Instituto Juan March
de Estudios e Investigaciones

62 CENTRO DE REUNIONES
INTERNACIONALES SOBRE BIOLOGÍA

1996
Annual Report

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Headquarters of the Fundación Juan March
(Home of the Centre for International Meetings on Biology)

Small, focused meetings of this kind allow the progress in a limited area of science to be critically evaluated. In the transcription field this is particularly valuable because the multiplicity of related proteins, the many target genes, and the complex regulation of activity can only be unraveled by integrating the efforts of many laboratories. Other fields would benefit from such focused meetings from which reports such as this can convey progress to the rest of the community.

Baeuerle, P.A. and Baltimore, D. (1996). NF-κB: Ten Years After. (Meeting Review). Cell 87, 13-20.

INSTITUTO JUAN MARCH DE ESTUDIOS E INVESTIGACIONES

CENTRE FOR INTERNATIONAL MEETINGS ON BIOLOGY

1996 ANNUAL REPORT

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FOREWORD

This publication covers the activities of the Centre for International Meetings on Biology during the year 1996. All of them were announced in brochures, posters, advertisements in scientific journals and articles in other periodicals.

The core of the Centre's work during 1996 was the organization of 13 workshops on different biological topics. An introduction to each of these meetings is presented here, followed by a list of invited speakers and participants selected from among the applications received. In total, 248 speakers were invited to these workshops, and 380 participants were chosen from among the 537 applications received.

A booklet was published on each of these meetings, which included the abstracts of the contributions presented by the participating scientists. About 400 copies of each booklet were distributed to research groups and laboratories working on problems relating to the subject of each meeting.

A new series of the Juan March Lectures on Biology, a tradition in the Centre since 1982, was organized in 1996. Information on these lectures is also included in the following pages. Another two sessions open to the general public were held to coincide with meetings mentioned above.

A short report is given of the reviews published during 1996 in scientific journals, regarding workshops organized by the Centre.

The schedule of meetings to take place in 1997 is also offered in this book.

Instituto Juan March de Estudios e Investigaciones

THE CENTRE FOR INTERNATIONAL MEETINGS ON BIOLOGY

The Centre for International Meetings on Biology endeavours actively and systematically to promote close cooperation and interaction among Spanish and foreign scientists working in the field of Biology. This scientific field is understood in the widest sense, and emphasis is given to advanced lines of research.

The Centre's activities stem from the Plan for International Meetings on Biology, initiated by the **Fundación Juan March** in January 1989 and ending in December 1991. A wide range of meetings and scientific activities were organized under this Plan. The Fundación Juan March, in addition to its well-known support of the fine arts and culture in general, has devoted particular attention to the biological sciences since its creation in 1955 by the Spanish financier Juan March Ordinas.

The Centre for International Meetings on Biology was established on January 1992 within the **Instituto Juan March de Estudios e Investigaciones**, a private foundation created in October 1986 and recognized by the Spanish Ministry of Education and Culture. This foundation complements the work of the Fundación Juan March, as an entity specializing in scientific activities. The Board of Trustees of the Instituto comprises: Juan March (Chairman), Carlos March (Deputy Chairman), Leonor March, Alfredo Lafita, Antonio Rodríguez Robles, Pablo Vallbona, Enrique Piñel and Jaime Prohens (Secretary). José Luis Yuste is the Managing Director of the Institute.

The Centre for International Meetings on Biology is located at Calle Castelló 77, Madrid. The Director of the Centre is Andrés González.

1996 Meetings Schedule

INSTITUTO JUAN MARCH

CENTRE FOR INTERNATIONAL MEETINGS ON BIOLOGY

1996 MEETINGS SCHEDULE

Date	Meeting Subject	Organizers
15-17 January	Transcriptional Regulation at Distance	**W. Schaffner.** Universität Zürich. **V. de Lorenzo.** Centro de Investigaciones Biológicas. Madrid. **J. Pérez-Martín.** Centro de Investigaciones Biológicas. Madrid.
11-13 March	From Transcript to Protein: mRNA Processing, Transport and Translation	**I. Mattaj.** European Molecular Biology Laboratory. Heidelberg. **J. Ortín.** Centro Nacional de Biotecnología. Madrid. **J. Valcárcel.** University of Massachusetts Medical Center. Worcester.
25-27 March	Mechanisms of Expression and Function of MHC Class II Molecules	**B. Mach.** University of Geneva. **A. Celada.** Facultad de Biología. Universidad de Barcelona.
15-17 April	Enzymology of DNA-Strand Transfer Mechanisms	**E. Lanka.** Max-Planck-Institut für Molekulare Genetik. Berlin. **F. de la Cruz.** Universidad de Cantabria. Santander.
20-22 May	Vascular Endothelium and Regulation of Leukocyte Traffic	**T. Springer.** Center for Blood Research. Boston. **M. O. de Landázuri.** Hospital de la Princesa. Madrid.
3-5 June	Cytokines in Infectious Diseases	**A. Sher.** National Institute of Health. Bethesda. **M. Fresno.** Centro de Biología Molecular «Severo Ochoa». Madrid. **L. Rivas.** Centro de Investigaciones Biológicas. Madrid.
17-19 June	Molecular Biology of Skin and Skin Diseases	**D. R. Roop.** Baylor College of Medicine. Houston. **J. L. Jorcano.** CIEMAT. Madrid.
1-3 July	Programmed Cell Death in the Developing Nervous System	**R. W. Oppenheim.** The Bowman Gray School of Medicine. Winston-Salem. **E. M. Johnson.** Washington University. St. Louis. **J. X. Comella.** Facultad de Medicina. Lérida.
8-10 July	NFκB/IκB Proteins. Their Role in Cell Growth, Differentiation and Development	**R. Bravo.** Bristol-Myers Squibb Pharmaceutical Research Institute. Princeton. **P. S. Lazo.** Facultad de Medicina. Oviedo.
23-25 September	Chromosome Behaviour: the Structure and Function of Telomeres and Centromeres	**B. Trask.** University of Washington. **Ch. Tyler-Smith.** University of Oxford. **F. Azorín.** Centro de Investigación y Desarrollo. Barcelona. **A. Villasante.** Centro de Biología Molecular «Severo Ochoa». Madrid.
7-9 October	RNA Viral Quasispecies	**S. Wain-Hobson.** Institut Pasteur. Paris. **E. Domingo.** Centro de Biología Molecular «Severo Ochoa». Madrid. **C. López Galíndez.** Centro Nacional de Biología Celular y Retrovirus. Madrid.
28-30 October	Abscisic Acid Signal Transduction in Plants	**R. Quatrano.** University of North Carolina. Chapel Hill. **M. Pagès.** Centro de Investigación y Desarrollo. Barcelona.
25-27 November	Oxygen Regulation of Ion Channels and Gene Expression	**E. Kenneth Weir.** University of Minnesota. **J. López-Barneo.** Facultad de Medicina. Sevilla.

All meetings will take place on the premises of the Instituto Juan March:

Castelló, 77
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Individual advertisements for every meeting, with more detailed information, are published with sufficient anticipation.

Transcriptional Regulation At a Distance

Organized by
W. Schaffner, V. de Lorenzo and J. Pérez-Martín
15th-17th January, 1996

The discovery of enhancer elements about one dozen years ago has been one of the major landmarks in modern Molecular Biology. The notion that discrete DNA sequences and cognate DNA-binding proteins can control the activity of promoters located at considerable distances has provided the key to understand the molecular basis of major biological phenomena such as tissue-related gene expression as well as the organization of complex regulatory cascades in developmental systems. The last few years have witnessed an amazing progress in the analysis of the various components which account for activation at a distance, in particular the nature of the regulatory proteins and auxiliary factors involved.

