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FINAL REPORT

INTERNATIONAL POSTGRADUATE COURSE
MODIFICATION OF ANTIBODIES BY GENETIC ENGINEERING:
EXPRESSION OF RECOMBINANT ANTIBODY FRAGMENTS IN BACTERIA.

VENUE:

Center for Genetic Engineering and Biotechnology (CIGBH) of Havana, Cuba.

HOST LABORATORY:

Laboratory for Recombinant Antibodies (RAL), Division of Immunotechnology and Diagnostics (DITD), CIGBH.

DATES:

September 5-18, 1993

INTRODUCTION:

Background.-

The possibility of fast cloning and modification of variable heavy (V_H) and light (V_L) region gene domains from antibody-secreting cells using the polymerase chain reaction (PCR) has opened a new era in the application of molecular biology methods to the engineering of antibodies and antibody fragments with increased efficacy or new properties.

Recombinant antibody fragments can be produced in bacteria and yeast, either as intracellular or secreted proteins. V_H and V_L region gene sequences can be expressed with (Fab fragments) or without (Fv fragments) constant region domains, or linking the carboxyterminus of one variable region with the aminoterminus of the other using hydrophilic peptides (single-chain Fv fragments; scFv). The small size and low immunogenicity of these molecules is an advantage for *in vivo* diagnostics and certain therapeutic applications.

Moreover, gene fusions can result in bacterial Fab and scFv with additional domains that confer toxic or regulatory properties, or provide "handles" for affinity purification and coupling of active groups. In this way, the need for further biochemical modifications of antibody fragments is prevented.

Motivation. Course Objectives.-

At the Recombinant Antibodies Laboratory (RAL) of the Division of Immunotechnology and Diagnostics (DITD) of the CIGBH, we have been engaged in the subject of antibody modification through genetic engineering since 1988, accumulating extensive practical experience in the bacterial production of single-chain antibody fragments (scFv).

Taking into account that the interest and diffusion of molecular biology and monoclonal antibody technology are growing steadily in Latinamerica, we envisaged that a regional postgraduate course on antibody modification using genetic engineering would be an attractive way of linking together both fields and promoting further development and exchange.

The course would have the following specific objectives:
(a) To provide participants with a theoretical view of the driving forces, rationale, and involved techniques that characterize the latest advances in the field of modification of antibodies using genetic engineering.
(b) To provide participants with a practical knowledge of the most common technical procedures used in the field, taking as an example the production of antibody fragments in bacteria.
(c) To provide participants with an opportunity of establishing contacts with other scientists of the area.

Facilities and External Support.-

The CIGBH is known as a very prestigious scientific institution in the region and around the World. The Center has modern laboratory and lecture facilities. The DITD has an important group of scientists with experience in the field that could act as professors and instructors, and has previously acted as a host for international courses, trainings, and project involving Latinamerican young scientists.

External support would be only needed to cover expenses involving housing for students, communications, reproduction of manuals, travel, board and lodging of foreign invited profesors, and the acquisition of some laboratory expendables and minor equipment. Such support was requested from the Center for Genetic Engineering and Biotechnology (ICGEBT), and the Biotechnology Regional Program for Latinamerica and the Caribbean (BRPLC:UNDP/UNESCO/UNIDO). These institutions have previously sponsored courses and projects organized and executed by the CIGBH.

The ICGEBT granted USD 20.000, that were used to cover board and lodging expenses for 10 students, fully finance the assistance of one invited professor from the ICGEBT, and acquire laboratory materials, reagents, and minor equipment (see ANNEX 1). The BRPLC granted an extra USD 15,000. These funds were used for the support of 10 additional students from the region (lodging, and air ticket), for a total of USD 8,000, to be delivered directly by UNIDO to each selected student. The remaining USD 7,000 were awarded to the DITD and employed in the full coverage of a second invited professor, communications, and organization expenses (see ANNEX 2).

The first payment of the financial support awarded through the BRPLC has not yet been received. This has motivated that the course organization has had to depend on borrowed funds from the CIGBH to cover the operation expenses.

