MINISTERIO DE CIENCIA E INNOVACIÓN

AGENCIA ESTATAL DE INVESTIGACIÓN

CURRICULUM VITAE (CVA)

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

CV date	19/06/2023

Part A. PERSONAL INFORMATION

First name	Bovolenta		
Family name	Paola		
Gender (*)	Female	Date of Birth	11/11/1957
Social Security, ID #	33534698P		
e-mail	pbovolenta@cbm.csic.es	URL Web	
Open Researcher and Contributor ID (ORCID) (*)		0000-0002-1870-751X	

A.1. Current position

Position	CBM-SO Director; Head of the CIBERER Unit 709		
Initial date	Research Professor since 2002		
Institution	Consejo Superior de Investigaciones Científicas		
Department/Centre	Centro de Biología Molecular Severo Ochoa		
Country	Spain	Phone number	911964718
Keywords	Morphogenesis, pattern formation, cell-cell communication, inborn eye defects, neurodegeneration, neuroinflammation, Alzheimer´s disease		

A.2. Previous positions (research activity interruptions)

Period	Position/Institution/Country/Cause of the interruption
2012-2022	Chair of the Tissue and Organ Homeostasis Program, CBM-SO
2008-2012	Head of the Biology and Biomedicine Area of the CSIC
2005-2009	Chair, Cell Mol. Dev Neurobiol. Dept., Instituto Cajal, CSIC
2005-2010	Full Professor, Instituto Cajal, CSIC
2002-2004	Associate Professor, Instituto Cajal, CSIC.
2000	Invited Professorship, École Normale Supérieure, Paris.
1995	Visiting Scientist, HSR-DIBIT, Milan, Italy
1993-2002	Staff Scientist, Instituto Cajal, CSIC.
1989-1993	Research Associate, Instituto Cajal, CSIC.

A.3. Education

PhD, Graduate Degree	University/Country	Year
BS	University of Florence, Florence, Italy	1981
MS	New York University, Sch. Med, NY, USA	1984
PhD	New York University, Sch. Med, NY, USA	1986
Postdoc	New York University, Sch. Med, NY, USA	1986
Postdoc	Columbia Univ., Col. Phys.& Surg, NY, USA	1986-1988

Part B. CV SUMMARY *(max. 5,000 characters, including spaces)*

PB's research currently focuses on 1) understanding the molecular mechanisms underlying early development of the visual system, with the aim of identifying, among others, those processes responsible for inborn pathologies. This latter aspect is further developed within the CIBER for Rare Diseases, to which the team belongs. Major findings in this field include the identification of gene regulatory networks and species-specific morphogenetic events leading to eye formation in vertebrates and European collaborative work elucidating the role of two transcription factors as causes of syndromic inborn eye pathologies. A more recent line of research that serendipitously stemmed from her long-lasting interest in eye development focuses on 2) understanding the role of the abnormal expression

levels of the secreted protein SFRP1 in neurodegeneration and neuroinflammation. These studies demonstrate that SFRP1 is a major player in Alzheimer's disease pathology, contributing not only to the regulation of APP processing but also to neuroinflammation and loss of synaptic plasticity, thereby representing a potential important therapeutic target for the disease. In support of this possibility, the team has demonstrated that antibody mediated neutralization of SFRP1 delays AD progression in mice and prevents loss of cognitive capacity. The antibodies are object of an international patent and their therapeutic potentials are further explored with support of international private funds (Cure Alzheimer Fund). As in the past, PB research is supported by local, national and international public and private funding agencies (e.g. CAM, AEI, PTI-Aging, ERA-NET, FP7, HFSP, Fundacion R. Areces, Fundacion Tatiana) and benefits from the interaction with national and international colleagues, among others, through two networks that she coordinates: the 4rd very successful edition of RedDevNeural a national Network of Excellence on Developmental Neurobiology, and the 2nd successful edition of an ERA-NET Neuron project on Developmental Visual disorders. She coordinated the 2020 CSIC White paper "The origin, (co)evolution, diversity and synthesis of life", from which the CSIC-LIFE-HUB, originated. This hub gathers CSIC researchers from different domains with aim of addressing truly interdisciplinary work on the topic of the white paper. She authors >130 articles peer reviewed (e.g. Nat Neurosci, Nat Comm, Dev Cell, EMBO Rep, eLife, EMBO Mol Med, PNAS, Neuron) most as senior author (>11.000 citations, h-index 59, GS). She is often invited as speaker in prestigious congress (e.g. Gordon Conferences, EMBO Workshop; FENS, etc); inventor of an internationally protected patent and received the Fundaluce award for her research on retinal diseases (2009 and 2012). She is member of EMBO (2012) and of the Academia Europæa (2022).

