BIOGRAPHICAL SKETCH

1. Personal data

Name: Jose Lopez-Barneo
Born: Torredonjimeno (Jaén), Spain, 1952
Status: married with two children
Position title: Professor of Physiology and Director
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2. Education/Training

University of Seville. Medical School. M.D. 1969-1975
University of Seville. Medical School. Ph.D. 1975-1977

Postdoctoral training
- Centre Nationale de la Recherche Scientifique, Department of Neurosensorial Physiology, Paris, France.
Postdoctoral work January-October 1978
- Department of Physiology. University of Pennsylvania Medical School and Marine Biological Laboratory (Woods Hole, Mass), USA.
Postdoctoral work January 1980- September 1982
- Department of Physiology and Biophysics. New York University Medical Center, USA. Postdoctoral work January-May 1983

3. Research and professional experience

3.1. Positions
2006-present. Director of the Institute of Biomedicine of Seville, University of Seville/Spanish Research Council/University Hospital Virgen del Rocío, Seville, Spain.
2006-2010. Director of CIBERNED, Spanish Network of Excellence for Research on Neurodegenerative Diseases.
1999-present. Director of Research, University Hospital Virgen del Rocío. University of Seville Medical School
1997-2001. Department Chairman, Department of Physiology, University of Seville Medical School
1991-1992 Visiting Professor. Stanford University. Sabbatical year supported by the Spanish Ministry of Science and Education
1987-1990 Department Chairman, Physiology, Department of Physiology, University of Seville Medical School
1986- present. Full Professor, Department of Physiology, University of Seville Medical School
1982-1985 Associate Professor, Department of Physiology, University of Seville Medical School
1979 Assistant Professor. Department of Physiology, University of Seville Medical School
1975-1978 Instructor of Physiology. Fellow of the "National Plan for the Training of Research Personnel". Department of Physiology, University of Seville Medical School

3.2. Membership of editorial boards of scientific journals
1986-2010. Editorial Board of the "Journal of Physiology and Biochemistry" (former Spanish Journal of Physiology)
1996-2003 Editorial Board "Physiological Reviews" (USA)
1997- 2005 Editorial Board of "The Journal of Physiology" (UK)
2000- 2008. Executive Editor of "Pflügers Archives-European Journal of Physiology" (Germany)
2001- present. Editorial Board of "Journal of Vascular Research" (Germany)
2003-present. Editorial Board of "Physiology" (USA)
2010-present. Editorial Board of "Pulmonary Circulation" (USA).

3.3. Membership of professional committees and boards
1988-1991 Commission of "Physiology and Pathophysiology" of the Spanish Medical Research Council
1988-1991 Coordinator of the Division of "Physiological Sciences" of the Commission of "Pathophysiology" of the Spanish Medical Research Council
1994-1997 President of the commission of "Physiology and Pathophysiology" of the Spanish National Research Council
1994-1998. President of the Spanish Neuroscience Association
1997. Member of the panel on "Vascular Physiology and Pathophysiology" of the International Union of Physiological Sciences
1996- present. Member of the "Dana Alliance for Brain Initiatives"
1999-present. Member of the "Academia Europaea"
2000- present. Member of the European Molecular Biology Organization
2001-2003. Member of the Scientific Committee of the Spanish Medical Research Council
2001- 2012. Member of the Advisory Board of the Spanish Ministry of Health
2002-2007 External Advisory Board of the European Neuroscience Institute (Göttingen, Germany)
2005-present. Member of the External Advisory Board of IDIBAPS (Barcelona).

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2005-present. Member of External Advisory Board of Institute of Research Vall de Hebron (Barcelona).
2008-present. Member of external Advisory Board of research institutes in hospitals: Ramón y Cajal (Madrid), San Pau (Barcelona), La Princesa (Madrid), Biodonostia (San Sebastián), Aragonés de Ciencias de la Salud (Zaragoza), Biomedicine (Salamanca).
2010-present. Member of the External Advisory Board of the Ludwig Boltzmann Institute for Pulmonary Vascular Research, Graz, Austria.
2007-2011 President of the Spanish Society of Gene and Cell Therapy.

