

CURRICULUM VITAE ABREVIADO (CVA)

Part A. PERSONAL INFORMATION

First name	Maria Ángeles (Marian)
Family name	Ros Lasierra

A.1. Current position

Position	Profesora de Investigación CSIC
Center	Instituto de Biomedicina y Biotecnología de Cantabria
Country	Spain
Key words	Developmental Biology; Limb development; Cell signaling; Hox genes; Mouse genetics; Lmx1b; transcriptional regulation

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

Period	Position/Institution/Country/Interruption cause
20/05/88-23/06/05	Profesora Titular de Universidad
24/06/05	Catedrática de Universidad

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
PhD in Medicine and Surgery	University of Cantabria	1986
MD	University of Cantabria	1982

Part B. CV SUMMARY

Marian Ros received her M.D. at the University of Cantabria, in 1982 with the special award of the year (Premio Extraordinario de la Promoción). In 1986, she obtained a PhD at the University of Cantabria, studying an animal model of polycystic kidney disease. After a postdoctoral stay in the laboratory of Dr. John Fallon (University of Wisconsin-Madison, USA) studying the role of *Msx* and *Hox* genes in limb development, she established her own research group in the Department of Anatomy and Cell Biology of the University of Cantabria in 1996. In 2005 she obtained a full professorship position at the University of Cantabria and in 2007 she moved to the Spanish Research Council (CSIC) when the Instituto de Biomedicina y Biotecnología de Cantabria (IBBTEC) was created. She is member of the Royal Academy of Medicine of Cantabria and the awardee the 2013 Prize of Investigation Consejo Social de la Universidad de Cantabria Juan María Parés. With a broad background in Developmental Biology, Human Anatomy and Embryology, Marian Ros research has consistently focused on understanding the molecular basis of morphogenesis: how the formation of a particular structure is genetically and molecularly controlled during vertebrate development. Using the limb as a paradigm, her team has made significant contributions by uncovering key molecules and mechanisms that influence organ shaping, always with a translational interest towards disease, repair and regeneration. Her lab's extensive experience in cutting-edge mouse genetic techniques and proficiency with the chick model, has resulted in the successful generation of animal models for various human genetic malformations, including phocomelia, sirenomelia, SHFM, and polydactyly to delve into the underlying mechanisms and etiological factors driving these conditions. In recent years, the lab has embraced state-of-the-art genomic technologies and harnessed the power of genome editing through CRISPR-Cas9 direct electroporation of mouse zygotes. This has substantially broadened the scope and impact of our research. Currently, the Ros' group research focuses on the following areas:

- Mechanisms regulating dorsoventral (DV) limb patterning and their relevance to Nail-Patella Syndrome.
- The involvement of SP and DLX transcription factors in the etiology of human ectrodactyly.
- Reevaluation of current limb development models using state-of-the-art technologies.

Part C. RELEVANT MERITS (sorted by typology)

C.1. Publications (Selected publications, organized by theme)

Dorso-ventral patterning and Lmx1b function

Hawkins MB, Zdras S, Naranjo S, Juliá M, Sanchez-Martin M, ...S, Harris MP*, Tena JJ*, **Ros MA*** (2025) Establishment, conservation, and innovation of dorsal determination mechanisms during the evolution of vertebrate paired appendages. *Current Biology* (in press).

Zdras S, Bordignon SG, Meyer A, **Ros MA**, Woltering JM (2025). Dorsoventral limb patterning in paired appendages emerged via regulatory repurposing of an ancestral posterior fin module. *Mol Biol Evol.* 2026 Jan 3;43(1):msaf331. doi: 10.1093/molbev/msaf331.

Skoufa E, Zhong J, ... Castilla-Ibeas A, Jang H, Weigert M, La Manno G, Lutolf M, **Ros M**, Aztekin C. 2025 *Sci Adv.* 11(48):eady7682. doi: 10.1126/sciadv.ady7682

Castilla-Ibeas A, Zdras S, Galán L ...**Ros MA*** (2023). Failure of digit tip regeneration in the absence of Lmx1b suggests Lmx1b functions disparate from dorsoventral polarity. *Cell Rep.* Jan 31;42(1):111975. Significance: We discovered persistent Lmx1b expression into adulthood and within the regeneration blastema suggesting novel roles for Lmx1b that go beyond dorsal-ventral patterning. <https://pubmed.ncbi.nlm.nih.gov/36641754/>

Haro E, Petit F, Pira CU ... **Ros MA***, Oberg KC* (2021) Identification of limb-specific *Lmx1b* auto-regulatory modules with Nail-Patella Syndrome pathogenicity. *Nat Commun.* Sep 20;12(1):5533. Significance: This work was pioneer in discovering Lmx1b transcriptional regulation and forms the basis for the DV part of this proposal. <https://pubmed.ncbi.nlm.nih.gov/34545091/>

