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	**Juan Carlos**		
Family name	**Espinosa Martín**		
Gender (*)	Male	Birth date	[redacted]
Social Security, Passport, ID number		[redacted]	
e-mail	espinosa.juan@inia.csic.es	https://www.researchgate.net/profile/Juan-Espinosa-5	
Open Researcher and Contributor ID (ORCID)		0000-0002-6719-9902	

A.1. Current position

Position	Senior scientist		
Initial date	5/10/2009		
Institution	Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria (INIA) - Consejo Superior de Investigaciones Científicas (CSIC)		
Department/Center	Centro de Investigación en Sanidad Animal (CISA)		
Country	Spain	Teleph. number	+34 916 202 300
Key words	Bovine Spongiform Encephalopathy, Prions, strains, PrP, Scrapie, transgenic mice, Transmissible Spongiform Encephalopathy		

A.2. Previous positions

Period	Position/Institution/Country/Interruption cause
2003-2009	Postdoctoral Researcher. Prions' research group of CISA-INIA-CSIC.
2001-2002	Postdoctoral Researcher. Instituto de Investigaciones Biomédicas Alberto-Sols (CSIC). Molecular Biology and Biochemistry of prion diseases.
2000-2001	Postdoctoral Researcher. University of Castilla-La Mancha (UCLM). Molecular Biotechnology.
1998-1999	Postdoctoral Researcher. CSIC. Centro de Biología Molecular Severo Ochoa (CBMSO). Molecular Microbiology
1993-1997	PhD student in Molecular Microbiology. CSIC-CBMSO.

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
Licensed in Sciences (Biology). Biochemistry and Molecular Biology	Universidad Autónoma de Madrid/Spain	1992
PhD in Sciences (Biology)	Universidad Autónoma de Madrid/Spain	1997

Part B. CV SUMMARY

I began my scientific career by completing my doctoral thesis at the Centre for Molecular Biology "Severo Ochoa," supervised by Dr. A. Jiménez. My thesis delved into characterizing all genes involved in puromycin biosynthesis and exploring properties of proteins in the biosynthetic pathway. A comprehensive molecular and *in silico* analysis enabled me **to describe, for the first time, all the biochemical steps in the biosynthesis of a natural antibiotic**. This research provided a robust foundation in molecular biology, protein biochemistry, molecular microbiology, and the interpretation, discussion, and dissemination of research results. Consequently, I published 7 peer-reviewed articles, firmly establishing the basis for describing the biosynthetic routes of these metabolites. I engaged in an exchange program, leading me to the laboratory of Dr. W. Piepersberg at the Bergische Universität in Wuppertal, Germany, where I conducted research on antibiotic glycosylation. Post-thesis, I undertook a research project at the Faculty of Chemical Sciences at UCLM in Ciudad Real, focusing on biotechnological yeast strain improvement in the wine industry. This project

