

COMMENTARY

Retirement of Désiré Collen

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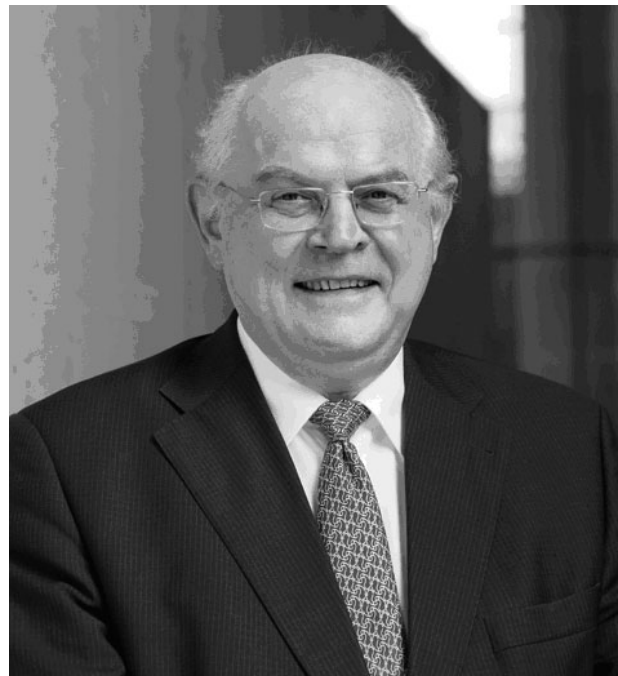
See also Rijken DC, Lijnen HR. New insights into the molecular mechanisms of the fibrinolytic system. This issue, pp 4–13; Van de Werf FJ, Topol EJ, Sobel BE. The impact of fibrinolytic therapy for ST-segment-elevation acute myocardial infarction. This issue, pp 14–20; Loges S, Roncal C, Carmeliet P. Development of targeted angiogenic medicine. This issue, pp 21–33.

Désiré Collen was born on 21 June 1943, and thus reached the official age of retirement this year. With this commentary we wish to highlight his exceptional contributions to research and development in thrombosis, hemostasis and fibrinolysis.

D. Collen obtained his MD degree in 1968 and his PhD in 1974, both at KU Leuven, Belgium. He subsequently went to the New York University Medical Center, New York (working with Allan Johnson), and to the Karolinska Institute in Stockholm (with Birger Blombäck). Besides being Professor at the Faculty of Medicine at KU Leuven, he has been Professor of Biochemistry and Medicine at the University of Vermont (VT), Visiting Professor at the Faculty of Medicine and Pharmacy of the Free University Brussels, Visiting Professor of Medicine at Harvard Medical School (Boston), Consultant in Medicine at Massachusetts General Hospital (Boston), and Visiting Professor at St Thomas' School of Medicine (London).

The scientific output of D. Collen between 1968 and 2008 consists of approximately 650 research papers in peer-reviewed international journals, 170 survey articles and 28 issued US patents. He ranked among the 100 most cited scientific authors of the 1980s and is listed with the highly cited authors of the 1980 and 1990s (<http://www.highlycited.com>).

In addition to his many other contributions to thrombosis, hemostasis and vascular biology, the landmark achievement has undoubtedly been the development of tissue-type plasminogen activator (t-PA) from a laboratory concept to a life-saving drug used worldwide for treatment of thromboembolic diseases. These initial studies were performed at the Center for Thrombosis and Vascular Research (now Center for Molecular and Vascular Biology) at KU Leuven. At the basis of the concept of fibrin specificity of t-PA was a molecular model for the regulation and control of fibrinolysis, developed together with B. Wiman, which was presented in a plenary



lecture (Edward Kowalski Memorial Lecture) at the VIIIth International Congress on Thrombosis and Haemostasis in 1979 in London. Initially, natural t-PA was purified from the Bowes melanoma cell line in sufficient amounts to study its biochemical properties and to develop quantitative assays (with D. Rijken, M. Hoylaerts, R. Lijnen, I. Juhan-Vague and C. Korninger). Its thrombolytic potential was evaluated in animal models (with O. Matsuo, B. Sobel and F. Van de Werf) and in 1981, in collaboration with W. Weimar, the first patient with renal transplant vein thrombosis was successfully treated with melanoma t-PA, followed in 1983 by patients with acute myocardial infarction (with F. Van de Werf and B. Sobel). Following the cloning and expression of the t-PA gene by D. Pennica of Genentech (published in *Nature* 1983), recombinant t-PA was studied in animal models (with H. Gold, T. Yasuda, I-K. Jang and W. Flameng). With the approval of the Food and Drug Administration, recombinant t-PA was first administered to a patient in 1984 by E. Topol. The subsequent