From the information available at the moment, we know that cis-acting regulatory elements of eukaryotic genes include promoter sequences located around the transcription initiation site and enhancer sequences located farther away. A promoter often consists of an initiator sequence, a TATA box and one or more upstream sequences where regulatory proteins can bind. Transcription initiation by RNA polymerase II involves the assembly of a multifactor complex at the TATA box and initiation site. While the promoter is the assembly site of the preinitiation complex, enhancers confer additional regulatory information (i.e. cell-type specificity) to the promoter. Eukaryotic transcription factors are divided, in one hand, into the *general transcription factors*, which bind to common motifs (TATA box, initiator motif) and constitute the preinitiation complex, and the *sequence-specific transcription factors* which bind to upstream promoter or enhancer elements. On the other hand, sequence-specific transcription factors are thought to influence the rate of transcription initiation by interacting with the general transcription factors, RNA polymerase II and chromatin components. The main features of a sequence-specific transcription factor include the DNA-binding domain, the nuclear localization signal and the transactivation domain. A common (and somewhat naive) view of the process assumes that once the initiation complex is assembled, the collection of transcription factors create a constellation of protein-protein interactions that, through a largely undisclosed mechanism, enables the polymerase to initiate transcription. On top of this, the pivotal role of chromatin and chromatin-associated proteins in transcriptional control is becoming an emerging (and expanding) issue in nearly every system where its role has been examined.

Needless to say that these views are under permanent challenge, since new factors and mechanisms are coming into play, mostly from research on transcriptional regulation in yeasts and *Drosophila*. These two experimental systems are the best beneficiaries at the power of the genetics that can be applied to solve otherwise intractable questions. Complex issues on the mechanism of transcription initiation by RNA polymerase II (for example, recruitment of the holoenzyme to the promoter mediated by transcriptional factors) are amenable to experimental scrutiny, to this day, almost exclusively through genetic means. In addition to the reverse genetics with mammalian cell cultures and the increasing availability of transgenic animals, yeast genetics has become the major driving force to raise a wealth of opportunities for fundamental explorations into the mechanisms of transcription in

eukaryotes. One example is the control of the mating types of *S. cerevisiae*, one of the most complex -and most fascinating- paradigms of regulation of gene expression in the biological world. Similarly, the study of novel elements such as the chromatin insulators of *Drosophila* that inhibit the function of enhancers, is greatly facilitated in systems with a good repertoire of tools for genetic analysis.

What was believed to be distinct of eukaryotic promoters happens to occur also in prokaryotic systems. A number of observations made in the mid-80s in the Laboratory of B. Magasanik on regulation of nitrogen-starvation systems of *Escherichia coli*, notably the *glnAp2* promoter and its cognate regulator, the protein NRI (widely known by its alternative name, NtrC), indicated that remote transcriptional control was not a privilege of higher cells. *glnAp2* turned out to be the prototype of a novel class of promoters depending on the alternative σ^{54}factor. These are unique in that they are activated at a distance by specific regulators bound to upstream, enhancer-like sequences (UAS). These unusual properties are to be explained by the eukaryotic-like structure of the σ^{54} factor itself and that of the cognate regulatory proteins. In a subset of σ^{54}-dependent promoters, a binding site for the histone-like protein IHF site is found between the binding sites of the RNAP- σ^{54} holoenzyme and the UAS. The major (but perhaps not the sole) role of IHF as co-activator in the σ^{54}-promoters is believed to assist formation of a DNA loop or even a nucleoprotein complex to stabilize contacts between the RNAP and the activator protein bound to the UAS. There is also an increasing evidence that other prokaryotic histone-like proteins (such as HU) play a role in the assembly of the transcription initiation complex.

Although σ^{54}-dependent promoters are the most extensively studied case of activation at a distance in prokaryotes, other systems are subjected also to transcriptional control by regulatory devices placed at distant sites. A notable case is that of the T4 enhancer, in which tracking (and not looping) of the replication protein accounts for the effect of distant sites in transcription initiation. Repression at a distance is also a well known phenomenon in prokaryotic systems: early observations can be traced back to the late 70s in the work by Bob Schleif on the arabinose (*ara*) operon of *E. coli*. In spite of having been studied for over two decades, the *ara* system seems to be a permanent source of surprises to this day -and surely the best documented case of remote negative control in bacteria.

What lessons can the prokaryotic systems learn from the more complex eukaryotic promoters and *vice versa*? Perhaps activation at a distance is a general evolutionary strategy to integrate multiple signals for the control of a single promoter. The architecture of some bacterial promoters subjected to distant control may therefore be better understood in light of its evolutionary history and not on the basis of a strict necessity for such a complex setup. An interesting lesson that comes from the prokaryotic side is that DNA structures play an active role in such *signal integration*, instead of being just docking sites for transcription

factors. It seems to be true also for some prokaryotic systems (those dependent of σ^{54}) that the assembly of an upstream nucleoprotein complex gives rise to an enzymatic activity that is not present in the non-assembled components of the complex, an issue rarely examined in eukaryotic promoters.

In summary, it appears that, in spite of the intrinsic differences in the mechanism of activation of prokaryotic and eukaryotic systems subjected to remote control, various common themes will help to gain a better insight in the general biological problem of transcriptional control.

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From Transcript to Protein: mRNA Processing, Transport and Translation

Organized by
I. Mattaj, J. Ortín and J. Valcárcel
11th-13th March, 1996

Biological research very frequently involves reductionist experimental approaches on very specialized aspects of the cell structure, regulation or fate. However, it is becoming more evident every day that biological phenomena are profoundly and extensively interrelated and interdependent. For a virologist like me, an outsider in the Cell Biology field, it was quite a surprise when work of our group, as well as others, showed that the influenza virus NS1 protein, a small non-structural protein, was able to alter several aspects of the gene expression program of the cell, including pre-mRNA splicing, nucleocytoplasmic transport and mRNA translation. Therefore, it was not a fully altruistic idea to propose to the Centre of International Meetings on Biology ("Instituto Juan March de Estudios e Investigaciones") a Workshop to integrate discussions on the post-transcriptional steps involved in gene expression. Looking at the state of the field, I felt that it was particularly appropriate to look at the recent advances with an integrative perspective and that the Spanish scientists, myself included, could learn very much from it.

The organization of such a meeting would have been impossible without the active role of relevant researchers in the field. I was very lucky to have Iain Mattaj and Juan Valcárcel as co-organizers, who helped very much in the difficult task of selecting, among the many excellent scientists covering these topics, those that would make an appropriate blend for a successful meeting.

It was the purpose of the meeting to find interconnections between the several steps that take place from the point a primary transcript is synthesized up to the moment its corresponding mRNA is actively translated and, eventually, degraded. After three days of intensive exchange of ideas, the outcome of the workshop exceeded our expectations. Indeed, both the oral and poster presentations, as well as the very active discussions,supported previously suspected connections and opened our minds to unexpected new ones. Thus, the mechanisms of nucleo-cytoplasmic trafficking can no longer be separated into nuclear import and export, since evidence is accumulating that suggest that both processes might be tightly connected and might share common factors.

In the same line, some of the newly discovered signals that stimulate the export from the nucleus (NESs) appear to overlap with nuclear import signals (NLSs).Furthermore, in addition to the long studied dependence of mRNA stability on its capacity to be translated, it appears now that a safe ward might exist to avoid the normal splicing of pre-mRNAs in which premature termination codons would impair the biological activity of the potential translation product. These observations, together with the known relationship between polyadenylation and mRNA translatability, indicate that profound feed-back information loops should exist between distant (both temporally and physically) post-transcriptional events in the gene expression process.

