CONTENIDO DEL DOCUMENTO

1. Requisitos de los solicitantes
2. Plan de formación
3. Resumen del proyecto
4. CVA IP, CoIP

REQUISITOS DE LOS SOLICITANTES:

- ✓ Graduadas y graduados en ciencias de la salud, preferentemente en el área de Biología Sanitaria.
- ✓ Máster preferente en el ámbito de la medicina traslacional.
- ✓ Estar en posesión de la capacitación para manejo de animales de experimentación (A, B y C).
- ✓ Conocimientos de inglés.
- ✓ Conocimientos en técnicas básicas de citometría, histología, microscopía confocal, orientadas preferentemente a la fisiopatología cardiaca.
- ✓ Experiencia previa de trabajo en el ámbito de la cardiología básica.

PLAN DE FORMACION:

The group can incorporate ***one predoctoral fellow*** who can be trained in immunology, metabolism and CVDs, and electrophysiology in an integrative way. In fact, the PI and Co-PI have been collaborating for more than 10 years under the CIBERCV and the RECAVA networks. The candidate will be trained in the study of the role of AhR in cardiac hypertrophy, fibrosis, cardiac calcium dynamics and HF. This incorporation is very important to boost and increase the research career of the post-doctoral and senior members of the group. The new fellow will work in the development of animal models, the design and use of cardiac 3D-structures oriented to translate the findings to human chronic HF, and all this in the context of the most prevalent CVDs. Special attention will be paid to the formation in the use of omic techniques, the analysis of the biomolecules involved and the design of biomarkers of adverse cardiac remodeling and HF progression. The targeting of AhR and ferroptosis is the nucleus of the formative activities. In terms of training, we suggest routinely our students to perform high-level courses relevant to their professional careers. All previous predoctoral fellows in the group have been doing short-term stays in other national and international laboratories for periods of 3-6 months, at the time that conducted specific experiments in laboratories where unique techniques were included in their routine. The aim was to boost their training and to encourage them to continue a research career, in some cases with relevant publications as predocs. Finally, at the moment of submission of the thesis, all predoctoral fellows in the group had various publications, and most of them received 'PhD extraordinary awards'. In summary, the formative activities involve: Organization and critical review of the research results, improvement of research skills and critical knowledge of the techniques acquired; formation in research management to guarantee the sustainability of our group; development of oral and written communication skills.

RESUMEN DEL PROYECTO

La insuficiencia cardíaca es un síndrome clínico complejo que constituye un problema importante de salud cuyo tratamiento sigue siendo ineficaz durante ca. más de la mitad de los pacientes, a pesar de la introducción de diferentes intervenciones terapéuticas. De hecho, la insuficiencia cardíaca sigue siendo una de las principales causas de morbilidad y mortalidad en todo el mundo, y representa una carga importante para los sistemas de salud. Las personas mayores representan hasta el 80% de los pacientes con insuficiencia cardíaca. Entre las causas de insuficiencia cardíaca subyacente se encuentran la isquemia cardíaca (y la reperfusión intervencionista), la miocarditis y las enfermedades hipertensivas. Muchos de estos pacientes progresan hacia una insuficiencia cardíaca incapacitante. La condición proinflamatoria asociada a la insuficiencia cardíaca es una de las causas más conocidas, ya sea por síndromes coronarios agudos, por patógenos cardíacos idiopáticos o por miocarditis autoinmune. La acción anti-inflamatoria del receptor nuclear AhR es bien conocida, y nuestro grupo ha demostrado que AhR se activa parcialmente tras un infarto de miocardio, aunque esta activación puede verse incrementada significativamente mediante agonistas farmacológicos. Esta activación fisiológica de AhR es importante para proteger la función cardíaca después de un infarto de miocardio, ya que los ratones que carecen de este receptor nuclear presentan una lesión cardíaca exacerbada, progresión a insuficiencia cardíaca y muerte súbita en el caso de los machos. El análisis de los mecanismos moleculares dependientes de la activación del AhR muestra la inhibición de la ferroptosis cardíaca como uno de los actores patogénicos clave en la progresión hacia la insuficiencia cardíaca. En este proyecto, proponemos estudiar las vías dependientes de AhR de las células cardíacas que permiten la protección de los cardiomiocitos y su reconfiguración hacia una condición más cercana a su condición

fisiológica. Para ello realizaremos: a) estudios cardíacos funcionales y moleculares; b) estudios electrofisiológicos y regulación de los flujos de calcio en respuesta a AhR; c) técnicas multiómicas y transcriptómica, para determinar las dianas clave en el proceso de protección e integrar los datos en mapas de flujo que aporten valor añadido, incluido el análisis de la lesión cardíaca mediante transcriptómica espacial; d) validación de la activación farmacológica de AhR en el curso del daño cardíaco. Para ello, proponemos el uso de animales deficientes en Ahr vs. sus correspondientes homólogos Wt y sometidos a isquemia/reperfusión miocárdica; un modelo murino de miocarditis autoinmune; y cultivos 3D de iPSC humanas diferenciadas a cardiomiocitos y sometidas a hipoxia/reperfusión. En este contexto, proponemos validar el concepto de que AhR representa una opción terapéutica para mejorar la recuperación de la función cardíaca después de una reperfusión deletérea tras un infarto de miocardio o un estrés inflamatorio cardíaco (miocarditis).

