

FOREWORD

Luis F. Leloir

This year Dr. Luis Federico Leloir reaches his sixtieth birthday. Born in a family whose members, apart from a few lawyers, were traditionally dedicated to large farming activities, he was the first to be interested in Science. After completing his medical studies and internship in 1932, he worked intensively in the Institute of Physiology of the Buenos Aires University Medical School, on a thesis about the role of the adrenals in carbohydrate metabolism. This was the prize for the best thesis of that year (1934).

At that time he told me about his decision to devote himself to scientific research in some fundamental problem of biochemistry or cellular physiology. Conscious of his insufficient training in chemistry, he studied in the School of Chemistry of the Faculty of Sciences in order to acquire knowledge, but without taking examinations or applying for a degree in chemistry.

From 1932 to 1943 he worked in the Institute of Physiology of the Medical School, where the chairs of Physiology, Biochemistry, and Biophysics were associated and linked together for teaching and research. In 1935, he went to the Institute of Biochemistry at Cambridge, then directed by Professor F. G. Hopkins, where he worked in 1936 with M. Dixon, D. E. Green, and N. L. Edson. On his return he worked in Buenos Aires. In 1943 the Government dismissed about 50% of the University professors, including myself. Dr. Leloir resigned and went to the United States, where he worked for six months with Professor C. Cori at the Washington University Medical School in St. Louis, Missouri, and later at the Columbia University Medical School, New York, with D. E. Green, for one year.

In 1946 he returned to the recently

founded private Institute of Biology and Experimental Medicine of Buenos Aires, where the former members of the Institute of Physiology had organized a place to work.

In 1947 Mr. Jaime Campomar, a wool industrialist, and his wife, asked for my opinion on the possibility of giving funds for a Research Institute of Biochemistry. I recommended Dr. Leloir as director and the Institute of Biochemistry of the Campomar Foundation was created. Important help for the equipment and maintenance was given by the Rockefeller Foundation and later by the National Institutes of Health.

Leloir and a few devoted collaborators began their work in a small room with very little equipment, but by persistent work and technical ingenuity they made important discoveries. The laboratory was later installed in a small house, but lack of space was still a problem; many apparatuses were installed in the patio or in the entrance lobby. These precarious conditions were completed by a leak in the roof. In spite of the difficulties the work continued without interruption.

In 1958 the Ministry of Public Health gave him a much better building of two floors which has been now transferred to the National Research Council. In 1958 he was appointed Research Professor of Biochemistry at the Faculty of Sciences of Buenos Aires University, and since 1962 he has been head of the Department of Biochemistry.

Under his direction, 25 graduates are working full time in original research and have made important findings. Team work and especially individual thinking and research is the rule. The activity in the laboratory is continuous during 6 days a week and on most holidays. It ceases only on Sundays and for a short yearly vacation.

After his work on the role of adrenals in carbohydrate metabolism (1930–1935), during his stay in Cambridge he did research on ketogenesis (1936 with Edson) and on dehydrogenases (1937, with Dixon and Green). When he returned to Buenos Aires he worked with Muñoz on alcohol oxidation (1938) and later on the oxidation of fatty acids *in vitro* (1939, 1944). They obtained the first preparation free from intact cells, containing mitochondria, that could oxidize fatty acids *in vitro*.

In 1935, in collaboration with Houssay, he demonstrated the diabetogenic action of anterior pituitary extract in the absence of adrenals. Normally, somatotropin and corticoids have a synergic effect.

In 1939 he discovered hypertensin (now called angiotensin) in the venous blood of the ischemic kidney, in collaboration with Fasciolo, Brauu Menéndez, and Muñoz. They demonstrated that in conditions of ischemia the kidney secretes into the blood a substance, renin, which acts on a gamma globulin (hypertensinogen) and releases a polypeptide, hypertensin (angiotensin), with hypertensive action. Recently its role in the stimulation of the secretion of aldosterone from the adrenal has been reported. Leloir and his collaborators demonstrated the specificity of renin, the formation and inactivation of hypertensin (hypertensinase), the formation of hypertensinogen, and the mechanism of nephrogenic hypertension. They published many papers, and books in Spanish (1939), English (1939), and Italian (1951).

In the United States, he studied the formation of citric acid (1945, with Hunter), the transaminases (1945, with Green), and histamine oxidase (1946, with Green).

Returning again to work in Buenos Aires, he studied the enzyme galactokinase (1948, with Caputto, Trucco, and Mittelman) and also found that glucose 1,6-diphosphate is a coenzyme necessary for the action of phosphoglucomutase. They postulated an interesting mechanism of *trans*-phosphorylation in the transformation of glucose 6-phosphate into glucose 1-phosphate.

The enzymic transformation of galactose into glucose (1949, with Caputto, Trucco, Cardini, and Paladini) was then studied. A

deficiency in this enzymic mechanism is the cause of galactosemia, a serious and in some cases lethal hereditary disease.