Program.-

The Program of the course was established following the principle that a reasonable theoretical background of the entire field of antibody modification

by genetic engineering was necessary for the students, in order to facilitate their development in the specific theme of bacterial recombinant antibody fragments. The topics would be developed through lectures in two days, with a final written evaluation.

The Theory Program covered the following: B cells and immune response. Antibody structure and genetic control. Monoclonal antibodies. Modification of antibodies by recombinant DNA technology. Expression of heterologous proteins in E.coli. Antibody fragments. PCR cloning and primer design for variable immunoglobulin regions. Production and purification strategies for heterologous proteins from recombinant bacteria. Combinatorial immunoglobulin libraries using phage.

The practical program was organized as laboratory demonstrations by members of the staff, with direct help from students. Taking as model the generation of bacterial scFv fragments, the Practical program included: RNA and cDNA from hybridomas. PCR amplification of variable immunoglobulin regions. Cloning of amplified V regions into vectors and sequencing. Construction of scFv inserts by PCR. Cloning into expression vectors. Transformation and expression analysis by SDS-PAGE and Western Blot. Testing for specificity of scFv fragments.

These practical demonstrations would be divided in operative blocks, under the guidance of staff professors, and projected to be developed in 8-9 working days. The students would also be divided in groups, and would rotate until developing all the practical blocks. A final evaluation of practical sessions would be programmed, per student group. Free time per group would allow study, and interaction with other aspects of the work of the Division, as per individual interests of the students.

A detailed practical manual, with selected references in support of the theory, and a review article on the subject of recombinant antibody fragments, would be prepared.

Selection of Staff.-

The final Staff of the course was composed by 7 Cubans and 2 foreigners. The latter were selected on the basis of their knowledge in the field, and previous connections with the host laboratory. A third foreign scientist, visiting the RAL, contributed to the sessions (ANNEX 3).

Students and Selection.-

As mentioned above, the students would be selected from the Latinamerican region (Spanish and Portuguese-speaking; Dominican Republic, Costa Rica, Guatemala, Honduras, Nicaragua, México, Panamá, Bolivia, Colombia, Ecuador, Perú, Venezuela, Argentina, Brasil, Uruguay, Paraguay, and Chile). The aspirants should be at least graduates with one-two years of laboratory practice in a field related to microbiology and molecular biology, and would have to be able to read and interpret scientific articles in English.

Selection of the students would be done on the basis of the information submitted by the aspirant, taking into account the eligibility criteria mentioned in the previous paragraph, as well as: institution letter explaining why the course was seen as important for the student and center, curriculum vitae (CV), and present working themes. Immediately after the deadline for submission of requests, the students would be selected taking also into account the date of request, and the principle of at least one student per country, unless the CV would clearly indicate the contrary.

Lodging.-

The CIGBH coordinated lodging for students and invited professors in hotel "Biocaribe", located a block away from the venue. A special and economic hotel "package" was negotiated. For students, accomodation was fully covered during the days of the course with ICGEBT or BRPLC funds. Meals at the CIGBH during the working days, or at the hotel (weekends), would be also provided free-of-charge by the CIGBH.

Announcement.-

Informative announcements were made using the channels of the ICGEBT and directly by the CIGBH (ANNEX 4). The announcement was also distributed by Dr. Rodolfo Quintero, Coordinator of the BRPLC.

DEVELOPMENT OF THE COURSE:

Selection of Students.-

Thirty-one applications were received: 12 from Argentina, 8 from Brazil, 4 from Mexico, 3 from Ecuador, 2 from Bolivia, 1 from Colombia, 2 from Perú, and 1 from Venezuela.

The eligibility criteria mentioned in the introductory section were strictly followed. As stated in the announcement, an initial selection was made immediately after June 30. A final list was prepared after receiving confirmation of assistance. This included: 9 students from Argentina, 2 from Brazil, 2 from Ecuador, 3 from Mexico, 1 from Bolivia, 1 from Colombia, 1 from Venezuela, 1 from Perú. Ten were chosen for extra support by the BRPLC, on the basis of: (a) at least one per country, (b) curriculum vitae, (c) date of arrival of application.