CURRICULUM VITAE ABREVIADO (CVA)

IMPORTANT – The Curriculum Vitae cannot exceed 4 pages. Instructions to fill this document are available in the website.

Part A. PERSONAL INFORMATION

First name	Lisardo		
Family name	Boscá Gomar		
Gender (*)	male	Birth date (dd/mm/yyyy)	21/08/1957
ID number	20404150E		
e-mail	lbosca@iib.uam.es	URL Web	IIBM_L_BOSCA
Open Researcher and Contributor ID (ORCID) (*)		0000-0002-0253-5469	

(*) Mandatory

A.1. Current position

Position	Research Professor		
Initial date	2006		
Institution	Insituto de Investigaciones Biomédicas Sols-Morreale (CSIC-UAM)		
Department/Center	Cell metabolism		
Country	Spain	Teleph. number	646328464
Key words	Inflammation; macrophage; cardiovascular pathology; heart failure; atherogenesis; immunometabolism; AhR; mTOR ; lipoxins, AKI; NO		

A.2. Previous positions (research activity interuptions, indicate total months)

Period	Position/Institution/Country/Interruption cause
1986-2008	Instituto de Bioquímica (CSIC-UCM). Research Investigator
2008-2013; 2015-present	IIBM Sols Morreale (CSIC-UAM) Research Professor
2013-14	ISCIII sub-director (FIS)

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
Lic. Chemistry	U. Valencia	1979
PhD sciences	U. Autónoma de Madrid	1983

(Include all the necessary rows)

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

In the last decade, we have been working on the regulation of inflammation as a common pathophysiological process, from inception to resolution, and applied this knowledge to understand the pathogenesis of cardiovascular diseases and cancer. In 2010, in J. Immunol., with more than 690 citations, we described the metabolic features associated with the phenotypic differentiation of macrophages, from a pro-inflammatory to an anti-inflammatory and pro-resolution profile. In addition, we have shown for the first time how bioactive lipids derived from cyclooxygenase and/or lipoxygenases are involved in the resolution of several cardiovascular pathologies, from atherothrombosis to myocardial infarction and autoimmune myocarditis. In atherogenesis, these lipid molecules (i.e. lipoxins) modulate macrophage viability and this is a critical step in the regulation of the innate response. Briefly, lipoxin A4 and its derivatives, through a mechanism operated by plasma membrane receptors, inhibit apoptosis and induce macrophage autophagy, extending their biological activity. This is important because, a) these molecules are synthesized by the macrophage itself in the course of the pro-inflammatory response without requiring precursors requiring intercellular trafficking; b) modulate Nrf-2-dependent gene expression that mediates adaptation to oxidative stress, a signature of the activated innate immune response; c) delay macrophage apoptosis until the resolution process of the inflammatory response is completed. This is important to avoid necrosis and necroptosis-related alterations; and d) generate a response that ensures autophagic concatenation of pro-resolution activities, both through lipids derived from *n*-6 PUFAs (lipoxins) and *n*-3 (resolvins and maresins) PUFAs. Several publications of the group