Juan Ortín

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Mechanisms of Expression and Function of MHC Class II Molecules

Organized by
B. Mach and A. Celada
25th-27th March, 1996

The idea of organizing the Workshop on "Mechanisms of expression and function of MHC class II molecules" in Madrid was to cover two objectives: first, to make the point of the recent discoveries in the field of MHC class II molecules. The second objective was to meet other Spanish colleagues working in this field. The major credit for the organization of this meeting is to the co-organizer, Bernard Mach, who helped me in contacting a selected list of brilliant and active investigators in the field of class II molecules. With his prestige, Bernard supported this meeting which, due to the small size and the good facilities of the Juan March Foundation, made for an easy interaction between participants. Without the effort of Bernard this meeting would not have been possible. Finally, I should thank all the participants who spent some of their busy schedules coming to Madrid and making the success of the meeting possible.

I would like to mention that Spanish research in the last 20 years has made a dramatic improvement. This is due, certainly, to the political and economical changes that have occurred with the return of democracy to Spain. The increase in the budgets for research programmes resulted in a large number of publications appearing in scientific journals, produced by groups working in Spain. Another important aspect to science is communication, and we are very glad that some private foundations such as Juan March decided to support with enthusiasm and organize these biology meetings that help the interactions between Spain and the rest of the scientific community. One of the results of this effort is that many of the invited scientists to the workshop made their first visit to Spain, where they could learn through the presentations carried out during the meeting that, although Spanish science still needs to develop, putting our emphasis on the quality of the research, we are traveling in the good direction.

The small number of participants allowed a good interaction during the presentations, the coffee breaks and lunches. Many cooperative projects will start from this meeting, helping all of us to do in a better way one of the things that we enjoy: research. Also, for young participants, it was a unique opportunity to meet one of the best groups of scientists working in the field of class II molecules. I am quite sure that soon some of these participants will apply for training as post-docs in some of the labs that made the presentations.

The immune system has two functions: one is to recognize what comes from outside and what comes from inside, and the other is to induce a reaction that eliminates what is foreign. MHC class II molecules play a key role in the immune system. These molecules are necessary to present to T lymphocytes the peptides that come from the processed antigens. It is very important to define the mechanisms that regulate the expression of MHC class II molecules. Once these molecules have been produced, it is also necessary to know the different steps from the endoplasmic reticulum until the molecules of class II are loaded with peptides and expressed at the cell surface. Therefore, the understanding of the regulation of the expression and functional activity of these molecules is one of the major steps to understand correctly the immune system.

The expression of class II genes is tissue specific and inducible in some cells by cytokines such as interferon gamma (IFNγ). For instance, in B lymphocytes the expression is constitutive, in macrophages it is inducible by IFNγ and in some other cells it is not expressed. This represents a good opportunity to study tissue specific and inducible transcription factors as a way to better understand the regulation of gene expression.

In the study of molecules such as IFNγ that induce the expression of class II molecules, the next step is to define the interaction with the cells at their surface. IFNγ-receptors are proteins in which, after the interaction with the ligands, two tyrosin-kinases, JAK1 and JAK2 become activated.

As a result of the ligand-receptor interaction, a cascade of second signals is produced inside the cell. Some of these signals induce in minutes the expression of some genes (early genes), such as Stat 1, that are required for the subsequent transcription of other genes directly related with the expression of class II molecules.

Upstream of all MHC class II genes there exist three relatively conserved sequences that play an essential role in the transcription regulation of these genes. Some binding proteins are defective in patients with combined immunodeficiency, a disease in which there is no MHC class II expression.

MHC class II molecules assemble with the Invariant chain in the endoplasmatic reticulum and are then moved to endosomal/lysosomal compartments. There, Ii is proteolytically digested but fragments of Ii, designed CLIP, remain in the groove of class II molecules and are removed by HLA-DM, a non-classical MHC class II molecule, so that peptide loading with antigenic peptides can proceed.

At the end of the meeting, I asked myself if we have answers to all the questions that this exciting workshop provoked. Obviously that is not the case, and not only that, but I think that we have more questions that remain open to new ideas, experiments, etc. This suggests to me that this interesting topic is alive and we will need the help of many scientist to answer all the questions.

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Enzymology of DNA-Strand Transfer Mechanisms

Organized by
E. Lanka and F. de la Cruz
15th-17th April, 1996

This year we celebrate the 50th anniversary of the discovery of bacterial conjugation by Lederberg and Tatum. Since then, conjugation has been a hot matter of active research at various levels: basic advance of knowledge, as a technological tool, by its implication in bacterial ecology (including medically important issues) and evolution, etc.

From a general point of view, we now know it involves the assembly and operation of a complicated structure that can be compared with the small ribosomal subunit, at least in the number of components. Conjugation allows the passage of a single-stranded DNA (that can be as large as the entire bacterial chromosome - a string of 5 million nucleotides) across four bacterial membranes. Amazingly, the process can be of very broad host range, with several known examples of trans-kingdom conjugation. By far the most conspicuous is T-DNA transfer from *Agrobacterium tumefaciens* to plant cells, a process considered to be a specialized form of bacterial conjugation.

Plasmid conjugation is of actuality also because of the use of exogenous DNA in release experiments, an ecological issue that was discussed at a related workshop in this Institute (Thomas et al., 1994).

The molecular complexity of bacterial conjugation allocates it to the intersection of apparently unrelated research topics, from rolling-circle replication and DNA-strand transfer mechanisms to macromolecular transport through biological membranes. We reasoned that first front research in bacterial conjugation should not limit itself to the knowledge produced by inbreeding. We considered it will most profit from the input of leading experts in the above mentioned flanking areas, by adopting an interdisciplinary approach. Thus, we organized the workshop with strong emphasis in the awareness that the contribution of the flanking areas can trigger in our field. As a nice by-product, the achievements of bacterial conjugation research will be better appreciated by a broader audience.

Hopefully, all participants will benefit from provoking questions and ideas launched across the different fields. With this idea in mind, the keynote lecture was chosen to alert the audience on the crucial importance of the knowledge of the 3D structures of proteins to investigate biochemical processes using topoisomerases as a model system.

The first section of the meeting focused on rolling-circle replication systems, which resemble the DNA processing reactions during conjugation. These were compared at a later section to other DNA-strand transferases, such as transposases and resolvases. The core sections included the topics of conjugation and T-DNA transfer. The utilization by bacterial conjugation of a complex DNA transport machinery bears analogies with other processes of macromolecular transport through membranes, which constituted another section of the workshop.

In our opinion, the meeting succeeded in presenting the facts of conjugation in a way that could be discussed as pertaining to the selected fields. Perhaps one of the most difficult

things was to find a suitable and inclusive title for our enterprise. Our initial idea ("Sources of inspiration for bacterial conjugation") found its way as the headline for the final Round Table discussion which involved many of the participants in a lively and "inspiring" discussion. Although gene transmission by bacterial conjugation is being studied now for 50 years, it is only since very recently that questions dealing with the mechanistic principle were asked and could be answered at the molecular level of enzymes. Consequently, "Enzymology of DNA-strand transfer mechanisms" was chosen as the most appropriate title to describe the aims of the workshop.

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Vascular Endothelium and Regulation of Leukocyte Traffic

Organized by
T. A. Springer and M. O. de Landázuri
20th-22nd May, 1996

The circulatory and migratory properties of white blood cells have evolved to allow efficient surveillance of tissues for infectious pathogens and rapid accumulation at sites of injury and infection. Lymphocytes continually patrol the body for foreign antigen by recirculating from blood, through tissue, into lymph, and back to blood. Lymphocytes acquire a predilection, based on the environment in which they first encounter foreign antigen, to home to or to recirculate through that same environment.

