

CURRICULUM VITAE (CVA)

IMPORTANT – The Curriculum Vitae cannot exceed 4 pages. The guidelines are available in the website.

Part A. PERSONA	AL INFORMATION C	/ date		21/07/2023
First name	Gonzalo			
Family name	Sanchez Duffhues			
Gender (*)	Male		Birth date (dd/mm/yyyy)	08/03/1980
ID number	30958263X			
e-mail	g.s.duffhues@cinn.es		URL Web https://cinn.es/equipo/	
Open Researcher and Contributor ID (ORCID) (*)			0000-0002-32	05-0710

(*) Mandatory

A.1. Current position

A. I. Guilein position				
Position	Ramon y Cajal fellow and group leader			
Initial date	01/01/2023			
Institution	CSIC (CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS)			
Department/Center	CINN (CENTRO DE INVESTIGACION EN NANOMATERIALES Y NANOTECNOLOGIA)	ISPA (INSTITUTO DE INVESTIGACION SANITARIA DEL PRINCIPADO DE ASTURIAS)		
Country	Spain		Teleph. number	+34 661546033
Key words	TGF-β, cardiovascular, signal transduction, bone.			

A.2. Previous positions (research activity interuptions, art. 13.2.b))

Period	Position/Institution/Country/Interruption cause		
	Assistant Professor. Leiden University Medical Center. The		
2020-2022 (25 months)	Netherlands. Prof. Marie-José Goumans lab. The		
	Netherlands		
	Senior Researcher. Leiden University Medical Center. The		
2017-2020 (38 months)	Netherlands. Prof. Marie-José Goumans lab. The		
	Netherlands		
2011-2017 (79 months)	Postdoctoral fellow. Leiden University Medical Center. The		
2011-2017 (79 1110111115)	Netherlands. Prof. Peter ten Dijke's lab. The Netherlands		
2007-2011 (48 months)	PhD student. University of Cordoba. Spain		
2004-2007 (25 months)	Research assistant. University of Cordoba. Spain		

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
PhD in Biomedicine	University of Cordoba, Spain.	2010
MSc in Nutrition and Metabolism	University of Cordoba, Spain.	2009
BSc in Biochemistry	University of Cordoba, Spain.	2005
Technical degree Chemistry Analysis and Quality Control	IES Maimonides, Cordoba, Spain.	2004



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

Following my education in Biochemistry, I enrolled in my PhD studies at the Department of Cell Biology, Physiology and Immunology in the University of Cordoba (ESP). During my PhD I published 12 peer-reviewed manuscripts where I investigated the signal transduction pathways activated by pro-inflammatory cytokines, and identified novel (semi)synthetic compounds and cellular factors modulating inflammatory signaling, using HIV as a surrogate model. I performed my postdoctoral studies as an active member of Prof. Peter ten Dijke's group (LUMC, NL), where I led the studies of the interplay between inflammatory signaling and Transforming growth factor (TGF)-B pathways in skeletal and cardiovascular diseases (CVD). I became particularly interested in endothelial cell plasticity, which contributes to a growing number of human pathologies (i.e., CVD, bone disorders, cancer, fibrosis). To gain deeper understanding in stem cell biology, I joined the group of Prof. Marie-José Goumans (LUMC, NL). Supported by my host institution and my own funding, I built my own team currently consisting in three PhD students and one undergraduate student. Very recently, I have been awarded with a Ramon y Cajal grant, that has allowed me to move back to Spain to the Nanomaterials and Nanotechnology Research Center (CINN) in Oviedo (Asturias) to expand my own team on Tissue-specific Bone morphogenetic protein (BMP) signaling. My objective is to study rare TGF-B monogenic human diseases (i.e., Fibrodysplasia ossificans progressiva (FOP), Pulmonary arterial hypertension) as models to identify druggable targets and therapies for TGF-b gain- and lossof-function pathologies (i.e., fibrosis, cancer, CVD and musculoskeletal disorders). I aim to achieve this goal combining the development of novel drug screening methods, complex cell culture 3D platforms (organ-on-chip), patient-derived cell lines and disease animal models.

In my career I have accumulated a **substantial publication record** (nearly 50 publications) and obtained **my own funding** (approximately €2M), through personal awards, competitive grant programs and biotech service fees and collaborative agreements. I have accumulated several prizes, including **major international recognition awards** (i.e., AO Berton Rahn Research award, elected member of the European Calcified Tissue Society (ECTS) Young Academy, 1st Marshall Urist young BMP investigator award) and **presentation prizes at conferences**. I belong to different scientific societies such as SEBBM (Spanish society of Biochemistry and molecular biology, since 2010), ECTS (since 2016) and the ECTS Young Academy (since 2021), EuroOCs (European organ-on-chips organization, since 2019), hDMT (Institute for human Organ and Disease Model technologies, since 2018). This has helped me to establish my **own research network with academic, clinicians, corporate partners and patient associations** all over the globe.