support our work in this area (J Immunol. 185:605-614; Autophagy 11:1729-1744; Cell Death Differ. 17:1179-1188). The sum of citations of our works is >12,200, including 52 references in patents (WoS).
From a preclinical and technology transfer point, our studies in collaboration with the group of Dr Narula (Mount Sinai Med. School, NY) on atherogenesis imaging to identify the presence of 'active' plates led us to introduce new PET-based tracers to improve the images based on the classic FDG incorporation, which offers a low-resolution. One of the most promising new substrates to characterize macrophage signatures is the uptake of ^{18}F-deoxymannose which shows an impressive increase in active atheromas. Our group identified the mechanisms by which this mannose tracer exceeds widely that of FDG, allowing a significant increase in the quality and specificity of the PET image without affecting costs, toxicity, or detection mechanism. This work has opened new perspectives for the characterization of alternative molecules to FDG in atherogenesis, with a clear application to biomedical imaging. These studies have been conducted in rodents, and rabbits and are being implemented in humans. With a cost of € 5-10 for each administration in humans and an increase of up to 3-5 times in the signal *vs.* noise ratio, represents a valid alternative for athero detection (Nature Med. 20:215-19), including the improvement by transient GMCSF administration (x10 increase in PET resolution). Collaboration with FAES Farma, allowed us to change the initial description of proprietary molecules (benzylamine and thenylamine-derived compounds), from the allergy to the oncology field, due to the analysis of their effects in macrophages. These compounds are in the pipeline of a Japanese pharma. We are collaborating with researchers of Pernambuco Fed. Univ. (BZ), we developed new PPARγ partial selective agonists. Also, in collaboration with SMEs (AptaTargets, PharmaMar), we have been working on the targeting of TLR4 with specific aptamer molecules, to prevent adverse myocardial effects after acute infarction. This strategy has been the subject of an international patent, and clinical trials are ongoing to evaluate the use of this therapeutic strategy in cardiovascular diseases associated with pro-inflammatory activation. With PharmaMar we are assaying the targets of ecteinascidins in human immune cells. New prognosis bioassays are ongoing in the context of personalized medicine.
Regarding social communication and formation, these points are detailed in sections 4.3, 4.4, 6.1 and 6.2 of the project. In summary, all the PhD formed in our group (27 and 3 ongoing) had between 4-6 articles published, and good professional profiles (CSIC, Universities, USA). Social communication and formation have been cared for during my career, participating as organizer in congresses, webinars, formation of pharmacy professionals and technicians.

Part C. RELEVANT MERITS *(sorted by typology)*
C.1. Publications *(see instructions)* ***Corresponding author BOLD***. Citations (Wos. Jan2024)

Indicators: 276 articles in WoS (12,676 citations, h-index 59); Google scholar: 17,922 citations, h-index 71, i10 237.

Paz-García M, Povo-Retana A, Jaén RI, et al., **Boscá L**. (2023) *Beneficial effect of TLR4 blockade by a specific aptamer antagonist after acute myocardial infarction*. **Biomed Pharmacother 158:114214**. doi: 10.1016/j.biopha.2023.114214. **17/17**. Citations: 2

Fernández-García V, González-Ramos S, Avendaño-Ortiz J, Martín-Sanz P, Gómez-Coronado D, Delgado C, Castrillo A, **Boscá L.** (2022) *High-fat diet activates splenic NOD1 and enhances neutrophil recruitment and neutrophil extracellular traps release in the spleen of ApoE-deficient mice*. **Cell Mol Life Sci. 79:396.** doi: 10.1007/s00018-022-04415-x. Citations: 4

Val-Blasco A, Prieto P, Jaén RI, et al. **Boscá L***, Fernández-Velasco M*. (2022) *Specialized proresolving mediators protect against experimental autoimmune myocarditis by modulating Ca^{2+} handling and NRF2 activation*. **JACC Basic Transl Sci. 7:544-560**. doi: 10.1016/j.jacbts.2022.01.009. *Corresponding authors **22/23**. Citations: 5

Haider N, **Boscá L**, Zandbergen HR, et al. Narula J. (2019) *Transition of macrophages to fibroblast-like cells in healing myocardial infarction*. **J Am Coll Cardiol. 74:3124-3135**. doi: 10.1016/j.jacc.2019.10.036. **2/14**. Citations: 70

Tawakol A, Singh P, Mojena M, et al **Boscá L.** (2015) *HIF-1α and PFKFB3 mediate a tight relationship between pro-inflammatory activation and anaerobic metabolism in atherosclerotic macrophages*. **Arteriorscler Thromb Vasc Biol 35:1463-1471.** doi: 10.1161/ATVBAHA.115.305551. **16/16**. Citations: 142

Prieto P, Rosales-Mendoza CE, Terrón V, et al. **Boscá L** (2015) *Activation of autophagy in macrophages by pro-resolving lipid mediators.* **Autophagy 11:1729-1744.** doi: 10.1080/15548627.2015.1078958. **10/10**. Citations: 52

Tahara N, Mukherjee J, de Haas HJ, et al, Boscá L, **Narula J** (2014) *[^{18}F]2-fluoro-2-deoxy-D-mannose positron emission tomography imaging in atherosclerosis*. **Nat Med. 20:215-19.** doi: 10.1038/nm.3437. **17/18**. Citations: 133

Rodríguez-Prados JC, Través PG, Cuenca J, Rico D, Aragonés J, Martín-Sanz P, Cascante M, **Boscá L** (2010) *Substrate fate in activated macrophages: A comparison between innate, classic and alternative activation*. **J Immunol. 185:605-614.** doi: 10.4049/jimmunol.0901698. Citations: 698