The first critical step in lymphocyte migration from circulation into tissue is the adhesion of lymphocytes to vascular endothelium. In lymphoid organs, lymphocyte adherence and transendothelial migration occur at specialized postcapillary vascular sites called high endothelial venules (HEVs). Although HEVs are particularly abundant in the T-cell areas surrounding the B-cell follicles, they serve as the sites of entry both for T and B lymphocytes. In humans, HEVs are found in all secondary lymphoid organs (with the exception of spleen, where lymphocyte emigration occurs via the blood sinusoids in the marginal zone), including hundreds of lymph nodes dispersed in the body, tonsils and adenoids in the pharynx, Peyer's patches in the small intestine, appendix, and small aggregates of lymphoid tissue in the stomach and large intestine. Moreover, HEV-like vessels are observed in chronically inflamed nonlymphoid tissues and are believed to support lymphocyte recruitment in these sites. In contrast to the endothelial cells from other vessels, the high endothelial cells of HEVs have a distinctive appearance, express specialized ligands for lymphocytes and are able to support high levels of lymphocyte extravasation.

The different homing and recirculation behaviors of lymphocytes depend on expression of specific adhesion receptors by lymphocytes, endothelial cells, and tissue cells and on interactions with the extracellular matrix. Expression of these receptors is finely regulated according to cell type, functional state, and anatomical localization, and builds up a complex network in interactions that simultaneously involve several of these receptors working as "traffic signals" or "postcodes" for lymphocyte migration and homing. There are five main families of adhesion molecules: immunoglobulin superfamily, integrins, selectins, cadherins, and mucin-like molecules.

Many different adhesion systems are known to be subject to regulation, but the most-studied and best-understood class is the integrin. Integrins are known to be regulated at several levels. Modulation of the affinity of the adhesion receptor for ligand (called affinity modulation) is a well-documented mechanism for the activation of platelet aggregation and is thought to underlie activation of leukocyte adhesion. Adhesive strengthening by the clustering of adhesion receptors or by cytoskeletal-dependent processes such as cell spreading is known to be crucial for strong cell attachment, the control of cell growth and cell motility. These regulatory changes occur either in response

to intracellular event (hence, sometimes called inside-out signalling), as a result of EC ligand binding (often called postreceptor occupancy events), or in many instances from both.

Regulation of integrin-mediated adhesion may involve conversions among several different states. For example, leukocyte exhibit several different adhesive behaviours as they interact with endothelial cells of vessel wall during homing or extravasation at sites of inflammation. In the now classic three-step model, under the high shear forces present in flowing blood, leukocytes first become tethered and then roll along the vessel surface. When a local signal (for example, a cytokine) is released in their vicinity, they arrest, develop firm adhesion, and then migrate across the endothelium. Until recently, it has been thought that the rolling phase was mediated solely by the selectins, a family of carbohydrate-binding adhesion molecules implicated in leukocyte homing. Arrest and tightening of adhesion are known to result from the activation of leukocyte integrins. However, it has been recently shown that a single type of integrin can mediate all adhesive phases, including the initial tethering and rolling. For example, $\alpha 4\beta 1$ (VLA-4) mediates tethering and rolling on vascular cell adhesion molecule 1 (VCAM-1), an endothelial integrin ligand belonging to the immunoglobulin superfamily. As expected, this integrin can also become activated to bring about arrest and tight adhesion. Thus, prior to activation, the integrin exhibits binding properties that support tethering and rolling.

The HEV endothelium is unique amongst vascular endothelium by virtue of its capacity to recruit large numbers of lymphocytes. In the human body it is estimated that as many as $5x10^6$ lymphocytes extravasate from the blood through HEVs every second. The specificity and efficiency of this process is explained by specialized features of the HEV endothelium, such as the expression of mucin-like glycoproteins decorated with HEV-specific oligosaccharide. In the future, it will be important to define precisely the molecular mechanisms involved in the induction and maintenance of the specialized HEV phenotype.

HEV-like vessels induced by chronic inflammation in extra lymphoid sites appear to be phenotypically and functionally similar to HEVs from lymphoid tissues. Thus, a better understanding of the mechanisms controlling development and maintenance of HEVs could provide the basis of a novel therapeutic approaches for the treatment of human chronic inflammatory diseases, including rheumatoid arthritis and inflammatory bowel diseases, in which HEV-like vessels facilitate large-scale influx of lymphocytes, leading to ampliation and maintenance of chronic inflammation.

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Cytokines in Infectious Diseases

Organized by
A. Sher, L. Rivas and M. Fresno
3rd-5th June, 1996

In recent years it has become clear that cytokines play an important role in controlling both the inductive and the effector arm of the immune response. Moreover, the host cytokines response is a key determinant of the outcome of infection-governing both host resistance and immunopathology. For this reason, prophylaxis or treatment with cytokines has emerged as an important strategy for immunologic intervention in many infectious diseases.

In addition, parasite infections provide paradigms for addressing some fundamental questions concerning the innate host response to infection. What parasite molecules stimulate cytokine production? What causes in some cases, the abnormally high cytokine production that lead to severe pathology? Is this genetically regulated? The study of cytokine function in infectious disease has been revolutionized by the advent of engineered mouse strains with genetic disruptions in cytokine and cytokine receptor genes. In addition to identifying cytokine requirements for host resistance and pathology, these animals have provided new insights into redundancies in the cytokine network itself. Such investigations have highlighted the important lessons learned from the infection disease models on the mechanism underlying the selective induction of different immune responses.

There are two main types of helper T (Th) cells according to cytokine secretion. Th1 cells produce IL-2, INF-γ, and TNF but not IL-4. By the contrary, Th2 cells preferentially secrete IL-4, but not no IFN-γ. Their polarized expression in different disease states frequently determines host resistance or susceptibility and it is strongly influenced by events triggered early in infection, involving innate recognition mechanisms. The early induction of IL-12 by APCs, which in turn trigger IFN-γ, is a key determinant of Th1 response induction while the initiation of Th2 responses depends on IL-4. Thus, the balance of IL-12 and IL-4 triggered early after pathogen invasion forms the basis of the subsequent selection of T cell subsets and their protective versus disease promoting influence on infection. In many diseases, such as Leishmaniasis, Toxoplasmosis, Tuberculosis, Th1 responses are protective whereas Th2 are detrimental. Others, as Chagas or Malaria have a more complex pattern.

Th cell polarization is a complicated process controlled by a number of factors including: the nature of the antigen and of the APCs, accessory molecules expressed on APCs that deliver different co-activation signals to T cells, cytokines produced early after exposure to a pathogenic agent or immunization with an antigen, etc. There is now growing evidence that cells other than APC, encountered by pathogens early after host entry, such as

neutrophils and epithelial cells are also capable of producing IL-12. Besides, $CD4^+NK1.1^+$ cells, and in the case of the *Leishmania* model, a subset of $CD4^+$ cells with a limited TCR repertoire, have been implicated as sources of the IL-4 in addition to T and mast cells.

In addition to their role in initiating T cell subset differentiation, cytokines are crucial for maintaining and regulating adaptive immune responses. The lymphokines IL-2, IL-4, IFN-γ and the anti-inflammatory cytokines IL-10 and TGF-β are key players at this stage. An important effector mechanism involved in the control of many different infectious agents is the production of nitric oxide (NO). The synthesis of this toxic metabolite is induced by the action of the Th1 cytokines and regulated by both Th2 and anti-inflammatory cytokines.

Pathogens have also evolved complex strategies to ensure survival in an immunologically hostile host environment. Thus, many parasites have coevolved molecules that can alter the production of either immunoregulatory or effector cytokines, important to control the infection, by macrophages.