All students were informed in July concerning their acceptance. Additional information on support, visa arrangements, deadlines for confirmation and flight schedule, etc. were included. The organizers of the course provided help with visa arrangements, whenever the information was sent before the stated deadline.

Two weeks before the onset of the course, a fax from Néstor Annibali, from Argentina, informed the organizers that due to medical problems he was not able to attend the course. In view of the little time left a Cuban student from the CIGBH was selected. Rodrigo Armijos, from Ecuador, and for which extra support of the BRPLC had been awarded, did not attend the course due to

unknown reasons. A detailed list of the 19 participants students is presented in ANNEX 5.

As in the ICGEBT announcement no notice was made of the regional character of the course, 29 applications from other countries were also received. These included: Italy, USA, Denmark, Finland, Mauritanie, Slovenia, China, Pakistan, Iran, India, Vietnam, Zimbabwe, Zaire and UK. Fax or letter answers explaining the situation were sent to all these applicants.

Development of the Program.-

The main contents of both the Theory and Practical Programs were carried on as originally designed. Three days were dedicated to theory, including the evaluation. The practical demonstrations took the other 10 working days. Students were divided in 4 groups of 4-5, and the demonstrations were done in 4 blocks. Due to this organization, all students directly participated in the experiments. A detailed description of the Final Program can be found in the first pages of the Manual (ANNEX 6). A total of 85 hours of effective course activities were developed.

An individual theoretical test (ANNEX 7) represented 40% of the total evaluation, while practice the other 60%. The latter was developed in groups. All course participants (students and professors) were provided with a Certificate (ANNEXES 8,9).

The students had access to the library of the CIGBH, and were provided with free-of-charge photocopy service.

Two special sessions, one conducted by the General Director of the CIGBH, Dr. Manuel Limonta, were devoted to discuss the history, structure, goals, and accomplishments of the Center, and the role of Biotechnology in Cuba and Latinamerica.

Conclusions.-

The shared contribution from ICGEBT and UNIDO allowed us to organize an ambitious course, in terms its postgraduate level, the high number of participants, and complexity of the program. Taking into account the way in which the Theory and Practical Programs were accomplished, the overall evaluation of the students (ANNEX 10), and the opinions gathered from students and foreign professors (ANNEX 11), we can conclude that the course was successful and its objectives accomplished.

The group of students was excellent, and warm contacts were established with the staff of the host laboratory and Division, and among themselves.

ANNEX 1.- Expenses covered with ICGEBT funds.-

A total of USD 20.000 were awarded (USD 16.000 as first payment and USD 4.000.00 after the Final Report). The CIGBH has covered temporarily the difference, from other sources.

Funds were used to cover:

1. Prof. Oscar Burrone's participation expenses: USD 2,376.00
- Air ticket: USD 1,740.00
- Board, lodging, and pocket money (September 4 to September 9): USD 106.00 x 6: USD 636.00

2. Board and lodging for 9 students (Hotel Biocaribe), from September 5 to September 18: USD 399.00 x 9: USD 3591.00

3. Minor Laboratory Equipment and Reagents.- USD 14,817.00
- Thermocycler for PCR, horizontal DNA electrophoresis apparatus, and vertical protein electrophoresis apparatus, reagents for electrophoresis: USD 7030.00
- Sequencing unit (including electrophoresis apparatus, power source, accessories, and reagents): USD 7,787.00

Total: USD 20.784.00

ANNEX 2.- Expenses covered with BRPLC funds.-

A total of USD 7,000 were awarded to the CIGBH. As a product of the delay in establishing the reference terms, the first payment of USD 6,000 to be received in advance, are still not available at the moment of preparation of this report. Consequently, the CIGBH has temporarily covered the expenses from other sources.