Ivaska J, Boscá L, **Parker PJ** (2003) *PKCε is a permissive link in integrin-dependent IFNγ signaling that facilitates JAK phosphorylation of STAT1.* **Nature Cell Biol. 5:363-369.** doi: 10.1038/ncb957. Citations: 59

Castrillo A, Díaz-Guerra MJM, Hortelano S, Martín-Sanz P, **Boscá L** (2000) *Inhibition of IκB kinase and IκB phosphorylation by 15-deoxy-Δ^{12,14}-prostaglandin J$_2$ in activated murine macrophages.* **Mol Cell Biol. 20:1692-1698.** doi: 10.1128/mcb.20.5.1692-1698.2000. Citations: 202

C.2. Congress, indicating the modality of their participation (invited conference, oral presentation, poster)
On average, we are invited to 1-2 congresses/year, and young researchers present their work (oral or poster) in 2-4 congresses (half-international

C.3. Research projects (from 2017), indicating your personal contribution. In the case of young researchers, indicate lines of research for which they have been responsible.
Fundación Ramón Areces. 1/17-12/19. **PI and center:** L. Boscá. IIB-AS (CSIC-UAM)**:** *Biomateriales basados en grafeno:macrófagos: caracterización funcional para su aplicación en patología cardiovascular*. 97.000 €

MINECO SAF2014-52492. 1/15-12/17. **PI:** L. Boscá. IIB-AS. *Estudio de la relación entre polarización funcional y metabolismo energético del macrófago en patologías inflamatorias*. 340.000 €

PharmaMar. 8/16-7/18. **PI:** L Boscá. IIB-AS. *Characterization of the immunometabolic actions of trabectedin and PM01183 in murine and human macrophages: An approach to understand the role of these drugs on tumor-associated macrophages* (TAM). 116.300 €

Com. Madrid. Biociencia S2017/BMD3686. 08/18-06/22. **PI:** L. Boscá. IIB-AS. (Coordinator). *Consorcio para el estudio del fracaso renal agudo: fisiopatologia, nuevas terapias, biomarcadores y modelos experimentales*. 748.650 €

SAF2017-02161. 01/18-12/20. **PI:** L. Boscá. IIB-AS**:** *Modulación inmunometabólica del macrófago a través de mTOR y de la señalización purinérgica para favorecer la estabilidad de la placa en la aterogénesis*. 240.000 €.

PID2020-113238RB-I00. 01/21-12/23. **PI:** L. Boscá. IIB-AS**:** *Papel de los receptores nucleares VDR y AhR en la respuesta anti-inflamatoria y pro-resolutiva en la insuficiencia cardiaca*. 340.000 €.

CPP2021-008392. 10/22-9/25. **PI**: L. Boscá. IIB-AS. *Desarrollo de nuevas estrategias terapéuticas basadas en la evidencia para el uso de calcifediol en el tratamiento del Linfoma Difuso de Células B Grandes y el infarto de miocardio*. 290.750 €

Com. Madrid. Biociencia P2022/BMD-7223. 01/23-12/26. **PI**: Lisardo Boscá (coordinador). IIB-AS. Consorcio para el estudio del fracaso renal y su impacto en la patología cardiovascular.Cantidad financiada: 923.000 € (140.000 L. Boscá)

C.4. Contracts, technological or transfer merits (from 2017), Include patents and other industrial or intellectual property activities

MINECO RTC-2015-3741-1. 10/15-12/17. **CO:** APTATARGETS SL. **PI**: L. Boscá. IIB-AS. *Desarrollo preclínico de una molécula basada en tecnología de aptámeros específica de TLR-4 y de aplicación en ictus agudo y enfermedades cardiovasculares*. 80.930,50 €

PharmaMar. 8/16-7/18. **PI:** Lisardo Boscá. IIB-AS. Characterization of the immunometabolic actions of trabectedin and PM01183 in murine and human macrophages: An approach to understand the role of these drugs on tumor-associated macrophages (TAM). 116.300 €

MINECO RTC-2017-6283-1. 9/18-12/19. **CO:** APTOLL/ APTATARGETS SL. **PI**: L. Boscá. IIB-AS. *SAFETOLL-Desarrollo de nuevas aplicaciones terapéuticas de ApTOLL en enfermedades vasculares y autoinmunes*. 83.381 €

PharmaMar: 2022-23. *Immunometabolic and functional effect of ecteinascidins in human macrophages and lymphocytes*. **PI**: L. Boscá. 101.000 €

PATENT: International Application **PCT/IB2020/054655** (Company: APTATARGETS. S.L.) Intl. Filling Date: May 16, 2020. Treatment of tlr-4 mediated diseases and conditions with aptamers targeting tlr-4.