Although clearly important in both the establishment and maintenance of resistance, the cytokine response to infectious agents can also be host detrimental and has been described as a "double-edged sword". Most of the pro-inflammatory cytokines and lymphokines associated with the Th1 response (e.g. TNF-α, IL-12 and IFN-γ) are toxic when induced in an excessive or uncontrolled manner. Some of this toxicity results from the subsequent production of NO but also from more complex down-stream phenomena. Cytokine biology offers an important approach for understanding the pathogenesis of these disorders. Finally, as should be obvious, the exogenous manipulation of deleterious cytokine responses offers a potentially powerful strategy for preventing or treating infectious disease pathology.

Animal studies on a number of important infectious diseases have provided testable strategies for the use of cytokines in disease treatment as well as prevention. The further elucidation of the function role of cytokine regulation in human infection and the continued introduction into the clinic of novel cytokine based strategies for disease intervention remain important goals for this field. The Juan March Workshop has provided a forum to address some of those questions in detail and to exchange knowledge from different infectious diseases in this dynamic field.

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Molecular Biology of Skin and Skin Diseases

Organized by
D. R. Roop and J. L. Jorcano
17th-19th June, 1996

The skin is the largest organ of the human body. Its importance is well known as a protective barrier against the aggression of many external agents, physical, chemical and biological (bacteria, fungus, virus, etc.). Nonetheless, attention to and research on this tissue have long been scarce, even though dermatological diseases affect a large number of patients (for instance, psoriasis, chronic ulcers and cutaneous tumors are high-incidence diseases in industrialized countries).

In recent years, this situation has changed. Recognition that the epidermis forms a complex, interesting and highly-ordered system in which the processes of proliferation, differentiation and cell death can be studied has attracted the attention of a growing number of investigators. In a spectacular race against the clock, the molecular basis of several skin diseases has been described and significant progress has been made in understanding the mechanisms controlling proliferation and differentiation in this tissue, as well as in the identification of the factors that intervene in these processes. Due to the barrier function of the skin, special attention should be given to the advances in cytoskeletal organization and its role in the maintenance of epithelial structure and function, and in particular to the keratins and to the molecules and structures of cell adhesion (desmosomes and hemidesmosomes, integrins, cadherins, etc.).

The external corporal localization of the skin and the identification of those sequences that direct gene activity in this tissue have made the use of transgenic animals a flexible and widely-used technique which permits the acquisition of important information *in vivo*. The skin has thus become one of the tissues on which more research is being done and more progress is being made.

From the clinical point of view, three novel characteristics have attracted considerable attention to this tissue:

1) The finding that the skin produces interleukins and other cytokines of enormous importance in the infectious and inflammatory processes of this tissue. Given the large area of the skin, it is hypothesized that these epidermal cytokines, after passing to the circulation, may also play a very important systemic role.

2) At present, the skin is the organ with the highest incidence of tumors, and this frequency continues to increase. There is evidence that many of these tumors are caused by increased exposure of the skin to ultraviolet radiation, due as much to the deteriorating ozone layer as to reigning esthetic fashions. Skin carcinogenesis is an area in which considerable work is being done.

3) *In vitro* culture and expansion of human keratinocytes are recently-developed methods of great relevance, both in patients with major cutaneous lesions (such as, for example, those with burns covering a large body area, insuperable until this new technique was introduced) and in the treatment of ulcers which do not respond to classical therapies. In addition, however, accumulated experience and the relative ease of *in vitro* culture of epidermal keratinocytes and their subsequent transplant in patients make the epidermis an ideal tissue for the development of gene therapy protocols, for both hereditary and tumoral diseases. Recent advances in the identification and isolation of epidermal stem cells are particularly relevant in this context, as is the development of methods which permit the stable or transitory expression of therapeutic genes in keratinocytes.

These subjects were addressed in depth and actively discussed in the present Workshop.

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Programmed Cell Death in the Developing Nervous System

Organized by
R. W. Oppenheim, E. M. Johnson and J. X. Comella
1st-3rd July, 1996

Although the existence of a large scale loss of cells during development has long been recognized, it is only in the last twenty years that the significance of programmed, naturally ocurring cell death has been appreciated. Because, with the possible exception of the immune system, the programmed cell death of developing neurons has been studied longer and more extensively than that of any other cell type, it is perhaps not surprising that knowledge about the normal biology of cell death in the nervous system is also more complete. However, even in the nervous system our understanding of many aspects of cell death is still fragmentary. Although many aspects of cell death in the nervous system (especially molecular pathways) appear to be similar to that of cell death outside of the nervous system, there are also important differences that make neuronal cell death novel and unique. For example, control of cell death of neurons often involves interactions between neurons and interconnecting populations of synaptic targets and afferents that are absent in other cell types undergoing cell death. Another difference is that physiological activity, including synaptic transmission, plays a role in the regulation of cell death in the nervous system, whereas similar signals are probably not involved outside of the nervous system. Collectively, it is these unique and shared properties of cell death in nervous and non-nervous tissue that provided a major rationale for the first workshop on *Programmed Cell Death in the Developing Nervous System* held at the Juan March Foundation in Madrid. Because of similarities between cell death in nervous and other tissues, the information discussed at the meeting will be of interest to a wide spectrum of investigators in the cell death field. By focusing the meeting on the developing nervous system, however, it was assured that the many unique aspects of neuronal and glial cell death were the major topic of discussion.

The participants at the workshop represented an international group of prominent investigators with diverse interests, backgrounds, research strategies, animal models and viewpoints. Because of this diversity it was possible to addres virtually all of the important issues in the field. These included the following topics: What is the biological significance of cell death in the nervous system and does this differ for cell types, brain regions and species; What role do targets and afferents play in the regulation of cell death and does this differ between vertebrates and invertebrates; What are the similarities and differences between cell death of neurons and glia; What neurotrophic agents and growth factors (and receptors) regulate survival in the nervous system and how do these act at the biochemical and molecular levels to promote survival; How are other cell-cell signals such as activity and hormones involved in regulating death and survival; What are the biochemical/molecular pathways that result in cellular degeneration and do these differ for different cells, brain regions and species; What genes are involved in mediating death and survival in the nervous system and how are these similar or different across species.

Although consensus was reached on our present understanding of many of these issues, for others there were differences of opinion and a general agreement that more information is needed for a final resolution. Despite the lingering differences of opinion on some key issues, however, all of the participants felt that the meeting was a great success in assessing the present state of knowledge in the field and in identifying the critical important issues that remain for future investigations. The organizers and participants would like to thank Andrés González and the staff of the Juan March Foundation for their hard work, generosity and perception in supporting this timely inaugural meeting on *Programmed Cell Death in the Developing Nervous System*.

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NF-κB/IκB Proteins. Their Role in Cell Growth, Differentiation and Development

Organized by
R. Bravo and P. S. Lazo
8th-10th July, 1996

Ten years ago the first paper reporting the existence of a kappa immunoglobulin enhancer binding protein was published and called NF-κB. This binding function presented a stage specific pattern of activation in B cells which led to a model that included an inhibitory protein (IκB) which could retain NF-κB in the cytoplasm. Upon activation of the cell, the inhibitor would be inactivated and NF-κB translocated to the nucleus to activate gene transcription.

Since then, NF-κB has been found to be an ubiquitous transcription factor composed of dimers and several homologous proteins have been identified, e.g., p50, p52, c-Rel, RelB, RelA (p65). The term Rel/NF−κB now refers to a family of closely related dimeric complexes which are able to regulate specific gene transcription. In the last six years, emphasis has been placed on isolating and cloning the various members of the Rel/NF−κB family, characterizing their structure and their interaction with DNA.

The family of inhibitory proteins, which includes the proto-oncogene Bcl-3, has also been the subject of active research as well as the study of the mechanisms by which different activators trigger NF-kB activation. It is now clear that phosphorylation and ubiquitin mediated proteolysis are implicated in the mechanism of activation of NF-κB. However, it remains unclear which kinases and proteases are responsible for these processes.

