

CURRICULUM VITAE - SUMMARY

PERSONAL INFORMATION

NAME: **Nuno Luis Costa Borges**

PROFESSIONAL ADDRESS: Embryotools, Parc Cientific de Barcelona, Av. Doctor Marañon, 8. 08028 Barcelona – Spain.

EMAIL: nuno.borges@embryotools.com

NATIONALITY: Portuguese

PLACE AND DATE OF BIRTH: Coimbra, Portugal, 19-11-1979

EDUCATION AND TRAINING

2006 to 2011: **PhD in Reproductive Biology**

2003 to 2005: **MSc in Cell Biology**

2002 to 2003: **Post-graduation in Biotechnology**

1997 to 2002: **Degree (4 years + 1 year of training) in Biochemistry**

SUMMARY

Nuno Costa-Borges is an embryologist with over 18 years of experience in both research and clinical practice. As a PhD fellow supported by the Portuguese National Funding Agency for Science (FCT), Nuno spent several years developing strategies to improve the efficiency of animal cloning, successfully achieving the first cloned animals in Spain in 2009. After completing his PhD at the Autonomous University of Barcelona, he joined the embryology team at IVI Barcelona, where he worked as a clinical embryologist.

Nuno later co-founded Embryotools, where he has focused on providing quality control tests, training, and consulting services to the global IVF community. As the scientific director of Embryotools, he has been committed to developing new IVF techniques, including the flicking method for blastocyst biopsy and the maternal spindle transfer technique. His work has resulted in several peer-reviewed publications, and he has been an invited speaker at numerous international conferences and scientific meetings. He has also received prestigious awards, including the Paper Prize from the American Society of Reproductive Medicine (ASRM) in 2017, the IVI Foundation Award in 2019, the Paper Prize from the Society for Reproductive Biology and Technology (SRBT) and ASRM in 2022, and the Robert Edwards Award for the best paper published in RBMO in 2023.

Nuno was instrumental in producing the embryos that led to the birth of the world's first babies following maternal spindle transfer for the treatment of infertility associated with poor oocyte quality. More recently, he was involved in the development of a semi-automated ICSI system, which resulted in the birth of the world's first babies using this technology in 2023.

WORKING EXPERIENCE

- 2013 to – Present: **Co-Founder, Scientific Director**
Embryotools SL, Barcelona, Spain
- 2010 to - Present: **Clinical Embryologist**
Instituto Valenciano de Infertilidad (IVI) de Barcelona, Spain
- 2007 to 2010: **PhD fellow**
Fellow of the Fundação para a Ciência e a Tecnologia, Ministerio da Educação e Ciência, Portugal
- 2006 to 2007: **Assistant Professor**
Universitat Autònoma de Barcelona – Departament de Biologia Cel•lular, Fisiologia i Immunologia, Facultat de Biociències, Spain

RESEARCH SKILLS AND COMPETENCES

AREA OF SCIENTIFIC ACTIVITY: Embryo Reproduction, Clinical Embryology and Developmental Biology.

PRESENT RESEARCH INTERESTS: Oocyte and Embryo Cryopreservation; Mitochondrial Replacement Therapies; Animal Cloning by Somatic Cell Nuclear Transfer; laboratory automation.

TECHNIQUES FAMILIARIZED WITH: Embryo biopsy on Day 3 and Day 5; Polar body biopsy; Intra-cytoplasmic sperm injection (ICSI); maternal spindle transfer (MST), Tubing of biopsied cells; Oocyte pick-up; Embryo grading and transfer; Vitrification / warming of human oocytes and embryos; Time-lapse embryo grading; Embryo and oocyte fixation for immunofluorescence analysis; Mouse Embryo Assays (MEA); Somatic cell nuclear transfer; Biopsy and ICSI in Equine Embryos.

PARTICIPATION IN RESEARCH PROJECTS:

Principal investigator in the project: “*Development of a new technique for spindle transfer in metaphase II oocytes*” funded by the Acció-Generalitat de Catalunya and the European Regional Development funds (ERDF, Ref. RD 15-1-0011.).

Full-time researcher in the project: “*Desarrollo de nuevas estrategias de obtención de células madre embrionarias*” funded by the Ministerio de Educación y Ciencia de España (BIO2006-11792).