involved participation in the biochemical and genetic analysis of **yeast to enhance wine production and quality, merging basic research with essential elements for regional economic development**. The outcome was the publication of 4 peer-reviewed articles. In 2001, I transitioned to prion biology during a CSIC research project, studying the aggregation properties of the prion protein, leading to a highly cited peer-reviewed article. After, in 2003, I joined the Prions research group at CISA. During this time, I made two research visits to the laboratory of Dr. Olivier Andréoletti at INRA-Toulouse, France, collaborating on joint projects. My research focused on prion strains and their alteration after passage in another species. To investigate this, I utilized different transgenic mouse models (Tg) expressing the prion protein (PrP) of interest in a background knockout for mouse-PrP, facilitating the characterization of prion strains and their evolution. Most of these Tg were generated and/or characterized by myself. Using these tools, we demonstrated that **epidemic Bovine Spongiform Encephalopathy (BSE) increased its ability to infect other species, including humans, after passing through another species**, such as sheep or goats. We also proposed that **the origin of the epidemic BSE could be related to sporadic atypical prions**, either from cattle (type H-BSE) or sheep or goats (atypical scrapie). In both cases, evolution from the presumably sporadic prion would occur in the context of bovine-PrP. This topic is important, as it could explain **the origin of the BSE epidemic in the UK**, which had a significant economic impact in the EU due to the recycling of animal tissues used for cattle feeding. Additionally, these findings highlight **the ability of prion strains to evolve from non-zoonotic prions to other strains transmissible to humans**. I also contributed to extensive work that established **the zoonotic potential of scrapie**. With a new Tg created by myself, I demonstrated **the role of two amino acid changes (Met166 and Glu168) in the human-PrP sequence in resistance to infection with different prion strains** and their implications in human evolution. During my period at CISA, this research allowed me to publish **>50 articles in first-quartile journals**, some of them highly cited, such as Nat. Commun., Proc Natl Acad SCI USA, or Acta Neuropathol. among others. Other laboratories were interested in both our research and conducting experiments with the cited Tg facilitating numerous collaborations with both national and international research groups. In many cases, these collaborations have evolved into funded collaborative projects led by myself. Specifically, my recent work has focused on three key areas: 1) investigating how specific **changes in the PrP sequence can impact the replication of different prions**; 2) exploring **how alterations in the PrP sequence can lead to the generation of spontaneous infectivity**; and 3) examining **how prion strains can modify the biochemical and pathobiological properties after passage in another species**. I have played an active role in mentoring and training young researchers (PhD, master's, and bachelor's degree students). In this sense, one student under my guidance on both her bachelor's and master's projects **earned the prestigious Arquímedes 2022 award and the highest academic qualification**, respectively. Additionally, I have served as a peer reviewer for several prominent journals in my field, as well as participating in project and research activity evaluations for research agencies in Spain and the UK. **Six-year and Five-years** periods awarded: **4.** Total publications citations: 87. Total citations: 1779. Average citations/year (last 5 years): 134 citations/year. Publications in the first quartile (Q1): 53. Index h: 23 (Scopus).

Part C. RELEVANT MERITS

C.1. Publications

These are the 10 most relevant publications from the last 10 years:

1. Espinosa JC*; Marín-Moreno A*; Aguilar-Calvo P; Torres JM(CA). Met(166)-Glu(168) residues in human PrP β2-α2 loop account for evolutionary resistance to prion infection. Neuropathology and applied neurobiology. 2021. 47 - 4, pp. 506 – 518. *Joint authorship. https://doi.org/10.1111/nan.12676

2. I Cali*, **Espinosa JC***(1/10), SK Nemani, … P Gambetti(CA). Two distinct conformers of PrP(D) type 1 of sporadic Creutzfeldt-Jakob disease with codon 129VV genotype faithfully propagate in vivo. Acta Neuropathol Commun. 2021. 9 - 1, pp. 55. *Joint authorship. https://doi.org/10.1186/s40478-021-01132-7

3. Espinosa JC*(1/12); Andreoletti*, O, Marín-Moreno, A,… JM Torres(CA). Allelic Interference in Prion Replication Is Modulated by the Convertibility of the Interfering PrP(C) and Other Host-

Specific Factors. mBio. 2021. 12 (2), e03508-20. *Joint authorship. https://doi.org/10.1128/mBio.03508-20
4. Espinosa JC(CA); A Marín-Moreno, P Aguilar-Calvo, SL Benestad; O Andreoletti; JM Torres. Porcine Prion Protein as a Paradigm of Limited Susceptibility to Prion Strain Propagation. The Journal of Infectious Diseases. 2020. 223 (6): 11103-1112. https://doi.org/10.1093/infdis/jiz646
5. Huor A*; **Espinosa JC***(1/20); Vidal E*;… O Andreoletti(CA). The emergence of classical BSE from atypical/Nor98 scrapie. Proc. Natl. Acad. Sci. USA. 2019. 116 (52), 26853-26862. *Joint authorship. https://doi.org/10.1073/pnas.1915737116
6. Espinosa JC, Comoy E, Marín-Moreno A, Aguilar-Calvo P, Birling MC, Pitarch JL, Deslys JP, Torres JM(CA). Transgenic mouse models expressing human and macaque prion protein exhibit similar prion susceptibility on a strain-dependent manner. Sci rep 2019; 9 (1), 1-9. https://doi.org/10.1038/s41598-019-52155-z
7. Fernández-Borges N*, **Espinosa JC***(1/9), Marín-Moreno A, … Torres JM(CA). Protective Effect of Val129-PrP against Bovine Spongiform Encephalopathy but not Variant Creutzfeldt-Jakob Disease. Emerg Infect Dis. 2017; 23: 1522. *Joint authorship.
doi: 10.3201/eid2309.161948
8. Espinosa JC(1/12), Nonno R, Bari MDi, ... Torres JM(CA). PrP^C governs susceptibility to prion strains in bank vole, while other host factors modulate strain features. J. Virol. 2016; 90 (23) 10660-10669. doi: 10.1128/JVI.01592-16
9. Cassard H, Torres JM, Lacroux C, … **Espinosa JC**(13/15), Beringue V, Andreoletti O(CA). Evidence for zoonotic potential of ovine scrapie prions. Nat Commun 2014; 5:5821. https://doi.org/10.1038/ncomms6821
10. Torres JM(CA), Castilla J, Pintado B, Gutierrez-Adan A, Andreoletti O, Aguilar-Calvo P, Arroba AI, Parra-Arrondo B, Ferrer I, Manzanares J, **Espinosa JC**(11/11)**.** Spontaneous generation of infectious prion disease in transgenic mice. Emerg Infect Dis 2013; 19:1938-1947. doi: 10.3201/eid1912.130106

