is among the isolated and characterized toxins. It has been utilized in the isolation of the acetylcholine receptor. The gamma toxin from *Tityus serrulatus* has been used in the isolation of the sodium channel. The specific Noxiustoxin for the potassium channel and, more recently, the blocking Taica toxin for the calcium channel, are new tools being used for the isolation of channel proteins.

All these natural peptides have been marked with radioactive isotopes or fluorescent chromophores for their use as biological tracers, or they have been utilized for the synthesis of affinity chromatography supports.

Specific projects

Isolation and characterization of potassium channel from mice brain.
H.H.F. Valdivia, A. Zentella, G., Szabo and L.D. Possani
1984/P/S/DBP/URIA/UB

The utilization of noxiustoxin and of taicatoxin for the study on the distribution of potassium and calcium channels in excitable membranes.
K.Angelides, Y. Srinivasan, J.M. Mochca, H.H.F. Valdivia and L.D. Possani
1986/I/S/DBP

Program 5.4 Functional characterization of toxin peptides.

Natural and synthetic peptides have been utilized as tools in the characterization of biological functions, from an electro-physiological, neurochemical, and morphological point of view.

The study of the opening and closing mechanism of ionic channels from excitable membranes has benefited from the discovery of peptidic toxins. Likewise, the studies on the liberation of neurotransmitters and experimental pancreatitis have been implemented thanks to the use of natural and synthetic peptides. Finally, morphologic alterations and immunohistochemical localizations have been visualized or understood thanks to the use of the above mentioned peptides.

Specific projects

Blockade of potassium channel of the squid´s axon by-Noxiustoxin; a toxin from *Centruroides noxius* scorpion-venom.
E. Carbone, G. Prestipino, L. Spadavecchia, F. Franciolini and L. D. Possani
1982/T/S/DBP

The effect of two toxins from the new world scorpions in sodium channels from the heart.
A. Yatani, L.D. Possani, G. Kirsch and A.M. Brown
1985/P/S/DBP

The effect of toxin II-10 and II-9.2.2 from *C. noxius* scorpion venom in the GABA liberation of synaptosomes from rat brain.
M. Sitges, L.D. Possani and A. Bayón
1984/P/S/DBP

Neurotoxins that act selectively on the voltage-dependent calcium channel of the heart.
A. Brown, A. Yatani, A. Lacerda, G.B. Gurrola and L.D. Possani
1985/P/S/DBP

Localization of scorpion toxin binding sites in the central nervous system of rats, by labelling anti-toxin monoclonal antibodies.
G.M. Villarreal, A.T. Cárabez, M.R.G. Sánchez and L.D. Possani
1985/P/S/DBP

The effect of *Tityus serrulatus* toxins on pancreatic secretion.
P.L. Fletcher, M. Fletcher and L.D. Possani
1984/P/S/DBP

Program 5.5 Purification and characterization of the plasminogen activator from the saliva of hematophage bats.

The *Desmodus rotundus* activator (desmokinase) degrades with great efficiency sanguineus clots from mammals. Our plan is to study this enzyme's molecular biochemistry and explore its possible use as a thrombolytic agent. The great dependence of desmokinases on fibrin specificity and low inmmunogencity allows its routine use in patients with profound thrombosis.

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Specific projects

The purification and chemical characterization of desmokinase, the plasminogen activator from the saliva of *Desmodus rotundus* vampire.
B. Sosa, R. Medellin and A. Alagón
1985/P/S/DBP

The dependence on the requirements of fibrin for the enzymatic action of desmokinase.
B. Sosa, A. Alagón and W.D. Schleuning
1985/P/S/DBP

Program 5.6 The development and optimization of methods and purification systems for proteins and peptides.

We intent to develop both general and specific methodologies for the purification of polypeptides utilizing mainly techniques such as: affinity chromatography, ionic interchange chromatography, gel permeation chromatography, high resolution chromatograpy, electrophoresis and diffusion through membranes. Likewise we work in the scaling up of purification methods for specific peptides.

Specific projects

Purification by ion exchange chromatography of human insulin chains produced in bacteria.
L. Güereca, X. Alvarado, G. Estrada, N. Cruz and F. Bolívar
1984/T/S/DBP/UPP

Analytical and semipreparative purification by HPLC of the human A and B insulin peptides produced in bacteria and the products of chemical association.
S. Antonio, N. Cruz and L. Güereca
1985/T/S/DBP/UPP

Separation of TRH and its metabolites by ion-paring reversed -phase HPLC.

S. Antonio, L. Güereca, M. Cisneros and J.L. Charli
1985/T/S/DBP/UPP

Development of immunoaffinity columns for TRH.
P. Joseph
1984/P/DBP/URIA

Design, synthesis and evaluation of supports for pseudo-affinity chromatography.
N. Cruz and L. Güereca
1985/P/S/DBP/UPP

Optimization of enzyme purification methods in nucleic acids research.
I. Vichido and N. Cruz
1986/I/DGBM/DBP/UPP/UCCRB

Program 5.7 Production of monoclonal antibodies against peptides and proteins.

We work on developing methodologies for the production of monoclonal antibodies directed against specific polypeptides. They will be used for quantification, characterization, and purification of such polypeptides.

Specific projects

Production of monoclonal antibodies against LHRH and its use in the hormone purification by affinity chromatography.
P. Hérion, R. Saavedra and P. Joseph
1983/P/S/DBP/UB/URIA

Program 5.8 Protein engineering.

This field has great implications in the molecular interpretation of physiological phenomena and in the biotechnological application of specific proteins. Our aim is to explore in depth the structural-functional relation of specific proteins. We intent to apply this knowledge in the design of improved proteins for diverse purposes. Genetic engineering and classic genetic methods will be applied during the initial period and graphic and dynamic molecular methods will be implemented in subsequente stages.

Specific project

Saturation mutagenesis for the selection of specificity mutants of *Eco*R1 endonuclease.
M. Alonso and X. Soberón
1985/P/DGBM/USQM

Isolation of the DNA which codes for non toxic immunogenic fragments from tetanus toxin.
J. Osuna and X. Soberón
1985/P/S/DGBM

Reseach line No. 6

Development of methodology in molecular biology

Programs

6.1 Construction and characterization of molecular vectors for the cloning and expression of DNA.

6.2 Isolation, characterization and production of enzymes used in recombinant DNA.

6.3 Preparation and maintenance of biological specimens.

6.4 Chemical synthesis of oligonucleotides.

6.5 Utilization of exponential RNA replication for hybridization assays.

6.6 Generation of fluorescent signals for the detection of pathogenic agents and for other bioassays.

Program 6.1 Construction and characterization of molecular vectors for the cloning and expression of DNA.

Recombinant DNA techniques make possible the isolation, characterization, and expression of native and synthetic DNA. We work in the design and construction of the genetic systems need to isolate, modify and express a specific DNA. For that purpose we have built various plasmid cloning vectors from which we expect to obtain expression vehicles by using DNA regions that make possible the transcription of specific genes in *E. coli*. The following regions are used: the regulatory region for the *lac* and *trp* operons of *E. coli* bacteria, the PL promoter of bacteriophage lambda, and a synthetic promoter-operator.

We have constructed several vectors for cloning DNA which are utilized by many laboratories around the world where genetic engineering is used. Likewise, our reseach group has developed vectors that allow high efficiency of expression of the cloned genetic material.

Specific projects

Construction of molecular vectors for specific DNA expression, using the promoter of the tryptophan operator.
P. Balbás, N. Flores, F. Valle and F. Bolívar
1984/T/S/DGBM

Construction of molecular vectors for specific DNA expression utilizing the PL promoter of bacteriophage lambda.
N. Flores, P. Balbás, R. de Anda, F. Valle and F. Bolívar
1984/T/S/DGBM

Construction of molecular vectors with copy numbers that are subject to regulations; study of various loci which affect stability.
M. Zurita, M.E. Munguía and X. Soberón.
1983/P/S/DGBM/USQM

Construction of molecular vectors for the synthesis of hybrid proteins using the gene that codes for the bacteriophage - lambda repressor.
N. Flores, R. de Anda, F. Bolívar and F. Valle
1984/P/S/DGBM

Design of a molecular vector for the production and easy purification of proteins.
C. Aranda and X. Soberón
1983/T/S/DGBM/USQM

Program 6.2 Isolation, characterization and production of enzymes used in recombinant DNA.