PATENT: Extensions: **WO2015197706** Aptamers specific for TLR-4 and uses thereof. and **USP 62/849,072** and **USP 62/849,072** (Treatment of ischemic stroke with aptamers targeting TLR-4). Patent USA, ES, RU and South Africa.

C.5. OTHER SCI & TECH ACTIVITIES.
Director of 25 doctoral theses and 4 ongoing (expected 2024, 2026 (2) and 2027)

Referee of articles from: Hepatology, Comparative Physiology and Biochemistry, Journal of Neurochemistry, Cancer Letters, BBRC, FASEB Journal, Circulation, Atherosclerosis, Journal of Hepatology, International J. Biochemistry, Life Sciences, Biochimica Biophysica Acta, Eur. J. Biochemistry, Nitric Oxide, Cardiovasc. Res., Redox Biol., Liver Intl. Biochem. J (editor, 2004-2012). World J. Gastroenterology (wjg; editor 2009-) Front Immunol (2019-).

Evaluator EU projects (INTAS), Human Frontier Science Program, Wellcome Trust, Italian System of Science and Technology (CINECA), Expert Spanish Representation FP6 and FP7 from the EU (HEALTH) (2003-2009). Director of the National System of R&D (Biomed program) from the Ministry of Science and Technology (2007-2012). Member of the Scientific Advisory Board of the IDIBAPS (2004-present); Member of the Scientific Advisory Board of the IDIBELL (2004-present); Member of the Scientific Advisory Board of the Fundación Jiménez Díaz (2009-present). Secretary Elected of the Spanish Society of Biochemistry and Molecular Biology (2000-2006). President of the Spanish Group of Free Radicals (GERLI; 2007-2009)

CURRICULUM VITAE ABREVIADO (CVA)

CVA Date	18/01/2024

Part A. PERSONAL INFORMATION

First name	Carmen		
Family name	Delgado Canencia		
Gender (*)	Female	Birth date (dd/mm/yyyy)	17/11/1958
Social Security, Passport, ID number	00677508C		
e-mail	cdelgado@iib.uam.es/carmen.delgado@csic.es	URL_LAB_CDELGADO	
Open Researcher and Contributor ID (ORCID) (*)		0000-0002-0047-4674	

(*) Mandatory

A.1. Current position

Position	Científico Titular		
Initial date	01/02/1987		
Institution	Consejo Superior de Investigaciones Científicas		
Department/Center	Metabolic and immune diseases/ The Sols-Morreale Biomedical Research Institute		
Country	Spain	Teleph. number	915854432/33
Key words	cardiac ionic currents, cardiac calcium handling, cardiac remodeling, cardiac hypertrophy, heart failure, cardioactive drugs.		

A.2. Previous positions (research activity interuptions, indicate total months)

Period	Position/Institution/Country/Interruption cause
2/06/2015-present	Científico Titular/ Instituto de Investigaciones Biomédicas Sols-Morreale. Madrid
2015-2008	Científico Titular/Centro de Investigaciones Biológicas (CSIC). Madrid
1/02/2008-1987	Científico Titular/Instituto de Farmacología y Toxicologia (CSIC-UCM). Madrid.
1989-1987 (24 months)	Becario Fulbright/ SUNY Health Science Center. Syracuse, NY (USA)
1986 (12 months)	Becario postdoctoral del CSIC. /Instituto de Farmacología y Toxicologia (CSIC-UCM). Madrid
1985 (12 months)	Becario Predoctoral/CAYCIT/Instituto de Farmacología y Toxicologia (CSIC-UCM). Madrid.

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
PhD on Pharmacy	Complutense	1984
Bachelor degree on Pharmacy	Complutense	1981

(Include all the necessary rows)

