



Part A. PERSONAL INFORMATION

CV date	09/12/21
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First name	David		
Family name	Macías Gutiérrez		
Gender (*)	Male	Birth date (dd/mm/yyyy)	30/01/1981
Social Security, Passport, ID number	77333662A		
e-mail	dmacias@us.es	URL Web	
Open Researcher and Contributor ID (ORCID) (*)	0000-0002-8676-1964		

(*) *Mandatory*

A.1. Current position

Position	Profesor Ayudante Doctor (Assistant Professor)		
Initial date	11/11/2021		
Institution	Universidad de Sevilla		
Department/Center	Fisiología Médica y Biofísica	Instituto de Biomedicina de Sevilla (IBiS)	
Country	Spain	Teleph. number	638975155
Key words	hypoxia, HIF, carotid body, senescence, pulmonary hypertension		

A.2. Previous positions (research activity interruptions, art. 14.2.b))

Period	Position/Institution/Country/Interruption cause
01/06/2018-10/11/2021	Research Associate/University of Cambridge/UK
21/11/2019-30/05/2020	Research Associate/University of Cambridge/UK/child birth
03/03/2014-31/05/2018	Research Associate/University of Cambridge/UK
09/10/2009-28/02/2014	Investigador postdoctoral/Universidad de Sevilla/Spain

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
PhD in Biology	Universidad de Jaén/Spain	2009
Degree in Biology	Universidad de Jaén/Spain	2003

Part B. CV SUMMARY (*max. 5000 characters, including spaces*)

After completing my bachelor's degree in Biology and a master's degree in cellular and molecular biology, I was awarded a fellowship to undertake a PhD degree at the University of Jaén (Spain) under the supervision of Dr Francisco Luque. In 2009, I completed my PhD in Biology with honours. My work was focused on eliminating the latent reservoir for HIV-1 in CD4+ T cells as eradication of HIV-1 will require a method to eliminate this reservoir (Macias, D. et al., Hum Gen Ther 2009). After concluding my PhD, I decided to change the topic of my research and I initiated a distinctive and independent line of research, first in the laboratory of Prof. José López Barneo (Instituto de Biomedicina de Sevilla IBiS, 2009-2014) and then in the laboratory of Prof Randall Johnson (Department of Physiology, Development and Neuroscience, University of Cambridge, 2014-2018). My line of research focused on how organisms respond and adapt to oxygen availability under normal and pathological conditions. In particular, I was interested in how hypoxia signalling pathway regulates the development and function of the carotid body, a peripheral chemoreceptor that controls respiratory and cardiovascular function in response to hypoxia. My studies were published in top journals for the field (EMBO Mol Med, 2014; J. Physiol, 2016 and eLife 2018 being co-corresponding author). In order to translate these findings to the clinic, I obtained funding from Peloton Therapeutics (343,092 GBP) with Dr Andrew Cowburn (Imperial College London). We showed that HIF-2a inhibition offered a beneficial effect in reverting most of the clinical parameters altered in an established preclinical model of pulmonary hypertension (Macías, D. et al., ERJ, 2020). My work was presented in multiple international



conferences including oral presentations in the prestigious Keystone Symposia (Oxford, UK, 2018 and Keystone CO, US, 2020). Additionally, I was invited to participate as a speaker in 2 local symposia in Cambridge (UK), and give seminars in London (UK), Dresden (Germany) and Cádiz (Spain).

In June 2018, I joined the laboratory of Dr Muñoz-Espín at the Department of Oncology of the University of Cambridge. Since then, my research is focused on the role of cellular senescence in lung cancer. In particular, how senescent cells communicate with neighbouring cancer cells to promote tumour growth and relapse. I am currently preparing 2 manuscripts for publication.

An important aspect of my scientific career is my ability to collaborate and interact with my colleagues helping them to achieve their goals while still delivering on my own projects. As a result, I was an essential collaborator in 14 articles (second author in 2 and third author in 7) published in very high-profile journals including 2 Nature, Cancer cell, Cell Metabolism, etc.

Besides my own research outputs, I have been committed to the supervision and mentoring of research students (1 undergraduate and 4 Master's students) as well. I have co-supervised a PhD student who passed her viva without corrections. Furthermore, I have been involved in the teaching in each of the departments I have been associated with; a total of more than 450 hours over my scientific career.