3.3. Honors and awards

1978 Award of the University of Seville to the M.D and Ph. D. Theses
1993 National Research Award "King Juan Carlos I" in Science and Technology
1994 Medal of the Andalusian Government
1994 Wellcome Visiting Professorship Award. University of Minnesota. USA
1998 National Research Award "King Jaime I" in Science and Technology
2000 National Research Grant of the Juan March Foundation
2002 Research prize "Maimónides" awarded by the Andalusian Government
2003 Honorary Lecture "Teófilo Hernando", Autonomous University of Madrid
2003 National Research Prize of the Lilly Foundation
2003 Medal of the Spanish Ministry of Health
2004 Member of the "Real Academia de Ciencias de Sevilla"
2005 Corresponding member of the "Real Academia Española de Ciencias Exactas y Naturales"
2006 Research prize Javier Benjumea awarded by the Focus-Abengoa Foundation
2009 Prize FAMA to the Research Career by the University of Seville
2010 Award Medal and Lectures "Chair Grisolía", Foundation "Ciudad de las Artes y las Ciencias", Valencia.
2010 Honorary Lecture "Carmen and Severo Ochoa", Foundation "Carmen and Severo Ochoa", Madrid
2012 Member of the "Real Academia de Medicina y Cirugía de Sevilla".

4. Scientific/academic activity and fields of interest

After obtaining his M.D degree, Dr. Lopez-Barneo combined for a short time his Ph.D. studies with work as a family doctor. However, he soon became a full time investigator. His first research interest was the neurophysiology of the oculomotor and vestibular systems using extracellular recordings in awake cats. He was one of the pioneers of modern neurophysiological research in Spain. His most significant contribution was the identification of neurons in the nucleus prepositus hypoglossi whose firing rate encoded eye velocity and position. This work demonstrated that the prepositus nucleus, located in the lower brainstem, is a major center for gaze control in mammals (see the most relevant contribution of this period in Lopez-Barneo et al., J. Neurophysiol., 1982).

During his postdoctoral work at the U.S.A., Dr. Lopez-Barneo performed the most complete electrophysiological study to date of the parathyroid gland. This work suggested the existence in parathyroid cells of a divalent cation membrane receptor to explain the dependence of parathyroid hormone secretion on extracellular calcium concentration (Lopez-Barneo & Armstrong, J. Gen. Physiol., 1983). This seminal observation served of inspiration for the cloning of the receptor (that besides in the parathyroid gland is also found in neurons and other cell types) and the opening of a new field of cellular physiology. During this time Lopez-Barneo became also interested in the study of ion channels in the squid giant axon and the intrinsic electrophysiological properties of central neurons (representative examples of the work performed in this period are in Armstrong & López Barneo, Science, 1987; Lopez-Barneo & Llinas, J. Neurophysiol., 1988).

In 1983 Dr. Lopez-Barneo established an independent research group in the University of Seville aiming to the study of ion channel function and modulation in different neuronal and non-neuronal preparations. His laboratory was among the first to set up in Spain several techniques, now broadly used in the study of cell physiology, such as voltage and patch-clamping, amperometry and microfluorimetry in single dispersed cells as well as in fresh slice preparations. In subsequent years, the laboratory incorporated a whole set of molecular and cell biology methodologies. The most relevant scientific achievements of Dr. Lopez-Barneo's group are:
a) Analysis of the intrinsic electrical properties of septal neurons and their relationship with the generation of the theta rhythm (Alvarez de Toledo & Lopez-Barneo, J. Physiol., 1988). This work also included recordings of intradendritic action potentials, which are among the first ever performed.
b) Identification of the first oxygen-sensitive potassium channels in glomus cells of the carotid body. This pioneer work, summarized in several publications (e.g. Lopez-Barneo et al., Science, 1988; Ganfornina & Lopez-Barneo, PNAS, 1991; Ureña et al., PNAS, 1994), served not only to explain the chemosensory properties of the carotid body but, in addition, stimulated research on acute oxygen sensing in other organs. Acute oxygen sensing has become a quite attractive area of modern cellular physiology and pathophysiology (see Lopez-Barneo et al., Ann. Rev. Physiol. 2001; Weir et al., N. Eng. J. Med. 2005).
c) During a sabbatical stay at Stanford University, Dr. Lopez-Barneo worked on the identification of the molecular determinants for C-type inactivation and the interaction of external cations with the outer mouth of potassium channels. His observations, of major impact in the field (see Lopez-Barneo et al., et al., Receptor and