Full-time researcher in the project: “*Desenvolupament d’un protocol d’enucleació química d’oòcits per al clonatge de mamífers per transferència nuclear*” funded by the Universitat Autònoma de Barcelona (2004-24).

MOST RELEVANT PUBLICATIONS

Parra A, Denkova D, Burgos-Artizzu XP, Aroca E, Casals M, Godeau A, Ares M, Ferrer-Vaquer A, Massafret O, Oliver-Vila I, Mestres E, Acacio M, **Costa-Borges N**, Rebollo E, Chiang HJ, Fraser SE, Cutrale F, Seriola A, Ojosnegros S. METAPHOR: Metabolic evaluation through phasor-based hyperspectral imaging and organelle recognition for mouse blastocysts and oocytes. Proc Natl Acad Sci U S A. 2024 Jul 9;121(28).

Martínez-Casado A, Acacio M, Matia-Algué Q, Casals A, Villamar A, Franco-Roig A, Mendoza M, Castelló C, Medina S, Calderón G, **Costa-Borges N**, Mestres E. Culture medium and protein supplementation affect sensitivity of the mouse embryo assay in detecting

Triton X-100. *Reprod Biomed Online*. 2024 May 18;49(4):104120. doi: 10.1016/j.rbmo.2024.104120. Online ahead of print.

Costa-Borges N, Munné S, Albó E, Mas S, Castelló C, Giralte G, Lu Z, Chau C, Acacio M, Mestres E, Matia Q, Marquès L, Rius M, Márquez C, Vanrell I, Pujol A, Mataró D, Seth-Smith M, Mollinedo L, Calderón G, Zhang J. First babies conceived with Automated Intracytoplasmic Sperm Injection. *Reprod Biomed Online*. 2023 May 25:103237. doi: 10.1016/j.rbmo.2023.05.009.

Costa-Borges N, Nikitos E, Späth K, Miguel-Escalada I, Ma H, Rink K, Coudereau C, Darby H, Koski A, Van Dyken C, Mestres E, Papakyriakou E, De Ziegler D, Kontopoulos G, Mantzavinos T, Vasilopoulos I, Grigorakis S, Prokopakis T, Dimitropoulos K, Polyzos P, Vlachos N, Kostaras K, Mitalipov S, Calderón G, Psathas P, Wells D. First pilot study of maternal spindle transfer for the treatment of repeated in vitro fertilization failures in couples with idiopathic infertility. *Fertil Steril*. 2023 Feb 12:S0015-0282(23)00136-X.

E Mestres, Q Matia-Algué, A Villamar, A Casals, M Acacio, M García-Jiménez, A Martínez-Casado, C Castelló, G Calderón, **N Costa-Borges**. Characterization and comparison of commercial oils used for human embryo culture. *Human Reproduction*, Volume 37, Issue 2, February 2022, Pages 212–225.

E Mestres, M García-Jiménez, A Casals, J Cohen, M Acacio, A Villamar, Q Matia-Algué, G Calderón, **N Costa-Borges**. Factors of the human embryo culture system that may affect media evaporation and osmolality. *Hum Reprod*. 2021 Feb 18;36(3):605-613.

Costa-Borges N; Katharina Späth; Irene Miguel-Escalada; Enric Mestres; Rosa Balmaseda; Maria Garcia, Ivette Vanrell; Jesús Gonzalez; Klaus Rink, Dagan Wells; Gloria Calderón. Meiotic spindle transfer overcomes embryo developmental arrest caused by ooplasmic defects in the mouse. *Elife*. 2020 Apr 29;9:e48591.

E.Mestres, M.Garcia-Jiménez, L.Faes, I.Vanrell, V.Bogaert, I.Jonckheere, A.Casals, C.Llop, M.Sentí, G.Calderón, **Costa-Borges N**. Parameters of the Mouse Embryo Assay that affect detection of peroxides in mineral oil. *Reprod Biomed Online*. 2019 Oct;39(4):547-555.

Castelló D, Cobo A, Mestres E, Garcia M, Vanrell I, Remohí JA, Calderón G, **Costa-Borges N**. 2018. Pre-clinical validation of a closed surface system (Cryotop SC) for the vitrification of oocytes and embryos in the mouse model. *Cryobiology* 2018 Apr;81:107-116.