Our effort, in conjunction with other research laboratories, is part of a strategy to provide the Center with molecular tools and specific methods in the isolation, characterizaton and expression of DNA. To accomplish some of our goals we have integrated a collection of microbial strains for the production of the enzymes involved in the handling of DNA *in vitro*. Some of these strains have been used for the production of enzymes.

Specific projects

Purification of *Pst*I restriction endonuclease.
I. Vichido
1984/T/DGBM/UCCRB

Purification of *Pal*I restriction endonuclease.
I. Vichido and F. Rosetti
1985/T/DGBM/UCCRB

Purification of *Sal*I restriction endonuclease.
I. Vichido
1986/I/DGBM/UCCRB

Purification of T4 DNA ligase.
I. Vichido and F. Rosetti
1986/I/DGBM/UCCRB

Purification of *Bam*H1 restriction endonuclease.
F. Rosetti and I. Vichido
1986/T/DGBM/UCCRB

Purification of *Cfo*I restriction endonuclease.
F. Rosetti and I. Vichido
1986/T/DGBM/UCCRB

Purification of *Eco*R1 restriction endonuclease.
I. Vichido
1986/T/DGBM/UCCRB

Program 6.3 Elaboration and maintenance of biological collections.

Our aim is to establish several biological collections: a) strains of microorganisms of research interest; b) genetic material (DNA) from plasmids and phages. Our long term plan is to establish a collection of microorganisms of industrial interest.

Specific projects

Integration of the Research Center's DNA bank.
I. Vichido, D.G. Hernández, J.A. Izquierdo and E.G. Me-

néndez
1985/P/DGBM/UCCRB

Integration of a collection of microorganism cellular pastes for the production of enzymes and plasmids.
I. Vichido
1985/P/DGBM/UCCRB

Preparation of cells suitable for transformation.
I. Vichido
1986/P/DGBM/UCCRB

Implementation of the Center's collection of microbial strains
I. Vichido
1986/P/DGBM/UCCRB

Program 6.4 Chemical synthesis of oligonucleotides.

Novel methods for DNA synthesis are implemented to bring up to date the Unit for Chemical Syntesis of Macromolecules. The Center's objective is to optimize the synthesis system utilizing automatized equipment, in order to speed up our contribution to the academic community of our country.

Specific projects

Standarization and optimization of techniques for automatic synthesis of oligonucleotides.
M.A. Cuevas and X. Soberón
1986/I/DGBM/USQM

Program 6.5 Utilization of exponential RNA replication for second generation hybridization assays.

The use of exponential RNA replication for the generation of signals in hybridization assays has great potential for diagnostic testing of infectious diseases. In the future, this method could be as useful as immunological methods for detecting pathogens. With this goal in mind, we have initiated a project to explore the use of amplification systems for the exponential replication of RNA and its application to hybridization assays. We propose to use a system derived from phage Q-Beta, in which the construction of recombinant RNA with the capability of autocatalytic replication in vitro has been demonstrated.

In collaboration with Dr. Fred Kramer from the Public Health Research Institute of the City of New York, and Dr. Donald Mills from Columbia University, new plasmids that facilitate the construction of recombinant RNA have been developed. With these plasmids, which contain a promoter for specific RNA transcription, we can construct recombinant RNA with optimal yield and purity.

For the initial experiments we are using repetitive DNA from malaria as a model. Its sequence is inserted in a specific locus inside the Q-Beta vector at the DNA level, using the plasmids mentioned above. The transcription of the desired recombinant sequence is obtainded utilizing phage T7 promoter in an in vitro system with T7 RNA polymerase. The RNA is used as a probe and then is replicated exponentially by Q-Beta replicase. In an alternative scheme, the replicatable RNA do not contain the probe sequence; the probe is coupled to the RNA by a 5' - 5' covalent union via disulfide; therefore, the probe sequence and the RNA can be separated by reduction after hybridization. We expect that the application of some of these systems for the generation of signals through exponential replication will result in a method of higher sensitivity and lower cost than the methods available today. If successful in the use of recombinant RNA for the development of diagnostic assays for malaria, we will attempt to use other analogous systems for assays in other pathogens of medical and veterinary importance.

Specific projects

Study of new replicatable recombinant RNA and its application to the amplification of signals.
H. Lomelí, F.R. Kramer, I. Tusie and P.M. Lizardi
1986/I/S/DBP

Development of byfunctional probes which contain replicatable RNA in covalent union with affinity molecules.
A. Alagón, C. González, C. Guerra, H. Lomelí, X. Soberón, L. Orgel and P.M. Lizardi
1986/I/S/DBP/DGBM/USQM

Study of RNA of Q–Beta phage in membranes with positive charges.
C. Guerra, C. González, A. Alagón and P.M. Lizardi
1986/I/S/DBP

Development of a method for the detection of pathogens based on the hybridization of DNA with generation of signals by replicatable RNA.

I. Tusie, H. Lomelí, C. Guerra, A. Alagón, F.R. Kramer and P.M. Lizardi

1986/P/S/DBP

Program 6.6 Generation of fluorescent signals for the detection of pathogenic agents and for general application in other bioassays.

The highly sensitive systems that are currently used for detecting pathogenic agents are based on immunologic techniques or in the hybridization of nucleic acids. They reveal the specific interaction through the following two modalities: the radioactive mode (i.e. autoradiography, radioimmunoassay), and the activity of some enzyme which transforms a colorless substrate into a colored product (i.e. enzymatic immunoassay, Ward's method for detecting hybridization of nucleic acids in nitrocellulose). Systems which employ radioactivity are higly sensitive but too costly and the storage life is extremely short. With enzymatic systems that genetate color is not always possible to achieve the level of sensitivity of radioactive systems; on the other hand, there is an advantage, they can be largely automated. Obviously there is a need to provide alternatives for the generation of extremely efficient and sensitive systems with the following characteristics: low cost, simple to perform, susceptible to automatization, and with the capability of being applied massively. Our effort is directed towards establishing strategies for the generation of fluorescent signals that will permit visualizing and quantifying the interaction of a specific DNA sequence (diagnostic probe) for *Plasmodium vivax* and parasite DNA in blood samples on a solid support (i.e. nitrocellulose membranes). If successful the procedure could be expanded to other diagnostic tests indistinctly if they are based on hybridization of nucleic acids or in other type of interaction (i.e. antigen-antibody).

In order to accomplish this objective we are taking advantage of the fluorescent properties of the ficobiliproteins; specially of ficoeritrin. In this project we collaborate with Dr. L. Strayer and Dr. A. Glaser from the Universities of Stanford and Berkely.

With the same objective in mind, and with the collaboration of the Gerencia General de Biologicos y Reactivos de la Secretaría de Salud (General Masagement for Biologicals and Reagents of the Health Secretariat), we are developing non-fluorescent synthetic pepetide substrates, which through an enzymatic transformation result in insoluble and highly fluorescent products.

With both types of fluorides we are assessing three ways of proceeding. In the following description the word "proteins" will refer indistrincly to ficobiliprotein or proteolytic enzyme: a) The protein is coupled directly and in covalent union to the diagnostic probe; b) The biotinylated protein is recognized by streptavidin previously anchored to a diagnostic probe that is biotinylated; c) The protein, derivatized with a hapten, is recognized by an antihapten polymeric antibody which has reacted previously with the same hapten in covalent union with the diagnostic probe.

In the case of the protease it involves a step further, in which a substrate is added to obtain the flourescent signal. The permanent registrer of the generated signals can be obtained with a photograph of the membranes under excitation with long wave ultraviolet light, using Polaroid film of high sensitivity.

Specific projects

Development of methods for the precipitation *in situ* of fluogenic aromatic amines.
M.L. Covarrubias, J. Martin-Polo and A. Alagón
1986/I/S/DBP

Synthesis of *ad hoc* fluorogenic peptides.
M.A. Torti, M.L. Covarrubias, J.Martín-Polo and A.Alagón
1986/P/S/DBP

Development of membranes derived from cellulose with positive charges and its application in the manipulation of macromolecules in bioassays.
C. González, M.A. Torti, C. Guerra, P.M. Lizardi and A. Alagón
1986/P/S/DBP

Development of schemes for the coupling of ficobiliproteins to oligonucleotide probes.
A. Alagón, P.M. Lizardi, L. Strayer, A. Glazer, L. Orgel and X.Soberón
1986/I/S/DBP/DGBM/USQM

Development of schemes for the coupling of proteases to oligonucleotide probes
A. Alagón, P.M. Lizardi and X. Soberón
1986/I/S/DBP/DGBM/USQM

Development of methods for detecting pathogens based in the use of DNA hybridization with the generation of fluorescent signals.
J. Cruz, I. Tusie, C. González, M.A. Torti, G. Gurrola, P.M. Lizardi, X. Soberón and A. Alagón
1986/I/S/DBP/DGBM/USQM

Research No. 7

Basic studies in Biotechnology

This line of research comprises basic studies relevant to key areas in the generation of biotechnologies. In many cases, these studies have resulted from the Center's need to develop its own specific technologies. Nevertheless, the programs and projects tend to develop areas of research with more general objectives.

