Scientific Report 2024

Advancing Women's Health

Carlos Simon
Foundation
FOR RESEARCH IN WOMEN´S HEALTH

Letter from the President

Reproductive health continues to raise important questions: How can we better diagnose gynecological conditions? How can we improve existing treatments? At the Carlos Simon Foundation, we seek not only answers, but real solutions. In 2024, we expanded our research, embraced new technologies, launched new projects, and strengthened collaborations with leading research groups to ensure science has a tangible impact on women's lives.

This report reflects that effort and our ongoing commitment to the future.
Thank you to everyone who makes it possible. We keep moving forward.

Carlos Simon

President of the Carlos Simon Foundation

Our Mission and Core Pillars

We believe in science that goes beyond the lab and reaches people. Our mission is to improve women's health, and it stands on three core pillars:

Biomedical Research

We conduct excellent biomedical research in women's health

Clinical Translation

We transform scientific knowledge from the lab into clinical and societal applications

Education

We pass on our knowledge and institutional culture to the next generation

2024 in Numbers

In 2024, we continued our research activity through pioneering projects, thanks to institutional support, a dedicated team, and the funding that allowed us to keep advancing reproductive health.

19

active research projects

6

peer-reviewed publications in Q1 journals (83% in D1, SJR 2023)

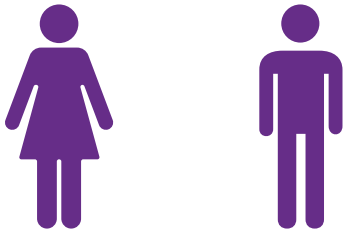
3.8M€

annual budget

Team and Talent

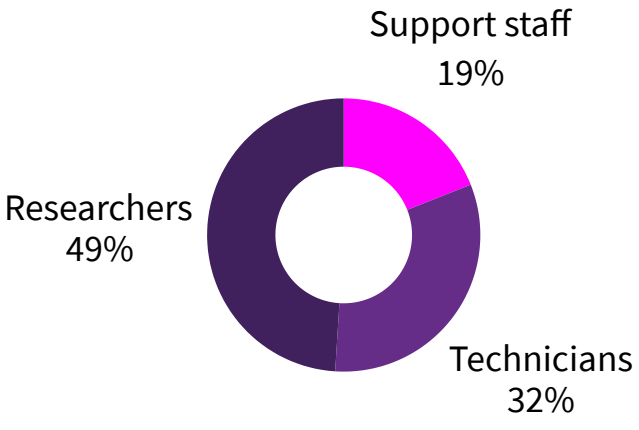
The Carlos Simon Foundation is more than a research center: it's a talent ecosystem. Our multidisciplinary team of 34 professionals is united by a shared commitment to transforming reproductive health.

Distribution by gender

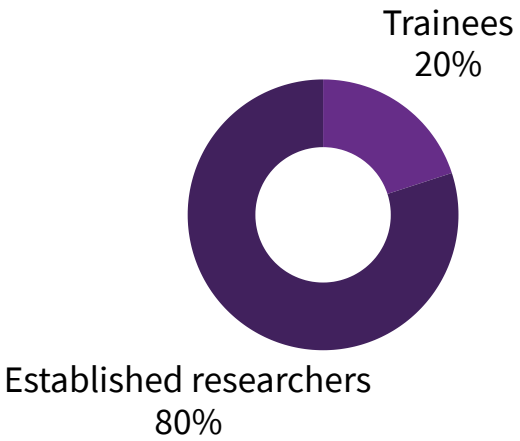


68% **32%**

Distribution by role



Distribution by training stage



Funding

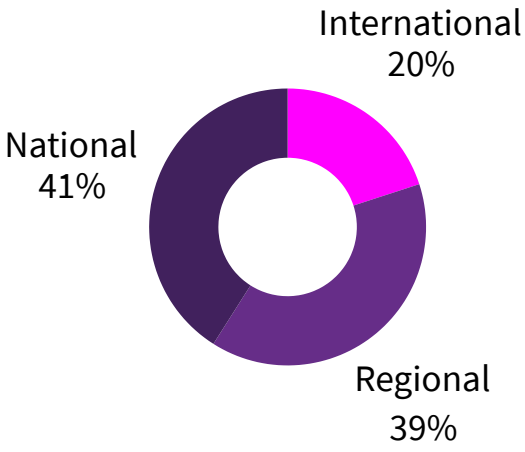
Thanks to the funding received in 2024, we launched new research lines and strengthened strategic partnerships.