Costa-Borges N, Bellés M, Meseguer M, Galliano D, Ballesteros A, Calderón G. 2016. Blastocyst development in single medium with or without renewal on day 3: a prospective cohort study on sibling donor oocytes in a time-lapse incubator. *Fertil Steril* 105 (3):707-713.

Costa-Borges N, González S, Santaló J, Ibáñez E. 2011. Effect of the enucleation procedure on the reprogramming potential and developmental capacity of mouse cloned embryos treated with valproic acid. *Reproduction*. *Reproduction*, 141:789-800.

Costa-Borges N, Paramio MT, Santaló J, Ibáñez E. 2011. Demecolcine- and nocodazole-induced enucleation in mouse and goat oocytes for the preparation of recipient cytoplasts in somatic cell nuclear transfer procedures. *Theriogenology*, 75:527-541.

Costa-Borges N, Santaló J, Ibáñez E. 2010. Comparison between the effects of valproic acid and trichostatin A on the in vitro development, blastocyst quality, and full-term development of mouse somatic cell nuclear transfer embryos. *Cellular Reprogramming (former Cloning and Stem Cells)*, 12:437-446.

Costa-Borges N, González S, Santaló J, Ibáñez. 2009. Collection and cryopreservation of hamster oocytes and mouse embryos. *J Vis Exp*. 27:1120. doi: 10.3791/1120.

Costa-Borges N, Paramio MT, Calderón G, Santaló J, Ibáñez. 2009. Antimitotic treatments for chemically assisted oocyte enucleation in nuclear transfer procedures. *Cloning and Stem Cells*, 11:153-166.

CONFERENCE PROCEEDINGS

Costa-Borges N, Nikitos E, Spath K, Kostaras K, Zervomanolakis I, Kontopoulos G, et al. First registered pilot trial to validate the safety and effectiveness of maternal spindle transfer to overcome infertility associated with poor oocyte quality. *Fertil Steril*. 2020;114(3,suppl):e71–2.

Costa-Borges N., Nikitos E., Rink IM-EK., Spath K., Wells D., Zervomanolakis I., Vasilopoulos I., Grigorakis DDZS., Kontopoulos G., Prokopakis T., Dimitropoulos K., Vlachos PPN., Kostaras K., Psathas P., Calderon G. 2018. Spindle transfer can enhance the potential of developmentally compromised human oocytes to reach the blastocyst stage: proof of concept with donor oocytes. *Human Reproduction*, 33, Supplement 1, i237-238.

Mestres E; Garcia-Jimenez M; Faes L; Vanrell I; Bogaert V; Jonckheere I; Casals A; Llop C.; **Costa-Borges N**, Calderón G. 2018. Development of a Mouse Embryo Assay with enhanced sensitivity for detection of peroxides in mineral oil samples. *Human Reproduction*, 33, Supplement 1, i239.

Costa-Borges, N, Mestres, E, Miguel-Escalada, I, Balmaseda R, Garcia, M, Vanrell I, Gonzalez J, Calderon, G. 2017. Meiotic Spindle transfer overcomes embryo developmental arrest in compromised oocyte: proof of concept in the mouse. *Fertility and Sterility*, Vol 108, Issue 3, Supplement, Page e41.

Costa-Borges N, Nikitos E, Rink K, Agapitou K, Kallergi S, Botzaki D, Makri C, Vassilopoulos G, Vlachos N, Zervomanolakis G, Polyzos P, Dimitropoulos K, Kontopoulos G, Prokopakis K, Kostaras, P. Psathas, G. Calderon. 2017. Meiotic spindle transfer between human donor oocytes using chemically-induced or HVJ-E karyoplast fusion: preliminary results. Word ART congress. New York.