Programs

7.1 Fermentation technology.

7.2 Enzyme technology.

7.3 Downstream processing.

7.4 Perspective studies in biotechnology.

Program 7.1 Fermentation technology.

The primary goal of this program is the development of technology to obtain a product of interest in the areas of food and health. Various types of microbial cultures are used. Our study focuses on the engineering parameters which affect a fermentation process, emphasizing the mass and heat transfer phenomena (fermentation engineering), the scale up criteria and the optimization of production processes. This optimization is done from an operative unit up to the integral process. Finally, we study the control of the process through the development of equipment and control strategies.

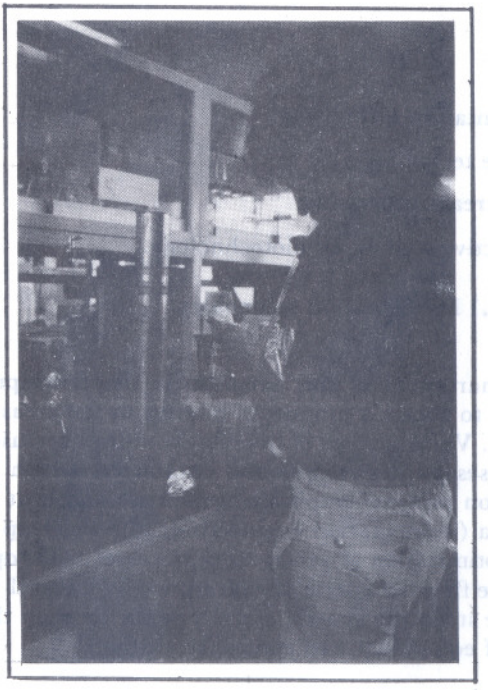
Specific projects

Projects directed towards the study of fermentation engineering;

Basis of engineering and scale up conditions in the production of xanthan gum.
B. Torrestiana, E. Brito, G. Delgado, R. Herrera, R.M. Corona and E. Galindo
1985/P/A/E/DBT/UEPP

Influence of superficial oxygen transfer on total transference.
A. Martínez and M. Salvador
1986/I/DBT/UEPP

Distribution of impellers and their influence in oxygen transfer in bioreactors.
A. Martínez and M. Salvador
1986/I/DBT/UEPP



Projects directed towards the study of optimization processes:

The influence of nitrogen sources in the production of single cell protein from milk whey.
M. García and M. Salvador
1986/T/W/C/DS T/UEPP

The influence of oxigen tension in the production of enzymes.
L. Pedraza, R. Mojica, S. Sánchzz and M. Salvador
1986/T/S/DBT/UEPP

The production of ethanol and its recovery during yeast fermentation.
M. Salvador
1986/ I/A/DBT/UEPP

Antibiotic production in plug flow columns: perspectives and modeling.
M.R. Celis and M. Salvador
1986/I/S/DBT/UEPP

Selection of scale up criteria in the production process of 6-APA.
L. Pedraza, M.E. Rodríguez, F. Neri and M. Salvador
1986/I/S/DBT/UEPP

Analysis of carbon source requirements in a feebback culture for the production of Beta-galactosidase in *Kluviveromyces fragilis* cells.
J. Torres, A. López and L. Casas
1985/T/P/S/DBT/UEPP

Projects directed to the study of scale up processes:

Relation of the oxygen transfer coefficient (Kla) on the production of Beta-galactosidase in *K. fragilis*.
J. Torres, A. López and L. Casas
1985/T/A/S/DBT/UEPP

Projects directed towards the designs of equipment:

Design and characterization of biosensors to measure compounds of clinical and industrial interest.
J. García, J. Pimentel, M. Alvarez and E. Galindo
1983/P/A/S/DBT

Program 7.2 Enzyme technology.

The aim of this program is to utilize the specific activity of an enzyme to procure a less expensive conversion. The enzymes can be used either in a purified form or contained in free or immobilized cells. To accomplish our goal, we carry on studies on the following: kinetic characterization of the enzyme of interest; development of new supports for the immobilization of the biocatalysts obtained and design and characterization of biocatalysts applied to enzymatic reactors.

Specific projects

Projects directed towards the kinetic characterization of enzymes;

Kinetic characterization of the Beta-galactosidase from *E. coli and K. fragilis.*
L. García, M. García, A. Canales, R. Quintero, A. López, E. Castillo, C. Peña and L. Casas
1983/P/A/S/DBT

Projects directed to the development and characterization of enzyme and cell supports:

Development and characterization of enzyme supports derived from galactans, galactomanans and polyoles.
F. Domínguez, E. Brito and L. Casas
1984/T/A/DBT

Characterization of various supports derived from cellulose acetate.
E. Castillo and L. Casas
1985/P/A/S/DBT

Projects directed towards development and characterization of biocatalysts:

Immobilization and characterization of a biocatalyst with Beta-galactosidase activity from *K. fragilis* cells immovilized in cellulose acetate fibers.
M. García, E. Castillo, A. López and L. Casas
1983/P/A/DBT

Development of an immobilization method for proteins in nylon.
J. García and E. Galindo
1983/P/A/S/DBT

Utilization of immobilized enzymes in the generation of hydrogen peroxide for milk conservation.
A. Luna, M. García and L. Casas
1986/P/A/DBT

Projects directed to the study and application of enzymatic reactors:

Design and characterization of an enzymatic reactor for the hydrolysis of lactose.
E. Castillo, L. Casas and A. López
1985/P/A/S/DBT/UEPP

Program 7.3 Downstream processing.

The aim of this program is to develop recovery processes suitable for the types of biotechnological applications on which the Center's research lines are focused.

Specific projects

Research studies on the recovery purification of xantan from a fermentation broth.
M.E. Ramírez, R. González, J. Torres, F. García, E. Brito and E. Galindo
1985/P/A/E/DBT/UEPP

Yeast recovery with Beta-galactosidase activity and without zimase activity from a fermentation broth.
C. Peña, J. Torres and L. Casas
1985/P/A/S/DBT/UEPP

Extraction and purification of the Beta-galactosidase from yeast.
S. Méndez, M. González and L. Casas
1985/P/A/S/DBT/UEPP

Studies on the recovery of single cell protein from fermented broths.
M. Salvador
1986/T/A/DBT/UEPP

Program 7.4 Prospective studies in biotechnology.

Through this program we inform researchers on the development of those projects which have potential for commercial applications. The specific areas we will cover include: technological policy, project evaluation, and industrial application.

Specific projects

Diagnostic kits: technological and market analysis.
E. Galindo
1986/I/S/DBT

Research line No. 8

Optimization and integration of processes and prototypes: Technology development

The objective of this area of research is to carry out the studies needed to integrate and optimize processes or prototypes that could be used by the productive sector. Consequently, this line of study presents the following distinct features: the incidence of various research groups at the Center sharing a common goal and the participation of other sectors and institutions.

Another characteristic is that the criteria used to delineate the plan of study is based on the final application of the product of interest. Examples of these criteria are: quality control norms, technical and economic feasibility, availability of raw materials, etc. The research studies will provide the necessary information to bring the product of interest to the level of production.

Due to these unique characteristics, each program belonging to this area of research is constituted not by isolated projects, but by a whole technological development within different stages of development.

Programs

8.1 Elaboration of products with lactase activity to be applied to milk or to sweet whey.

8.2 Development of a process at a semipilot level for the production of food grade xanthan gum.

8.3 Development of a prototype of a electroenzymatic analyzer for fast and simple quantification of compounds that have an industrial and clinical interest.

8.4 Production of human insulin synthetized by bacteria.

8.5 Development of hyperproducing strains of penicillin acylase utilizing recombinant DNA techniques.

8.6 Biochemical, functional, and genetic characterization of yeasts for the production and development of a method for their consevation.