The important role of NF-κB/IκB proteins in growth regulation and differentiation can be deduced from their involvement in the transcriptional activation by growth factors, the oncogenic activities of some of the family members, and their activation by mitogens. However, the role of each individual protein has not been clearly established probably because of the ability of NF-kB proteins to substitute for each other in the heterodimeric complexes.

The workshop dealt with the most recent advances in this active field of research, from the molecular level to the most complex biological models. Thus, it was discussed the characterization of the molecular interaction between DNA and NF−κB proteins using crystallography data as well as biochemical studies on the interaction of the different NF-κB proteins and their inhibitors, including the new inhibitor IkBε.

From the data presented at the workshop, it is apparent that signal transduction from the cell membrane to NF-κB is rather complex, with different pathways being implicated.

It also appears that different kinases may be involved in the phosphorylation of IκB proteins and that these inhibitory proteins play different roles in the activation process of NF-κB.

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Chromosome Behaviour: The Structure and Function of Telomeres and Centromeres

Organized by
B. J. Trask, C. Tyler-Smith, F. Azorín and A. Villasante.
23rd-25th September, 1996

As previously mentioned, results presented focused on several organisms including ciliated protozoa and *Drosophila*. Most eukaryotic telomeres are made by G-rich repeats which are generated by telomerase. A contrast is represented by *Drosophila*, where telomeres do not have those simple repeats; instead telomere-specific transposable elements are found. Data on telomerase-independent mechanisms for telomere maintenance in *Drosophila* were presented.

Interest was shown not only on the very end of chromosomes, but also on several structural and functional aspects of the subtelomeric regions. Results presented at the meeting indicate that DNA near end of human chromosomes has large blocks of duplicated material and is highly polymorphic. Furthermore, the large-scale polymorphic duplications can contain genes, such as members of the olfactory receptor gene family.

Unlike telomeres, where functional sequences are well conserved, the repeated sequences found at many centromeres vary widely between species. The identity of the functional sequence has been well characterized only in yeast.

There has been debate about whether the small centromere of *S. cerevisiae* provides a model for the larger centromeres of most other organisms: are *cerevisiae*-like "magic sequences" embedded in the centromeric repeats of other organisms?. In his summary of the meeting, John Carbon identified the demise of the "magic sequence" hypothesis as one of its major conclusions. New evidence presented at the workshop suggested that repeated sequences alone are sufficient to form the centromeres of multicellular eukaryotes.

Schizosaccharomyces pombe can be seen as providing a model for the centromeric DNA of higher eukaryotes, and the identification of the *S. pombe* centromere binding protein Abp1 with extensive homology to the mammalian centromere protein CENP-B allows the model to be extended to include proteins as well. The centromeric DNA of a *Drosophila* minichromosome has now been characterised: only satellite DNAs and transposons were found. None of these sequences were detected at all other *Drosophila* centromeres and each sequence had non-centromeric locations. These findings, together with the observation that deleted minichromosomes lacking the centromeric DNA can show surprising stability, led to the thought-provoking suggestion that there may be nothing at all special about the centromeric DNA: perhaps, after suitable epigenetic activation, any sequence whatsoever can show centromeric activity.

The relevance of some structural features of *Drosophila* centromeric satellites and the functions of specific proteins that interact with mammalian centromeres were also discussed. Workers on mammalian chromosomes have been trying for years to emulate the success of those working with yeast, and create mammalian artificial chromosomes starting

from DNA elements. The first reports of success from this approach provided some of the highlights of the meeting. Evidence is mounting that alphoid satellite DNA introduced into a cell may be sufficient to form a human centromere. Although more work is still required, the techniques are now at hand to create functioning human minichromosomes. Chromosome based vectors will allow the cis-acting DNA requirements for mammalian chromosome function to be rigorously defined. Furthermore, synthetic chromosomes could be extremely useful tools in the field of gene therapy.

In conclusion, findings reported at the workshop provided new insights into this dynamic field, giving a stimulating overview on the structure and function of two essential chromosomal structures. Undoubtedly, detailed function and structure may vary considerably from system to system; however, the workshop provided a wonderful opportunity to learn and to reflect about the possible links of chromosome behaviour among species, from yeast to human.

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RNA Viral Quasispecies

Organized by
S. Wain-Hobson, C. López Galíndez and E. Domingo
7th-9th October, 1996

The workshop on RNA viral quasispecies gathered a number of experts on topics related to RNA virus evolution. It was indeed a broad scope of topics ranging from the molecular basis of copying fidelity of viral polymerases to the contribution of virus variation to pathogenesis and to the emergence of new viruses. As is often the case in a gathering of stout scientists with long personal histories in unique environments, agreement in some issues parelleled disagreement in many others.

Few virologists would now question that the quasispecies model of molecular evolution of macromolecules, proposed by M. Eigen a quarter of a century ago, is exerting a great influence in our current understanding of RNA viruses. Several examples were identified that document that specific mutations arising during viral replication are directly associated to new pathogenic potential of the evolved genomes. It is not yet possible to design experiments involving infections with viruses replicating with very high copying fidelity to test the effect of replication errors on virus pathogenesis. In spite of this, it is becoming increasingly clear that adaptability, measured as the ability to gain fitness, or the ability to cope with environmental changes (presence of antibodies, drugs) are directly related to the high mutation rates and quasispecies structure of viral populations.

There was much less agreement on the limits of applicability of the quasispecies concept. Are human populations quasispecies? And retrotransposons? Fortunately Eigen himself was there to clarify the origins of the concept, as also emphasized in several of his recent papers: Quasispecies implies a related set of simple replicons subjected to competitive selection. The main departure from previous models of population genetics is the consideration of the wild type as an ensemble of genomes instead of one genome with a defined nucleotide sequence. It is this mutant swarm - the preferred word of H. Temin- that offers sufficient plasticity for the ensemble to become an easy prey of selective forces and genetic drift.

The process of mutant generation, competition and selection can be analyzed in a controlled fashion in the replication of short-chained RNA species derived from bacteriophage Qβ. Several more complex model systems were discussed. The classical influenza viruses -which preceded other viral systems in defining concepts of structural and evolutionary virology- poliovirus, foot-and-mouth disease virus, vesicular stomatitis virus, hepatitis C virus, human respiratory syncytial virus, retrotransposons and, of course, the human immunodeficiency viruses and their chimeric simian/human versions, among other animal and plant RNA viruses and genetic elements. Although several important concepts are emerging from these studies (limitations in the cloud of mutant swarms, multiple mutational pathways associated to escape from antibodies or to resistance to antiviral inhibitors, identification of mutations associated to deep fitness losses, the effect of viral population size on selective dominance of some classes of mutants, etc.) it was also quite

clear that additional input from population genetics would be of great help to virology. Some connexions between classical population biology theory and quasispecies have already been established but more are needed to assess the value of viruses to approach evolutionary problems.

New possibilities of antiviral intervention based on the error prone replication of viruses were also discussed. Copying fidelity of reverse transcriptase can be modified by structural alterations of the enzyme and the manipulation of fidelity to drive viral replication into error catastrophe is no longer a dream. An elegant exploitation of error-prone replication is the generation of heavily substituted nucleic acids and proteins. *In vitro* hypermutagenesis constitutes an impressive tool to explore the functional space of enzymes, and a means to generate molecules with new biological properties.

In conclusion, the meeting offered a lot to most and, fortunately, there were sufficient points of disagreement to lend ourselves to believing that Fundación Juan March may consider a similar meeting some years from now.