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Channels, 1993), were followed by several contributions on the structure/function relationship in ion channels done at his laboratory in Spain. Among these, the most representative was the identification of the first non-conducting regulatory alpha subunit in potassium channels (Castellano et al., J. Neurosci. 1997).
d) A further step toward the full understanding of carotid body physiology was the development of the carotid body slice preparation (Pardal et al., PNAS, 2000). This allowed to show that, besides sensing changes of blood oxygen tension, carotid body glomus cells are also physiologically relevant glucose receptors (Pardal & Lopez-Barneo, Nature Neurosci., 2002; García-Fernández et al., Diabetes, 2007).
e) In parallel with the studies of the effect of acute hypoxia on ion channels, Lopez-Barneo's group has also explored the possibility that ion channel-encoding genes are upregulated by chronic hypoxia. The first ion channel gene shown to be upregulated by hypoxia-inducible transcription factors is the T-type (alpha 1H subunit) calcium channel (del Toro et al., J. Biol. Chem., 2003). This group has also reported that the maxi-K+ channel beta1 subunit (a gene whose expression is almost restricted to the cardiovascular system) is down regulated by chronic hypoxia (Navarro-Antolin et al., Circulation, 2005). This observation helps to explain why in some chronically hypoxic subjects (as for example in sleep apnea patients) altered vasoregulation can lead to hypertension. It also helps understand the mechanisms underlying hypoxic conditioning in heart muscle (Bautista et al., Circ. Res. 2009).
f) The studies on smooth muscle cells have lead Lopez-Barneo's group to the description of a new metabotropic role for voltage gated calcium channels, which might have major physiological and clinical interest. In the absence of calcium influx, activation of L-type calcium channels induce in arterial smooth muscle cells stimulation of the G protein-phospholipase C pathway, inositol trisphosphate production and calcium release (del Valle-Rodriguez et al., EMBO J., 2003; del Valle Rodriguez et al., PNAS, 2006, Fernández-Tenorio et al., Circ. Res. 2010, 2011).
g) The dopaminergic nature of carotid body cells suggested that they could be used for cell therapy applied to Parkinson's disease. In 1997 Dr. Lopez-Barneo's laboratory initiated a quite original project designed to test the efficacy of intrastriatal autotransplants of glomus cells to improve parkinsonism. The excellent results observed in preclinical research in rodents (Espejo et al., Neuron, 1998; Toledo-Aral et al., J. Neurosci., 2003) and monkeys (Luquin et al., Neuron, 1999) models, lead to carry out two pilot clinical trials in patients. A first safety trial, with moderately optimistic results, (Arjona et al., Neurosurgery, 2003) was followed by a second trial using PET-scan analysis (Minguez-Castellano et al., J. Neurol. Neurosurg. Psychiatry 2007). The technology used to prepare dopaminergic glomus cells and their transplantation to Parkinson's patients is being refined based on the ability of carotid bodies to be expanded *in vitro* using stem cell techniques. Recently, Dr. López-Barneo's group has reported the discovery of stem cells in the carotid body (Pardal et al., Cell, 2007). This is the first time neurogenesis is observed in the adult peripheral nervous system in mammals, an observation that may boost further developments on cell therapy applied to neurological disorders. Indeed, a patent derived from the stem cell work performed by Dr. López-Barneo's group has been licensed by a biotechnological company, with the idea of facilitating the transference of this basic research to the clinics.
h) The increase in funding (mainly due to grants awarded by the Juan March and the Marcelino Botín Foundations) allowed Dr. Lopez-Barneo's group to setup independently the infrastructure necessary for the design and generation of genetically modified mice. The first knockout (Piruat et al., Mol. Cell. Biol., 2004) and transgenic (Mejias et al., J. Neurosci., 2006) mice ever produced in southern Spain have already been published. In addition, several other genetic animal models are being generated to study the mechanisms of oxygen sensing as well the processes underlying both cell death and neuroprotection in the nigrostriatal pathway. Recently, the absolute requirement of GDNF for maintenance of adult catecholaminergic neurons has been published (Pascual et al., Nature Neurosci, 2008). Identification of the GDNF-producing cells in the rodent striatum has also been recently achieved (Hidalgo-Figueroa et al., J. Neurosci. 2012). Other animal models with major phenotype are under study.