8.7 Development and validation of diagnostic tests for protozoan parasites by DNA hybridization methods.

8.8 Design and chemical synthesis of pepetides and their possible uses.

8.9 Development of a diagnostic system for cystic fibrosis, based on nucleic acid hybridization.

Program 8.1 Elaboration of products with lactase activity to be applied to milk or to sweet whey.
J. Torres, E. Castillo, A. López, C. Peña, J. Rios, M. González, G. Ramírez and L. Casas
1985/P/A/S/DBT/UEPP

The objective of this program is to develop a product for hydrolyzing lactose, preferably from milk. Subsequently we pretend to apply the product to whey. The following partial goals are essential in accomplishing our objective: a) obtainment of an enzymatic extract; b) obtainment of a biocatalyst through immobilized cells; c) obtainment of cells with high enzymatic activity.

The products must have the following characteristics to be of industrial use: high enzymatic activity, operational stability, availability of raw materials and services in its elaboration, and technically and economically feasible.

Program 8.2 Development of a process at a semipilot level for the production of food grade xantan gum.
M.E. Ramírez, R. González, J. Torres, E. Brito, F. García and E. Galindo
1985/P/A/DBT/UEPP

This project aims to develop a technology for the production of food grade xanthan gum. It is based on the developed process for the production of technical grade xanthan. Aspects

to consider are the following: a) selection and trial of raw materials in the fermentation that will facilitate the purification steps of the product; b) selection of the necessary unitary operations for its recovery and purification; c) tests of the obtained product (both bromatological and for specific application in food products).

Program 8.3 Development of a prototype of a electroenzymatic analyzer for fast and simple quantification of compounds that have an industrial or clinical interest.
J. García, J. Pimentel, M. Alvarez and E. Galindo
1985/P/S/DBT

We seek to develop an enzymatic analyzer that could be used for fast and simple quantification of compoundus such as; sugars, organic acids and alcohols. To achieve this goal the following studies are in progress: a) immobilization of the specific enzymes involved in an inert membrane support; b) costruction of transducers and adequate electronic systems for each substrate; c) construction of a multipurpose module that integrates the mechanical, electrical, electronic and enzymatic aspects of the meter; d) functional testing of the electrode; e) testing of the apparatus in clinical and industrial settings.

Program 8.4 Production of human insulin synthetized by bacteria.
P. Balbás, L. Güereca, N. Cruz, S. Antonio, X. Alvarado, G. Estrada, I. Flores, R. De Anda, F. Valle and F. Bolívar
1981/P/S/DGBM/UPP/DBP

Human insulin is a peptidic hormone that consists of two chains of aminoacids, A and B. Using recombinant DNA, diverse strains from bacteria, which carry specific genes for chain A or chain B from human insulin, have been developed. The systems for the detection of these chains from animal (commercial) and bacterial origin have been established.

The resulting experiments show that those strains that carry the genes for A an B chains do produce these peptides. At the present time, we work on the optimization of the isolation processes for these peptides. On the other hand, we have established the systems that can reassociate the A and B chains into insulin, and we have developed conditions for crystallization and detection of insulin. Finally, we work on the conditions for scaling up the growth of the producing microorganisms.

Program 8.5 Development of hyperproducing strains of penicillin acylase utilizing recombinant DNA techniques.
F. Valle, N. Flores, R. De Anda and F. Bolivar.
1985/P/S/DGBM

The enzyme penicillin acylase is utilized for converting penicillin intro 6-aminopenicillinic acid. This molecule is the precursor of semisynthetic penicillins. The gene that codes for this enzyme has been isolated and sequenced and we have determined which is the region that allows its expression.

Through fine DNA manipulation and through the use of *E. coli* strains with altered permeability, we have obtained an *E. coli* strain that shows five to six times more specific activity than the original ATCC-11105 strain.

Our research grupo is also exploring suitable conditions for optimal stability and growth of this new strain designed by genetic engineering with the objective of utilizing this strain in an enzymatic technology process developed at the Center.

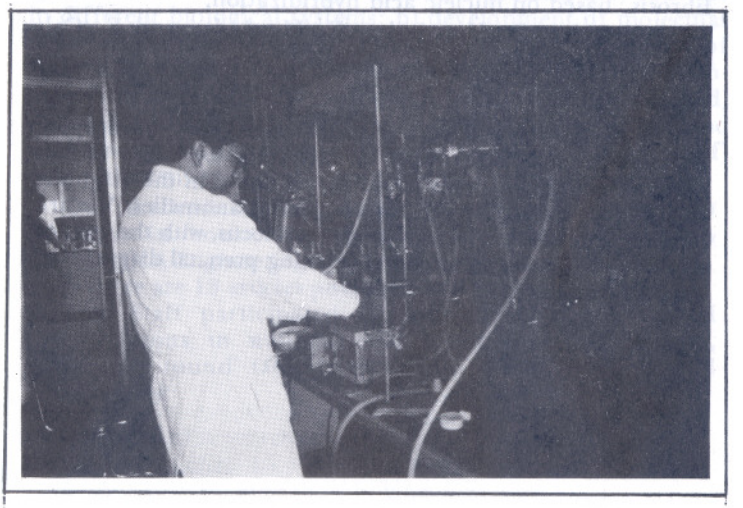
Prrogram 8.6 Biochemical, functional and genetic characterization of yeast strains and development of methods for their conservation.
E. Arriaga, M. Fernández, L. Casas, E. Galindo, A. González and M. García-Garibay.
1986/P/A/DBT

Our group seeks to characterize five yeast strains of industrial origin utilized in the production of ethanol from molasses. The characterization of yeast strains will take place based on biochemical tests, and the analysis of genetic material with the purpose of establishing their taxonomic identity, and the differences between them and in relation to collection strains. Likewise, we will characterize these yeasts with the goal of establishing their utility as industrially relevant strains for the production of ethanol obtained from sugar cane molasses. In parallel to the work mentioned above, we will evaluate different conservation techniques. Our target is to find the optimal conditions for the preservation of the strain viability and function for long periods of time.

Program 8.7 Development and validation of diagnostic tests for protozoan parasites by DNA hybridization methods.
A. Alagón, H. Muñóz, H. Lomelí and P.M. Lizardi
1986/P/S/DBP

The advancement of diagnostic techniques on genetic manipulation and DNA cloning have made feasible the design of new types of diagnostic analysis, based on the hybridization of nucleic acids. This novel methodolgy permits an alternative to microscopic, serologic, or inmunologic assays presently used for detecting microorganisms. Recently published research studies demonstrate the utility of hybridization probes which can detect malaria parasites (*P. falciparum*), with absolute specificity and great sensitivity. Radioactive probes were used in the original studies, but the utilization of non-radioactive probes is feasible. The technology of non-radioactive DNA probes promises to have a technological impact of a magnitude similar to that of the utilization of monoclonal antibodies for clinical diagnosis.

Considering the potential of this new technology on diagnostics and epidemiologic vigilance on malaria, and, in the long term, of other infectious diseases, we plan to develop and validate diagnostics of this kind in México.



Program 8.9 Design and chemical synthesis of peptides and their possible uses .
G. Gurrola, L.A. Vaca, F. Zamudio, R.S. Saavedra, A.H. Muñoz, M.A. Sánchez and L. Possani
1986/P/S/DBP

The determination of the primary structure of scorpion toxins has permitted the design and synthesis of specific peptide

fragments. Using the Merrifield solid-phase synthesis technique, we have synthesized a dozen peptides which correspond to scorpion toxin sequences, including the complete sequence of Noxiustoxin. Likewise, using liquid-phase synthesis, we have synthesized for the determination of epitope sequences in monoclonal antibodies.

From immunological studies on synthetic peptides, and from the displacement curves of antibody binding to native toxin versus synthetic peptides, and the determination of some epittopes from natural toxins, we expect to obtain the information needed to design a synthetic anti-toxin vaccine for scorpion sting.

By being able to obtain and study venoms, we have been able to generate hyperimmune sera which is one of the few effective medications against scorpion sting.

Program 8.9 Development of a diagnostic system for cystic fibrosis, based on nucleic acid hybridization.
M. Fernández, D. Hernández, E. Menéndez and E. Calva
1986/I/S/DGBM

The purpose of this work is to determine how polymorphic sites on human DNA vary in different segments of the mexican population. This knowledge is useful in the diagnosis of defective genes for various congenital anomalies. We are focusing our effort on the cystic fibrosis locus, with the goal of detecting heterozygote carriers, or doing prenatal diagnosis of affected fetuses.