C.2. Congress

Throughout my career, I have had the privilege of contributing to over one hundred international congresses, presenting my work in a variety of formats, including oral presentations and invited conferences. These opportunities have allowed me to share my research and ideas with colleagues from around the world, and have helped me to stay at the forefront of my field. Some highlights of my contributions are provided below:
1. Congress: 9th Iberian Prion Congress. City: Jaca (Spain). Title: Strain dependent susceptibility to prion infection modulated by R171 or K176 sheep-PrP polymorphic variants. Authors: **Espinosa JC**; Marín-Moreno A; Sara Canoyra Sánchez; Fernández-Borges N; Aguilar-Calvo P; González L; Andreoletti A; Benestad SL; Torres JM. Date: 12/2021. Type: **oral presentation**.
2. Congress: 8th Iberian Prion Congress. City: Castelo Branco (Portugal). Title: Amino acid residues in beta2-alfa2 loop of human-PrP regulate prion strain susceptibility. Authors: **Espinosa JC**; Marín-Moreno A; Aguilar-Calvo P; Lorenzo P; Villa A; Prieto A; Torres JM. Date: 10/2019. Type: **oral presentation**.
3. Congress: Prion 2018. Back to basics: Understanding prions. Santiago de Compostela (Spain). Title: Pig-PrP as a paradigm of resistance to prion propagation. Authors: **Espinosa JC**; Aguilar-Calvo P; Marín-Moreno A; Pitarch JL, Puntero I, Benestad SL; Andreoletti A; Torres JM. Date: 05/2018. Type: **oral presentation**.
4. Congress: 6th Iberian Prion Congress. Córdoba (Spain). Title: Role of polymorphic variants of the prion protein in the differential susceptibility to prion strain infection. Authors: **Espinosa JC**; Aguilar-Calvo P; Marín-Moreno A; González L; Andreoletti, O.; Benestad S.; Torres JM. Date: 10/2017. Type: **oral presentation**.
5. Congress: 4th Iberian Prion Congress. Lisbon (Portugal). Title: Comparison of the transmission features of several prion strains in a transgenic mouse model and in its natural counterpart. Authors: **Espinosa JC**; Nonno R; Di Bari; Aguilar-Calvo P; Pirisinu P; Prieto I; Lorenzo P; Frassanito P; Villa A; Agrimi U; Torres JM; Date: 12/2015. Type: **oral presentation**.
6. Congress: 3th Iberian Prion Congress. Zaragoza (Spain). Title: Porcine species is resistant to a broad diversity of prions. Authors: **Espinosa JC**; Aguilar-Calvo P; Villa A; Prieto I; Lorenzo P; Esteban A; Piquer J; Torres JM; Date: 12/2014. Type: **oral presentation**.