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

I currently direct the laboratory of "Cellular Electrophysiology and Regulation of Hypertrophy and Heart Failure" at the Department of Metabolic and Immunological Diseases/Sols-Morreale Biomedical Research Institute (IIBM-UAM) in Madrid. I have been granted 6 research six-year terms (the last 2015-2020). **My Research focuses** on delving deeper into the cellular and molecular mechanisms involved in the development and maintenance of cardiac hypertrophy (CH) and heart failure (HF). CH that appears in response to pathological stimuli and predisposes to HF and arrhythmias or even sudden death. My Group has provided relevant information on the changes in the expression and/or function of the main ion channels involved in the deleterious electrical remodeling of the adult heart in response to **pro-hypertrophic stimuli** such as **hypertension (**DOI**:**10.1006/jmcc.1999.0998; 10.1113/jphysiol.1993.sp019807;10.1152/ajpheart.1997.272.3.H1078;10.1113/jphysiol.2003.041954 ;10.1161/HYPERTENSIONAHA.107.093666;10.1093/cvr/cvq063),**obesity** (DOI: org/10.1113/JP274030) or **inflammatory mediators** (DOI: 10.1152/ajpheart.01122.2006 ; 10.1093/cvr/cvs234). Regarding HF, it appears as a final syndrome common to several pathologies frequently associated with aging, such as ischemic and hypertensive heart disease, chronic obstructive pulmonary disease or diabetes. Despite some advances in therapeutics, HF continues to represent a very important clinical challenge due to its high prevalence, morbidity and mortality. Many deaths occur suddenly and unexpectedly, presumably as a result of fatal ventricular arrhythmias. Improving the prognosis of these patients is essential, and to do so my group works to elucidate the pathophysiological mechanisms involved in the genesis and progression of HF, with special focus on contractile dysfunction and arrhythmogenesis, in order to identify new therapeutic targets, that help us to obtain new safe and effective drugs that can be co-administered with the other treatments that the patient receives. **Currently our work is funded by** MICINN-AEI: Ref. PID2020-113238RB-I00 (2021-2024); Ref. CPP2021-008392 (2022-2025) and Ref:UCRAN20050 (2022-2024) and focuses on studying the role of aryl hydrocarbon receptors (AhR) and vitamin D receptors (VDR) in HF (DOI: org/10.3390/ijms23105403; 10.1111/bph.15048 ;10.1016/j.hrthm.2016.12.013). **We have established collaborations** in the line of HF and kidney disease with Dr. Ruiz.Hurtado (H12Oct): (DOI: 10.1186/s12916-021-02209-9 ; org/10.1093/ndt/gfy392; 10.1111/eci.12902) ; and in the line of HF and immunity/inflammation with Dr.Fernández-Velasco (IdiPAZ) and Dr. Boscá (IIBm) (DOI: 10.1016/j.biopha.2023.114214; 10.1016/j.biopha.2022.112769 ; 10.1111/apha.13691 ; 10.1016/j.jacbts.2020.03.015 ; 10.3389/fphys.2018.00702 ; 10.1016/j.jacc.2016.10.073 ; 10.1093/cvr/cvv118 . **Scientific Responsibilities**: European Society of Cardiology: 2004-2008 Member of the Steering Committee of the Working Group on Cardiac Cellular Electrophysiology (WGCCE). **Projects as IP**: **National** Total = 15 (CICYT MEC/MCYT/MINECO/MICINN-AEI), **International** Total = 4 (Ukraine, BioMED2 Program, 2 Spanish-French Integrated Actions) and **Private** Total =3 (Lacer S.A 2003-2004, Spanish Society of Cardiology 2018-20022, FAES Pharma 2022-2025). **International Collaborations as IP**: U195 of INSERM in Clermont Ferrand (Dr. Lorente) and Unit-637 of INSERM in Montpellier (Dr. Ana Gómez) Spanish-French Integrated Actions Program of the MEC (Ref. HF-254B- 1992-1993 and Ref. 2005FR00202016-2017). European Project BioMED2 Concerted Action Program. (ref: PL 95-0287) (1996-1999); 6 months stay U. John Hopkins, Baltimore, USA. Salvador de Madariaga Program (MEC) (PR2006-0062); Collaboration project with Ukraine (2022-2024) (Ref: UCRA50). **Training of young researchers**: I have directed 7 Doctoral Theses and now I am directing 1 and co-directing 2 more. All of them obtained the highest qualification, 2 were Extraordinary Prizes and 1 European Doctorate Mention. **Four of the Doctors have followed a research career:** Ana María Gómez. UCM1994 (Director INSERM UMR-S 1180, Paris), María Fernández Velasco. UCM2005 (Miguel Servet 3 IDIPAZ), Gema Ruiz Hurtado UCM2008 (Miguel Servet 1, H12Oct), María Tamayo. UAM2020 (Hired Margarita Salas, Iata, CSIC, Valencia). **Publications**: 68 articles, 72 communications to International Congresses, 6 book chapters. 1 Patent.

Part C. RELEVANT MERITS *(sorted by typology)*

C.1. Most important publications in books and scientific journals with "peer review" and conferences (see instructions).*CA: correspondin author; (nº x / nº y): position/ total authos.* If applicable, indicate the number of citations and average per year.