Research achievements
(April 1982–December 1987)

Basic Research

One of the principal achievements has been the generation of knowledge in the following areas: a) Genetic organization of specific DNA and RNA regions and the proteins they code for in different biological systems; b) development of molecular tools and methodology for the isolation and expression of specific segments of the genetic material; c) physiology, biochemistry and molecular biology of specific neuropeptides; d) determination of parameters for the design of fermentors and microbiological electrodes; e) development of bioreactors; f) characterization of proteic toxins from poisonous animals.

Our Academic Staff published 57 articles in journals, 30 chapters in books. Two books were published, one in Biochemical Engineering and the other in Organic Chemistry. Also there are 13 articles published in Annals and Reviews.

Our Staff participated in approximately 250 formal presentations in national and international congresses, seminars, round table discussions, poster sessions and conferences.

Applied Research and technological development

Other important achievements have been the use of some of this information along with the one already present literature for:

A) The development and the transference of six biotechnologies developed at the Research Center to mexican industry: I) development of an enzymatic technology for the production of semisynthetic penicillins and cephalosporins; II) development of a fermentation process for the production of xantan; III) development of two fermentation processes for the production of unicellular protein from milk serum; IV) development of a process, at laboratory and pilot plant scale, for the production of inoculum from *Saccharomyces cerevisiae* towards the production of alcohol; V) development of a fermentation process to produce unicellular protein from methanol; VI) biological and biochemical characterization of alcohol producing yeast strains.

B) Two patents have been accepted and six more are under review.

C) Building of microorganisms that produce human proteins (Such as human interferon, A and B chains of human insulin) and industrially important polymers (xantan).

D) Development of a system for the detection of malaria, using DNA probes.

E) Development of a multienzymatic meter for fast and sample quantization of simple compounds.

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*Articles in which X. Soberón is co–author, published during his stay in City of Hope, National Medical Center, Duarte, CA. (USA).
**Works partially realized at the Instituto de Investigaciones Biomédicas, UNAM (UNAM's Institute from Biomedical Research) by A. Alagón and L.D. Possani.
***Works partially realized at the Rockefeller University, New York (USA) by P.M. Lizardi.
****Work partially realized at Institute de Investigaciones Biomédicas, UNAM, by C. Arias and S. López.

c) Articles in memoirs and reviews.

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d) Books.

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J. Rubio and P. Joseph–Bravo Química Orgánica para Estudiantes del Area Biomédica. CINVESTAV–Offset, méxico (1986).

II) Participation in congresses

The Center's Staff has actively participated in various National and International Congresses with more than 250 presentations.

III) Reports

The development of 37 project contracts and agreements have generated 68 technical reports.

IV) Patents

a) Registered patents.

82/1691 D. Carranco, L. Casas, R. Quintero, F. Bastarrachea and F. Bolívar. "Separación y purificación del acido 6–aminopenicilánico producido por hidrólisis enzimática". UNAM–CONACYT.

83/2064 L. Casas, F. Bastarrachea, R. Quintero, D. Carranco, E. Galindo and F. Bolívar. "Producción de la enzima penicilino–amidasa en células de *E. coli*". UNAM–CONACYT.

b) Patents in process.

L. Casas, D. Carranco, R. Quintero, F. Bolívar and F. Bastarrachea. "Producción del acido 6–aminopenicilánico por hidrólisis enzimática de la penicilina–G, con penicilino–amidasa contenida en células de *E. coli* inmovilizadas en colágena". UNAM–CONACYT.

L. Casas, D. Carranco, R. Quintero, E. Galindo, F. Bolívar and F. Bastarrachea. "Producción del acido 6–aminopenicilánico por hidrólisis enzimática de la penicilina–G con penicilina–amidasa contenida en celulas de E. coli inmovilizadas en carragenina". UNAM–CONACYT.

R. Quintero, E. Galindo, M. Ruíz, M. Maya and F. Serrano. "Procedimiento para la obtención de plisacáridos por degradación bacteriana de carbohidratos". UNAM–IMP.

M. García, L. Casas, A. López–Munguía and R. Quintero. "Procedimiento para la producción de un biocatalizador con actividad enzimática de Beta–galactosidasa". UNAM–CONACYT.

E. Galindo, J. García, M. Alvarez and J. Pimentel. "Procedimiento para la utilización de enzimas en mallas de nylon en la construcción de electrodos enzimáticos". UNAM–CONACYT.

L. Possani and G. Gurrola. "Utilización de un péptido sintético correspondiente a una secuencia parcial a la noxiustoxina, bloqueador especifico del canal de potasio". UNAM–CONACYT.

V) Transfered technological developments

"Obtainment of unicellular protein from milk serum". PROMITER QUESO FINO, S.A. November (1983).

"Xantan production". INSTITUTO MEXICANO DEL PETROLEO (IMP) July (1984).

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towards the production of alcohol". BACARDI & CIA., S.A. July (1985).

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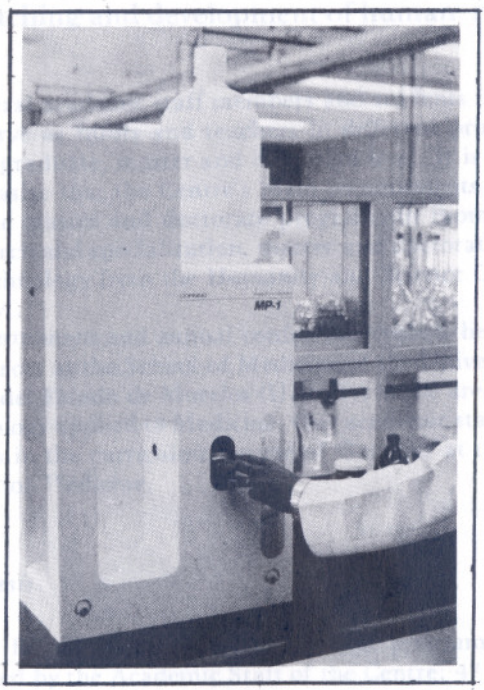
"Production of unicellular proteins from milk serum at pilot plant level". KEMFUDS DE MEXICO. S.A. June (1986).

"Biochemical and genetical characterization of yeast strains needed in the production of alcohol". BACARDI & CIA., S.A. September (1987).



Teaching and development of human resources

Several academic staff members and students from the Centre serve as tutors and teachers in different programs at the undergraduate, master and doctorate level. It is important to emphasize that the Centre's main commitments in education are the master and doctorate programs in Biomedical Basic Research and specialization, master and doctorate program in Biotechnology from the Humanity and Science College of the UNAM.

A permanent and annual conference cycle is held by several Professors at the School of Medicine of the Universidad Autónoma del Estado de Morelos (UAEM), in the area of Molecular Biology applied to Medicine. Our academic staff also participates in the curriculum course of Genetics at the UAEM's School of Medicine.

a) Thesis.

The following thesis, from different programs, have been directed by the Academic Staff of the Centre; 47 at undergradute level, 21 at the master level and 5 at the doctorate level.

The following thesis are in process:
28 Undergraduate
25 master
11 doctorate

Directed thesis.

Undergraduate Level

1982

Mario Zurita
Science Faculty/UNAM
(Bolívar F.)

Laura López
Chemistry Faculty/UNAM.
(Quintero R.)

Georgina Ponce
ENEP Zaragoza/ UNAM.
(Charli J.L.)

Patricia De Gortari
Universidad Iberoamericana.
(Bolívar F. and Joseph P.)

1983

Salvador Antonio
ENEP Zaragoza UNAM.
(Huerta I.)

