

PROFESSIONAL PROFILE OF CARLOS BELMONTE

Professor Carlos Belmonte, born in Albacete, Spain in 1943, obtained his MD and PhD degree with honors at the University of Madrid Medical School. He completed his research training as a NIH international Fellow in the University of Utah, where he worked with C. Eyzaguirre and the Nobel Laureate H.K. Hartline, and returned to Valladolid, Spain in 1973 as the youngest Full Professor and Chairman in a Medical School of the country. Apart of his sabbatical periods as Visiting professor in Harvard, Utah and New South Wales University of Australia, Carlos Belmonte's academic and research work, that has received international recognition, has been entirely developed in his laboratory in Spain.

Belmonte's general research interest has been centered in sensory neurophysiology, studying the cellular and molecular mechanisms of peripheral somatosensory transduction and pain. On sensory transduction Belmonte's group first demonstrated that electrical properties of primary sensory neurons are dependent on the type of peripheral sensory receptor to which they are connected. He also obtained the first direct proof in single pain corneal nerve fibers, that nociceptors have separate membrane mechanisms for transduction of mechanical and chemical noxious stimuli, and also recorded for the first time the electrical activity of a single mammalian nociceptive nerve terminal. More recently, his work in trigeminal ganglion neurons defined the contribution of non-specific ion currents to the transduction and threshold of cold thermoreceptor neurons, the modulation of TRPM8 channels by inflammatory mediators and osmolality and of TRPA1 by bacterial endotoxins. He also contributed to prove that the analgesic effect of intra-articular injection of sodium hyaluronan is due both to its buffering effect on the transmission of mechanical forces and also by the binding of HA molecules to TRPV1 channels, reducing their enhanced excitability by local inflammation.

Professor Belmonte is responsible in a large extent for our current understanding of the non-visual sensory physiology of the eye. Aside from his key demonstration of the functional modalities of corneal sensory innervation, his research has embodied a highly targeted translational element which has been of great clinical value. Professor Belmonte showed experimentally that trigeminal fibers innervating the cornea subserve the modalities of polymodal nociception, mechanoreception and thermal reception and have additional roles related to epithelial healing and ocular inflammation. This research has involved the electrophysiological characterization of these fiber types by ocular neuron intracellular and extracellular recordings, and the extracellular measurement of single parent axon and nerve terminal activity. He developed a novel aesthesiometer which allowed him to confirm the existence of qualitatively different sensory modalities in the human eye and to determine the relative contribution to sensations of the different fiber types. The breadth of his research has ranged from the study of recombinant receptor channels, the use of gene knockouts, the identification and functional characterization of receptors in sensory nerve terminals, electrophysiological studies in cultured neurons and in living animals, and the application of his findings to significant human disease. Professor Belmonte's research has identified the role the channel receptor TRPM8 as one transducer of low temperatures and osmolarity. He further showed that cold fiber activation is concerned in the regulation basal lacrimal secretion, spontaneous blinking and in the symptoms of Dry Eye Disease (DED), aging and of so-called, LASIK dry eye. Professor Belmonte's research has also identified the role of TRPV1 in ocular nociception and contributed to the development of lipid-conjugated peptides, modelled on the shape of key, conserved, functional TRP domains, which are capable of specific modulation of

TRP excitation and inhibition. This research has strong therapeutic implications. The LASIK dry eye story is an excellent example of Professor Belmonte's translational research, in areas of clinical importance. He recognized that the symptoms of LASIK dry eye were likely to entail a major neuropathic element, due to the neuropathic firing of damaged trigeminal nerve fibers. He was able to show, however, in experiments in a LASIK animal model, that the likely cause of symptoms was not a general firing of the full complement of damaged sensory fibers, but primarily, the selective firing of damaged cold fibers alone. A subtle outcome of this research is an explanation for the paradox, not yet fully explored, that the severance of trigeminal nerve fibers by LASIK surgery, can at one and the same time lead to a reduced drive to spontaneous blinking and lacrimal secretion and yet give rise to noxious symptoms. Professor Belmonte's contributions to our understanding of the sensory neurophysiology of the eye, and its contributions to ocular health and disease. Three of his patented inventions to treat pain are currently under clinical study.

In addition to the scientific achievements, Professor Belmonte has dedicated a significant effort to the advancement of medical education in Spain and to the promotion of neurosciences and eye research worldwide. He played a direct and critical role in the development of Spanish medical education as Professor of Human Physiology in Madrid and Valladolid and as Vice Chancellor for Academic Affairs and Dean of the Medical School of the University of Alicante that he contributed to create in 1980, through the implementation of novel teaching strategies and an innovative medical curriculum in Alicante that were later adopted by many medical schools in Spain, where he was President of the Spanish Society of Medical Education

Carlos Belmonte also developed a very active and prominent role in the development of world's neuroscience as Secretary-General first and later President for 6 years of the International Brain Research Organization (IBRO), that under his leadership became the largest and most influential world's neurosciences federation. Carlos Belmonte created in Alicante in 1987 the Institute of Neurosciences, a Joint Center of the Spanish National Research Council (CSIC) and the University Miguel Hernandez (UMH) that he directed continuously until 2007. The Institute of Neurosciences is today the largest neuroscience research center in the country, and one of the Excellence Research Institutions for the Government of Spain. A large number of Spanish leading university professors and researchers in physiology and neuroscience today have been trained in Belmonte's laboratory. This dedicated work was recognized internationally with the Nature 2017 Lifetime Award for Outstanding Mentorship of the journal Nature. Dr. Belmonte served in the boards of many international research institutions (Human Frontiers, European Research Council, Hellen Keller Prize, ERA-NET Neuron), as part of the Editorial board of the journals *Exp Eye Res*, *Pain*, *Mol Pain* and *Eur J Neurosci*, among others. Dr. Belmonte served in the boards of many international research institutions and belongs to the international scientific board of numerous research institutes and Foundations in Spain, Portugal, Germany, France, UK, Mexico, Japan and USA.

Dr. Belmonte's contributions have been recognized in Spain, among others, with the National Research Award "Rey Jaime I", the National Prize for Biology and Biomedicine "Severo Ochoa" and the National Award in Medicine "Gregorio Marañón", all presented by the Kings of Spain. Internationally, with the Luis Federico Leloir Award of the Government of Argentina. In eye research, he received the EA Balazs Medal of the German Ophthalmological Society, the Eucornea Medal and the European Vision Award (Europe). He is ARVO Golden Fellow and Honoree of the ARVO Foundation (USA). He has been awarded with the EA Balazs Prize of the International Society of Eye Research. Belmonte is a member of the Academia Europaea, the

National Academy of Sciences of Spain and the Akademie der Wissenschaften und der Literatur, Mainz (Germany) and *Doctor Honoris Causa* by the Universities of Castilla la Mancha, Spain and by the University of Cordoba, Argentina. Presently, he continues his academic activities as Emeritus Professor and Senior Researcher at the Instituto de Neurociencias, UMH-CSIC in Alicante, Spain.