Throughout her career, PB mentored 21 PhD Students (4 ongoing) and 18 postdocs, most of whom successfully lead their own research groups in Spain or abroad and are themselves leaders in the fields of developmental biology and neuroscience. PB also mentors and supports her past lab members as well as several young researchers within and outside of the CBM-SO. She participates in outreach activities and is leading author of 18 outreach science-related articles in different venues.

She is the Director of the CBM and the Scientific Director of the CBM Severo Ochoa Excellence Award. She has been member of the ERC Scientific Council (2017-2022) chaired the ERC Open Science Working group (2019-2022) and participated in the UE Core Group on Reform of Research Assessment (EU Directorate, 2022). She belongs to SAB of the ERA-NET Neuron Program since 2016; is member of the Scientific Advisory Committee of the Armenise-Harvard, Bettencourt-Schueller and Gadea Foundations (all since 2017) and Italian Telethon (since 2021). She is also member of the SAB of different Research Institutes (C. Darwin Institute, La Sapienza Roma, Centre Interdisciplinary Research in Biology, CdF, Paris; Institut de la Vision in Paris; Institut de Biologie de Dev de Marseille; PSI-Neuro, Gif-sur-Yvette; IBENS, ENS, Paris; and IBTEEC, Santander). She is Senior Editor of the *Eur J Neurosci* (FENS official journal), *eLife* Reviewing Editor, Associate editor of *Vision Research* and *Front Dev Neurosci* member of the editorial board of other journals (*Cells & Devel, Dev Dyn; Fron Anat*) . She is the current President of the Spanish Society for Neuroscience (SENC) and co-chair of the program committee for the upcoming IBRO world congress 2023. Among the most notable past activities, she acted as Coordinator of the Biology and Biomedicine Area of the CSIC (2008-2012) and has been member of the selection committee for national and international private and public funding agencies and for scientific awards' selection. She served in the FENS and SfN societies and participated in the organization of national and international workshop and mtgs.

Part C. RELEVANT MERITS

C.1. Main recent Publications

Cardozo MJ, Sanchez-Bustamante E and **Bovolenta P** (2023) Optic cup morphogenesis across species and related inborn human eye defects. ***Development*** 150, dev200399

Hernández-Bejarano M., Gestri G., Monfries C., Tucker L., Dragomir E.I., Bianco IH, **Bovolenta P.**, Wilson SW and Cavodeassi E. (2022) Foxd1 dependent induction of temporal retinal character is required for visual function. ***Development*** 149, dev200938

Moreno-Marmol, T, Ledesma M, Tabanera N, Martin-Bermejo MJ, Cardozo, MJ, Cavodeassi F, and **Bovolenta P.** (2021) Stretching of the retinal pigment epithelium contributes to zebrafish optic cup morphogenesis. ***eLife*** 10:e63396. (*eLife digest*)

Buono L, Corbacho J., Naranjo S., et al. **Bovolenta P***, Martínez-Morales JR* (2021) Analysis of gene network bifurcation during optic cup morphogenesis in zebrafish. ***Nat Commun***. 12: 3866 ***co**-corresponding.

Moreno-Marmol, T., Cavodeassi, F. and **Bovolenta P.** (2018) Setting eyes on the retinal pigment epithelium. ***Front Cell Dev Biol,*** 6, 145.

Cardozo MJ*, Almuedo-Castillo*, M and **Bovolenta, P.** (2020) Patterning the vertebrate retina through morphogenetic signaling pathways. ***Neuroscientist***, 26, 185-196.

The above set of articles provide novel views on the cellular and molecular mechanisms by which the retinal pigmented epithelium (RPE) contributes to early eye morphogenesis, explaining species-specific differences between fish and amniotes, including humans. These findings add on our previous seminal work on RPE development.