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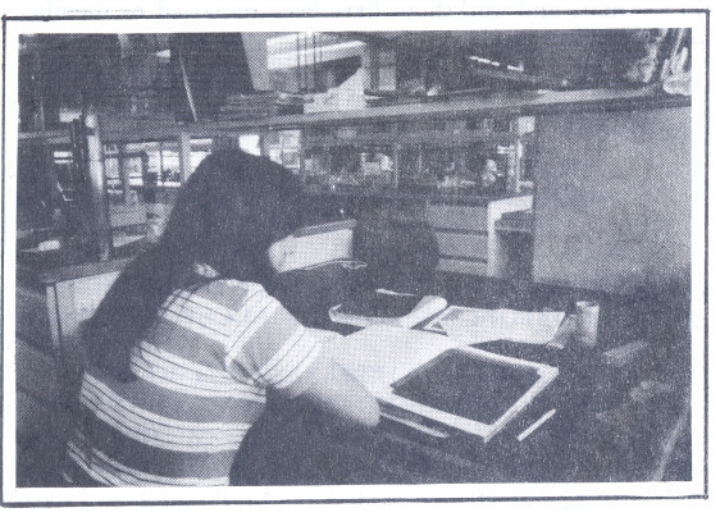
b) Courses given

Undergradute level:

Biochemistry; Biomedical engineering; Neuronal development; Genetics I; Molecular biology; Genetics II; Physical chemistry I and II; Evaluation of the projects for the field of Engineering of Industrial Biochemistry; Biotechnology.



Gradute level:

Regulation of the genetic expression in prokaryotes I; Neuroendocrine integration; Molecular aspects of neuropeptides; Theoretical basis and practical approaches used in characterization and separation methods for macromolecules; Transcrip tion and translation processes in prokaryotes; Transport of macromolecules in cellular systems; Regulation of genetic expression in prokaryotes II; Molecular endocrinology; Fermentations and enzymatic technology; Genetic and molecular aspects of DNA recombination in prokaryotes; Enzymology principles applied to biotechnology; Relevant aspects in biocatalysis; Genetic engineering; Directed mutagenesis and its applica tions to genetic engineering; Chemical synthesis of DNA and its applications; Aspects on global genetic regulation in prokar yotes; Molecular biology and human diseases; Microbiology; Instrumentation and control of biotechnological processes; Fer mentation technology; Industrial biotechnology; New approaches to biocatalysis; Biochemical engineering; Chemical syn-

thesis of DNA directed mutagenesis; Structure and engineering of proteins; Medical genetics; Transport phenomena in biological systems; Biochemical engineering; Evolution of the prokaryotic genome; Physical chemistry of macromolecules; Biochemistry.

c) Educational and Informational Seminars Workshops:

74 seminars and workshops have been imparted by members of the academy staff.

Fundings and standing agreements

EQUIPAMIENTO DEL CENTRO DE INVESTIGACION SOBRE INGENIERIA GENETICA Y BIOTECNOLOGIA, UNAM.
EQUIPING OF THE RESEARCH CENTRE FOR GENETIC ENGINEERING AND BIOTECHNOLOGY, UNAM.
Key: PFT/QU/NAL/82/1730
Responsible: Dr. Francisco Bolívar.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

ESTUDIO Y CARACTERIZACION DE LAS REGIONES REGULATORIAS DE LOS GENES ESTRUCTURALES QUE CODIFICAN PARA LAS ENZIMAS GLUTAMATO DESHIDROGENASA Y GLUTAMATO SINTASA.
STUDY AND CHARACTERIZATION OF THE REGULATORY REGIONS OF THE STRUCTURAL GENES CODING FOR ENZYMES GLUTAMATE DEHYDROGENASE AND GLUTAMATE SYNTASE.
Key: PCCBBNA/022584.
Responsible: Dr. Francisco Bolívar.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

FORTALECIMIENTO A LA ESPECIALIZACION, MAESTRIA Y DOCTORADO EN BIOTECNOLOGIA.
FORTIFYING THE SPECIALIZATION, MASTER AND DOCTORATE PROGRAMS IN BIOTECHNOLOGY.
Key: without number

Responsible: Dr. Francisco Bolívar.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

PRODUCCION DE ENZIMAS DE RESTRICCION PARA INVESTIGACION EN INGENIERIA GENETICA Y BIOTECNOLOGIA.
PRODUCTION OF RESTRICTION ENZYMES FOR RESEARCH IN GENETIC ENGINEERING AND BIOTECHNOLOGY.
Key: PVT/AI/NAL/86/3405
Responsible: Biol. Irma Vichido
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

PRODUCCION DE LA ENZIMA B-GALACTOSIDASA EN CELULAS DE LEVADURA. SU INMOVILIZACION EN LA ELABORACION DE UN BIOCATALIZADOR QUE HIDROLICE A LA LACTOSA PRESENTE EN LECHE Y EN SUERO DULCE DE LECHE.
PRODUCTION OF B-GALACTOSIDASE FROM YEAST CELLS; ITS IMMOBILIZATION IN THE MANUFACTURE OF A BIOCATALYZER THAT HYDROLYSES THE LACTOSE PRESENT IN MILK AND SWEET MILK SERUM.
Key: PVT/AG/NAL/84/243
Responsible: M. in Sc. Lidia Casas
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

PRODUCCION DE LA ENZIMA B-GALACTOSIDASA EN CELULAS DE K. FRAGILIS ELABORACION DE UN PRODUCTO CON ACTIVIDAD B-GALACTOSIDASA PARA SU UTILIZACION EN LECHE Y SUERO DULCE DE LECHE.
PRODUCTION OF THE ENZYME B-GALACTOSIDASE FROM K. FRAGILIS CELLS MANUFACTURE OF A PRODUCT WITH B-GALACTOSIDASE ACTIVITY TO BE USED IN MILK AND SWEET MILK SERUM.
Key: PVT/AI/NAL/84/2584
Responsible: M. in Sc. Lidia Casas.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

OBTENCION Y PURIFICACION DE LA B-GALACTOSIDASA PRODUCIDA POR CELULAS DE K. FRAGILIS.
PURIFICATION OF THE B-GALACTOSIDASE PRODU-

CED BY K. FRAGILIS CELLS.
Key: PVT/AG/NAL/85/3182
Responsible: M. in Sc. Lidia Casas
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

COLABORACION E INTERCAMBIO MEXICO-FRANCIA EN EL AREA DE NEUROPEPTIDOS. ESTUDIO DEL METABOLISMO DE PEPTIDOS.
MEXICO-FRANCE COLABORACION AND EXCHARGE IN THE NEUROPEPTIDE AREA. STUDY OF PEPTIDE METABOLISM.
Key: PCCBBNA/021044
Responsible: Dra. Patricia Joseph
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

DESARROLLO DE UN PROTOTIPO DE MEDIDOR ELEC TROENZIMATICO PARA LA CUATIFICACION RAPIDA Y SENCILLA DE COMPUESTOS DE INTERES INDUSTRIAL Y CLINICO.
DEVELOPMENT OF AN ELECTROENZYMATIC MEASURING DEVICE PROTOTYPE TO QUANTIFY IN A QUICK AND EASY MANNER INDUSTRIALLY AND CLINICALLY IMPORTANT COMPOUNDS.
Key: PVT/NAL/85/ 2744
Responsible: M. in Sc. Enrique Galindo.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

REGULACION DE LA BIOSINTESIS DE LHRH, TRH Y SRIF EN EL HIPOTALAMO DE LA RATA.
REGULATION OF THE BIOSYNTHESIS OF LHRH, TRH AND SRIF IN RAT HYPOTHALAMUS.
Key: ICSAXNA/030915
Responsible: Dr. Jean Luis Charli
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

ESTUDIOS SOBRE EL GENOMA DE SALMONELLA TYPHI. I. GENES PARA PROTEINAS DE MEMBRANA EXTERNA.
STUDIES ON THE GENOME OF SALMONELLA TYPHI. I. GENES FOR OUTER MEMBRANE PROTEINS.
Key: ICSAXNA/O30735
Responsible: Dr. Edmundo Calva

Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

BASES DE INGENIERIA Y ESCALAMIENTO DE LA PRODUCCION DE GOMA XANTANA.
ENGINEERING AND SCALING UP BASES FOR THE PRODUCTION OF XANTAN GUM.
Key: PVT/AI/NAL/85/2743
Responsible: M. in Sc. Enrique Galindo.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

DESARROLLO DE UN PROCESO A NIVEL SEMI-PILOTO PARA LA PRODUCCION DE GOMA XANTANA GRADO ALIMENTICIO.
DEVELOPMENT OF A PROCESS AT A SEMI-PILOT LEVEL FOR THE PRODUCTION OF FOOD GRADE XANTAN GUM.
Key: PVT/AI/NSL/2745
Responsible: M. in Sc. Enrique Galindo
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

ESTUDIOS SOBRE LA BIOSINTESIS, LIBERACION E INACTIVACION DE LA HORMONA LIBERADORA DE TIROTROPINA (TRH) EN EL SISTEMA NERVIOSO CENTRAL.
STUDIES ON THE BIOSYNTHESIS, RELEASE AND INACTIVATION OF THE THYROTROPIN HORMONE RELEASING FACTOR (TRH) IN THE CENTRAL NERVOUS SYSTEM.
Key: without number.
Responsible: Dr. Jean Louis Charli.
Given by Fondo de Investigación Ricardo J. Zevada.