Costa-Borges N, E. Nikitos, K. Agapitou, S. Kallergi, D. Botzaki, C. Makri, G. Vassilopoulos, N. Vlachos, G. Zervomanolakis, P. Polyzos, K. Dimitropoulos, K. Kostaras, P. Psathas, K. Rink, G. Calderon. 2017. Zona thinning and classic assisted hatching preformed with systematic

- multipulse laser settings result in significant improvements of clinical outcomes in frozen embryo transfer cycles. *Human Reproduction*, 32, Supplement 1, i242.
- E. Mestres, I. Vanrell, M. Garcia-Jimenez, G. Calderon, **Costa-Borges N.** 2017. Pre-clinical validation of the meiotic spindle transfer technique in the mouse model. *Human Reproduction*, 32, Supplement 1, i239.
- Mestres E; Balmaseda R; Miguel-Escalada I; Garcia M; Vanrell I, Gonzalez J; Palacios J; Calderón G; **Costa-Borges N.** 2017. La transferencia de huso meiótico mejora el desarrollo embrionario de ovocitos con potencial limitado: prueba de concepto en el modelo murino. *ASEBIR*.
- Herrero L, Basile N., Garcia Velasco J, **Costa-Borges N**, Calderon G. 2016. A systematic study using a laser reveals differences in blastocyst hatching rate and clinical outcomes between two different methods: classic assisted hatching (AH) and zona thinning (ZT). *Fertility and Sterility* Vol 106, Issue 3, Supplement, Page e309.
- E. Mestres, I. Vanrell, **Costa- Borges N**, G. Calderon. 2015. Details to consider when setting-up dishes and heated stages in the IVF lab: how to minimize the impact of temperature fluctuations outside the incubator. *Human Reproduction*, 30, Supplement 1, i222.
- Vanrell Barbat I, Mestres E, García M; **Costa-Borges N**; Calderón G. 2015. Efecto del tipo de incubador utilizado en la recuperación de la temperatura de las microgotas en medio de cultivo. *ASEBIR*.
- Simjanovska L., Mestres E., Calderon G., **Costa-Borges N.** 2015. Analysis of the influence of an enriched negative ions atmosphere on mouse embryo development. *COGEN*.
- Bellés M., **Costa-Borges N.**, Molina J. Pellicer, A. Ballesteros A, Esbert M. 2014. Embryo quality and clinical outcomes using embryoscope™, minc™ and heracell™ 150i incubators: preliminary results from a randomized study with donor oocyte. *Human Reproduction*, 29, Supplement 1, i160
- Bellés M., **Costa-Borges N.**, Molina J. Pellicer, A. Ballesteros A, Esbert M. 2013. Exposure of embryos to oxygen at low concentration in an oocyte donation program with cleavage stage transfer. *Fertility and Sterility* Vol. 100, Issue 3, Supplement, Page S250.
- Costa-Borges N**, Bellés M, Herreros J, Ballesteros A, Pellicer A, Calderón G. 2013. Single medium culture in a time-lapse incubator until the blastocyst stage with or without medium renewal on Day-3: a prospective randomized study with donor oocytes. *Hum. Reprod.* (2013) 28 (suppl 1): i149-i206.
- Costa-Borges N**, González S, Santaló J, Ibáñez. 2009 Comparison between chemically-assisted, chemically-induced and mechanical enucleation of mouse oocytes. *Reproduction, Fertility and Development*, 21(1):113.
- González S, Ibáñez E, **Costa-Borges N**, Santaló J. 2008. Comparison between three different methods for establishing mouse embryonic stem cells from single blastomeres. *Human Reproduction*, 23, Supplement 1, i93.

Costa-Borges N, Santaló S, Ibáñez E. 2007. Enucleation of pre-activated mouse oocytes induced by demecolcine, nocodazole and vinblastine. *Reproduction, Fertility and Development*, 19:135.

González S, Ibáñez E, **Costa-Borges N**, Santaló J. 2007. Derivation of mouse ESC lines from isolated blastomeres. *Human Reproduction*, 22, Supplement 1, i171.

Costa-Borges N, Paramio MT, Santaló J, Ibáñez E. 2005. Enucleación química de ovocitos de ratón y de cabra: una alternativa para la preparación de citoplastos receptores en transferencia nuclear. *ASEBIR*, 3: 42-43.

OTHER PUBLICATIONS

Costa-Borges N, Mestres E, Garcia M, Vanrell I, Calderón G, Sandra Stobrawa. 2017. Intracytoplasmic Sperm Injection (ICSI) in the Mouse with the Eppendorf PiezoXpert®: How to Increase Oocyte Survival Rates After Injection. *Eppendorf Userguide* 395.

Costa-Borges N, Mestres E, Garcia M, Vanrell I, Rink K, Levtonov M, Calderón G. 2016. Trophectoderm biopsy of blastocysts using the Eppendorf TransferMan® 4m micromanipulators assisted by a laser system. *Eppendorf Userguide* 351.