R&D Budget

€3.05M own funding (81%)

€750K competitive funding (19%)

Competitive funding by origin



Selected projects with competitive funding in 2024 (full list available in Annex I)

eprObes Project

European consortium for the prevention of obesity starting in the periconceptional stage.

Project No. 101080219

13 partner institutions

€9.8M

Funded by the European Commission

PREMIC Project

Investigating the role of endometrial infection as a possible cause of preeclampsia.

PROMETEO Program (CIPROM/2022/41)

€600K

Funded by the Valencian Ministry of Education

HETEROGENEITY Project

Aims to develop a reference cellular atlas of the tumor microenvironment in gynecological cancers to support more precise, personalized treatments.

Ref. PI23/00536

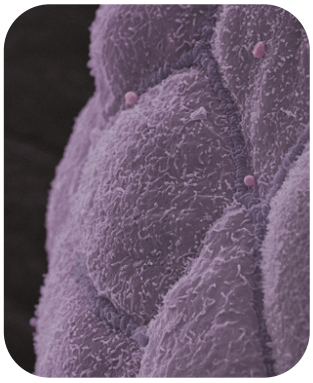
€226K

Funded by Instituto de Salud Carlos III

Research Lines

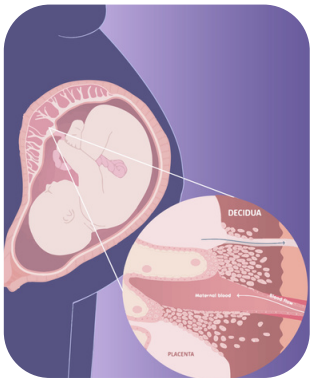
The Endometrial Microbiome in Human Reproduction

We study how endometrial microbiota influences local immunity and affects embryo implantation and reproductive outcomes.



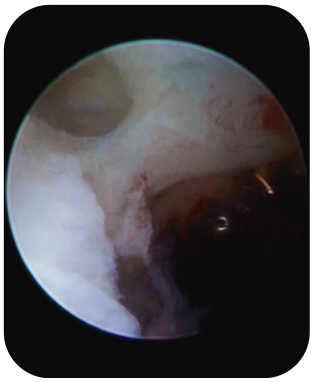
Maternal-Embryonic Cross-Talk

We investigate the genetic and epigenetic exchange between the endometrium and the embryo during implantation and its effect on embryo programming.



Maternal Implications in the Origin of Preeclampsia

We characterize defective decidualization of the endometrium as a maternal origin of preeclampsia using single-cell transcriptomics and longitudinal studies.

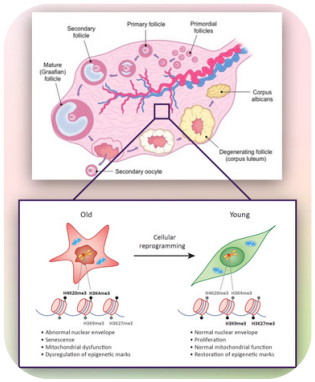


Endometrial Regenerative Therapies

We develop advanced therapies using autologous CD133+ stem cells to regenerate the endometrium in patients with Asherman's syndrome.

Molecular and Cellular Origins of Gynecological Tumors

We generate cellular atlases of gynecological tumors to identify initiating cells and their niches, moving toward personalized treatments.