GENETICA MOLECULAR DE POBLACIONES DEL GENE DE LA FENILALANINA HIDROXILASA EN MEXICO.
MOLECULAR GENETICS IN THE MEXICAN POPULATION OF THE GENE FOR PHENYLALANINE HYDROXYLASE.
Key: PVT/QF/NAL/86/2040
Responsible: Dr. Edmundo Calva
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

DESARROLLO Y VALIDACION DE PRUEBAS DIAGNOSTICAS PARA PALUDISMO POR EL METODO DE HIBRIDIZACION DE ADN.
DEVELOPMENT AND VALIDATION OF DIAGNOSTIC TEST FOR MALARIA USING DNA HYBRIDIZATION.
Key: PVT/QF/NAL/85/2941
Responsibles: Dr. Paul Lizardi and Dr. Alejandro Alagón.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

* DESARROLLO METODOLOGICO EN BIOLOGIA MOLECULAR.
METHODOLOGIC DEVELOPMENT IN MOLECULAR BIOLOGY.
Key: ICCBBITD/80/12/34
Given by Consejo Nacional de Ciencia y Tecnología (CONACYT) to several mexican institutions including UNAM.

REACTIVOS DE DIAGNOSTICO: ANALISIS TECNOLOGICO Y DE MERCADO.
DIAGNOSTIC REACTIVES: TECHNOLOGICAL AND MARKETING ANALYSIS.
Key: without number.
Responsible: Dra. Aurora del Rio and M. in Sc. Enrique Galindo.
Project in conjuction with Gerencia General de Biológicos y Reactivos de la Secretaría de Salud and Centro de Investigación sobre Ingeniería Genética y Biotecnología/UNAM.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

PROGRAMA DE VACUNAS SINTETICAS: PROYECTO ANTITOXINA TETANICA.
SYNTHETIC VACCINES PROGRAM: TETANUS ANTITOXIN PROJECT.
Key: PVT/AI/NAL/85/3079
Responsibles: Dra. Aurora del Rio and Xavier Soberón.
Project in conjunction with the Gerencia General de Biológicos y Reactivos de la Secretaría de Salud and Centro de Investigación sobre Ingeniería Genética y Biotecnología/UNAM. Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT).

DONATIVO AL CENTRO DE INVESTIGACION SOBRE INGENIERIA GENETICA Y BIOTECNOLOGIA DE LA COMPAÑIA SHERWIN WILLIAMS DE MEXICO, S.A. DE C. V. PARA EL DESARROLLO DE ESTA DEPENCIA DE LA UNAM.
FUNDING FOR THE CENTRO DE INVESTIGACION SOBRE INGENIERIA GENETICA Y BIOTECNOLOGIA GIVEN BY SHERWIN WILLIAMS DE MEXICO, S. A. DE C. V. FOR THE DEVELOPMENT OF THIS CENTRE.
Key: without number.
Responsible: Dr. Francisco Bolívar.
This grant was given through the program México 2000, Dirección de Transferencia de Tecnología de la Secretaría de Comercio y Fomento Industrial.

* Project in which the Centro de Investigación sobre Ingeniería genética is co–responsible together wich Centro de Investigación sobre Fijación de Nitrógeno, UNAM, and Centro de Investigaciones y de Estudios avanzados, I.P.N.

Fundings and Closed Agreements

PRODUCCION DE PROTEINA UNICELULAR A PARTIR DE SUERO DULCE DE LECHE.
UNICELLULAR PROTEIN PRODUCTION FROM SWEET MILK SERUM.
Key: without number.
Responsible: M. in Sc. Miguel Salvador.
Given by KEMFUDS.

AISLAMIENTO, CARACTERIZACION Y SOBREEXPRESION DEL GENE QUE CODIFICA PARA LA ENZIMA PENICILINO AMIDASA.
ISOLATION, CHARACTERIZATION AND OVEREXPRESSION OF THE GENE THAT CODES FOR ENZYME PENICILLIN AMIDASE.
Key: PCBBNAL/020164
Responsible: Dr. Francisco Bolívar.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

ESTUDIOS GENETICOS EN AZOSPIRILLUM.
GENETIC STUDIES IN AZOSPIRILLUM .

Key: PCBBNA/001903
Responsible: Dr. Fernando Bastarrachea.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

DISEÑO, CONSTRUCCION Y APLICACION DE SENSORES MICROBIOLOGICOS.
DESIGN, CONSTRUCTION AND APPLICATION OF MICROBIOLOGIC SENSORS.
Key: IVT/QU/NAL/81/1261
Responsible: Dr. Rodolfo Quintero.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

DESARROLLO DEL PROCESO PARA LA TRANSFORMACION DE DL-HIDANTOINA A D-AMINOACIDO, VIA ENZIMATICA A NIVEL LABORATORIO.
DEVELOPMENT OF A PROCESS FOR THE TRANSFORMATION OF DL-HYDANTOIN TO D-AMINOACID UTILIZING AN ENZYME AT LABORATORY LEVEL.
Key: without number.
Responsible: Dr. Rodolfo Quintero.
Given by ENZIMOLOGA, S.A.

ESCALAMIENTO DE UN PROCESO DE PRODUCCION DE UN BIOPOLIMERO.
SCALING UP OF A PRODUCTION PROCESS FOR A BIOPOLYMER.
Key: Without number.
Responsible: Dr. Rodolfo Quintero.
Given by Instituto Mexicano del Petroleo (I.M.P.)

REGULACION DEL METABOLISMO Y LIBERACION DE DE NEUROHORMONAS HIPOTALAMICAS ESTUDIOS "IN VITRO".
METABOLISM REGULATION AND RELEASE OF HYPOTHALAMIC NEUROHORMONES STUDIES "IN VITRO".
Key: without number.
Responsible: Dr. Jean Louis Charli.
Given by Fondo de Investigación Ricardo J. Zevada

HIDROLISIS DE LACTOSA EN LECHE.
HYDROLYSIS OF LACTOSE IN MILK.
Key: without number.

Responsible: M. in Sc. Lidia Casas.
Given by Programa Universitario de Alimentos/UNAM (PUAL).

OPTIMIZACION DE LAS CONDICIONES DE PRODUCCION DE INOCULOS DE SACCHAROMYCES CEREVISIAE EN EL PROCESO DE LA ELABORACION DE ALCOHOL.
OPTIMIZATION IN PRODUCTION CONDITIONS OF SACCHAROMYCES CEREVISIAE INOCULA IN THE ELABORATION PROCESS OF ALCOHOL.
Key: without number.
Responsible: M. in Sc. Enrique Galindo.
Given by BACARDI Y CIA. S.A.

INGENIERIA GENETICA PARA LA PRODUCCION DE POLIPEPTIDOS.
GENETIC ENGINEERING FOR THE PRODUCTION OF POLYPEPTIDES.
Key: PCCSABNAL/05341
Responsible: Dr. Francisco Bolívar.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

HORMONA LIBERADORA DE TIROTROPINA (TRH): CAPTACION Y DEGRADACION EN EL SISTEMA NERVIOSO CENTRAL.
THYROTROPIN RELEASING HORMONE (TRH): SEINZURE AND DEGRADATION IN THE CENTRAL NERVOUS SYSTEM.
Key: PSCNAL/800590
Responsible: Dr. Jean Louis Charli.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

DESARROLLO DE LA INGENIERIA GENETICA EN MEXICO (PRODUCCION DE INSULINA HUMANA).
DEVELOPMENT OF GENETIC ENGINEERING IN MEXICO (PRODUCTION OF HUMAN INSULIN).
Key: without number.
Responsible: Dr. Francisco Bolívar.
Given by Instituto Mexicano del Seguro Social (IMSS).

