The Year of Louis Pasteur International Symposium: "From Spontaneous Generation to Molecular Evolution"

The year 1995 was designated "The Year of Louis Pasteur" to commemorate the centenary of his death. The Institut Pasteur and UNESCO organized International Symposia, one in each of the five continents of the world, to allow the scientific community to pay a tribute to Pasteur and discuss the current progress and new perspectives on Pasteur's major discoveries and their impact on health, agriculture, industry and environment.

The first International Symposium of the "The Year of Louis Pasteur" was related to one of the most exciting discussions in science - spontaneous generation and molecular evolution - and held at Rio de Janeiro, Brazil, February 19 - 24, 1995. The event organized jointly by the Institut Pasteur, UNESCO and the Oswaldo Cruz Foundation (FIOCRUZ) brought together 310 scientists from Latin America, USA and Europe and 30 invited speakers from all over the world.

The organizers of the Symposium François Jacob (Institut Pasteur), Ignès Ullmann (Institut Pasteur), Luiz Hildebrando Pereira da Silva (Institut Pasteur) and Eloi S. Garcia (FIOCRUZ) set out to assess the state of the art of the origin of life and its evolution, including a discussion of some parasites. These points are more than merely of scientific interest. Far from being the great unknowns, genes are presently intensively studied and by about the year 2000, the complete sequence of the three thousand million letters of the human DNA should have been determined. Furthermore, two out of three people will die for reasons connected directly with the genes they carry or with genes of virus, bacteria or parasites with which they are infected. Molecular biology is bringing the hope of curing and controlling pathologies and, most of all, has transformed our view of life and nature. Based on these considerations thirty lectures were selected and organized into four sessions: 1 - Catalysis, 2 - Metabolism, 3 - Macromolecules and 4 - Cells.

The Introductory Remarks of the first session were made by François Jacob (Paris, France) with a review of Pasteur's work that demonstrated that life exists only when and where there was already life. Pasteur posed in clear terms the problems of the origin of life and subsequent evolution, and since that time, the study of the origins of life has become an active focus of research for biologists. Leslie Orgel (San Diego, USA), Jack Stozostak (Boston, USA) and Steven Benner (Zürich, Switzerland) reported works on catalysis and the origin of life. They discussed the possibility that activated nucleotides generated by synthesis of random sequence chains of RNA or of some RNA precursors might be the origin on the primitive earth of ribozymes capable of catalyzing the replication of RNA. François Michel (Gif/Yvette, France) described work which showed the patterns of the diversifying evolution of catalytic introns and intron-encoded proteins. The session closed with Daniel Koshland Jr (Berkeley, USA) who reviewed the nature of conformational changes and their dramatic effects on binding and enzyme catalysis.

The second session began with A. Graham Cairns-Smith (Glasgow, UK) who presented data on the evolution of primary metabolism and the question whether metabolic pathways evolve backwards or forwards. Antoine Danchin (Paris, France) reviewed the relationship of the intermediary metabolism and the origin of translation. He pointed out the role of peptides or related compounds in their own synthesis and also the synthesis of coenzymes and nucleotides. The enigma of secondary metabolism and its possible function as a protector against predators as transporting or signaling molecules and as an antibiotic was reported by Julian Davies (Vancouver, Canada). He pointed out the role of secondary metabolites as chemical fossil molecules effective in early biosynthetic reactions, prior to the appearance of enzymes. Philipe Marlière (Paris, France) reported the question of the enormous diversity of living organisms and the remodeling of the chemical constitution of living organisms based on different arrangements of a limited number of building-blocks, mainly amino acids, nucleotides and coenzymes. Jorge Allende (Santiago, Chile) described the structure and function of nuclear protein kinases and their roles in signal transduction, metabolic regulation and cell proliferation. Monica Riley (Woods Hole, USA) closed the session reviewing genes, proteins, enzymes and reactions of *Escherichia coli*. She reported on the complexity of genes responsible for the catalytic competence of enzymes of this microorganism.