I have followed **supervision and management training** (*Leadership in Science*, ElroyCOM Training, 2018) and hold **broad supervision experience** (1 postdoc, 9 PhD students, 7 MSc students, 4 BSc students, 3 undergraduates and 1 technician). I have **two PhDs awarded as co-promotor**: Marian Wesseling (2020) and Jin Ma (2021), and I have been solicited as **PhD thesis committee member** of 5 theses: David van de IJzendoorn (2020); Xiaoqing Sun (2021); Sarah Ouahoud (2022), Jose Valdes Fernandez (2022), Carolina Pimienta Costa (2023). I performed extensive **educational duties** in the LUMC (over 2500 teaching hours). In addition, I have **been invited lecturer** in **the ECTS PhD training course** (Laage Vuursche, NL, 2018), the 27th Medical Genetics Center course (Rotterdam, NL, 2017) and the XIV Corso di Aggiornamento in Genetica Clinica (Genoa, IT, 2015).

I am **reviewer** of national (Dutch Research Council NWO. Open competition XS. 2019, 2020; Dioraphte, NL, 2022) and European (European Research Council, Consolidator Grant CoG-2020; Telethon Italia, 2021, 2023) **grant agencies**. I am regular reviewer of **scientific journals** (i.e., Nature Communications, Journal of Clinical Investigation) and was a member of the LUMC-CCB **Scientific Committee** (assessing grant applications from my department), the LUMC *Microscope Facility Committee* (2019) and founder of the *BMP-LUMC workgroup*, including research groups working on BMP signal transduction within the LUMC (2021). I am (**Bio)medical advisor** for AEFOP (FOP Spain Association, since 2017) and IPSEN Pharma SAS (in the FOP field, since 2021).

I am an **advisory editorial board member** of Current Pharmaceutical Biotechnology and guest editor of the Special issue of Biomolecules "TGF- β signaling in Physiology and Pathology". I participate in dissemination activities through my **twitter** account (@DrEndMT), where I briefly introduce and discuss recent publications in the field of BMP signaling and EndMT and advertise related events. I also participate in FOP patients' **gatherings** where I give lectures in a lay-understandable manner.

Part C. RELEVANT MERITS (sorted by typology)

C.1. Publications (see instructions)



In my career I have accumulated an extensive publication record ("h" index 25; 330,029 accumulated IF), including first/second (26) and second last/last (10) author manuscripts (Google scholar profile). I have published 47 scientific manuscripts, 2 editorials, 1 book/thesis, 2 book chapters, 1 press release, 1 newsletter, been interviewed in a scientific podcast and I have hosted one Special issue as guest editor.