ESTUDIO Y MANIPULACION DE LOS ORIGENES DE REPLICACION DE VEHICULOS DE CLONACION MOLECULAR DE DNA. FORMACION DE RECURSOS HUMANOS EN INGENIERIA GENETICA.
STUDY AND MANIPULATION OF THE REPLICATION ORIGINS OF DNA MOLECULAR CLONING VECTORS.
Key: PCCBBNA/020642
Responsible: Dr. Xavier Soberón.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

ESTUDIO DE LA HORMONA LIBERADORA DE TIROTROPINA (TRH).
STUDY OF THE THYROTROPIN RELEASING HORMONE (TRH).
Key: PSCABNA/005590
Responsible: Dr. Jean Louis Charli
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

ESTUDIO DE LOS PROCESOS REGULADORES DE HORMONAS HIPOFISIARIAS. OPTIMIZACION DE UN SISTEMA DE CULTIVO DE CELULAS DISPERSAS PRIMARIAS DE HIPOTALAMO.
STUDIES OF THE PROCESSES REGULATING HYPOPHISIS HORMONES. OPTIMIZATION OF A CULTURE SYSTEM OF DISPERSE PRIMARY CELLS FROM HIPOTHALAMUS.
Key: PCSABNA/001117
Responsible: Dra. Patricia Joseph.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

ESTUDIO SOBRE LA BIOSINTESIS DE LHRH (HORMONA LIBERADORA DE LA HORMONA LUTEINIZANTE). CLONACION Y UTILIZACION DEL ADN COMPLEMENTARIO.
STUDIES ON THE BIOSYNTHESIS OF LHRH (RELEASING HORMONE OF THE LUTEINIZING HORMONE). CLONING AND USE OF COMPLEMENTARY DNA.
Key: PCCBBNA/001926
Responsible: Dra. Patricia Joseph.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

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Francisco Bolívar Ph.D
Edmundo Calva Ph.D.
Jean Louis Charli Ph.D.
Patricia Joseph Ph.D.
Paul M. Lizardi Ph.D.
Lourival D. Possani Ph.D.
Xavier Soberón Ph.D.

Associate Investigators:

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Milagros Méndez M.Sc.
Guillermo Ramírez M.Sc.
Luis Servín Ph.D.
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Academic Technicians

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Edmundo Castillo Biol. Chem.
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Norberto Cruz Biol. Chem.
Mario Cuevas Biol. Chem.
Ramón de Anda Biol. Chem.
Georgina Estrada Biol. Chem
Marcos Fernández Biol. Chem.
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Rosa Ma. López Biol. Chem.
Alfredo Martínez Biol. Chem.
Elizabeth Mata Veterinary
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Myriam Ortíz Biol. Chem.
Rodolfo Ramírez Eng.
Beatriz Torrestiana Biochem. Eng.

Auxiliary Academic Technicians

Fernando Chávez Biol.
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Miguel Angel Vargas Biol.

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Key: PCBBNA/001903
Responsible: Dr. Fernando Bastarrachea.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

DISEÑO, CONSTRUCCION Y APLICACIÒN DE SENSORES MICROBIOLOGICOS.
DESIGN, CONSTRUCTION AND APPLICATION OF MICROBIOLOGIC SENSORS.
Key: IVT/QU/NAL/81/1261
Responsible: Dr. Rodolfo Quintero.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

DESARROLLO DEL PROCESO PARA LA TRANSFORMACION DE DL-HIDANTOINA A D-AMINOACIDO, VIA ENZIMATICA A NIVEL LABORATORIO.
DEVELOPMENT OF A PROCESS FOR THE TRANSFORMATION OF DL-HYDANTOIN TO D-AMINOACID UTILIZING AN ENZYME AT LABORATORY LEVEL.
Key: without number.
Responsible: Dr. Rodolfo Quintero.
Given by ENZIMOLOGA, S.A.

ESCALAMIENTO DE UN PROCESO DE PRODUCCION DE UN BIOPOLIMERO.
SCALING UP OF A PRODUCTION PROCESS FOR A BIOPOLYMER.
Key: Without number.
Responsible: Dr. Rodolfo Quintero.
Given by Instituto Mexicano del Petroleo (I.M.P.)

REGULACION DEL METABOLISMO Y LIBERACION DE DE NEUROHORMONAS HIPOTALAMICAS ESTUDIOS "IN VITRO".
METABOLISM REGULATION AND RELEASE OF HYPOTHALAMIC NEUROHORMONES STUDIES "IN VITRO".
Key: without number.
Responsible: Dr. Jean Louis Charli.
Given by Fondo de Investigación Ricardo J. Zevada

HIDROLISIS DE LACTOSA EN LECHE.
HYDROLYSIS OF LACTOSE IN MILK.
Key: without number.

Responsible: M. in Sc. Lidia Casas.
Given by Programa Universitario de Alimentos/UNAM (PUAL).

OPTIMIZACION DE LAS CONDICIONES DE PRODUCCION DE INOCULOS DE SACCHAROMYCES CEREVISIAE EN EL PROCESO DE LA ELABORACION DE ALCOHOL.
OPTIMIZATION IN PRODUCTION CONDITIONS OF SACCHAROMYCES CEREVISIAE INOCULA IN THE ELABORATION PROCESS OF ALCOHOL.
Key: without number.
Responsible: M. in Sc. Enrique Galindo.
Given by BACARDI Y CIA. S.A.

INGENIERIA GENETICA PARA LA PRODUCCION DE POLIPEPTIDOS.
GENETIC ENGINEERING FOR THE PRODUCTION OF POLYPEPTIDES.
Key: PCCSABNAL/05341
Responsible: Dr. Francisco Bolívar.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

HORMONA LIBERADORA DE TIROTROPINA (TRH): CAPTACION Y DEGRADACION EN EL SISTEMA NERVIOSO CENTRAL.
THYROTROPIN RELEASING HORMONE (TRH): SEINZURE AND DEGRADATION IN THE CENTRAL NERVOUS SYSTEM.
Key: PSCNAL/800590
Responsible: Dr. Jean Louis Charli.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

DESARROLLO DE LA INGENIERIA GENETICA EN MEXICO (PRODUCCION DE INSULINA HUMANA).
DEVELOPMENT OF GENETIC ENGINEERING IN MEXICO (PRODUCTION OF HUMAN INSULIN).
Key: without number.
Responsible: Dr. Francisco Bolívar.
Given by Instituto Mexicano del Seguro Social (IMSS).

ESTUDIO Y MANIPULACION DE LOS ORIGENES DE REPLICACION DE VEHICULOS DE CLONACION MOLECULAR DE DNA. FORMACION DE RECURSOS HUMANOS EN INGENIERIA GENETICA.
STUDY AND MANIPULATION OF THE REPLICATION ORIGINS OF DNA MOLECULAR CLONING VECTORS.
Key: PCCBBNA/020642
Responsible: Dr. Xavier Soberón.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

ESTUDIO DE LA HORMONA LIBERADORA DE TIROTROPINA (TRH).
STUDY OF THE THYROTROPIN RELEASING HORMONE (TRH).
Key: PSCABNA/005590
Responsible: Dr. Jean Louis Charli
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

ESTUDIO DE LOS PROCESOS REGULADORES DE HORMONAS HIPOFISIARIAS. OPTIMIZACION DE UN SISTEMA DE CULTIVO DE CELULAS DISPERSAS PRIMARIAS DE HIPOTALAMO.
STUDIES OF THE PROCESSES REGULATING HYPOPHISIS HORMONES. OPTIMIZATION OF A CULTURE SYSTEM OF DISPERSE PRIMARY CELLS FROM HIPOTHALAMUS.
Key: PCSABNA/001117
Responsible: Dra. Patricia Joseph.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

ESTUDIO SOBRE LA BIOSINTESIS DE LHRH (HORMONA LIBERADORA DE LA HORMONA LUTEINIZANTE). CLONACION Y UTILIZACION DEL ADN COMPLEMENTARIO.
STUDIES ON THE BIOSYNTHESIS OF LHRH (RELEASING HORMONE OF THE LUTEINIZING HORMONE). CLONING AND USE OF COMPLEMENTARY DNA.
Key: PCCBBNA/001926
Responsible: Dra. Patricia Joseph.
Given by Consejo Nacional de Ciencia y Tecnología. (CONACYT)

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Lourival D. Possani Ph.D.
Xavier Soberón Ph.D.

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Miguel Cisneros Biol. Chem.
Fredy Coronas Chem.
Norberto Cruz Biol. Chem.
Mario Cuevas Biol. Chem.
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Georgina Estrada Biol. Chem
Marcos Fernández Biol. Chem.
Noemí Flores Biol.
Rosa Ma. López Biol. Chem.
Alfredo Martínez Biol. Chem.
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