Session three began with Walter Gilbert (Cambridge, USA) who reported data on the evolution of introns and exons and hypothesized that the first genes were assembled by recombination with introns and used the exons as modular units to synthesize proteins. Peter Starlinger (Köln, Germany) described the transposable elements as objects of study and tools for research. Giorgio Bernard (Paris, France) discussed the isochore organization, gene distribution and the evolution of the vertebrate genome. Computational approaches to the comparison and clustering of protein folds into superfamilies, were reported by Tom Blundell (London, UK) to explain the nature of the folds, their functions and various models of the evolution of proteins. August Böck (München, Germany) reviewed the flexibility of the genetic code using as a model the amino acid selenocysteine which is pre-

sent in the active site of several enzymes, and the incorporation into the respective protein that is directed by a TGA codon in the DNA. Kenneth Stuart (Seattle, USA) presented data on (i) the complexity of the RNA editing mechanism in kinetoplastids; (ii) the correlation between extensive editing that is primitive and early divergence of a species, and (iii) the loss of the need for editing of an RNA may induce a retrotransposition of edited sequence into the structural gene. The structure and the immunodominant domains of trans-sialidase and trans-sialidase-like glycoproteins and their essential role in the invasion of *Trypanosoma cruzi* into mammalian cells were discussed by Alberto Carlos Frach (Buenos Aires, Argentina). The session closed with Charles Weissman (Zürich, Switzerland) who presented work on the transmissible agent that causes spongiform encephalpathies such as scrapie, the prion, which is believed to be devoid of nucleic acid and identical to a modified form of a host protein encoded by a single copy gene, and found predominantly on the surface of neurons.

The final day set the "cells" under the spotlight. Guy Ourisson (Strasbourg, France) began with data on the origin of cell membranes (terpenoid theory) and evolution of terpenoids, present in sediments like shales, petroleum or coals, into cholesterol. Miroslav Radman (Paris, France) reported experiments that showed interspecies gene exchange in bacteria and the role of SOS and mismatch repair systems in sequence divergence (evolution) and in genetic isolation (speciation) of species. Rafael Palacios (Cuernavaca, Mexico) summarized the evolution of bacterial genomes with emphasis on the gene amplification in *Rhizobium*, the bacteria that establish nitrogen-fixing symbioses with the roots of leguminous plants, and proposed a model of the *Rhizobium* genome based on the presence of amplicons. Luis Pereira da Silva (Paris, France) attended to recent information on the evolution of *Plasmodium* and its genetic polymorphism mainly on allelic polymorphism, gene duplication, polymerization of gene segments and antigenic variation, and eventual construction of new open reading frames sequences. Zigman Brener (Belo Horizonte, Brazil) introduced *Trypanosoma cruzi* as a model for cell biology studies. He presented data on the different genetic characteristics that cause intriguing intraspecific population of this parasite. Nancy Saravia (Cali, Colombia) discussed the host-parasite interaction between human host/*Leishmania* of the *braziliensis* complex, and the cellular and molecular bases of human susceptibility and resistance to the parasite. Yeast and its EEC genes and *Saccharomyces* as a model for understanding the integrated circuitry of a eukaryotic cell and for isolation and functional characters of the genes/proteins from higher organisms were discussed by Piotr Slonimski (Gif/Yvette, France). The concluding remarks were made by Joshua Lederberg (New York, USA) who gave a fascinating conference on the reconstruction of origin of life, eobiology, the ultimate creation myth of science. He gave insights for three fields of investigation on the origin of life: (i) the reconstruction of plausible emulations of biopoiesis in the laboratory; (ii) observational evidence and palaetiological interpretation of geo- and cosmos-chemical history of organic molecules in free space and in condensates such as meteorites and comets; and (iii) the research for independent evolutions of life beyond constricted terrestrial limits - an exobiology beyond our own esobiology.

During the week of the Symposium an exhibition called "LIFE" jointly conceived by FIOCRUZ and Institut Pasteur was held where several aspects and theories of the origin of life were demonstrated. Also, FIOCRUZ invited all participants to visit its campus and to participate in a round table with the title "History of Brazilian science: relationship between Louis Pasteur and Oswaldo Cruz". In this special session François Jacob (Institut Pasteur), Nara Brito (FIOCRUZ) and Carlos M. Morel (FIOCRUZ), discussed the scientific interaction between Louis Pasteur and Oswaldo Cruz, and the common points between the creation of the Institut Pasteur in Paris and what now is known as the Oswaldo Cruz Foundation (formerly named Institute Soroterapico and later Oswaldo Cruz Institute). In the evening, a bust of Louis Pasteur (by the French artist Aronson) was unveiled at the Pasteur's square at FIOCRUZ, nearby the Castle of Manguinhos. It was a distinction for our Institution to make these tributes to Louis Pasteur and to the Symposium, and an honor that since Pasteur's time FIOCRUZ continuously maintains an excellent alliance and collaboration with the Institut Pasteur.

Therefore, the Symposium was successful and my feeling after it is that we are just in the beginning of the understanding of who we are, what we were, how nature makes us, why we age and die, and what we may become. Maybe in the year 2095, to mark the second hundredth anniversary of Pasteur's death, scientists may explain the life in our planet.

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