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Abscisic Acid Signal Transduction in Plants

Organized by
R. Quatrano and M. Pagès
28th-30th October, 1996

The mechanism(s) by which phytohormones trigger physiological responses have long eluded plant physiologists. How these relatively small and simple molecules can elicit such major responses that differ from tissue to tissue during plant development has been a very difficult question to approach. However, through the use of molecular and genetic approaches, tremendous strides have been made within the last decade to elucidate the molecular basis of phytohormone action. These advances have been most notable with responses elicited by the phytohormones ethylene, auxin and abscisic acid. Overall progress in this important area of plant science research is represented in this meeting that focuses on one of these phytohormones, abscisic acid (ABA). It is clear that the data accumulated from recent research has led to considerable progress in our understanding of the ABA response pathway; from perception of the ABA signal, through the expression and function of specific genes in a given physiological response. Future research, using the approaches outlined in this workshop, will undoubtedly lead to the further clarification of the role of ABA in plant development and serve as paradigm by which the modes of action of other phytohormones and plant signals can be better understood.

The role of ABA in the typical life cycle of a higher plant is mostly confined to the development of the seed, and in response to environmental stresses in vegetative tissue. Levels of endogenous ABA increase during the development of the seed, and is part of a developmental pathway which promotes maturation of the seed and the acquisition of desiccation tolerance, as well as prevents precocious germination. Evidence from genetic and molecular data, as well as from embryo culture indicates that this pathway is an integral component of the developmental program within all higher plants. An early response of vegetative plant tissue to environmental stresses, such as osmotic and temperature extremes, involves increases in the endogenous levels of ABA and or in the sensitivity of cells to ABA, as an internal signal to trigger a set of responses to protect immobile plants from these perturbations. Although the signaling pathway from ABA to gene expression may be similar in seeds and in vegetative tissue, it is clear that different sets of genes are expressed in the different tissues. Hence, the importance of understanding the molecular and genetic basis of the ABA response pathway has enormous implications in agricultural practices and in engineering crops in the future with improved traits in seeds and in tolerance of environmental stresses.

Genetic approaches using the model plant *Arabidopsis* have identified mutants whose phenotypes are defective in ABA responses in both vegetative and reproductive tissues. Since one can easily map these mutant loci in *Arabidopsis*, which consists of an extremely small genome, positional cloning techniques are available to isolate the mutated genes. Also, insertional mutagenesis in *Arabidopsis*, as well as in maize, has also led to the further isolation and characterization of genes active in the ABA response pathway. Studies of two such ABA-insensitive mutants, *abi1* and *abi3*(*vp1*), have resulted in the isolation of genes

that have been identified as a phosphatase and a transcriptional activator, respectively. The identification of other genes that interact with each of these gene products, as well as the substrates for their action, is the subject of intense genetic and biochemical research and study. More biochemical/cytological approaches have identified the ionic intermediates and the membrane channels responsible for these ionic fluxes that transduce the ABA signal (e.g. Ca) and drive various physiological responses to ABA (e.g. stomatal closure).

Direct microinjection techniques have identified unique intermediates (e.g. cyclic ADP-ribose) that are responsible for specific gene expression at the level of ABA-responsive promoters. Furthermore, molecular approaches have detailed the cis-elements and several transacting factors (including VP1) that are critical for the transcription of ABA-responsive genes. Although the initial receptor of ABA has not been identified, new approaches are being targeted to this major unknown. Likewise, although the function of ABA-responsive genes in various physiological processes (e.g. desiccation tolerance) are not known in molecular terms, considerable progress has been made on the molecular structure and important domains of these proteins.

It is clear from these recent studies outlined in this workshop, that our knowledge of the ABA signal transduction pathway has progressed greatly in the last several years, but major gaps still exist in our understanding. For example, what is the nature of the ABA receptor, what are the critical changes that occur in response to the ABA signal at the level of transcription resulting in ABA-dependent gene expression, and, what is the link between the proteins that appear in response to ABA and the tissue-specific physiological responses ?

Ralph S. Quatrano
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Oxygen Regulation of Ion Channels and Gene Expression

Organized by
E. Kenneth Weir and J. López Barneo
24th-26th November, 1996

This workshop concentrated on a relatively new but rapidly growing research field. The influence of O_2 sensing on cellular functions is an emergent topic that in the coming years will certainly have a broad impact in biomedicine. The initial progress in the field has been achieved independently by researchers with different background and technical expertise, without much communication among them. Thus, we thought that the gathering of a selection of scientists, representative of the various disciplines with interest in the subject, would render an enormous conceptual enrichment and could lead to a breakthrough in the maturation and development of the field. This was among the first international workshops on the subject aimed at the interchange of ideas and concepts among scientists from areas as diverse as molecular biology, biochemistry, physiology, pharmacology and clinical research.

Oxygen, one of the most abundant elements in the biosphere, is crucial for the maintenance of most life forms on earth. It has a major biological role as acceptor of the electrons in the mitochondrial respiratory chain and in doing so enables the synthesis of ATP by phosphorylative oxidation. Despite its paramount importance, little is known about how organisms are capable of sensing O_2 availability and adjusting the gas uptake to their changing needs, in different habitats or physiological situations. Because, in mammals, O_2 is taken up in the respiratory system and transported to the tissues by the blood, the most immediate adaptative response to the lack of environmental O_2 is an increase in the frequency of breathing. Acute hypoxia also produces dilatation in most arteries, which is an important mechanism participating in the local regulation of vascular tone. Besides these fast physiological responses, long-term hypoxia can induce in specific cells modifications in gene expression and enzymatic activity. Well-known examples of these chronic adaptations to the lack of O_2 are the induction of erythropoietin, the hormone that stimulates the production of red blood cells, and of vascular endothelial growth factor, which may mediate hypoxia-initiated angiogenesis.

Research in recent years has begun to shed light on the basic cellular and molecular mechanisms underlying acute and chronic adaptations to low O_2 tension. The cardiorespiratory responses to hypoxia seem to be mediated by O_2-sensitive ion channels, expressed in glomus cells of the carotid body (the primary O_2-sensitive arterial chemoreceptors), arterial smooth muscle cells, neuroepithelial bodies of the lung, pheochromocytoma and brain cells. The molecular nature of the intrinsic O_2-sensors associated with ion channels, or those O_2-sensitive molecules capable of triggering the signal pathway(s) regulating transcription, although unknown, is currently being investigated in several laboratories. The molecular characterization of the O_2 sensitive molecules will surely lead to a better understanding of many pathophysiological processes (such as hypertension or the responses of brain and heart cells to ischemia) and will generate new strategies for the pharmacological treatment of human diseases.

E. Kenneth Weir and José López-Barneo.

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XV Juan March Lectures

The Juan March lectures were first organized in 1982, and since then have been held every year without interruption. The purpose of these lectures is to put Spanish students and professionals in the field of Biology in direct contact with some outstanding world figures in this field. The invited lecturers often take advantage of their visit to Spain to give additional seminars in different laboratories.

In 1996, the XV lectures series took place, with the general theme of **TRANSCRIPTION FACTORS**. The speakers and topics were as follows:

19 February

DAVID BALTIMORE

Department of Biology
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Cambridge, MA (USA)
1975 Nobel Prize in Physiology or Medicine

The NF-κB transcription factor and lymphoid cell activation.

Introduced by: **Manuel Fresno.**

Centro de Biología Molecular "Severo Ochoa"
Universidad Autónoma de Madrid (Spain)

26 February

MARK PTASHNE

Department of Molecular and Cellular Biology
Harvard University
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Molecular mechanisms of gene regulation.

Introduced by: **Ana Aranda.**

Instituto de Investigaciones Biomédicas
Madrid (Spain)

4 March

WALTER J. GEHRING

Biozentrum
University of Basel (Switzerland)

The role of *eyeless* as a master control gene in eye morphogenesis and evolution.

