

Dr. Adolfo José de Bold

*Students often ask how to proceed to succeed in research; my usual answer is:
“Have a dream, don’t think small, work hard, and believe in yourselves.”*

I conclude by thinking to myself: “...and pray not to make a mistake.”

Adolfo José de Bold

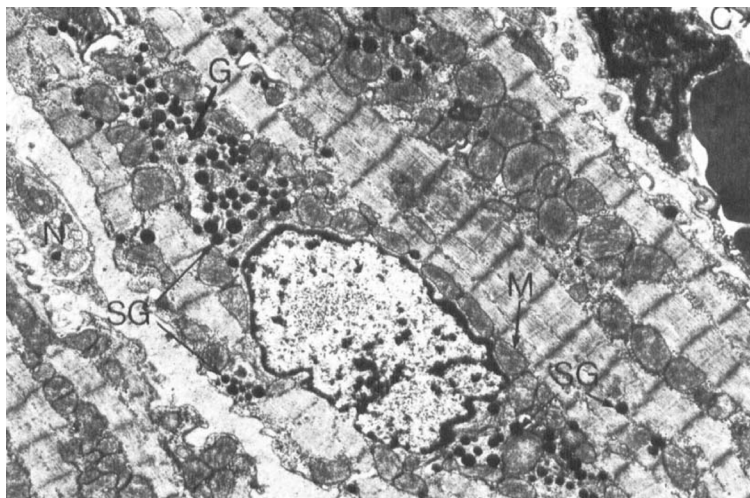


Fig. 1. Section through a portion of the rat atrial wall. Central sarcoplasmic core from an atrial muscle. The cell shows numerous specific granules (SG), mitochondria (M), and Golgi complex profiles. From: De Bold AJ, Bencosme SA. Studies on the relationship between the catecholamine distribution in the atrium and the specific granules present in atrial muscle cells. 1. Isolation of a purified specific granule subfraction. *Cardiovasc Res.* 1973 May;7(3):351-63. doi: 10.1093/cvr/7.3.351



Fig. 2. Adolfo J. de Bold receives the 2014 Lefoulon-Delalande Award of the French Academy of Sciences presented by Alain Carpentier.

Investigations into the mixed muscle–secretory phenotype of cardiomyocytes from the atrial appendages of the heart led to the discovery that these cells produce, in a regulated manner, two polypeptide hormones, the natriuretic peptides, referred to as atrial natriuretic factor or atrial natriuretic peptide (ANP) and brain or B-type natriuretic peptide (BNP), thereby demon-

strating an endocrine function for the heart. Studies on the gene encoding ANP (NPPA) initiated the field of modern research into gene regulation in the cardiovascular system. Additionally, ANP and BNP were found to be the natural ligands for cell membrane-bound guanylyl cyclase receptors that mediate the effects of natriuretic peptides through the generation

of intracellular cGMP, which interacts with specific enzymes and ion channels. Natriuretic peptides have many physiological actions and participate in numerous pathophysiological processes. Important clinical entities associated with natriuretic peptide research include heart failure, obesity and systemic hypertension. Plasma levels of natriuretic peptides have proven to be powerful diagnostic and prognostic biomarkers of heart disease. Development of pharmacological agents that are based on natriuretic peptides is an area of active research, with vast potential benefits for the treatment of cardiovascular disease.

Goetze JP, Bruneau BG, Ramos HR, Ogawa T, de Bold MK, de Bold AJ. Cardiac natriuretic peptides. *Nat Rev Cardiol.* 2020 Nov;17(11):698-717. doi: 10.1038/s41569-020-0381-0.

Dr. Adolfo J. de Bold, the Argentine researcher who discovered atrial natriuretic peptide, passed away on October 22, 2021, in Ottawa, Canada.

Some years ago, one of the authors of this obituary (ARdIS) had the idea of writing a book on "Argentines who Improved the World's Medicine" and invited another of the authors (CAB) to write the chapter dedicated to Adolfo de Bold, as they were old friends and he shared with Dr. de Bold a long and fruitful epistolary dialogue.