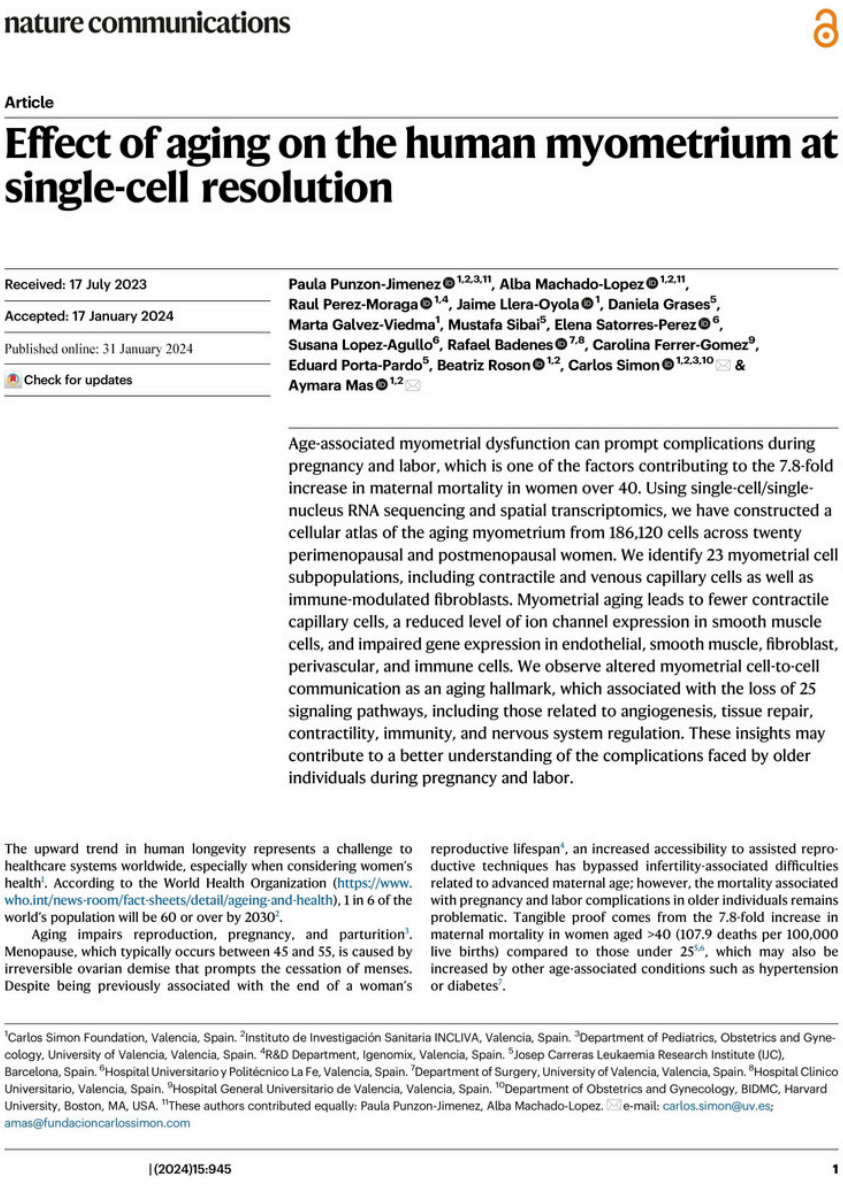
Ovarian Rejuvenation Through Partial Cellular Reprogramming

The CAROLINA project explores ovarian perfusion with partial reprogramming factors to reverse reproductive aging.

Scientific Output

In 2024, we published 6 scientific papers in indexed journals, 5 of which were in D1. These results reflect the quality and relevance of our research.

Featured publication:



nature communications

Article

Effect of aging on the human myometrium at single-cell resolution

Received: 17 July 2023

Accepted: 17 January 2024

Published online: 31 January 2024

Check for updates

Paula Punzon-Jimenez[1,2,3,11], Alba Machado-Lopez[1,2,11], Raul Perez-Moraga[1,4], Jaime Llera-Oyola[1], Daniela Grases[5], Marta Galvez-Viedma[1], Mustafa Sibai[5], Elena Satorres-Perez[6], Susana Lopez-Agullo[6], Rafael Badenes[7,8], Carolina Ferrer-Gomez[9], Eduard Porta-Pardo[5], Beatriz Roson[1,2], Carlos Simon[1,2,3,10] & Aymara Mas[1,2]

Age-associated myometrial dysfunction can prompt complications during pregnancy and labor, which is one of the factors contributing to the 7.8-fold increase in maternal mortality in women over 40. Using single-cell/single-nucleus RNA sequencing and spatial transcriptomics, we have constructed a cellular atlas of the aging myometrium from 186,120 cells across twenty perimenopausal and postmenopausal women. We identify 23 myometrial cell subpopulations, including contractile and venous capillary cells as well as immune-modulated fibroblasts. Myometrial aging leads to fewer contractile capillary cells, a reduced level of ion channel expression in smooth muscle cells, and impaired gene expression in endothelial, smooth muscle, fibroblast, perivascular, and immune cells. We observe altered myometrial cell-to-cell communication as an aging hallmark, which associated with the loss of 25 signaling pathways, including those related to angiogenesis, tissue repair, contractility, immunity, and nervous system regulation. These insights may contribute to a better understanding of the complications faced by older individuals during pregnancy and labor.