The funds have been used to cover:

1. Prof. Eva Harris participation expenses:
- air ticket: USD 840.00
- lodging at Biocaribe Hotel (September 5 to September 15): USD 615.00

2. Course materials:
- Photocopier with accessories: USD 4,200.00

3. Information and communication expenses (fax, telex, e-mail):
   USD 1,300.00

Total: USD 6,925.00

ANNEX 3.- Composition of the Staff.

Cuban participants were:

(1) Jorge V. Gavilondo, Ph.D., head of the Division of Immunotechnology and Diagnostics of the CIGBH, who acted as course Director and lecturer.

(2) Marta Ayala, M.Sc., head of the Recombinant Antibody Laboratory (RAL) of the Division, who acted as co-Director of the course, lecturer, and commanded a practical session.

(3) Antonieta Herrera, Ph.D., of the Division of Vaccines of the CIGB, that who as lecturer and commanded a practical session.

(4) Javier Vázquez, M.Sc., of the RAL, who commanded a practical session.

(5) Manuel Llano, M.D., M.Sc., head of the Therapeutic Antibodies Laboratory of the Division, who acted as lecturer.

(6) Giuvel Fontirrochi, M.D., M.Sc., head of the Monoclonal Antibody Laboratory of the Center for Genetic Engineering and Biotechnology of Camaguey (CIGBC), Cuba, who commanded a practical session.

(7) Lincidio Pérez, of the Monoclonal Antibody Laboratory of the Center for Genetic Engineering and Biotechnology of Santi-Spitirus, (CIGBSS), Cuba, who assisted a practical session.

Two invited professors were asked to contribute with the Theoretical Program:

(1) Prof. Oscar Burrone, M.D., Ph.D., head of the Dept. of Molecular Immunology of the ICGEBT, Trieste, Italy. Prof. Burrone maintains collaborative links with the host laboratory, within a ICGEBT-CIGBH funded project.

(2) Eva Harris, Ph.D., of the Molecular Biology Dept. of the University of California at San Francisco, USA. Dr. Harris has been present in Biotechnology Congresses in Havana, and has a long-standing collaborative position with Latinamerican scientists, being organizer of several courses on diagnostic methods using molecular biology techniques, particularly PCR.

Additionally, Dr. Alessandro Sidoli, from the Department of Biotechnological Research of the Hospital "San Raffaele" of Milan, Italy, attended the course. Dr. Sidoli is a collaborative partner with the host laboratory for a common project on recombinant antibody fragments, and participated on his own in the course, as a way by which increase his links with the host laboratory, and exchange ideas and experience with the students.

ANNEX 4.-

CURSO TEORICO PRACTICO
INTERNACIONAL DE POSGRADO

MODIFICACION DE ANTICUERPOS POR INGENIERIA GENETICA: EXPRESION DE FRAGMENTOS DE ANTICUERPOS EN BACTERIA

La Habana, Cuba. Septiembre 5-18, 1993

Organiza: Centro de Ingeniería Genética y Biotecnología (CIGB), La Habana, Cuba.

Auspician: International Center for Genetic Engineering andBiotechnology, Trieste, Italia, Programa Regional de Biotecnología, Comité Cubano de Biotecnología

Lugar: División de Inmunotecnología y Diagnóstico. CIGB, Avenida 31 entre 158 y 190, Cubanacán, La Habana 10600, Cuba. Fax: 53-7-218070, 336008. Teléfonos: 53-7-203297, 218854. Telex: 512330. 511702.

La **DIVISION DE INMUNOTECNOLOGIA Y DIAGNOSTICO** del CIGB, con casi 80 científicos y técnicos, se dedica fundamentalmente a la investigación, el desarrollo y la producción de sistemas diagnósticos y anticuerpos monoclonales. Del trabajo en los últimos 6 años han salido los sistemas diagnósticos ELISA y de formato simple para HIV-1/2, p24, Hepatitis C, HTLV-I/II, y Toxoplasma gondii, basados en antígenos recombinantes, naturales y péptidos sintéticos. El catálogo de anticuerpos monoclonales para agentes infecciosos, factores de crecimiento, hormonas, linfocinas y moléculas relacionadas a los problemas vasculares, abarca 43 renglones. La División ha acumulado también una importante experiencia en la producción de anticuerpos monoclonales humanos y en las nuevas técnicas de modificación de anticuerpos por ingeniería genética.