Rueda-Carrasco, J, Martin-Bermejo MJ*, Pereyra, G*, Mateo, MI*, et al., and **Bovolenta, P.** (2021) SFRP1 modulates astrocyte to microglia cross-talk in acute and chronic neuroinflammation ***EMBO Rep***. Sep 27:e51696. *equal contribution

Cisneros, E., Di Marco, F, Rueda-Carrasco, J, et al., and **Bovolenta, P.** (2020) Sfrp1 deficiency makes retinal photoreceptors prone to degeneration. ***Sci. Rep*** 10:5115

Esteve P, Rueda-Carrasco J., Mateo, I., et al., and **Bovolenta P.** (2019) Elevated levels of Secreted-Frizzled-Related-Protein1 contribute to Alzheimer's disease pathogenesis. ***Nat. Neurosci***. 22: 1258-1268. **(*Editors' choice in Sci. Transl. Med, 2019, 11, eaay7697*)**

Esteve P.* Crespo I.*, Kaimakis, P., Sandonís A. and **Bovolenta P**. (2019) Sfrp1 modulates cell-signaling events underlying telencephalic patterning, growth and differentiation. ***Cer Cortex*** 229, 1059–1074.

The above set of articles builds on our previous discovery that the secreted protein SFRP1 acts as an endogenous negative modulator of the ADAM10 sheddase (Esteve et al. 2011 Nat. Neurosci. 14, 562-569). Opening a new line of research in the lab, we have now demonstrated that alterations in this SFRP1 activity participate in neurodegenerative disease' pathogenesis (i.e. Alzheimer's disease) by controlling APP processing and neuroinflammation, thereby representing a potentially useful therapeutic target.

Bertacchi M., Gruart, A., Kaimakis P., et al., **Bovolenta P.**, and Studer M. (2019) Mouse Nr2f1 haploinsufficiency unveils new pathological mechanisms of human BBSOA syndrome. ***EMBO Mol Med***. 11: e10291 ***(cover caption article***)

Bertolini, J.*, Favaro R.*, Zhu, Y.*, et al., **Bovolenta P.,** Pavesi G., Guillemot F., Nicolis SK* and Wei CL*. (2019) SOX2 mediates transcriptional regulation through global functional chromatin connectivity in brain-derived neural stem cells. ***Cell Stem Cell,*** 24, 462-476.

Mercurio S, Serra L, Motta A, et al., **Bovolenta P** and Nicolis SK. (2019) Sox2 functions in thalamic neurons to control the development of retina-thalamus-cortex connectivity. ***iScience*** 15, 257-273 (***cover caption of issue 16***)

The above articles are among the collaborative output of the successful ERA-NET Neuron project ImprovVision coordinated by PB, demonstrating a critical link of two transcription factors, SOX2 and NR2F1, in human CNS developmental disorders. These findings are at the basis of the recently awarded Brain4Sight, ERA-NET Neuron project, again coordinated by PB

Books

Bovolenta P, Manzanares M, Buceta J (2020). Origins, (Co)Evolution Diversity and Synthesis of Life. CSIC Scientific Challenge. Vol 2.

Castelli-Gair Hombria, J and **Bovolenta P.** (2016) Organogenetic gene networks. Springer.

C.2. Main recent invited participations to Congresses

Bovolenta P (2022) Multiple roles of SFRP1 in Alzheimer's disease pathogenesis and its potential relevance as a therapeutic target. *18th Symposium Neuroscience at the Edge: Frontiers of Knowledge*. The Armenise-Harvard Foundation. June 19–22, Palazzo di Varignana, Italy (**invited closing lecture**)

Bovolenta P (2022) Eye morphogenesis as a mean to understand developmental visual disorders. CNRS-*Jacques Monod Conference* "Genetics, environment, signalling & synaptic plasticity in developmental brain disorders: from bench to bedside" Roscoff France, April 11-15 (**invited speaker**)

Bovolenta P. (2020) From Florence to New York to Madrid: a journey with Cajal. Cajal Club Mini-conference, *FENS Forum* 2020, Virtual, 11 July. **(invited speaker)**