In 2020, I was awarded a MSCA-IF to return to IBiS at the laboratory of Dr Alberto Pascual. Recently, I was appointed Assistant Professor at the University of Seville where I continue my synergistic collaboration with Dr Pascual at IBiS.

Part C. RELEVANT MERITS (sorted by typology)

C.1. Publications (see instructions)

I have published a total of 23 peer-reviewed articles (20 original articles and 3 reviews) and 2 book chapters. For a complete list of publications please visit my Orcid profile.

1. **David Macias***, Stephen Moore*, Alexi Crosby, Mark Southwood, Xinlin Du, Huiling Tan, Sanhai Xie, Arlette Vassallo, Alex JT Wood, Eli M Wallace, and Andrew S Cowburn. Targeting HIF2 α -ARNT hetero-dimerisation as a novel therapeutic strategy for pulmonary arterial hypertension. **ERJ**, 2020. doi: 10.1183/13993003.02061-2019.

***joint first authors.**

2. Estela González-Gualda†, Marta Pàez-Ribes†, Beatriz Lozano-Torres†, **David Macias**, Joseph R Wilson III, Cristina González-López, Hui-Ling Ou, Zhenguang Zhang, Araceli Lérida-Viso, Juan F Blandez, Andrea Bernardos, Félix Sancenón, Miguel Rovira, Ljiljana Fruk, Carla P Martins, Manuel Serrano, Gary J Doherty, Ramón Martínez-Máñez*, Daniel Muñoz-Espín*. Galacto-conjugation of navitoclax as an efficient strategy to increase senolytic specificity and reduce platelet toxicity. **Aging Cell**, 2020. doi:10.1111/ace.13142. † joint first authors.

3. Hortensia Torres Torreló, Patricia Ortega Saenz, **David Macias**, Masayo Omura, Ting Zhou, Hiroaki Matsunami, Randall Johnson, Peter Mombaerts, Jose Lopez Barneo. The role of Olfr78 in the breathing circuit of mice. **Nature**, 2018. doi:10.1038/s41586-018-0545-9.

4. **David Macias***, Andrew S. Cowburn, Hortensia Torres-Torreló, Patricia Ortega-Sáenz, José López-Barneo, Randall S. Johnson*. HIF-2 α is essential for carotid body development and function. **eLife**, 2018. doi:10.7554/eLife.34681. ***Corresponding authors.**

5. Asis Palazon, Petros A. Tyrakis, **David Macias**, Pedro Velica, Helene Rundqvist, Susan Fitzpatrick, Nikola Vojnovic, Anthony T. Phan, Niklas Loman, Ingrid Hedenfalk, Thomas Hatschek, John Lovrot, Theodoros Foukakis, Ananda W. Goldrath, Jonas Bergh, and Randall S. Johnson. An HIF-1 α /VEGF-A Axis in Cytotoxic T Cells Regulates Tumor Progression. **Cancer Cell**, 2017. doi:10.1016/j.ccell.2017.10.003. **Feature on the cover.**

6. Andrew S Cowburn, **David Macias**, Charlotte Summers, Edwin R Chilvers, Randall S Johnson. Cardiovascular adaptation to hypoxia and the role of peripheral resistance. **eLife**, 2017. doi: 10.7554/eLife.28755.

7. Petros A. Tyrakis, Asis Palazon, **David Macias**, Kian. L. Lee, Anthony. T. Phan, Pedro. Veliça, Jia You, Grace S. Chia, Jingwei Sim, Andrew Doedens, Alice Abelanet, Colin E. Evans, John R. Griffiths, Lorenz Poellinger, Ananda. W. Goldrath, and Randall S. Johnson. S-2-hydroxyglutarate regulates CD8+ T-lymphocyte fate. **Nature**, 2016. doi:10.1038/nature20165.

8. Andrew S Cowburn, Alexi Crosby, **David Macias**, Cristina Branco, Renato Colaço, Mark Southwood, Mark Toshner, Laura Crotty Alexander, Nicholas W Morrell, Edwin R Chilvers, Randall S Johnson. A HIF2 α -arginase axis is essential for the development of pulmonary hypertension. **PNAS**, 2016. doi:10.1073/pnas.1602978113.