Fernandez-Guerrero M, Yakushiji-Kaminatsui N, Lopez-Delisle L, ... Duboule D,* and **Ros MA*** (2020) Specific ectodermal enhancers control the expression of *Hoxc* genes in developing mammalian integuments. *Proc Natl Acad Sci U S A* 117(48):30509-30519 Significance: In collaboration with the Duboule's group, we discovered the enhancers controlling HoxC gene cluster expression in the ectoderm which jointly regulate hair and nail organ development. <https://doi.org/10.1073/pnas.2011078117>

Pérez-Gómez R, Fernández-Guerrero M, Campa V, Lopez-Gimenez JF, Rada-Iglesias A and **Ros MA*** (2024) Sp8 regulatory function in the limb bud ectoderm. submitted. Significance: We unveiled the dual mechanism of Sp8 in activating Fgf8 and DV patterning genes: direct DNA binding at Sp consensus sequences and indirect engagement through Dlx5 interaction. bioRxiv 2020.02.26.965178; <https://doi.org/10.1101/2020.02.26.965178>

Haro E, Delgado I, Junco M, Yamada Y, Mansouri A, Oberg KC, **Ros MA*** (2014) Sp6 and Sp8 transcription factors control AER formation and dorsoventral patterning in limb development. *PLoS Genet.* 2014 Aug 28;10(8):e1004468. Significance: We discovered the critical role of Sp6 and Sp8 as key regulators of Fgf8 and En1 in limb development. <https://doi.org/10.1371/journal.pgen.1004468>

Role of Hox genes in digit formation:

Bastida MF, Pérez-Gómez R, Trofka A, ... **Ros MA*** (2020) The formation of the thumb requires direct modulation of *Gli3* transcription by *Hoxa13*. *Proc Natl Acad Sci U S A.* 117(2):1090-1096. Significance: We found that the mutual antagonism between Gli3 and Hox13 paralogs controls handplate asymmetry and triggers thumb formation. <https://doi.org/10.1073/pnas.1919470117>

Sheth R, Marcon L, Bastida MF, Junco M, Quintana L, Dahn R, Kmita M*, Sharpe J*, **Ros MA*** (2012) Hox genes regulate digit patterning by controlling the wavelength of a Turing-type mechanism. *Science* 338: 1476-1480 Significance: First to demonstrate a Turing-type self-organizing mechanism modulated by Hox genes as the basis for digit patterning. <https://doi.org/10.1126/science.1226804>

González-Martín MC, Mallo M, **Ros MA*** (2014) Long bone development requires a threshold of Hox function. *Dev Biol.* 392(2):454-65. Significance: The dose of 5'Hoxd genes determines long versus short bone development. doi: <https://doi.org/10.1016/j.ydbio.2014.06.004>
Models for proximo-distal specification in limb development

Pickering J, Rich CA, Stainton H, Aceituno C, Chinnaiya K, Saiz-Lopez P, **Ros MA***, Towers M* (2018) An intrinsic cell cycle timer terminates limb bud outgrowth. *Elife*. Sep 3;7. pii: e37429. *Significance: We indentified that a progressive intrinsic increase in Bmp expression is responsible for termination of the limb bud outgrowth.* doi: <https://doi.org/10.7554/eLife.37429.001>

Saiz-Lopez P, Chinnaiya K, Campa VM, Delgado I, **Ros MA***, Towers M* (2015) An intrinsic timer specifies distal structures of the vertebrate limb. *Nat Commun*. 6:8108. *Significance: We proposed a complete model for limb proximo-distal specification that involves the switch from extrinsic signals to intrinsic timing.* doi: <https://doi.org/10.1038/ncomms9108>

C.2. Congress, indicating the modality of their participation (invited conference, oral presentation, poster):

- Multiple participations in international conferences each year, usually by invitation.
- Invited speaker at every International Limb Meeting (biannual) since 2000.
- Keynote speaker at the International Limb Development and Regeneration Meeting, Edinburgh, July 2017.
- Keynote speaker at the Limb Development and Regeneration Meeting. July 2017, UK.
- Keynote speaker at the EMBO Workshop Limb development: Fundamental mechanisms, evolution, disease and regeneration. June 2024, Dresden, Germany.

C.3. Research projects.