Bovolenta P. (2020) Is there a common regulatory network that orchestrates the assembly of visual circuits? *Symposium Ramón Areces:* Understanding and reprogramming developmental visual disorders. 30-31 January 2020. Madrid (**invited speaker**; **co-organizer**)

Bovolenta P. (2019) Secreted Frizzled Related Protein 1 in neurodegeneration. *6th Venusberg Meeting on Neuroinflammation*, Bonn, Mayo-9-11 **(invited speaker)**

Bovolenta P. (2019) The role of Sfrp1 in axon guidance and synaptic plasticity. "Circuits Development & Axon Regeneration" - *3rd AXON Meeting*, Alicante September 11-13 **(invited speaker)**

Bovolenta P., Moreno-Marmol T., Ledesma M, Cavodeassi F. (2018) Specification of the retinal pigment epithelium and its implication in vertebrate optic cup morphogenesis. *5th European Zebrafish PI meeting (*5th EZPM) Trento **(invited speaker)**

Bovolenta P. (2018) Specification of the retina pigment epithelium and its implication in vertebrate optic cup morphogenesis. *XXIII Biennial Meeting of the International Society for Eye Research* September 9-13, 2018. Belfast, Northern Ireland, UK **(invited speaker)**

C.3. Recent research projects

Center of Excelence Severo Ochoa: CMB-SO, Acronym: I3M. (**AEI, CEX2021-001154-S).** 2023-2026. Funding 4.000.000 €. **PI**

SFRP1 as a target in the fight against Alzheimer's disease. **Fundacion Tatiana**. 2023-2025. Funding 85.250 €. **PI**

Deconstructing gene regulatory networks for improving sight and brain disabilities (Brains4Sight). (***ERA-NET Neuron***, ***NEURON_NDD-255***) 2022-2024. ***Coordinator*** and ***Principal Investigator*** (**PI** 4 teams). Funding for the team: 250.000 €

Development of human 3D organoids to understand the differential impact of DYRK1A haploinsufficiency syndrome in the CNS. ***CIBERER-ACCI***. 2022-2023. PI. Mariona Arbones and PB co-PI. Funding: 56.000 €

CSIC Interdisciplinary Thematic Platform (PTI+) NEURO-AGINGl+. (**PTI-NEURO-AGING+**), CSIC Strategic Funds. 2022- 2023. Funding for the team: 100.000 €. ***PI***

New approaches to understand prevalent and neurodegenerative diseases. Agencia Estatal de Investigacion (**AEI, PID2019-104186RB-100**) 2020-2023. ***PI.*** Funding: 387.200 €

Sfrp1 as a therapeutic target and diagnostic/prognostic factor in Alzheimer's disease. **Cure Alzheimer´s Fund**. 2020-2022. ***PI.*** Funding: 345.000 $

RedDevNeural.3.0. An integrative approach to understandthe logic of neural development ***AEI (RED2018-102553-T)***. 2020-2022. ***Project Coordinator*** (10 teams) Funding: 22.000 €

Understanding and reprogramming developmental visual disorders: from anophthalmia to cortical impairments (ImprovVision). ***ERA-NET Neuron***. 2015-2018. ***Project Coordinator*** and ***PI*** (5 teams). Funding for the team: 149.000 €

Cellular and molecular interactions during nervous system development and degeneration. ***MINECO (BFU2016-75412-R***). 2017-2019. ***PI*** Funding: 387.200 €

Cdon-Hh Interaction: functional in vivo analysis in Cdon-Hh Interaction: functional in vivo analysis in zebrafish (CHI-ZEF). EU Horizon 2020 (740916-CHI-ZEF-H2020-MSCA-IF-2016). 01/07/17-30/06/19 ***Supervisor.*** Funding: 158.121 €

C.4. Technology/Knowledge transfer

Therapeutic target and monoclonal antibodies against it for the diagnosis and treatment of Alzheimer´s - Disease". Inventores: **Paola Bovolenta**, Pilar Esteve, Javier Rueda Carrasco, Maria Inés Mateo Ruiz, Maria Jesús Martin Bermejo (CSIC); Mercedes Dominguez Rodriguez Inmaculada Moreno Iruela (ISCIII). Ref. PCT/EP2020/054045