Costa-Borges N, Santamaria X, Calderon G. 2013. Maternal spindle transfer to prevent mitochondrial diseases: closer to clinical application. *ASEBIR*, June 18, vol I, 6-9.

Costa-Borges N, Sanchez-Arbouin R. 2012. Biopsy of Equine Embryos with the Eppendorf PiezoXpert® for Preimplantation Genetic Diagnosis. *Eppendorf Userguide* 047.

Costa-Borges N, González S, Santaló S, Ibáñez E. 2007. Enucleació químicament induïda d'òcits de ratolí per a la seva aplicació en protocols de transferència nuclear. *Societat Catalana de Biologia, Biologia de la Reproducció*, 10:53-57.

González S, Ibáñez E, **Costa-Borges N**, Santaló J. 2007. Derivació de cèl·lules mare embrionàries a partir de blastòmers aïllats de ratolí. *Societat Catalana de Biologia, Biologia de la Reproducció*, 10:65-69.

Costa-Borges N, Santaló J, Ibáñez. 2006. Preparation of recipient cytoplasts for nuclear transfer by chemical oocyte enucleation. *IberoAmericana de Fertilidad y Reproducción Humana*, 23:163-172.

Costa-Borges N, Paramio MT, Santaló J, Ibáñez E. 2005. Avaluació de l'eficiència del colcemid, nocodazol i vinblastina per l'enucleació químicament assistida d'òcits de ratolí i de cabra. *Societat Catalana de Biologia, Biologia de la Reproducció*, 9:73-79.

THESIS COMMITTEES

Member of the PhD thesis committee of Bladimir Lenin Cordova Veizaga. 2011.

Thesis title: “Estrategias de cultivo para optimizar la maduración in vitro de ovocitos de terneras prepúberes”.

Directors: Dr. Maria Teresa Mogas Amorós and Dr. Maria Dolors Izquierdo Tugas.

Degree awarded by the Universitat Autònoma de Barcelona

Member of the PhD thesis committee of Nuria Arcarons Deseures. 2017.

Thesis title: “OPTIMITZACIÓ DE LA VITRIFICACIÓ DELS OÒCITS BOVINS MADURATS IN VITRO”.

Director: Dr. Maria Teresa Mogas

Degree awarded by the Universitat Autònoma de Barcelona.

Member of the PhD thesis committee of Iris Martínez Rodero. 2023.

Thesis title: “In vitro production of bovine embryos: different approaches to optimize their vitrification”.

Director: Dr. Maria Teresa Mogas

Degree awarded by the Universitat Autònoma de Barcelona.

Member of the PhD thesis committee of Antonia Christodoulaki. 2023.

Thesis title: “: Germline nuclear transfer to overcome oocyte cytoplasmic immaturity of in vitro matured oocytes”.

Director: Dr. Björn Heindryckx

Degree awarded by the Ghent University Hospital.

PhD thesis director

Enric Mestres, 2022. Identifying the factors that influence the stability of the embryo culture system and the sensitivity of the Mouse Embryo Assay. Classification: Cum Laude.

Damià Castelló Salom, 2018. Development and validation of a new completely closed vitrification system for human IVF. Cum laude. Classification: Cum Laude.

PRIZES AWARDED, MERITS

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- **PaperPrize award SARBT-ASRM 2023.**
- **IVI foundation Award 2019.**
- **PaperPrize award ASRM 2017.**
- **First Horses born in Europe after embryo biopsy** using Piezo drill micromanipulation and sex selection by PCR. Paul Schockemöhle’s farm. Lewitz (Germany), 2012.
- First horses by ICSI made in Spain in 2018.
- **“Best Poster Award”,** IV Scientific Meeting of the Departament Biologia Cel·lular, Fisiologia i Immunologia, Universitat Autònoma de Barcelona, 2010.
- **First successfully cloned animals** in Spain, 2009.
- **Merit award from the Rector of the Universitat Autònoma de Barcelona,** Dr. Anna Ripoll, in recognition for the successful cloning of the first animals in Spain, 2009.
- Second prize in the Students’ Competition at the 25th Scientific meeting of the European Embryo Transfer Association. Poznan (Poland), 2009.