The upward trend in human longevity represents a challenge to healthcare systems worldwide, especially when considering women's health[1]. According to the World Health Organization (https://www.who.int/news-room/fact-sheets/detail/ageing-and-health), 1 in 6 of the world's population will be 60 or over by 2030[2].

Aging impairs reproduction, pregnancy, and parturition[3]. Menopause, which typically occurs between 45 and 55, is caused by irreversible ovarian demise that prompts the cessation of menses. Despite being previously associated with the end of a woman's reproductive lifespan[4], an increased accessibility to assisted reproductive techniques has bypassed infertility-associated difficulties related to advanced maternal age; however, the mortality associated with pregnancy and labor complications in older individuals remains problematic. Tangible proof comes from the 7.8-fold increase in maternal mortality in women aged >40 (107.9 deaths per 100,000 live births) compared to those under 25[5,6], which may also be increased by other age-associated conditions such as hypertension or diabetes[7].

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The full list of publications is available in Annex II.

Participation in Scientific Conferences

We took part in leading international congresses on reproductive medicine, presenting results and expanding scientific collaboration networks.

Highlights:

SRI 2024

ESHRE 2024

ASRM 2024

The full list of conference participations is available in Annex III.

Innovation and Knowledge Transfer

We drive the transformation of scientific knowledge into new technologies, therapies, and diagnostic tools that improve clinical practice in reproductive health.

1

patent

Non-invasive method of cell imaging

PCT/EP2023/078547

4

start-ups

ASHERMAN Therapy

iPremom

ECTOLIFE

Premium Fertility

Strategic Collaborations and Partnerships

We collaborate closely with top universities, research centers, hospitals, and biomedical companies:

Education and Training

Education drives the future of research. We not only generate knowledge, but also share it with future scientists, physicians, and reproductive medicine professionals.

Official Training Programs

Master's Degree in Clinical Genomics, Precision Medicine and Genetic Counseling (University of Valencia)

Specialist Diploma in Genetic Counseling and Clinical Genomics (University of Valencia)

In-House Training Programs

Summer School for Young Scientists

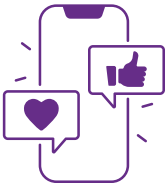
Doctoral Theses Defended

Molecular Diagnosis of Uterine Leiomyoma by Next Generation Sequencing. Doctoral candidate: Alba Machado. Supervisors: Aymara Mas, Carlos Simon, Diana Valbuena

Deciphering Interactions at the Single-Cell Level of the Human Uterus Microbiome in Health and Disease. Doctoral candidate: Bruno Toson. Supervisors: Inmaculada Moreno, Carlos Simon

Media Presence and Public Impact

We have strengthened our presence in the media and on social platforms. This has helped increase our institutional visibility as a reference in reproductive health.



10.5%

engagement rate on social media

17

mentions in general and specialized media

677,850

total media impressions

Our research in the media:

LA VANGUARDIA · El Confidencial · infosalus.com · ONDA CERO · ConSalud.es · COPE

Awards and Recognition

The Carlos Simon Foundation was honored with the CaixaBank Private Banking Philanthropy Award and presented the Carlos Simon Excellence in Translational Research Award to Dr. Dennis Lo for his pioneering contribution to non-invasive prenatal diagnosis.

CaixaBank Philanthropy Award

Recognizing excellence in philanthropic initiatives with social impac

Carlos Simon Excellence in Translational Research Award

For his groundbreaking work in non-invasive prenatal testing through fetal DNA in maternal plasma

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Each discovery brings us closer to a future where all women have access to personalized treatments for their health and well-being. Thanks to our team, collaborators, and funders, we continue to drive science as a foundation for progress.