The research work of Dr. Lopez-Barneo has been published in more than 150 publications in highly ranked international journals indexed in PubMed and books. He has given numerous lectures and seminars in international meeting and research institutions all over the world. Dr. Lopez-Barneo is one of the most cited physiologists in Spain and has been (or is being) serving as a member in the editorial committees of the most prestigious international journals in Physiology (Journal of Physiology, Pflügers Archives, Physiological Reviews, Physiology, etc) .

In parallel with his research career, Dr. Lopez-Barneo has carried out an intense academic activity with a high teaching load to medical and graduate students. He has already sponsored 25 Ph.D. students and more that 20 postdocs from Spain, the USA and several other countries. Numerous former Lopez-Barneo's graduate students are currently either physiology full/assistant professors or staff clinicians in Spanish hospitals and universities. From the beginning of his career, Dr. Lopez-Barneo has been fully committed to the development of independent research in Andalusia, a Spanish region with little academic tradition. Dr. Lopez Barneo's has also devotedly worked for the development of high quality biomedical research within the university hospitals, to favor the connection between basic research and clinical practice. He has greatly contributed to the creation of one of the first biomedical institutes (Instituto de Biomedicina de Sevilla) that bas been built within a Spanish university hospital. Dr. Lopez-Barneo has also served as coordinator of the ENI (European Neuroscience Institute) in Seville and from 2007-2010 he was Director of the National Center of Excellence for Research on Neurodegenerative Diseases (CIBERNED).

5. List of 50 selected publications

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1. López-Barneo J, Darlot C, Berthoz A, Baker R. Neuronal activity in the prepositus nucleus correlated with eye movements in the alert cat. Journal of Neurophysiology 1981; 47: 329-352.

2. López-Barneo J, Armstrong CM. Depolarizing response of rat parathyroid cells to divalent cations. Journal of General Physiology 1983; 82: 269-294.

3. Armstrong CM, López-Barneo J. External calcium ions are required for potassium channel gating in squid neurons. Science 1987; 236: 712-714.

4. Alvarez de Toledo G, López-Barneo J. Ionic basis of the differential neuronal activity of guinea pig septal nucleus studied "in vitro". Journal of Physiology 1988; 396: 399-415.

5. López-Barneo J, López-López J, Ureña J, González, C. Chemotransduction in the carotid body: potassium current modulated by pO_2 in type I chemoreceptor cells. Science 1988; 241: 580-582.

6. López-Barneo J, Llinás R. Electrophysiology of mammalian tectal neurons "in vitro". I. Transient ionic conductances. Journal of Neurophysiology 1988; 60: 853-868.

7. López-López J, González C, Ureña J, López-Barneo J. Low pO_2 selectively inhibits K^+ channel activity in chemoreceptor cells of the mammalian carotid body. Journal of General Physiology 1989; 93: 1001-1015.

8. López-Barneo J, Castellano J, Toledo-Aral J. Tyrotropin-releasing-hormone and its physiological derivative TRH-OH inhibit Na^+ channel activity in septal neurons. Proceedings of the National Academy of Sciences (USA) 1990; 87: 8150-8154.

9. Ganfornina MD, López-Barneo J. Single K^+ channels in membrane patches of arterial chemoreceptor cells are modulated by O_2 tension. Proceedings of the National Academy of Sciences (USA). 1991; 88: 2927-2930.

10. Ganfornina MD, López-Barneo J. Potassium channel types in arterial chemoreceptor cells and their selective modulation by oxygen. Journal of General Physiology 1992; 100: 401-426.