- -Marius Wits, Clarissa Becher, Frances de Man, <u>Gonzalo Sanchez-Duffhues (CA)</u>, Marie-José Goumans. (5/4). 2023. Sex-biased TGFβ signaling in Pulmonary arterial Hypertension. *Cardiovasc. Res.* In press. IF₂₀₂₂: 13.081
- -Gonzalo Sanchez-Duffhues (CA), Amaya Garcia de Vinuesa, Esmeralda Blaney-Davidson... Peter ten Dijke. (11/1). 2021. Cripto favours chondrocyte hypertrophy via TGF-β SMAD1/5 signaling during development of Osteoarthritis. *J Pathology*. 255(3): 330-342. DOI: 10.1002/path.5774 IF₂₀₂₂: 9.883
- <u>-Gonzalo Sánchez-Duffhues</u>, Keane Jared Guillaume Kenswil, Paola Pisterzi ... Marc Hermanus Gerardus Petrus Raaijmakers (CA). (23/1). 2021. Endothelium-derived stromal cells contribute to hematopoietic bone marrow niche formation. *Cell Stem Cell.* 28(4): 653-670. DOI: 10.1016/j.stem.2021.01.006 IF₂₀₂₂: 25.269
- -Robert Szulcek, <u>Gonzalo Sanchez-Duffhues</u>, Nina Rol... Marie-José Goumans (CA). (15/1). 2020. Exacerbated inflammatory signaling underlies aberrant response to BMP9 in pulmonary arterial hypertension lung endothelial cells. *Angiogenesis*. **23**(4): 699-714. DOI: <u>10.1007/s10456-020-09741-x</u> <u>IF₂₀₂₂: 10.658.</u>
- -Jerome Fortin, Ruxiao Tian, Ida Zarrabi... Tak W Mak (CA). (19/6). 2020. A Diffuse Intrinsic Pontine Glioma-Driving *ACVR1* Mutation Causes Oligodendroglial Lineage Cell Expansion and Differentiation Arrest. *Cancer Cell*. 37(3): 308-323 e312. DOI: 10.1016/j.ccell.2020.02.002 **IF**₂₀₂₂: 38.585.
- -Shirley Man, <u>Gonzalo Sanchez Duffhues</u>... David Baker (CA). (4/2). 2019. The Therapeutic potential of targeting the Endothelial-to-mesenchymal transition. *Angiogenesis*. 22(1): 3-13. DOI: <u>10.1007/s10456-018-9639-0</u> **IF**₂₀₂₂: **10.658**
- -Maria Catalina Gomez Puerto, Prasanna Vasudevan Iyengar, Amaya Garcia de Vinuesa... <u>Gonzalo Sánchez-Duffhues (CA)</u>. (5/5). 2018. Bone morphogenetic protein receptor signal transduction in human diseases. *J Pathology*. 247(1): 9-20. DOI: <u>10.1002/path.5170</u> **IF**₂₀₂₂: **9.883**
- -Lai-Ming Yung, <u>Gonzalo Sánchez-Duffhues</u>... Paul B Yu (CA). (4/2). 2015. Bone morphogenetic protein 6 and oxidized low-density lipoprotein synergistically recruit osteogenic differentiation in endothelial cells. *Cardiovasc. Res.* vol 108(2): 278-87. DOI: <u>10.1093/cvr/cvv221</u> **IF**₂₀₂₂: **13.081**
- <u>-Gonzalo Sánchez-Duffhues</u>, Theodore Fotsis, Peter ten Dijke (CA). (3/1). 2015. Signal Transduction: Gain of Activin Turns Muscle into Bone. *Current Biol*. vol 25(23): R1136-8. DOI: 10.1016/j.cub.2015.10.005 IF₂₀₂₂: 10.9
- -Gonzalo Sánchez-Duffhues (CA), Amaya García de Vinuesa, Jan H. Lindeman... Peter ten Dijke. (9/1). 2015. SLUG is expressed in endothelial cells lacking primary cilia to promote cellular calcification. *Arterioscler Thromb Vasc Biol*. Vol 35(3): 616-27. DOI: 10.1161/ATVBAHA.115.305268 IF₂₀₂₂: 10.514

C.2. Congress

- **-IFOPA Drug Development Forum.** Dallas, USA. November 2022. *International*. Invited speaker: Treatment with the PI3Kalpha inhibitor BYL719 unveils a differential regulation of AP-1 by Activin in Fibrodysplasia ossificans progressiva.
- -13th BMP International Conference. Dubrovnik, HR. Oct 2022. *International*. Invited speaker. New Voices in BMP Research: In vitro modelling of endothelial function through TGF-b signaling. *Marshall Urist BMP young investigator award.
- -The TGF-b superfamily conference: Signaling in development and disease. FASEB meeting. Online. July 2021. *International*. Selected oral communication: Cripto favors chondrocyte hypertrophy via TGF-b SMAD1/5 signaling in experimental Osteoarthritis. *Best short talk award.
- **-12th BMP International Conference.** Tokyo, JP. October 2018. *International*. Selected oral communication: Identification of Novel Macrocyclic ALK2 inhibitors for Fibrodysplasia ossificans progressiva using patient-derived endothelial colony forming cells. *Travel grant award.
- **-Dutch German Molecular Cardiology meeting.** Göttingen, GE. March 2019. *International.* Selected poster: Inflammation-induced EndMT facilitates BMP-mediated vascular calcification in a BMP type II receptor (BMPR2) dependent manner. *Best poster prize award.
- **-LICR-LUMC TGF-β Meeting**. Uppsala, SW. August 2017. *International*. Selected poster: Inflammation-induced EndMT facilitates BMP-mediated vascular calcification in a BMP type II receptor (BMPR2) dependent manner. *Best poster prize award.



- **-7th BMP International Conference**. Lake Tahoe (Reno), USA. July 2012. *International*. Selected poster: JNK inhibitor SP600125 potentiates BMP-induced endothelial-to-osteoblast transdifferentiation. *Selected for short presentation
- **-International patient gatherings (invited speaker):** FOP Stichting Nederland (NL: 2011, 2013, 2015, 2016, 2017, 2019), FOP Italia (IT: 2013, 2014, 2015, 2020, 2022), AEFOP (ESP: 2014), FOP Argentina (2021).