OBJETIVOS DEL CURSO

El curso pasará revista al estado actual del campo de modificación de anticuerpos por ingeniería genética, y demostrará los elementos prácticos fundamentales mediante los cuales es posible construir genes que codifiquen para fragmentos de anticuerpos tipo scFv de simple cadena y su expresión en E. coli.

NIVEL

Teniendo en cuenta el temario y el staff de profesores y asistentes, el curso puede ser considerado como de posgrado (maestría y/o doctorado).

CONTENIDO

Teoría (24 horas): Células B y respuesta inmune. Estructura y genética de las inmunoglobulinas. Anticuerpos monoclonales en el diagnóstico y tratamiento. Modificación de anticuerpos por ingeniería genética. Estrategias para la clonación de

los genes de las inmunoglobulinas empleando la reacción en cadena de la polimerasa (PCR). Expresión de anticuerpos quiméricos y "humanizados" en células eucariotas superiores. Expresión de fragmentos de anticuerpos en E. coli. Librerías combinatorias en fagos filamentosos.

Prácticas Demostrativas (60 horas; organizadas en grupos de estudiantes y conducidas por un miembro del staff): Aislamiento y modificación de las regiones variables mediante PCR. Secuenciación. Construcción y clonación de un inserto para fragmento Fv de simple cadena en un vector de expresión. Transformación de E. coli, selección de clones y análisis de expresión.

STAFF DE PROFESORES

Director del Curso: Dr. Jorge V. Gavilondo (CIGB), **Profesores Invitados:** Dr. Oscar Burrone, ICGEBT, Trieste, Italia, Dr. Eva Harris, UC Berkely, California, EEUU. **Profesores Cubanos (todos del CIGB):** Lic. Marta Ayala, Lic. Antonieta Herrera, Dr. Manuel Llano, Lic. Javier Vázquez, Lic. Mayté Pérez, Lic. Marta Dueñas

PARTICIPANTES Y REQUISITOS

El curso tendrá cupo para 20 estudiantes extranjeros provenientes de países de habla hispana y portuguesa de la región latinoamericana. Los estudiantes deben ser graduados universitarios en planes de posgrado, con un mínimo de 2 años de experiencia práctica en el laboratorio, relacionada con los campos de la microbiología, inmunología y/o biología molecular. El conocimiento del inglés es indispensable para el análisis de artículos científicos y la comprensión de conferencias.

ADMISION Y APOYO

El staff de profesores seleccionará a los participantes sobre la base de documentos de su institución de origen que certifiquen el nivel de posgrado, sus actividades investigativas actuales y experiencia práctica, y las razones que motivan su interés en el campo de la modificación de anticuerpos por ingeniería genética. La selección tendrá en cuenta el balance de asistencia entre los diferentes países y la fecha de llegada de las solicitudes. Se recomienda emplear el fax o correo DHL para hacer llegar la información pertinente a la dirección del curso.

Existirá un fondo limitado de ayuda económica para los participantes que cubrirá: (a) USD 400.00 del costo del pasaje a La Habana para 10 estudiantes, (b) alojamiento y alimentación por 14 días, para una mayoría de los participantes. Los candidatos deben incluir en su solicitud la necesidad detallada de apoyo financiero. La fecha límite para la recepción de las solicitudes de participación es el **30 de JUNIO de 1993.**

EVALUACION

Los participantes tendrán un evaluación sobre la base de un examen escrito al final de las sesiones teóricas. Las prácticas demostrativas serán evaluadas por equipo de trabajo, en base a presentaciones orales. Se emitirá un certificado final de asistencia y evaluación por la Vice-Dirección de Docencia del CIGB.