11. López-Barneo J, Hoshi T, Heinemann S, Aldrich RW. Effect of external cations and mutations in the pore region on C-type inactivation of *Shaker* potassium channels. Receptors and Channels 1993; 1: 61-71.

12. Ureña J, Fernández-Chacón R, Benot A, Alvarez de Toledo G, López-Barneo J. Hypoxia induces voltage-dependent Ca^{2+} entry and quantal dopamine secretion in carotid body glomus cells. Proceedings of the National Academy of Sciences (USA) 1994; 91:10208-10211.

13. Franco-Obregón A, Ureña J, López-Barneo J. Oxygen-sensitive calcium channels in vascular smooth muscle and their possible role in hypoxic arterial relaxation. Proceedings of the National Academy of Sciences (USA) 1995; 92: 4715-4719.

14. Montoro R, Ureña J, Fernández-Chacón R, Alvarez de Toledo G, López-Barneo J. O_2-sensing by ion channels and chemotransduction in single glomus cells. Journal of General Physiology 1996; 107: 133-143.

15. Franco-Obregón A, López-Barneo J. Differential oxygen-sensitivity of calcium channels in smooth muscle cells of conduit and resistance pulmonary arteries. Journal of Physiology 1996; 491: 511-518.

16. López-Barneo J. O_2-sensing by ion channels and the regulation of cellular functions. Trends in Neurosciences 1996; 19: 435-440.

17. Molina J, Castellano A, López-Barneo J. Pore mutations in *Shaker* K^+ channels distinguish between the sites of TEA blockade and C-type inactivation. Journal of Physiology 1997; 499: 361-367.

18. Castellano A, Chiara MD, Mellström B, Molina A, Monje F, Naranjo JR, López-Barneo J. Identification and functional characterization of a K^+ channel a-subunit with regulatory properties specific of brain. The Journal of Neuroscience 1997; 17: 4652-4661.

19. Espejo EF, Montoro RJ, Armengol JA, López-Barneo J. Cellular and functional recovery of parkinsonian rats after intrastriatal transplantation of carotid body cell aggregates. Neuron 1998; 20: 197-206.

20. Luquin R, Montoro R, Guillén J, Saldise L, Insausti R, del Río J, López-Barneo J. Recovery of chronic parkinsonian monkeys after autotransplants of carotid body cell aggregates. Neuron 1999; 22: 743-750.

21. Pardal R, Ludewig U, García-Hirschfeld J, López-Barneo J. Secretory responses to hypoxia and tetraethylammonium of intact glomus cells in thin slices of rat carotid body. Proceedings of the National Academy of Sciences (USA) 2000; 97: 2361-2366.

22. Ortega-Sáenz P, Pardal R, Castellano A, López-Barneo J. Collapse of conductance is prevented by a glutamate residue conserved in voltage-gated K+ channels. Journal of General Physiology 2000; 116: 181-190.

23. López-Barneo J, Pardal R, Ortega-Sáenz P. Cellular mechanisms of oxygen-sensing. Annual Review of Physiology 2001; 63:259-287.

24. Pardal R, López-Barneo J. Low glucose-sensing cells in the carotid body. Nature Neuroscience 2002; 5: 197-198.

25. Toledo-Aral J, Méndez-Ferrer S, Pardal R, Echevarría M, López-Barneo J. Throfic restoration of the nigrostriatal dopaminergic pathway in long-term carotid body grafted parkinsonian rats. The Journal of Neuroscience 2003; 23: 141-148.

26. Ortega-Sáenz P, Pardal R, García-Fernández M, López-Barneo, J. Rotenone selectively blocks sensitivity to hypoxia in rat carotid body glomus cells. Journal of Physiology 2003; 548: 789-800.

27. del Toro R, Levitsky C, López-Barneo J, Chiara MD. Induction of T-type calcium channel gene expression by chronic hypoxia. Journal of Biological Chemistry 2003; 278: 22316-22324.

28. Arjona V, Mínguez-Castellanos A, Montoro RJ, Ortega A, Escamilla F, Toledo-Aral JJ, Pardal R, Méndez-Ferrer S, Martín JM, Pérez M, Katati MJ, Valencia E, García T, López-Barneo J. Autotransplantation of carotid body cell aggregates for treatment of Parkinson's disease. Neurosurgery 2003; 53:321-330.

29. López-Barneo J. Oxygen and glucose sensing by carotid body cells. Current Opinion in Neurobiology 2003; 13: 493-499.

30. Del Valle-Rodríguez A, López-Barneo J, Ureña J. Ca^{2+} channel-sarcoplasmic reticulum coupling: a mechanism of arterial myocyte contraction without Ca2+ influx. EMBO Journal 2003; 22: 4337-4345.

31. Piruat J, Pintado CO, Ortega-Sáenz P, Roche M, López-Barneo J. The mitochondrial *SDHD* gene is required for early embryogenesis and its partial deficiency results in persistent carotid body glomus cell activation with full responsiveness to hypoxia. Molecular and Cellular Biology 2004; 24: 10933-10940.

32. Villadiego J, Méndez-Ferrer S, Valdés-Sánchez T, Silos-Santiago I, Fariñas I, López-Barneo J, Toledo-Aral JJ. Selective glial cel line-derived neurotrophic factor production in adult dopaminergic carotid body cells *in situ* and after intrastriatal transplantation. The Journal of Neuroscience 2005; 25: 4091-4098.

33. Muñoz-Cabello A, Toledo-Aral JJ, López-Barneo J, Echevarría M. Rat adrenal chromaffin cells are neonatal CO_2 sensors. The Journal of Neuroscience 2005; 25: 6631-6640.

34. Navarro-Antolín J, Levitsky KL, Calderón E, Ordóñez A, López-Barneo J. Decreased expression of maxi-K^+ channel b1 subunit and altered vasoregulation in hypoxia. Circulation 2005; 112: 1309-1315.

35. Weir EK, López-Barneo J, Buckler K, Archer S. Acute Oxygen Sensing. New England Journal of Medicine 2005; 353: 1042-1055.

36. del Valle-Rodríguez A, Calderón E, Ruiz M, Ordoñez A, López-Barneo J, Ureña, J. Metabotropic Ca2+-channel induced Ca2+ release and ATP-dependent facilitation of arterial myocyte contraction. Proceedings of the National Academy of Sciences (USA) 2006; 103: 4316-4321.

37. Mejías R, Villadiego J, Pintado CO, Vime PJ, Gao L, Toledo-Aral J, Echevarría M, López-Barneo, J. Neuroprotection by transgenic expression of glucose-6-phosphate dehydrogenase in dopaminergic nigrostriatal neurons of mice. The Journal of Neuroscience 2006; 26: 4500-4508.

38. Ortega-Sáenz P, Pascual A, Gómez R, López-Barneo J. Acute oxygen sensing in heme oxygenase-2 null mice. The Journal of General Physiology 2006;128: 405-411.

39. Minguez-Castellanos A, Escamilla-Sevilla F, Hotton GR, Toledo-Aral JJ, Ortega-Moreno A, Mendez-Ferrer S, Martin-Linares JM, Katati MJ, Mir P, Villadiego J, Meersmans M, Perez-Garcia M, Brooks DJ, Arjona V, López-Barneo J. Carotid body autotransplantation in Parkinson disease: A clinical and PET study. Journal of Neurology, Neurosurgery and Psychiatry, 2007; 78: 825-831.

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41. Pardal R, Ortega-Sáenz P, Duran R, López-Barneo J. Glia-like stem cells sustain physiologic neurogenesis in the adult carotid body. Cell 2007;131:364-377.

42. García-Fernández M, Ortega-Sáenz P, Castellano A, López-Barneo J. Mechanisms of low-glucose sensitivity in carotid body cells. Diabetes 2007; 56:2893-2900.

43. Pascual A, Hidalgo-Figueroa M, Piruat JI, Pintado CO, Gómez-Díaz R, López-Barneo J. Absolute requirement of GDNF for adult catecholaminergic neuron survival. Nature Neuroscience, 2008; 11:755-761.

44. Levitsky KL, López-Barneo J. Developmental change of T-type Ca2+ channel expression and its role in rat chromaffin cell responsiveness to acute hypoxia. Journal of Physiology, 2009; 587:1917-1929.

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