Carlos Simon
Foundation
FOR RESEARCH IN WOMEN´S HEALTH

Follow us on social media

Annex I – List of Active Competitive Projects in 2024

- **Study of the impact of the endometrial microbiome on human endometrium under physiological and pathological conditions at single-cell level.** Instituto de Salud Carlos III – Health Research Projects (PI) PI21/00235. PI: Inmaculada Moreno. Duration: 01/01/2022 – 30/12/2024. Funding: €169,279.00

- **Transcriptomic characterization of human embryo implantation at single-cell level using a 3D endometrium in a microfluidic chip.** Instituto de Salud Carlos III – Health Research Projects (PI) PI21/00528. PI: Felip Vilella. Duration: 01/01/2022 – 30/12/2024. Funding: €90,750.00

- **Preventing lifetime obesity by early risk-factor identification, prognosis and intervention (EPROBES).** European Commission – Horizon Europe Program 101080219-2. PIs: Carlos Simon / Felip Vilella. Duration: 01/05/2023 – 30/04/2028. Funding: €480,072.50

- **Identification of progenitor cells in human endometrium and demonstration of their regenerative capacity.** Agencia Estatal de Investigación (AEI) – Consolidation CNS2022-135696. PI: Felip Vilella. Duration: 01/07/2023 – 30/06/2025. Funding: €198,986.00

- **Deciphering a microbial footprint leading to onset and long-term risk of preeclampsia (PREMIC).** Generalitat Valenciana – PROMETEO Program CIPROM/2022/41. PIs: Carlos Simon, Tamara Garrido, Inmaculada Moreno. Duration: 01/01/2023 – 31/12/2026. Funding: €600,000.00

- **Grants for attracting European or other international program projects.** Generalitat Valenciana – APE 2023 CIAPE/2022/7. PI: Aymara Mas. Duration: 01/06/2023 – 31/12/2024. Funding: €9,000.00

- **Identification of maternal cellular and molecular targets at single-cell level for early prediction and treatment of preeclampsia.** Agencia Estatal de Investigación (AEI) – Knowledge Generation PID2022-140744OB-I00. PIs: Carlos Simon and Tamara Garrido. Duration: 01/09/2023 – 31/08/2027. Funding: €383,750.00

- **Effect of CD133+ bone marrow-derived stem cells on the maternal-fetal interface in patients with Asherman Syndrome.** American Society for Reproductive Medicine (ASRM) – KY Cha Award 2023. PI: Xavier Santamaría. Duration: 01/09/2023 – 31/08/2025. Funding: $18,338.53 USD

- **Identification of progenitor cells in human endometrial tissue.** Generalitat Valenciana – AICO 2023 CIAICO/2022/242. PI: Felip Vilella. Duration: 01/01/2023 – 31/12/2025. Funding: €90,000.00

- **Tumor heterogeneity inferred by single-cell RNA sequencing: new insights into therapeutic targets of uterine tumors.** Instituto de Salud Carlos III – Health Research Projects PI23/00536. PI: Aymara Mas. Duration: 01/01/2024 – 30/12/2026. Funding: €226,875.00

- **Study of the molecular and epigenetic mechanisms driving ovarian aging.** Generalitat Valenciana – Emerging Program CIGE/2023/217. PI: Ana Monteagudo. Duration: 16/07/2024 – 15/07/2026. Funding: €20,000.00

- **Study of the impact of the endometrial microbiota on the pathogenesis of endometriosis.** Ministry of Science, Innovation and Universities (MICIN) – Predoctoral FPU FPU23/02496. PI: Inma Moreno (PhD student: María Graciano). Duration: 01/12/2024 – 30/11/2028. Funding: €114,761.00

- **Development of an early, non-invasive diagnostic model for ovarian cancer based on global genomics/transcriptomics and circulating tumor DNA.** Generalitat Valenciana – Predoctoral Fellowship ACIF 2021 ACIF/2021/348. PI: Aymara Mas (PhD student: Paula Punzón). Duration: 01/10/2021 – 30/09/2025. Funding: €93,878.00

- **Identification of maternal cellular and molecular targets at single-cell level for early prediction and treatment of preeclampsia.** Agencia Estatal de Investigación (AEI) – Predoctoral FPI PREP2022-000534. PIs: Carlos Simon and Tamara Garrido (PhD student: Carla Montagud). Duration: 01/03/2024 – 29/02/2028. Funding: €76,750.00

Annex II – List of Scientific Publications in 2024

- López-Martínez S, Simon C, Santamaria X. **Normothermic Machine Perfusion Systems: Where Do We Go From Here?**. Transplantation. 2024 Jan 1;108(1):22-44. doi: 10.1097/TP.0000000000004573. Epub 2023 Dec 13. Review. PubMed PMID: 37026713.