1. Tamayo M, Martín-Nunes L, Piedras MJ and **Delgado C**. The Aryl hydrocarbon receptor ligand FICZ improves left ventricular remodeling and cardiac function at the onset of pressure overload-

induced heart failure in Mice. **Int. J. Mol. Sci**. **2022**. 23, 5403. **DOI:** 10.3390/ijms23105403 . **CA: Fernández-Velasco M and Delgado C; 11/11; NC=3**

2. Fernández-García V, González-Ramos S, Avendaño-Ortiz J, Martín-Sanz P, **Delgado C**, Castrillo A, Boscá L. NOD1 splenic activation confers ferroptosis protection and reduces macrophage recruitment under pro-atherogenic conditions. **Biomed Pharmacother. 2022 Apr;148:112769. 2022. DOI:** 10.1016/j.biopha.2022.112769 . Epub **2022** Mar 3. **CA: Bosca L; 5/7; NC=9**
3. Navarro-García JA, Salguero-Bodes R, González-Lafuente L, and **Ruiz-Hurtado G**. The antiaging factor klotho protects against acquired long QT syndrome induced by uremia and promoted by FGF-23. **BMC Med. 2022** Jan 19;20(1):14. **DOI**: 10.1186/s12916-021-02209-9 **. CA: Delgado C and Ruiz-Hurtado G; 16/17; NC=7**
4. Tamayo, M; Fulgencio-Covián A; Navarro-García and Fernández-Velasco M. Intracellular calcium mishandling leads to cardiac dysfunction and ventricular arrhythmias in a mouse model of propionic acidemia. **Biochim Biophys Acta Mol Basis Dis. 2020** 1866 (1), 165586. **DOI:** 10.1016/J.BBADIS.2019.165586 . **CA: DELGADO C, Richard E, Fernández-Velasco M; 10/12; NC=20**
5. Tamayo M, Martin-Nunes l, Val-Blasco A and **Delgado C.** Beneficial effects of paricalcitol on cardiac dysfunction and remodelling in a model of established heart failure. **Br J Pharmacol. 2020**. 177 (14):3273-3290. **DOI:** 10.1111/BPH.15048. **CA: Fernández-Velasco M and Delgado C; 10/10; NC=10**
6. Tamayo M, Martín-Nunes L, Val-Blasco A, Piedras MJ, Larriba MJ, Gómez-Hurtado N, Fernández-Velasco M, Delgado C. Calcitriol, the bioactive metabolite of vitamin D, increases ventricular K^+ currents in isolated mouse cardiomyocytes. **Front Physio**l. **2018** Aug 24;9:1186. **DOI**: 10.3389/fphys.2018.01186. **CA: Fernández-Velasco M and Delgado C. 8/8; NC=9**
7. Tamayo M, Manzanares E, Bas M, Martin-Nunes L, Val-Blasco A, Fernandez-Velasco M, Delgado C. Calcitriol (1,25-Dihydroxy vitamin D3) increases L-type calcium current via PKA signalling and modulates calcium cycling and contractility in isolated ventricular myocytes. **Heart Rhythm. 2017**. 14:432-439. **DOI:** 10.1016/j.hrthm.2016.12.013. **CA: Fernández-Velasco M and Delgado C; 6/6; NC=17**
8. Fernández-Velasco, M, Ruiz-Hurtado, G, Hurtado, O, Moro, MA, Delgado C. TNF-alpha downregulates transient outward potassium current in rat ventricular myocytes through iNOS overexpression and oxidant species generation**. Am. J. Physiol. Heart Circ. Physiol. 2007.** 293(1): H238-45. **DOI:** 10.1152/ajpheart.01122.2006. **CA: Delgado C; 5/5; NC=114**
9. Fernández-Velasco, M , Goren, N, Benito, G , Blanco-Rivero, J, Boscá, L , Delgado C. Regional distribution of hyperpolarization-activated current (If) and hyperpolarization-activated cyclic nucleotide-gated channel mRNA expression in ventricular cells from control and hypertrophied rat hearts. **J. Physiol. (Lond.) 2003.** 553(Pt 2): 395-405 **DOI:** 10.1113/jphysiol.2003.041954. **CA: Delgado C; 6/6; NC=149**
10. Martínez, ML, Heredia, MP, Delgado C . Expression of T-type Ca(2+) channels in ventricular cells from hypertrophied rat hearts. **J. Mol. Cell. Cardiol. 1999**. 31(9): 1617-1625 DOI: 10.1006/jmcc.1999.0998 **CA: Delgado C; 3/3; NC=201.**

C.2. **Research Proyects and lines in which you have participated, indicating your contribution (last 10 years).**

1. Papel de los receptores nucleares VDR y AhR en la respuesta anti-inflamatoria y pro-resolutiva en la insuficiencia cardiaca. MINECO (Ref. PID2020-113238RB-I00). Instituto de Investigaciones Biomédicas "Sols-Morreale", CSIC. 323.070,00 €. IPs: **Lisardo Bosca and Carmen Delgado.** 2021 – 2024.
2. Development of new evidence-based therapeutic strategies for the use of calcifediol in the treatment of Diffuse Large B-Cell Lymphoma (DLBCL) and myocardial infarction (Acronym: BIOFEROL). Colaboración público-privada –Ministerio de Ciencia e Innovación –Agencia Estatal de Investigación (AEI) (Ref: CPP2021-008392. Instituto de Investigaciones Biomédicas "Sols-Morreale", CSIC; Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla, Hospital Virgen del Rocío; FAES Farma. 588.177,00 €; IIBm: 304.500,00 €. IPs: **Lisardo Boscá and Carmen Delgado.** 01/06/2022 – 2025.