ANNEX 5. Selected and participating Students.-
Numbers 1-9 were awarded extra support by the Biotechnology Regional Program for Latinamerica and the Caribbean. Rodrigo Armijos from Ecuador did not attend the course, due to unknown reasons. Néstor Annibali, from Argentina, failed to travel due to medical problems, and Freya Milagros Freyre, from Cuba, was selected as substitute.

1. Roger Carvajal, Ph.D.
Director, Instituto de Servicios de Laboratorio de Diagnóstico en Salud,
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Ave. Saavedra, No.2224, Casilla M10362, La Paz, Bolivia
Teléfonos: 591-2-322436, Fax: 591-2-367399

2. Nunciada Salma
Laboratorio de Hibridomas, Instituto de Biomedicina
Apartado 4043, Caracas 1010A, Venezuela, Fax: 58-2-8611258

3. Marcia Regina Brochetto-Braga, Ph.D.
Profesora del Depto. de Biología
UNESP, 13506-900 Rio Claro, Sao Paulo, Brasil, P.O.Box 199
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4. Carlos Alberto Pérez
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Teléfonos: 54-41-300309, Fax: 54-41-240445 ó 0446

5. Carlos A. González
Inst.de Biotecnología UNAM, Cuernavaca, Morelos, México, Fax: 52-73-172388

6. Alexei F. Licea Navarro
Depto. de Bioquímica, Instituto de Biotecnología, UNAM
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7 Hélmer H. Lezama, M.Sc.
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8. Miriam Nakamura Goubea
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9. Jorge Almanza
Sección de Biotecnología Pecuaria, ICA-CI TIBAITATA, A.A 151123, Eldorado Bogotá, Colombia

10. Mariana L. Papouchado.
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11. Andrés D. Zambelli
Instituto Multidisciplinario de Biología Celular
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12. Ana Maria Roccamo
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Fax: 54-91-553933

13. René Hernández Vargas
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14. Adriana Gruppi
Inmunología- Dpto Bioquímica Clínica, Facultad de Ciencias Químicas-UNC
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15. Irina Mathov
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16. Nidia Maria Modesti, Ph.D.
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17. Ana Vargas Cuero
Hosp. del Seguro Social, Ave. 25 de julio s/n, Guayaquil, Ecuador
Fax: 539-4-490-846

18. Virginia Rivero
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Universidad Nacional de Córdoba, Argentina, Fax: 54-51-694724

19. Freya Milagros Freyre
Lab.de Anticuerpos Recombinantes, Div. Inmunotecnología y Diagnóstico,
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Cuba. Fax: 53-7-218070, 336008

ANNEX 7.-

Curso Internacional de Posgrado
"Modificación de Anticuerpos por Ingeniería Genética:
Expresión de Fragmentos de Anticuerpos en Bacterias"

Nombre y apellidos:

1. Anticuerpos quiméricos (10 puntos).
(a) En qué consisten. Motivaciones principales que llevaron a este desarrollo tecnológico. Aplicaciones.
(b) Describa los elementos más importantes que se requieren para obtener la expresión y secreción de una inmunoglobulina recombinante en una célula eucariota.

2. Reacción en cadena de la polimerasa (10 puntos).
(a) Mencione tres aspectos que tienen que ver con la optimización de una PCR.
(b) Mencione 3 formas de prevenir la contaminación en una PCR.
(c) Mencione 3 aplicaciones de la PCR.

3. Fragmentos de anticuerpos en bacteria (20 puntos).
(a) Tipos de fragmentos recombinantes. Aplicaciones.
(b) Estrategias para la expresión de fragmentos en E. coli.
(c) Describa una estrategia posible para la construcción de un fragmento tipo scFv.

ANNEX 8.-

Centro de Ingeniería Genética
y Biotecnología.

International Center for Genetic Engineering
and Biotechnology, Trieste, Italy.

Programa Regional de Biotecnología
PNUD/ UNESCO/ ONUDI.
para América Latina y el Caribe.

