

Editorial

Kinins 1925–2000

This volume contains selected contributions from an international conference held June 1–3, 2000, in Munich, which was devoted to the 75th anniversary of the discovery of kinins. The surgeon Emil-Karl Frey, a scholar of the famous 'Geheimrat' Ferdinand Sauerbruch, observed in 1925 a considerable reduction in blood pressure when he injected the urine of humans into dogs. Unlike many other contemporary scientists he did not attribute this effect to a toxic action of urine, but to the specific response to a substance with potential biological functions (Frey, 1926; Frey and Kraut, 1926): 'It is a substance that probably originates from several organs, is eliminated by the kidneys and has a pronounced cardioactive and vasoactive effect; a substance that is assigned the role of a hormone in the organism'. This F-substance was later termed kallikrein (Kraut *et al.*, 1930). Ten years later Eugen Werle (Werle *et al.*, 1937) found out that kallikrein is a proteolytic enzyme ('ferment'), which liberates the biologically highly active, basic polypeptide 'DK' or kallidin from a blood plasma protein, kallidinogen or kininogen. Hence, kallidin was the first of the basic tissue hormones, later known as kinins, to be described in greater detail, especially regarding its manifold pharmacological effects (Frey *et al.*, 1950). Werle also observed for the first time irreversible 'fermental degradation' of kallidin by 'kininases' and identified the kininases as peptidases (Werle and Grunz, 1939). Hence, the fundament of the system that we refer to today as the kallikrein-kinin system was set up by Frey, Kraut and Werle (see Figure 1).

The vital importance of the kallikrein-kinin system for fundamental mechanisms in biochemistry, patho/physiology, pharmacology, and more recently in molecular bi-

ology and cell biology, which are also of great interest and practical benefit to medicine, has stimulated scientists of various disciplines worldwide to become involved in kallikrein-kinin research. Included are also those scientists working on numerous regulatory or mediator systems cooperating with the kallikrein-kinin system. In this issue of *Biological Chemistry*, leading experts in their particular field have reviewed present knowledge or reported recent developments in topics of major interest, especially regarding the regulation, intracellular signaling events and functions of kinin receptors, the regulatory or therapeutic potential of kinin receptor antagonists in biology, pharmacology and medicine, as well as special cellular events associated with the kallikrein-kinin system. In view of the present political and economic pressure to produce applicable results in science in a minimum of time, we would like to mention that only recently, *i. e.* 70 years after the discovery of the kininases, was the therapeutic effectiveness of a drug for coronary heart disease proven in extensive clinical studies that were based on the seminal discoveries outlined above (The HOPE Study Investigators, 1996; The Heart Outcome Prevention Evaluation Study Investigators, 2000). This drug, an angiotensin I converting enzyme inhibitor, simultaneously blocks the degradation of kinins and the generation of angiotensin II, two tissue hormones exhibiting opposite biological or pharmacological effects.

A sense of tradition, combined with the concentration in Munich of research activities associated with the kallikrein-kinin system, kept the memory of the two scientists from the University of Munich, Emil-Karl Frey and Eugen Werle, alive and led to the establishment of the 'E.K. Frey-E. Werle Foundation of the Henning L. Voigt Family' in 1985 (see Figure 2). The purpose of the Foundation is the promotion of science and research in the fields of cardiology, hemostasiology and metabolism, to elucidate the functional role of the kallikrein-kinin system as well as of systems communicating with it. The Foundation bestows two types of awards: The Commemorative E.K. Frey-E. Werle Medal in Gold, to honor outstanding achievements in the kallikrein-kinin and related fields, and the E.K. Frey-E. Werle Promotion Prize for younger scientists who have made important contributions to contemporary research. The Honorary Membership Medal of the Foundation in Silver is awarded to scientists who contributed to our knowledge on the role of the kallikrein-kinin system in health and disease over decades so that their research activities have significantly influenced the development in the field, and also to scientists or persons with special merits regarding the objectives of the Foundation.



Fig. 1 The Surgeon Emil-Karl Frey (left), the Chemist Eugen Werle, and the Physiologist Heinrich Kraut (right).



Fig. 2 The Family of the Founder Henning L. Voigt (right), his son Jason and Mrs. Gerda Voigt-Garcia.

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