9. Patricia Ortega-Saenz*, **David Macias***, Konstantin L. Levitsky, Jose A. Rodriguez-Gomez, Patricia Gonzalez-Rodriguez, Victoria Bonilla-Henao, Ignacio Arias-Mayenco and Jose Lopez-Barneo. Selective accumulation of biotin in arterial chemoreceptors: requirement for carotid body exocytotic dopamine secretion. **Journal of Physiology**, 2016. doi:10.1113/JP272961. *Joint first authors. Feature on the cover.

10. **David Macias**, M. Carmen Fernández-Agüera, Victoria Bonilla-Henao, and José López-Barneo. Deletion of the von Hippel-Lindau gene in sympathoadrenal cells impairs chemoreceptor function and tolerance to hypoxia. **EMBO Molecular Medicine**, 2014. doi:10.15252/emmm.201404153. **Featured on the cover.**

C.2. Congress

My work has been presented in 23 international conferences. I will highlight those where I am first or corresponding author.

Speaker

- 2020 Keystone symposia: Hypoxia: Molecules, Mechanisms and Disease. Keystone, CO, USA. Targeting HIF2 α hetero-dimerisation as a novel therapeutic strategy for Pulmonary Arterial Hypertension
- 2018 Keystone Symposia: Therapeutic Targeting of Hypoxia-Sensitive Pathways. Oxford, UK. HIF-2 α Is Essential for Carotid Body Development and Function.

Poster presentations as first author.

- 2017 Keystone Symposia: Adaptations to Hypoxia in Physiology and Disease. Whistler, Canada. Sympathoadrenal HIF-2 α deletion impairs carotid body development and impacts on adaptive homeostasis.
- 2014 ITRIBIS: Hypoxia, molecular mechanisms and clinical translation. Seville, Spain. Deletion of the von Hippel-Lindau gene causes sympathoadrenal defects and impairs chemoreceptor-mediated adaptation to hypoxia.
- 2013 European Society of Gene and Cell Therapy. Madrid, Spain. Expansion of differentiated GDNF-producing carotid body cells by reversible lentiviral gene transfer: potential use in cell therapy.
- 2013 Oxygen 2013 meeting. Oulu, Finland. Survival in chronic hypoxia requires a proper VHL-dependent carotid body and sympathoadrenal development.
- 2012 22nd IUBMB and 37th FEBS Congress. Seville, Spain. Ablation of Vhl in tyrosine hydroxylase positive cells results in abnormal sympathoadrenal development and altered acclimatization to chronic hypoxia.
- 2012 Keystone Symposia: Advances in hypoxic signaling: from bench to bedside. Banff, Canada. Ablation of Vhl in tyrosine hydroxylase positive cells results in abnormal sympathoadrenal development and altered acclimatization to chronic hypoxia.
- 2009 Spanish Society of Gene and Cell Therapy. Granada, Spain. A lentiviral vector that activates latent HIV-1 proviruses by the overexpression of Tat and that kills the infected cells.
- 2008 XVIth Annual Congress of the European Society of Gene and Cell Therapy. Brugges, Belgium. A lentiviral vector for regulated tat expression activates HIV-1 silent proviruses in latently infected cells.

C.3. Research projects

Principal investigator:

1. Hypoxic regulation of the senescent secretome in cancer and Alzheimer's disease. **David Macias Gutierrez**. 10/01/2021-09/01/2023. European Commission (H2020-MSCA-IF-2020). 172,932.48 EUR. Grant number: 101029004.

2. The role of HIF2 α in the initiation and development of PAH. Peloton Therapeutics Inc. **David Macias Gutiérrez**. 2017-01/01/2019. 343,092 GBP. **Co-applicant.**

Co-investigator:

1 Targeting senescence in lung cancer. CRUK-Programme Foundation Award. Daniel Muñoz Espin. (University of Cambridge). 01/10/2020-30/09/2026. 1.584.852,4 €. Co-investigator.

2 Cellular plasticity and senescence at the origin of lung cancer. Medical Research Council (MRC). Daniel Muñoz Espin. (University of Cambridge). 01/06/2018-31/05/2020. Co-investigator.

3. The Physiology of hypoxic response. Wellcome Trust. Randall S. Johnson. (University of Cambridge). 01/08/2011-31/07/2018. 5.000.000 €. Co-investigator.