CERTIFICAN que:

Participó como Profesor del CURSO INTERNACIONAL
DE POSTGRADO **"MODIFICACION DE ANTICUERPOS POR INGENIERIA GENETICA: PRODUCCION DE FRAGMENTOS DE ANTICUERPOS EN BACTERIAS".**

realizado en La Habana, Cuba,
del 5 al 18 de Septiembre de 1993,

Francisco Alea
Subdirector Docente C.I.G.B.

Jorge V. Gavilondo Ph.D.
Director del Curso,
División de Inmunotecnología y Diagnóstico C.I.G.B.

ANNEX 9.-

Centro de Ingeniería Genética
y Biotecnología.

International Center for Genetic Engineering
and Biotechnology, Trieste, Italy.

Programa Regional de Biotecnología
PNUD/ UNESCO/ ONUDI.
para América Latina y el Caribe.

CERTIFICAN que

Asistió al CURSO INTERNACIONAL

DE POSTGRADO **"MODIFICACION DE ANTICUERPOS POR INGENIERIA GENETICA: PRODUCCION DE FRAGMENTOS DE ANTICUERPOS EN BACTERIAS".**

realizado en La Habana, Cuba,
del 5 al 18 de Septiembre de 1993,

con una duración de _____ horas,

y calificación de _____

Francisco Alea
Subdirector Docente C.I.G.B

Jorge V. Gavilondo Ph.D.
Director del Curso,
División de Inmunotecnología y Diagnóstico C.I.G.B.

ANNEX 10.- Results of the Theoretical and Practical Evaluations.

Student:	Theory	Practice	Total
1. Roger Carvajal	37/40	60/60	97/100
2. Nunciada Salma	40/40	60/60	100/100
3. Marcia R. Brochetto	36/40	60/60	96/100
4. Carlos Alberto Pérez	40/40	60/60	100/100
5. Carlos A. González	38/40	60/60	98/100
6. Alexei F. Licea Navarro	40/40	60/60	100/100
7. Hélmer H. Lezama	35/40	60/60	95/100
8. Miriam Nakamura Goubea	39/40	60/60	99/100
9. Jorge Almanza	31/40	60/60	91/100
10. Mariana L. Papouchado	39/40	60/60	99/100
11. Andrés D. Zambelli	40/40	60/60	100/100
12. Ana Maria Roccamo	34/40	60/60	94/100
13. René Hernández Vargas	32/40	60/60	92/100
14. Adriana Gruppi	37/40	60/60	97/100
15. Irina Mathov	37/40	60/60	97/100
16. Nidia Maria Modesti	40/40	60/60	100/100
17. Ana Vargas Cuero	32/40	60/60	92/100
18. Virginia Rivero	38/40	60/60	98/100
19. Freya M. Freyre	37/40	60/60	97/100

ANNEX II.-

CURSO INTERNACIONAL DE POSGRADO
La Habana, Cuba. Septiembre 5 al 18, 1993

MODIFICACION DE ANTICUERPOS POR INGENIERIA GENETICA:
PRODUCCION DE FRAGMENTOS DE ANTICUERPOS EN BACTERIA

Con vistas a tener criterios para una evaluación general del desarrollo del curso, así como recoger detalles que puedan servir para futuros eventos de este tipo, le rogamos que llene con sus opiniones los acápites que se adjuntan.

Gracias,

Profesor: [illegible]

Calidad de las conferencias (E, B, R):

E Células B y respuesta inmune.
E Estructura y genética de las immunoglobulinas.
E Modificación de anticuerpos por ingeniería genética.
___ Reacción en cadena de la polimerasa (PCR).
E Expresión de genes en células superiores.
E Expresión de anticuerpos quiméricos.
E Expresión de proteinas heterólogas en procariotes.
E Expresión de fragmentos de anticuerpos en E.coli.
___ Expresión de anticuerpos en fagos filamentosos.

Evaluación general del curso:

Excelente ✓ Buena _____ Regular _____

Observaciones: