Discurso de investidura como Doctor "Honoris Causa" del Excmo. Sr. D. Willy Malaisse

25 de mayo de 2009

Illustrissimo Senor Rector Carlos Berzosa Alonso-Martinez
Ladies and Gentlemen

I am most honoured by the nomination as Doctor Honoris Causa of the Universidad Complutense de Madrid. I wish first to express my deep gratitude to Professor Enrique Blasquez, Professor Jorge Tamarit and Doctor Isabel Valverde for their generous support on this occasion. I want also to thank you, Professor Enrique Blasquez, for your flattering laudatio.

Dear Colleagues,

The very short novel that I am about to tell you starts some 40 years ago in the late sixties of last century when Isabel Valverde was characterizing different circulating molecules of glucagon under the guidance of Professor Roger Unger in Dallas, Texas, whilst I had developed a new method for the measurement of insulin secretion in vivo and was initiated to pancreatic islet research under the guidance of the late Professors James Ashmore and Peter Wright in Indianapolis, Indiana, and Paul Lacy in St Louis, Missouri. If my recollection is correct, Isabel and I first met when we participated in 1967 in Atlantic City to the Annual Meeting of the American Diabetes Association.

A few years later, in 1972, I was invited to deliver the Oscar Minkowski Lecture of the European Association for the Study of Diabetes with the following title: Insulin secretion: multifactorial regulation for a single process of release [1]. This lecture was given in Madrid and since this was my first visit to Madrid, I greatly enjoyed the presence of Isabel who, on that occasion, acted as a charming guide in this impressive city.

We later decided to conduct some collaborative investigations and Isabel spent a postdoctoral year from July 1978 to June 1979 in Brussels at the Laboratory of Experimental Medicine of Brussels Free University. This research resulted in a first common publication in Science on the activation by calmodulin of adenylate cyclase in pancreatic islets [2]. From thereon and up to the present time, we further collaborated together. In this respect, and in my opinion, a most significant report was published in a much more modest journal than Science, namely Diabetes Research, it dealing with the perturbation of the anomeric specificity of glucose-induced insulin release in type 2 diabetic subjects [3]. This was the first description of a specific feature relative to the perturbation of insulin secretion in diabetes mellitus. I later proposed, with an obvious touch of immodesty, to refer to this phenomenon as an anomeric

malaise and suggested that it could be attributed to the accumulation of glycogen in the insulin-producing cells of diabetic patients.

Over the years, the interaction between our two research groups also resulted in no less than 10 doctoral theses by Spanish colleagues.

As a matter of fact, my collaboration with Spanish colleagues not only resulted in the publication of 117 original and review articles with Isabel Valverde and, since 1991, with Marisa Villanueva-Peñacarrillo and their colleagues, but also in 49 other publications with Professor Ramon Gomis from Barcelona and several of his colleagues, including Anna Novials, Ignacio Conget and Josep Vidal, to cite only a few of them, and another 30 publications with Spanish scientists from other cities in Spain such as Begonia Manuel y Keenoy, Remedios Ramirez, Carmen Segura and Bernat Soria.

In this respect, I wish to underline the most fruitful collaboration with Professor Ramond Gomis, who first also spent a sabbatical leave of one year in Brussels from September 1982 to October 1983 and later played a key role in obtaining both my nomination as Visiting Professor at the Department of Medicine of the Universidad de Barcelona from 1992 to 1994 and the attribution in 1998 of the Premio Endocrinologia of the Sociedad Española de Endocrinology y Nutricíon. Once again, a most significant study conducted by Ramond Gomis and his colleagues was not published in a quite prestigious journal but revealed a second typical feature concerning the perturbation of insulin secretion in type 2 diabetic subjects, namely a paradoxical early and transient inhibition of insulin release in response to the intravenous administration of glucose [4]. It eventually proposed that this phenomenon could also be accounted for by the accumulation of glycogen in the insulin-producing cells of diabetic patients. Incidentally, my comments so far are not meant to ignore my gratitude to about one hundred other Belgian and foreign coworkers, with a special mention for Professor Abdullah Sener with whom I am closely associated since 1972.

We are close to the end of this very shot novel.

In 2001, I was invited to deliver the Claude Bernard Lecture of the European Association for the Study of Diabetes during its annual meeting in Jerusalem [5]. It was the first time in the history of this European Association that the Claude Bernard Lectureship, usually given by a scientist close to retirement, was conferred to an investigator that had already received the Oscar Minkowski Award restricted in those early days to young research fellows below the age of 40 years. On this occasion, I proposed two new tools for the non-invasive imaging and quantification of insulin-producing cells in diabetic patients or subjects at high risk of developing diabetes mellitus.

The first tool precisely takes advantage of the accumulation of glycogen in insulin-producing pancreatic islet cells as distinct from acinar cells in situations of sustained hyperglycemia, and not surprisingly, I again called on

Isabel, Marisa and their colleagues to document that in hyperglycemic rats the glycogen content is about 75 times higher in insulin-producing cells than other pancreatic cells [6].

The second tool that I proposed for the non-invasive imaging of insulin-producing cells is mannoheptulose because we found that this heptose is transported into ß-cells at the intervention of GLUT2. Once again, I called on Spanish colleagues, in this case Ramon Gomis and Carmen Benito to refute the objection that GLUT2 is too poorly expressed in human as distinct from rodent pancreatic islet cells to allow the use of mannoheptulose as a marker of human ß-cells [7].

In conclusion, Ladies and Gentlemen, it is obvious that I would never have gained access to this podium today without the generous and valuable collaboration of these several devoted, perseverant and creative Spanish colleagues.

Please allow me, therefore, with your permission, Senor Rector, to join you now so that we may all together express, by our applause, our consideration to these several estimated Spanish scientists.

Thank you for your permission.

Thank you for your attention.

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