This investigation led to the discovery of uridine diphosphate glucose (UDPG), the coenzyme of galactose-glucose conversion. This substance was the first nucleoside diphosphate sugar to be isolated. This type of compound has later been found to be of fundamental importance in the transformations of carbohydrates and in the transfer of glycosyl groups.

Uridine diphosphate acetylglucosamine (1952, 1953, with Cabib and Cardini), guanosine diphosphate mannose (1954, with Cabib), adenosine diphosphate glucose (1963, with Dankert and Recondo), adenosine diphosphate mannose, adenosine diphosphate galactose, adenosine diphosphate acetylglucosamine (1964, with Dankert, Recondo, and Passeron), and other nucleoside diphosphate sugars were isolated and studied in Leloir's laboratory.

The study of nucleoside diphosphate sugars has produced a revolutionary advance in the biochemistry of carbohydrates and has elucidated the biosynthesis of oligo- and polysaccharides (sucrose, trehalose, lactose, glycogen, starch, callose, cellulose, glucosamines, chitins, bacterial saccharides, glucosides, gentiobiosides, and glucuronides), the formation of pentoses, conjugation of bilirubin, biosynthesis of cerebrosides, components of the connective tissue and of plant cell walls, etc. It is a great and original achievement in modern biochemistry.

Among the highlights are the biosynthesis of trehalose (1953, with Cabib) and sucrose (1955, with Cardini and Chiriboga), and later the finding that glycogen can be formed from UDPG (1959 and 1961, with Cardini, Olavarría, Carminatti, and Goldenberg). It was later ascertained that this is the normal way of biosynthesis of glycogen, whereas phosphorylase usually only acts in the degradation of this polysaccharide.

The enzymic formation of starch was also obtained with UDPG (1960 and 1961, with Cardini and Fekete). A more efficient precursor is adenosine diphosphate glucose (1961, with Recondo).

Leloir's current interest is mainly directed toward particulate glycogen, a high mole-

cular weight form of the polysaccharide, found in the liver. Recently he and his collaborators (1965, with Krisman and Mordoh) have been able to synthesize particulate glycogen "in vitro."

Dr. Leloir is thoughtful, quiet, and prefers to work on fundamental processes or mechanisms, not in just the accumulation of isolated facts. He publishes as little as possible. He has a horror of publicity and tries with tenacity to avoid distractions.

He is stoical and meets without apparent emotion sickness and disasters or success and satisfactions. He speaks little, but with great accuracy and humor. He has a great capacity for concentration and tries to avoid travelling, committees, or lectures. He does not like routine teaching, but is ready to discuss with or give advice to his collaborators or to graduates preparing these theses. At lunch time every day there are lectures or discussions.

He has consented to give only a few lectures in scientific congresses, and has accepted positions only for the sake of helping in the training of young scientists. He has been president of the Argentine Association for the Advancement of Science and a member of the National Research Council, and of committees for the selection of professors.

Many professors have been trained in his Institute, such as C. E. Cardini, E. Cabib, A. C. Paladini, R. E. Trucco, and J. L. Reissig (University of Buenos Aires); R. Caputto (Córdoba); and J. M. Olavarría and E. Recondo (Tucumán). He has trained research students from the United States, Brasil, Japan, Israel, Peru, Spain, etc.

He is a member of the Argentine Academies of Sciences (1957) and of Medicine (1959), an Associate member of the National Academy of Sciences of the United States (1960), the Academy of Arts and Sciences

(1961), the American Philosophical Society (1963), Doctor *honoris causa* of the University of Paris (1963), Honorary President of the Spanish Society of Biochemistry, and President of the Argentine Society of Biochemistry.

He has received many prizes: for the best thesis (1934, University of Buenos Aires), Argentine Commission of Culture (1942), Biology Award of the Argentina Scientific Society (1950), awards of the Helen Hay Whitney Foundation (1958), Vaccaro Foundation (1962), and Bunge and Born (1965). He has given special lectures: Squibb Centennial (1959), Harvey Lecture (1960), Dunham Lecture at Harvard (1961), Hopkins Memorial Lecture (1963), and plenary lectures in the International Congresses of Biochemistry in Brussels (1955) and New York (1964).

Many factors explain Leloir's career: his methodic training for research in medicine, physiology, and biochemistry; and his accurate work on important subjects, without haste but without pause. He is thoughtful and works in depth with originality; he is modest, calm, and firm and works for the sake of science, not for success or the satisfaction of vanity; he publishes only the necessary minimum; he protects himself from distractions; and he loves young people and tries to train and help them. He is respected and beloved by everybody but especially by his associates. He has trained many young students of very high quality.

The scientific achievements of Leloir and his school are of great value and have opened new important avenues in science. He is a leader and also an outstanding example for the young generations. We expect that his activity will continue for many years to come.

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