



## Prof. Héctor Croxatto

Professor Emeritus at the Pontificia Universidad Católica de Chile, Presidente y Fundador, Fundación Chilena de Hipertensión Arterial 'Dr. Héctor Croxatto Rezzio'



### **Most important awards, prizes and academies**

*Awards:* National Award of Science, Educational Board of the Chilean Government, Chile (1979); Bernardo Houssay Award, Organization of American States (1981); J. Gomez-Millas medal in recognition of his activities as a Scientist-Humanist (1994). *Academies:* Academia Chilena de las Ciencias; Academia Chilena de Medicina; Academy of History; Pontifical Academy of Sciences; Sociedad Médica de Santiago, Sociedad Chilena de Medicina Interna. Since 1990 President of the Academia Ciencias LatinoAmericanas, succeeding the illustrious Professor Carlos Chagas. *Honours:* Doctor Scientiae et Honoris Causa, Pontificia Universidad Católica de Chile (1983); Hijo Ilustre de la Ciudad de Temuco (1989); Reconocimiento Ciencia y Sociedad, de la Comisión Nacional de Investigación Científica y Tecnológica, Conicyt (2001); Grado de Doctor Honoris Causa, Universidad Metropolitana de Ciencias de la Educación (2002).

### **Summary of scientific research**

Since 1938 most of the research work of H.R. Croxatto was devoted to the biological actions of vasoactive peptides, particularly in the realm of circulatory homeostasis. One of the first

discoveries showed that the proteolytic hydrolysis (with pepsin) of plasma proteins (globulins) gives rise to potent peptides acting upon smooth muscles (vessels, uterus) and kidney functions. These findings provided strong support to the concept that still unknown peptidic molecules could have a broad and fundamental role in biological regulations. In the decade 1940-50, several peptide fractions released under the action of pepsin upon blood proteins were identified: pepsitensin, pepsitocin, pepsanurin and later anephrotensin. Among these peptides, pepsitensin and pepsitocin were of particular interest because, according to studies done in other laboratories, they were identical to angiotensin I (which is the precursor of angiotensin II, the most potent vasoconstrictor substance) and a precursor of bradykinin (one of the most potent vasodilator substances in vertebrates) respectively. Angiotensin and bradykinin have an important role in blood pressure regulation. In his final years Dr. H.R. Croxatto was engaged in the study of the renal kallikrein-kinin system, which appears to be involved in the mechanism of arterial hypertension. In 1970, he discovered that the urine of hypertensive rats has significantly lower amounts of kallikrein than the urine of normotensive rats. This finding opened up a wide field of research in order to elucidate the role of this system in the mechanism of blood pressure regulation in animals and human beings.