7. Congress: 2th Iberian Prion Congress. Title: Co-expression of two species PrP^{C} can interfere PrP^{Sc} replication depending on their amino acid sequences. Authors: **Espinosa JC**; Aguilar-Calvo P; Andreoletti O; Torres JM; Date: 12/2013. Type: **oral presentation**
8. Congress: 1th Iberian Prion Congress. Title: Human susceptibility to BSE from different species as assayed in transgenic mice. Authors: **Espinosa JC**; Aguilar-Calvo P; Padilla D; Morales M; Pintado B; Gutiérrez-Adán A; Esteban A; Andreoletti O; Torres JM; Date: 12/2012. Type: **oral presentation.**

C.3. Research projects

1. Project: PCI2023-143365. Classical Scrapie in Iceland, a model for prion diseases worldwide (ICRAD-ERANET 2nd call. ScIce; ID:54; 2021). Start-end: 01/04/2023 - 31/03/2026. **IP: Espinosa JC.** Budget: 172.000 €. Funded by: Agencia Estatal de Investigación.
2. Project: PCI2023-143384. Classical scrapie in genetically resistant goats: questioning current concepts and policies (ICRAD-ERANET 2nd call. ScIce; ID:59; 2021). Start-end: 01/04/2023 - 31/03/2026. IP: Fernandez–Borges N**.** Budget: 172.000 €. Funded by: Agencia Estatal de Investigación. Researcher in the project: **Espinosa JC.**
3. Project: PID2019-105837RB-I00. Zoonotic potential evolution of emerging prions through the species barrier (2019A I+D+I Projects). Zoonotic-prions. Start-end: 01/06/2020 - 31/05/2024. Co-IP: **Espinosa JC.** Budget: 193.842 €. Funded by: Agencia Estatal de Investigación.
4. Project: PCI2020-120680-2. Tackling chronic wasting disease in Europe (ICRAD-ERANET 1st call TCWDE). Start-end: 31/03/2021 - 30/03/2024. **IP: Espinosa JC.** Budget: 150.000 €. Funded by: Agencia Estatal de Investigación.
5. Project: Atyprion 201821-31. Evaluation of the public health risk of atypical and emerging prions. (2017 Infectious diseases. Atyprion; 201821-31). Start-end: 1/08/2019 - 31/01/2023. **IP: Espinosa JC.** Budget: 160.000 €. Funded by: Fundació La Marató de TV3.
6. Project: AGL2016-78054-R. Deciphering the molecular mechanisms involved in prion strain diversity and stability; (2016 I+D+I Projects). Start-end: 01/01/2017 - 31/12/2019. Co-**IP: Espinosa JC.** Budget: 150.000 €. Funded by: Ministerio de Economía y Competitividad.
7. Project: AGL2012-37988-C04-04. *In vitro* and *in vivo* dissection of the molecular mechanisms of prion replication by overcoming transmission barriers naturally pre-established; (2011 I+D+I Projects.). Start-end: 01/01/2013 - 31/12/2015. **IP**: **Espinosa JC.** Budget: 163.800 €. Funded by: Ministerio de Economía y Competitividad.
8. Project: 2013-0144332. Deciphering the role of α-synuclein strains in prion-like synucleopathy induction and spreading. Start-end: 3/16/2015 - 3/15/2018. IP: Torres JM. Budget: 150.000 €. Funded by: Fundació La Marató de TV3. Researcher in the project: **Espinosa JC.**
9. Project: 219235. Towards breeding of goats for genetically determined TSEs resistance. (FP7 ERA-NET EMIDA). Start-end: 01/09/2012 - 01/12/2015. **IP**: **Espinosa JC.** Budget: 229.500 €. Funded by: Ministerio de Economía y Competitividad.
10. Project: FSA-M3043. Exploring Permeability of human species barrier to circulating TSE agent. Start-end: 01/01/2007 - 01/30/2018. IP: Torres JM. Budget: 498.000 €. Funded by: Food Standards Agency, UK. Researcher in the project: **Espinosa JC.**

C.4. Contracts, technological or transfer merits

1. Contract: Transmissible spongiform encephalopathy (TSE) testing in CHO cells from CEVA. Start-end: 15/12/2023 - 14/12/2025. Responsible researcher: **Espinosa JC.** Budget: 14.000 €. Entity: Ceva Santé Animale S.A.
2. Contract: Evaluation of the potential infectivity of the RT-QuIC product to avoid iatrogenic TSE. Start-end: 20/10/2018 - 19/04/2023. Responsible researcher: Torres JM. Researcher in the contract: **Espinosa JC.** Budget: 42.900 €. Entity: Department of Neurology/Prion Research Group. University Medical School Robert Koch.
3. Member of the “Cervid and production animal surveillance, laboratory capacity, planning and disese” Chronic Wasting Disease Working Group. Center for Infectious Disease Research and Policy (CIDRAP). University of Minnessotta. USA.