Adolfo José de Bold was born on February 14, 1942, in Parana, Entre Rios. His family was made up of his father, who was secretary of the Mid-Parana section of the Ministry of Public Works, his mother, a housewife, school and piano teacher, and his elder sister, who was also a school teacher. He attended elementary school and up to the 3rd year of high school at *Escuela Normal Superior José María Torres* and completed high school at the *Colegio Nacional Domingo F. Sarmiento*. As a student he played many sports, from basketball and rugby to competitive rowing. He learned soccer and tango in Canada. Although he had never played soccer or danced tango, both remained as stigmas of an exiled Argentinean. He began studying biochemistry at the National University of Litoral, in Rosario, but the political instability in 1966 with the fall of President Arturo U. Illia, and the advent of the so-called *Revolución Argentina*, unleashed student demonstrations that finally led to the loss of the academic year. Then, de Bold enrolled in the career of biochemistry at the National University of Cordoba, where he was able to make up for the academic year by sitting for all the exams as an independent student. Of his time in Cordoba, de Bold recalled his love for Argentine folk music and his early passion for astronomy. Two years before graduating, he joined the Chair of Pathology directed by Prof. Enrique Mosquera at *Hospital de Clínicas* as volunteer teaching assistant, where he developed a prolific scientific activity and also met his future wife, the biochemistry student Mercedes

Lina Kuroski. De Bold also worked as teaching assistant in Physics and then in Normal and Pathological Histology and completed his undergraduate training at the Faculty of Chemical Sciences of the National University of Cordoba, where he graduated as a clinical biochemist in 1968. Dr. Juan Lechago made the arrangements so that de Bold could then move to Queen's University in Canada to work with his wife in the service directed by Dr. Sergio A. Bencosme Ruíz. While Dr. Kuroski was involved in matters related with pancreatic beta cells, de Bold gained enthusiasm for the atrial cells of the mammalian heart. These cells had granules but nothing was known about their chemical composition and functions. Kuroski and de Bold enrolled in a Master's program and then in the Ph.D. program at the School of Graduate Studies of Queen's University, Kingston, Ontario, Canada, for a total of six years. In 1985 de Bold became a professor at that university and in 1986, director of research at the University of Ottawa Heart Institute, a position he held until 1993. In 2008, de Bold was appointed Director of the Cardiovascular Endocrinology Laboratory at the University of Ottawa Heart Institute and Professor of Pathology and Cellular and Molecular Medicine at the University of Ottawa.

De Bold began his research studying the storage granules found in the atria, and hypothesized that these structures are linked to a hormone secreted by the heart that regulates blood pressure in relation to fluid and sodium balance. The studies by de Bold and Kuroski, together with Harold Sonnenberg, a physiologist at the University of Toronto, showed that a substance contained in the atrial granules has a potent hypotensive and natriuretic action, similar to that of a potent diuretic drug such as furosemide. In 1980, this research led to the discovery and isolation of atrial natriuretic peptide (ANP), a polypeptide hormone released by cardiac atrial muscle cells of mammals. This was the first demonstration of the endocrine function of the heart. De Bold's team then began studying how the heart modulates blood pressure, blood volume and cardiovascular growth through natriuretic peptides. De Bold published more than 100 papers, most of them related to these peptides. His discoveries opened up new fields of research that have led to multiple applications for diagnosis, prognosis and therapy, particularly in heart failure.

De Bold received countless awards for his work and was a member of the Royal Society of Canada and the American Association for the Advancement of Science. In 1992, he was made an Officer of the Order of Canada and in 2014, he was inducted into the Canadian Medical Hall of Fame.

As CAB comments in an intimate mood, "...I could not meet him on his last visit to Buenos Aires in 2018, as it coincided with my granddaughter Josefina's birth in Chile." ARdIS invited him for dinner

after a brilliant lecture at the National Academy of Medicine in Buenos Aires. Dr. de Bold was an exceptional and simple person, with an affable character and good humor. Apart from his achievements as a researcher in advanced science, youth education was one of his main concerns and a frequent topic of his lectures. This is a tribute to an eminent scientist who made an enormous contribution to medicine in

general and specially to cardiology, and who should have been awarded the Nobel Prize in Chemistry or Physiology because of the clinical implications of his discovery.

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