Introduced by: **Ginés Morata.**

Centro de Biología Molecular "Severo Ochoa"
Universidad Autónoma de Madrid (Spain)

11 March

FRANÇOIS JACOB

Institut Pasteur
Paris (France)
1965 Nobel Prize in Physiology or Medicine

Regulatory circuits in transcription.

Introduced by: **Antonio Garcia-Bellido.**

Centro de Biología Molecular "Severo Ochoa"
Universidad Autónoma de Madrid (Spain)

Sessions Open to the Public

In conection with some workshops, prominent invited speakers have also given additional lectures in sessions open to the public. In 1996, these were as follows:

During the workshop on **RNA Viral quasispecies** (7-9 October):

- JOHN HOLLAND

Department of Biology
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The population behaviour of RNA virus quasispecies and significance for virus diseases.

- SIMON WAIN-HOBSON

Unité de Rétrovirologie Moleculaire
Institut Pasteur
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Genetic variation reveals the biology and dynamics of retroviral infections.

Introduced by: **Esteban Domingo.**

Centro de Biología Molecular "Severo Ochoa"
Universidad Autónoma de Madrid (Spain)

During the workshop on **Abscisic Acid signal transduction in plants** (28-30 October):

- NAM-HAI CHUA

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New York (USA)

Phytochrome phototransduction pathways.

Introduced by: **Montserrat Pagès.**

Centro de Investigación y Desarrollo
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Reviews in Scientific Journals

During 1996 the meetings organized by the Centre have been reviewed in the following articles:

- **Neurobiology of Nociceptors** (1996). Eds. C. Belmonte and F. Cerveró. Oxford University Press (Oxford).
  (Based on the workshop *What do nociceptors tell the brain?*, held in February 1992).

- Vicente, M. and Errington, J. (1996) Structure, Function and Controls in Microbial Division. **Molecular Microbiology 20**(1): 1-7.
  (On the workshop of the same title, held in May 1995)

- López-Botet, M., Moretta, L. and Strominger, J. (1996) NK-Cell Receptors and Recognition of MHC Class I Molecules. **Immunology Today 17**: 214-217.
  (On the workshop *NK-Cell Receptors and Recognition of the Major Histocompatibility Complex Antigens*, held in September 1995).

- Dreyfuss, G., Hentze, M. and Lamond, A.I. (1996) From Transcript to Protein. **Cell 85**: 963-972.
  (On the workshop of the same title, held in March 1996).

- Henderson, C.E. (1996) Programmed Cell Death in the Developing Nervous System. **Neuron 17**: 579-585.
  (On the workshop of the same title, held in July 1996).

- Baeuerle, P.A. and Baltimore, D. (1996). NF-κB: Ten Years After. (Meeting Review). **Cell 87:** 13-20.
  (On the workshop on *NF-κB/IκB Proteins. Their Role in Cell Growth, Differentiation and Development*, held in July, 1996).

- Siebenlist, U. (1996). NF-κB/IκB Proteins. Their Role in Cell Growth, Differentiation and Development. **Biochimica et Biophysica Acta. (Reviews on Cancer) 1332(1):** R7-R13.
  (On the workshop of the same title, held in July, 1996).

- Nichol, S. (1996). RNA viruses. Life on the edge of catastrophe. **Nature 384:**218-219.
  (On the workshop on *RNA viral quasispecies*, held in October, 1996).

- Fresno, M., Kopf, M. and Rivas, L. Cytokines in Infectious Diseases. **Immunology Today**(In press).
  (On the workshop of the same title, held in June, 1996).

- Barthels, D., Ho, T.H.D. and Quatrano, R. **Plant Cell**.(submitted)
  (On the workshop on *Abscisic Acid Signal Transduction in Plants* held in October, 1996).

1997 Meetings Schedule

INSTITUTO JUAN MARCH

CENTRE FOR INTERNATIONAL MEETINGS ON BIOLOGY

1997 MEETINGS SCHEDULE

Date	Meeting Subject	Organizers
10-12 February	TGF-ß Signalling in Development and Cell Cycle Control	**J. Massagué.** Howard Hughes Medical Institute. New York. **C. Bernabeu.** Centro de Investigaciones Biológicas. Madrid.
10-12 March	Novel Biocatalysts	**S. J. Benkovic.** The Pennsylvania State University. University Park. **A. Ballesteros.** Instituto de Catálisis y Petroleoquímica. Madrid.
21-23 April	Signal Transduction in Neuronal Development and Recognition	**M. Barbacid.** Bristol-Myers Squibb Pharmaceutical Research Institute.Princeton. **D. Pulido.** Centro de Biología Molecular "Severo Ochoa". Madrid.
12-13 May	100th Meeting: Biology at the Edge of the Next Century	**Centre for International Meetings on Biology. Madrid.**
26-28 May	Membrane Fusion	**V. Malhotra.** University of California, San Diego. La Jolla. **A. Velasco.** Facultad de Biología. Universidad de Sevilla.
9-11 June	DNA Repair and Genome Instability	**T. Lindahl.** Imperial Cancer Research Fund. Herts. **C. Pueyo.** Facultad de Ciencias. Universidad de Córdoba.
7-19 July *	Biochemistry and Molecular Biology of Non-conventional Yeasts	**J. M. Cregg.** Oregon Graduate Institute of Science and Technology. Portland. **C. Gancedo.** Instituto de Investigaciones Biomédicas. Madrid. **J. M. Siverio.** Facultad de Biología. Universidad de La Laguna.
22-24 September	Principles of Neural Integration	**C. Gilbert.** The Rockefeller University. New York. **G. Gasic.** Neuron Editorial Offices. Cell Press. Cambridge. **C. Acuña.** Facultad de Medicina. Universidad de Santiago de Compostela.
6-8 October	Programmed Gene Rearrangement: Site-Specific Recombination	**N. D. F. Grindley.** Yale University. New Haven. **J. C. Alonso.** Centro Nacional de Biotecnología. Madrid.
20-22 October	Plant Morphogenesis	**M. Van Montagu.** University of Gent. **J. L. Micol.** Facultad de Ciencias. Universidad de Alicante.
3-5 November	Development and Evolution	**W. Gehring.** Biozentrum. University of Basel. **G. Morata.** Centro de Biología Molecular "Severo Ochoa". Madrid.
1-3 December	Plant Viroids and Viroid-Like Satellite RNAs from Plants, Animals and Fungi	**H. L. Sänger.** Max-Planck-Institut für Biochemie. Martinsried. **R. Flores.** Instituto de Biología Molecular y Celular de Plantas. Valencia.

All meetings, with the exception marked *, will take place on the premises of the Instituto Juan March:

Castelló, 77
Telephone: 34 - 1 - 435 42 40
Fax: 34 - 1 - 576 34 20
28006 Madrid (Spain)

Individual advertisements for every meeting, with more detailed information, are published with sufficient anticipation.

The Scientific Council

The Scientific Council of the Centre comprises the following members:

Miguel Beato
Institut für Molekularbiologie und Tumorforschung. Marburg (Germany).

José A. Campos-Ortega
Institut für Entwicklungsbiologie. Köln (Germany).

Gregory Gasic
Neuron Editorial Offices. Cambridge (USA).

César Milstein
Medical Research Council. Cambridge. (United Kingdom).

Margarita Salas
Centro de Biología Molecular. CSIC - Universidad Autónoma de Madrid. (Spain).

The Scientific Council determines the priorities for the Centre's activities. It may put forward initiatives to be carried out in collaboration with Spanish or foreign laboratories. It also considers proposals of meetings submitted to the Centre by Spanish or foreign scientists, selecting and approving those it feels deserve support.

In general terms, the Scientific Council advises the Centre for International Meetings on Biology on any scientific subject or issue falling within the scope of the Center's activities.

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