### Main publications

Croxatto, H.R., Huidobro, F., Croxatto, R. et Salvestrini, H., 'Action cholinestérasique du sang veineux pendant l'excitation musculaire directe et indirecte', *Compt. Rend. Seanc. Soc. Biol. Paris*, 130, p. 326 (1939); Croxatto, H.R. and Croxatto, R., 'Pepsitensin – A hypertensin-like substance produced by peptidic digestion of proteins', *Science*, 95, p. 101 (1942); Croxatto, H.R., Rojas, G. and Barnafi, L., 'The liberation of antidi- uretic factor by the hypertensinogen pepsin reaction', *Acta Physiol. Latinoamer.*, 2, p. 178 (1951); Croxatto, H.R., Pereda, T. and Mellada, R., 'Peptides with oxytocin and pressor activity obtained from acidified rat serum', *Nature*, 184, p. 1496 (1959); Croxatto, H.R. and Barnafi, L., 'Hormone and hormone-like activity of active polypeptides', *Rec. Prog. Horm. Res.*, 16, p. 236 (1961); Croxatto, H.R. and Belmar, J., 'Hypertensive effects of bradykinin in rats', *Nature*, 192 (4805), p. 879 (1961); Croxatto, H.R., Pereda, T., Belmar, J. and Labarca, E., 'Polypeptides formed by acidification of blood serum', *Ann. N.Y. Acad. Sci.*, 104, p. 146 (1963); Croxatto, H.R. and San Martin, M., 'Kallikrein-like activity in the urine of renal hypertensive rats', *Experientia*, 26, p. 1216 (1970); Roblero, J., Croxatto, H.R., García, R. and Corthorn, J., 'Kininogenase in urine produced by isolated perfused Rat Kidneys', *Experientia*, 30 (7), p. 771 (1974); Porcelli, G., Marini-Bettòlo, G.B., Croxatto, H.R. and Di Iorio, M., 'Purification and chemical studies on rabbit urinary kallikrein', *Italian J. Biochem.*, 23 (3), p. 154 (1974); Porcelli, G., Bianchi, G. and Croxatto, H.R., 'Altered urinary kallikrein in spontaneously hypertensive rats, selectively bred', *Life Sci.*, 16 (5), p. 818 (1974); Croxatto, H.R., Albertini, R., Arriagada, R., Roblero, J., Rojas, M. and Rosas, R., 'Renal urinary kallikrein in normotensive and hypertensive rats under enhanced urinary excretion of water electrolytes', *Clin. Sci. Mol. Med.*, 51, p. 3259 (1976); Roblero, J.S., Croxatto, H.R. and Albertini, R.B., 'Release of renal kallikrein to the perfusate by isolated rat kidney', *Experientia*, 32, p. 1440 (1976); Croxatto, H.R., Silva, G. and

Boric, P.M., 'Inhibition of kallikrein excretion by renin purified extracts', *Clin. Sci. and Mol. Med.*, 57, pp. 243-5 (1979); Rosar, R., Albertini, R. and Croxatto, H.R., 'Arterial pressure, plasma volume and the renal Kallikrein System in rats', *Hypertension*, pp. 13-20 (H. Villareal, ed.), published by J. Wiley and Sons, Inc., copyright (1981); Croxatto, H.R., 'Changes in renal kallikrein activity during pregnancy in rats', *Arch. Biol. Med. Exp.*, 15, pp. 305-8 (1982); Croxatto, H.R., Rosas and Gengler, J., 'Potentiating effect of Aldosterone in the diuretic action of atrial extract', *Exp.*, 43, pp. 604-66 (1987); Croxatto, H.R., 'Blood plasma proteins as substrates for the formation of Peptide Hormones', in *International Symposium on Biologically Active Proteins and Peptides* (S.H. Chiou, K.T. Wang and Sh. Wu, eds.), pp. 23-7 (1988); Boric, P.M., Croxatto, H.R., Albertini, R. and Roblero, S.J., 'Inhibition of Atrial Natriuretic Peptide-Induced Natriuresis by Plasma Hydrolysates Containing Pepsanurin', *Hypertension*, pp. 243-50 (1992); Croxatto, H.R., Boric, P.M., Roblero, S.J. and Albertini, R., 'Blunting effect of Pepsanurin Introduced in the Duodenum on ANP Diuretic Action in Rats', *Proc. Soc. Exp. Biol. and Med.*, 202, pp. 321-76 (1993); Croxatto, H.R., Silva, R., Figueroa, X., Albertini, R., Roblero, J. and Boric, M., 'A Peptide Released by Pepsin from Kininogen Domain 1 is a Potent Blocker of ANP Mediated Diuresis Natriuresis in the rat', *Hypertension*, 30, pp. 897-904 (1997); Croxatto, H.R., Figueroa, X., Roblero, J., Albertini, R., Ross and Boric, M., 'A fragment of human kininogen containing Bradykinin blunts the Diuretic Effect of Atrial Natriuretic Peptide', *Proc. Soc. Exp. Biol. and Med.*, pp. 212-34 (1996); Croxatto, H.R., Figueroa, X., Roblero, J., Boric, M., 'Kinin B2 receptors mediate of ANP Natriuresis Induced by Glucose or feeding in fasted rats', *Hypertension*, accepted for publication (1999).