4. Sensibilidad al oxígeno y neurodegeneración. Ministerio de Ciencia e Innovación. Investigación. José López Barneo. (INSTITUTO DE BIOMEDICINA DE SEVILLA). 01/01/2013-31/12/2015. 468.000 €. Co-investigador.
5. Myeloid vascular endothelial growth factor expression and its role in tumorigenesis. National Institute of Health. Randall S. Johnson. (University of Cambridge). 01/01/2012-31/12/2015. Co-investigador.
6. Mecanismos moleculares de formación de tumores en modelos genéticos animales con defectos mitocondriales. Consejería de Innovación, C^a y Empresa. Junta Andalucía. José Ignacio Piruat Palomo. (INSTITUTO DE BIOMEDICINA DE SEVILLA). 03/02/2010-31/12/2014. 238.517,68 €. Co-investigador.
7. Sensibilidad al oxígeno y neurodegeneración. CIBER enfermedades neurodegenerativas (CIBERNED). José López Barneo. (INSTITUTO DE BIOMEDICINA DE SEVILLA). 01/01/2010-31/12/2012. 605.000 €. Co-investigador.
8. Sensibilidad al oxígeno y neurodegeneración Fundación Marcelino Botín. José López Barneo. (INSTITUTO DE BIOMEDICINA DE SEVILLA). 01/01/2007-31/12/2012. 220.000 €. Co-investigador.

C.4. Contracts, technological or transfer merits

Aug 2017-Mar 2018. Consultant for Apollo Therapeutics. Project: Development of CAR-T technologies to improve CD8+ T-cell memory formation and its use in immunotherapy.

C.5. Research student supervision

PhD:

1. Cellular Senescence in Non-Small Cell Lung Cancer: from mechanisms to therapeutic opportunities. Author: Estela González-Gualda. University of Cambridge, UK. Passed with no corrections the 23/11/21. Co-supervisor.

Master and undergraduate students:

1. Targeting senescence in lung cancer. Author: Joshep Wilson. Master's degree. University of Cambridge, UK. 28/01/2020. Co-supervisor.
2. Defining the paracrine effects of cellular senescence in lung cancer. Author: Estela González-Gualda. Master's degree. University of Cambridge, UK. 11/09/2018. Co-supervisor.
3. Role of sympathetic nervous system derived vascular endothelial growth factor in endothelial permeability and metastatic potential. Author: Amer Jibrán. Undergraduate final year. University of Cambridge, UK. 2017. Co-supervisor.
4. Role of Sympathetic nervous system-derived VEGF on tumoral growth and dissemination. Author: Elia Colin. Master's degree. University of Cambridge, UK. 2016. Co-supervisor.
5. Generación de vectores lentivirales para la transducción de células glómicas de cuerpo catotídeo. Author: Daniel Enterrías Morales. University of Sevilla, Spain. 2014. Co-supervisor.

C.6. Teaching

1. Department of Experimental Biology. University of Jaén. 2006-2009. 200 hours.
2. Department of Medical Physiology and Biophysics. University of Sevilla. 2011-2014. 75 hours.
3. Department of Physiology, Development and Neuroscience. University of Cambridge. 2016-2021. 228 hours.

C.7. Positions of trust.

- Reviewer for the Czech Science Foundation, the main public funding agency in the Czech Republic supporting all areas of basic research (2020).
- I was evaluator in 3 thesis dissertations: 1) 2021, Title: "Efectos de la sobreexpresión de HIF-2a en la homeostasis del páncreas exocrino"; 1) 2019, Title: "Succinate dehydrogenase: tumour suppressive role in paragangliomas"; 2) 2016, Title: "Role of GDNF and Wnt/ β -catenin signaling in pancreas development and physiology".
- I was invited to give seminars and talks at INIBICA (2021), Imperial College London (2019), Medical Faculty of the Technical University Dresden (2017), and 3 workshops in Cambridge (2017, 2016, 2014).

C.8. Outreach activities.

- 2019. Cambridge Science Festival. Design and presentation of scientific activities to lay public, particularly kids.
- 2019. Speaker at the "Pint of Knowledge". Public engagement scientific seminars organized by the Spanish Society of Researchers in UK (SRUK).