Consistently funded by the Spanish Government's (Plan Estatal) since establishing myself as an independent researcher, always in the role of Principal Investigator. The four most recent projects here:

“El eje dorsoventral de la extremidad: investigando el papel de *Lmx1b* en desarrollo, evolución y regeneración” Ministerio de Ciencia e Innovación (PID2023-147771NB-I00)
2025-2028
IP: M.A. Ros

“Dorso-ventral polaridad de la extremidad y su implicación en morfogénesis y regeneración”
Ministerio de Ciencia e Innovación (PID2020-114525GB-I00)
01/09/2021 - 30/09/2024.
IP: M.A. Ros

“Descifrando las redes génicas reguladoras de *Sps* y *Hoxc* en el ectodermo de la extremidad”
Ministerio de Economía, Industria y Competitividad (BFU2017-88265-P)
01/01/2018 - 31/12/2020.
IP: M.A. Ros

“Análisis de la dinámica de la expresión génica durante las interacciones epitelio-mesenquimatosas en la extremidad”
Ministerio de Economía, Industria y Competitividad (BFU2014-57216-P)
01/01/2015 - 31/12/2017.
IP: M.A. Ros

Application for ERC Advanced Grant reaching the final stage but unfortunately not securing funding. Titled project: "Dorsal Ventral Limb Polarity Impact in Development, Evolution and Regeneration"

C.4. Institutional Responsibilities

2013 – present Chair - Department of Cell and Molecular Signaling- IBBTEC.
2007 – present Member of the Board of directors- IBBTEC
2009 – 2015 Founder and Scientific Director of the Advanced Microscopy Service at the IBBTEC
2006 – 2019 Member of the Bioethics Committee of the University of Cantabria
2020 – present Member of the Bioethics Committee of the Spanish Research Council

C.5. Editorial Service

Associate Editor *Developmental Dynamics* (since 2009)

C.6. Fellowships and Awards

- Member of the Royal Academy of Medicine of Cantabria (2016)
- Research Award University of Cantabria (2013)

C.7. Teaching activities: Representative of a rich history of dedication to teaching medical students:

- 1992 –2021 Human Anatomy and Embryology Course. Medical School. Univ of Cantabria.
- 1996 –2021 Neuroanatomy Course. Medical School. Univ of Cantabria.
- 1996 –2002 Developmental Biology for Medical Students. Univ of Cantabria.
- Since 1996 – Biomedicine and Molecular Biology Master Degree (UC-UPV).
- Since 2007– Collaborating Professor in Master's degrees of the University of Barcelona and Universidad Autónoma Madrid

C.8. Society/Meeting co-organization (selected)

- 2019 EMBO Workshop on Limb Dev and Regeneration, July 2019-Barcelona
- 2014-2018 Co-organizer of the 38th-39th-40th and 41st Conference of the SEBBM
- 2014 X Conference of the Spanish Society for Developmental Biology
- 2008 10th International Conference on Limb Development
- 2004 IV Conference of the Spanish Society for Developmental Biology
- 2002 Workshop Juan March Foundation

C.9. Professional Societies

Founding Member of the Spanish Society for Developmental Biology (SEBD)

Member of the Spanish Society for Biochemistry and Molecular Biology (SEBBM)

Member of the American Association for Anatomy (AAA)

C.10. Invited presentations (selected)

Seminars: Centro de Investigaciones Biológicas (CSIC; Madrid); Instituto de Biología Molecular de Barcelona; Fundación IFIMAV (Santander); Universidad de Cantabria; Universidad Autónoma de Madrid; Universidad del País Vasco (Spain); University Pierre et Marie Curie (Paris, France); Instituto de Biología y Genética Molecular (Valladolid); CBMSO (Madrid); University of Utrech (Países Bajos). University of Loma Linda (CA, USA); University of Würzburg (Alemania); University of Braunschweig (Alemania); University of Aberdeen (Scotland, UK); University of Basel (Switzerland); University of Geneve (Switzerland); University of Washington (San Luis, USA).

C.11. Reviewer:

Ad hoc reviewer for Scientific Journals *Science; Nature; Dev Cell; Nature Rev Mol Cell Biol; Nat. Rev. Genet.; Nat. Genet.; Nat. Commun.; PLOS Biology; Genes Dev.; EMBO Journal; PNAS USA; PLOS Genetics; Development; Dev Biol; Dev Dyn; Mech. Dev.*

Ad hoc reviewer funding agencies: National (Spain): Agencia Nacional de Evaluación y Prospectiva; BBV Foundation; - Fondo de Investigaciones Sanitarias; - Agencia Comunidad Autónoma de Castilla-León;- La Caixa Foundation. International: - Czech Science Foundation;- Deutsche Forschungsgemeinschaft (GER);- Fondo Nacional de Ciencia y Técnica (Argentina);- French National Research Agency (France);- Fundação para a Ciência e Tecnologia (Portugal);- Human Frontier Science Program (HFSP);- Israel Science Foundation; Israel Ministry of Health;- March of Dimes (USA);- National Science Foundation (USA);- Research Foundation Flanders (FWO) (Belgium);- Telethon Fondazione (Italy)