3. Mechanisms underlying the cardioprotective effects of nuclear vitamin D receptor activation in heart failure. Entidad financiadora: CSIC (Ref:UCRAN20050). Programa CSIC de cooperación científica con Ucrania. 2/09/2022- 26/09/2024. IP: **Carmen Delgado.** 104.393,47 €.
4. Efectos del Paricalcitol, un activador del receptor de vitamina D, sobre el acoplamiento excitación-contracción cardiaco y el remodelado eléctrico deletéreo arritmogénico en un modelo experimental de insuficiencia cardiaca en el ratón. SOCIEDAD ESPAÑOLA DE CARDIOLOGÍA (Convocatoria Proyectos 2018). Instituto de Investigaciones Biomédicas "Sols-Morreale", CSIC. 2018-2022. IP: **Carmen Delgado.** 15.000 €.
5. Papel del receptor de hidrocarburos de arilos (AhR) en el infarto agudo de miocardio. Entidad financiadora: MINECO (Ref. SAF2017-84777-R). Instituto de Investigaciones Biomédicas "Sols-Morreale". 121.000,00 €. IIP: **Carmen Delgado**. CSIC. January 2018- September 2021
6. Mecanismos celulares y moleculares implicados en el efecto cardioprotector de la vitamina D. Entidad financiadora: MINECO (Ref. SAF2014-57190-R). Instituto de Investigaciones Biomédicas (Sols-Morreale), CSIC. Cuantía de la subvención: 108.900,00 €. IP: **Carmen Delgado**. 2015-2018.

C3. Patents.

Inventores (p.o. de firma): Gutierrez Rodriguez M, Valenzuela Miranda C, Martin Martinez M, **Delgado Canencia C**, Naranjo Orovio JR. Título: Modulating compounds of KCHIP2 and its use for the treatment of cardiovascular pathologies. Nº de solicitud: 18382890.4- Entidad titular: Consejo Superior de Investigaciones Científicas. Países a los que se ha extendido: EUROPA. Fecha de solicitud: 04/12/18.

C4: R&D management.

- Member of the Panel of external evaluators of scientific projects of the ANEP/AEI from 2006 to the present and also of the Panel of the Ministry of Equality, Health and Social Policies of the Government of Andalusia from 2013 to the present. I have evaluated scientific projects for "The Research Foundation Flanders" (Bélgica) on 2018 and for the Spanish Society of Cardiology (SEC) 2020-2023.
- Member of the Steering Committee of the Working Group on Cardiac Cellular Electrophysiology (WGCCE) of the European Society of Cardiology (ESC). From 2004 to 2008.

C5 Participation in Collaborative Networks and CIBER. My research group has been part of the Spanish Thematic Network of Cardiovascular Diseases (RECAVA) from 2009 to 2016 (RD06-0014/0007) (RD12/0042/0019). Currently it is part of the CIBER Cardiovascular (CIBERCV) (CB/11/0022). Since 2017 we have also been part of the Spanish Network of Ionic Channels (RECI).

C6. Doctoral Theses Direction (last 10 years).

Título: Mecanismos implicados en el efecto cardioprotector de la vitamina D. **Doctoranda:** María Tamayo García. **University:** Autónoma de Madrid. School of Medicine. **Fecha:** 29 de septiembre de 2020 Sobresaliente "Cum Laude".

Título: Mecanismos implicados en los efectos cardiacos de leptina. Doctoranda: Nieves Gómez Hurtado. **University: Complutense de Madrid. School of Medicine. Fecha:** 19 de diciembre de 2013 Sobresaliente "Cum Laude" y **Premio Extraordinario de Doctorado**.

C7. Speaker at conferences, courses, seminars.

Pre-Congreso de la Sociedad Mexicana de Bioquímica. Nuevas tendencias de investigación en la señalización celular: Fisiopatologías relevantes en la era post-Covid. Título: Mechanisms involved in the beneficial effects of vitamin D on experimental heart failure. Speaker: Dra. Carmen Delgado Canencia. México DF: Octubre 25-29, 2021.

VII Red Española de Canales Iónicos (RECI): New Horizons in ion channel research. Symposium 3. Calcium Signaling and cell function.Título: Beneficial effects of paricalcitol on cardiac dysfunction and deleterious remodeling after established heart failure. Speaker: Dra. Carmen Delgado Canencia. Cáceres (España): Mayo 15-17, 2019