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NIH Thrombolysis in Acute Myocardial Infarction (TIMI) trials (led by E. Braunwald) in the USA, and the European Cooperative Study Group trials (led by M. Verstraete) provided the foundation for numerous clinical trials, culminating in the GUSTO trial (led by E. Topol and monitored by D. Stump on behalf of Genetech), which conclusively established the potential of t-PA for treatment of acute myocardial infarction.

Since the foundation of the Center for Transgene Technology and Gene Therapy (now Vesalius Research Center) of the Flemish Institute for Biotechnology, together with Peter Carmeliet and colleagues, landmark contributions were also made to the fields of vascular biology, tumour biology and neurobiology.

For his scientific achievements, Désiré Collen was awarded the degree of Doctor Honoris Causa at the Erasmus University (Rotterdam, 1988), the Free University of Brussels (Brussels 1994), the University of Notre Dame (Notre Dame IN, 1995) and the Université de la Méditerranée (Marseille, 1999). He is also a member of the Royal Academy of Medicine of Belgium. He was also awarded numerous national and international scientific prizes, including the prestigious 'Francqui-Prijs' (1984), the 'Prix Louis Jeantet de Médecine' (1986), the 'Bristol-Myers-Squibb Award for Cardiovascular Research' (1994, jointly with M. Verstraete) and the 'Health Prize of the Interbrew-Baillet Latour Fund' (2005, jointly with P. Carmeliet).

D. Collen, together with M.M. Samama, F. Bachmann, P. Brakman and J.F. Davidson, is one of the founders of the International Society for Fibrinolysis and Proteolysis (ISFP), a not-for-profit organization that aims at the 'furtherance of scientific research relating to fundamental and medical aspects of fibrinolysis, thrombolysis and proteolysis' (<http://www.fibrinolysis.org>). At present, the Journal of Thrombosis and Haemostasis is also the official journal of the ISFP, with R. Medcalf as Associate Editor for the section on Fibrinolysis.

D. Collen was Vice-President of the XIth International Congress on Thrombosis and Haemostasis (Brussels 1987) and President of the XIIth International Congress on Fibrinolysis (Leuven, 1994). He also served on the Council of the ISTH and was chairman of the Subcommittee on Fibrinolysis.

In 1988, the 'D. Collen Research Foundation' was created with a mission to use part of the royalties earned on the t-PA patent to further scientific research. This Foundation has over the years generously supported scientific meetings and young investigator grants. In addition, part of the royalty income was invested in the infrastructure of the laboratory in Leuven, making it a true state-of-the-art facility. In 2007, the name of the Foundation was changed into 'Life Sciences Research Partners, VZW' of which Désiré is the statutory Chairman.

In addition, the successful creation of the spin-off company ThromboGenics testifies for his managerial and business talents. He had indeed been doing translational research before the term was coined. Recently a strategic alliance was concluded with Roche, for the development of a PIGF neutralizing antibody for anticancer therapy.

In this issue, three review articles are dedicated to the main research topics of D. Collen, spanning almost 40 years: regulation of fibrinolysis, development and improvement of thrombolytic agents, and vascular biology focusing on angiogenesis. In the first contribution, D. Rijken and H.R. Lijnen review new insights into the regulatory mechanisms of fibrinolysis. F. Van de Werf, E. Topol and B. Sobel discuss the impact of fibrinolytic therapy on treatment of acute myocardial infarction over the past decades. In the third review, S. Loges, C. Roncal and P. Carmeliet focus on the development of targeted angiogenic medicine.

The most generous way in which D. Collen has always shared reagents, sometimes uniquely available from his laboratory, has greatly promoted research on fibrinolysis and thrombolysis and has had a major impact on the career of many colleagues in the field.

On behalf of his many colleagues and friends we thank him for this and wish him good health, happiness, success and exciting new experiences during the years to come.

Disclosure of Conflict of Interests

The author states that he has no conflict of interest.