C.3. Research projects

- 1) a) MACHINA; b) MechAnostimulation on-Chip: INterrogating Activin signaling; c) Spanish Ministry of Science and Innovation, Proyectos de Generacion del Conocimiento 2022; d) G. Sanchez-Duffhues; e) 2023-2026; f) €311,758; g) Principal Investigator.
- 2) a) PROMETHEUS; b) Pulmonary hypertension induced Right heart failure: Occurrence of genetic variations and disturbed BMP & TGFb signaling explaining impaired mechanotransduction and heterogenous adaptation to pressure overload; c) BHF-DZHK-DHF International Cardiovascular research partnership awards, 2022/23; d) Dr. Frances de Man, AUMC, Amsterdam, NL; Andrew Swift Sheffield University, UK; Soni Pullamsetti, Max Planck Institute for Heart and Lung Research, GE; e) 2022-2026; f) (€1,500,000 total. €27,650 allocated); g) Co-applicant.
- **3)** a) Rembrandt Research Grant 2021; b) Rejuvenating the heart in pulmonary arterial hypertension by targeting the bone morphogenetic protein 10; c) Rembrandt Institute of Cardiovascular Science, 2021; d) G. Sanchez-Duffhues, Leiden University Medical Center (Leiden, NL), together with Dr. Frances de Man, AUMC, Amsterdam, NL; e) 2022-2026; f) 1 PhD student + €7,5K/year bench fee (€283,328); g) Principal Investigator.
- **4)** a) #202038; b) Disrupting the ACVR1-PI3K axis in Fibrodysplasia ossificans progressiva: towards novel therapies for heterotopic ossification; c) FUNDACIÓ LA MARATÓ DE TV3, 2020; d) G. Sanchez-Duffhues, Leiden University Medical Center (Leiden, NL), together with Dr. Francesc Ventura, University of Barcelona, ESP; e) 2021-2024; f) €289,875; g) Principal Investigator.
- **5)** a) Grant Italia 2020; b) PI3K inhibitors as a new therapy for FOP; c) FOP Italia, 2020; d) G. Sanchez-Duffhues, Leiden University Medical Center (Leiden, NL), together with Dr. Francesc Ventura, University of Barcelona, ESP; e) 2021-2022; f) €100,000; g) Principal Investigator.
- **6)** a) Trampoline grant #22379; b) *Normalization of the vasculature to prevent heterotopic ossification in Fibrodysplasia ossificans progressiva*; c) AFM-Telethon, 2018; d) G. Sanchez-Duffhues, Leiden University Medical Center (Leiden, NL); e) 2018-2019; f) €50,000; g) Principal Investigator.
- 7) a) Postdoctoral fellowship #18365; b) *Putting the brakes on FOP. Development of Novel strategies to block heterotopic ossification*; c) AFM-Telethon, 2015; d) G. Sanchez-Duffhues, Leiden University Medical Center (Leiden, NL); e) 2015-2016; f) €51,500; g) Principal Investigator.
- **8)** a) Start Up Grant S12-27S; b) *Targeting EndMT in FOP*; c) AO-Foundation, 2012; d) G. Sanchez-Duffhues, Leiden University Medical Center (Leiden, NL); e) 2012-2014; f) €120,000; g) Principal Investigator.
- 9) a) LEDUCQ 2010; b) Multidisciplinary Program to Elucidate the Role of Bone Morphogenetic Protein Signaling in the Pathogenesis of Pulmonary and Systemic Vascular Diseases; c) Leducq Foundation, 2010; d) Prof. Nicholas Morrell (University of Cambridge, UK), Prof. Kenneth Bloch and Dr. Paul Yu (Harvard School of Medicine, Boston, US), Prof. Akiko Hata (University of San Francisco, US), Prof. James Smith (MRC National Institute for Medical Research, London, UK), Prof. Peter ten Dijke, Leiden University Medical Center (Leiden, NL); e) 2010-2015; f) \$6M; g) Postdoctoral researcher.

C.4. Contracts, technological or transfer merits

I have established the following service fee-based contracts with companies for them to use the technologies developed by my team:

- 1) a) BMP kinase receptor target assays for novel small molecule inhibitors; b) Galapagos NV (Leiden, NL); c) G. Sanchez-Duffhues, Leiden University Medical Center, Leiden, NL; d) 2022; e) €40,000.
- 2) a) ALK2 target assays for novel small molecule inhibitors; b) Galapagos NV (Leiden, NL); c) G. Sanchez-Duffhues, Leiden University Medical Center, Leiden, NL; d) 2021; e) \in 30,750.
- 3) a) Evaluation of novel ALK2 specific inhibitors in vitro; b) Oncodesign SA (Dijon, FR); c) G. Sanchez-Duffhues, Leiden University Medical Center, Leiden, NL; d) 2019; e) €15,000.
- 4) a) Development of a vascular calcification model in the Organoplate©; b) Mimetas (Leiden, NL); c) G. Sanchez-Duffhues, Leiden University Medical Center, Leiden, NL; d) 2017; e) €10,000 (in kind).