- Punzon-Jimenez P, Machado-Lopez A, Perez-Moraga R, Llera-Oyola J, Grases D, Galvez-Viedma M, Sibai M, Satorres-Perez E, Lopez-Agullo S, Badenes R, Ferrer-Gomez C, Porta-Pardo E, Roson B, Simon C, Mas A. **Effect of aging on the human myometrium at single-cell resolution.** Nat Commun. 2024 Jan 31;15(1):945. doi: 10.1038/s41467-024-45143-z. PubMed PMID: 38296945; PubMed Central PMCID: PMC10830479.

- Loid M, Obukhova D, Kask K, Apostolov A, Meltsov A, Tserpelis D, van den Wijngaard A, Altmäe S, Yahubyan G, Baev V, Saare M, Peters M, Minajeva A, Adler P, Acharya G, Krjutškov K, Nikolova M, Vilella F, Simon C, Zamani Esteki M, Salumets A. **Aging promotes accumulation of senescent and multiciliated cells in human endometrial epithelium.** Hum Reprod Open. 2024;2024(3):hoae048. doi: 10.1093/hropen/hoae048. eCollection 2024. PubMed PMID: 39185250; PubMed Central PMCID: PMC11344589.

- Sakkas D, Navarro-Sánchez L, Ardestani G, Barroso G, Bisioli C, Boynukalin K, Cimadomo D, Frantz N, Kopcow L, Andrade GM, Ozturk B, Rienzi L, Weiser A, Valbuena D, Simon C, Rubio C. **The impact of implementing a non-invasive preimplantation genetic testing for aneuploidies (niPGT-A) embryo culture protocol on embryo viability and clinical outcomes.** Hum Reprod. 2024 Sep 1;39(9):1952-1959. doi: 10.1093/humrep/deae156. PubMed PMID: 39059790.

- Ardestani G, Banti M, García-Pascual CM, Navarro-Sánchez L, Van Zyl E, Castellón JA, Simon C, Sakkas D, Rubio C. **Culture time to optimize embryo cell-free DNA analysis for frozen-thawed blastocysts undergoing noninvasive preimplantation genetic testing for aneuploidy.** Fertil Steril. 2024 Sep;122(3):465-473. doi: 10.1016/j.fertnstert.2024.04.037. Epub 2024 May 7. PubMed PMID: 38718960.

- Bellver J, Gonzalez-Monfort M, González S, Toson B, Labarta E, Castillón G, Mariani G, Vidal C, Giles J, Cruz F, Ballesteros A, Ferrando M, García-Velasco JA, Valbuena D, Vilella F, Parras-Molto M, Tercero-Atencia E, Simon C, Moreno I. **An Analysis of the Digestive and Reproductive Tract Microbiota in Infertile Women with Obesity.** Int J Mol Sci. 2024 Nov 23;25(23). doi: 10.3390/ijms252312600. PubMed PMID: 39684312; PubMed Central PMCID: PMC11641297.

Annex III – Conference Participation in 2024

- **RMN Facility Inauguration, CIC bioGUNE.** Bilbao, Spain. February. "Innovations in Reproductive Medicine. From the Bench to the Bedside."

- **XXI Peruvian and International Congress of Reproductive Medicine.** Peruvian Society of Fertility; Lima, Peru. February. 2 lectures: "Endometrial diagnostic tests to improve embryo implantation in clinical practice", "Advances in assisted reproduction: What more is possible?"

- **Society for Reproductive Investigation (SRI)**; Vancouver, Canada. March. 2 oral communications and 1 poster.

- **Grand Round Boston IVF**; Quincy, Massachusetts, USA. March. Online Lecture. "What single-cell transcriptomics teach us about the endometrium in health and disease."

- **Microbes in Women's Health Congress.** Copenhagen, Denmark. April. "The Endometrial Microbiome is Associated with Reproductive Outcomes in IVF."

- **46th International Dexeus Congress**; Barcelona, Spain. April. "Looking at the microbiome."

- **5th EBART International Congress**; Barcelona, Spain. April. "The impact of endometrial dysbiosis in women with recurrent implantation failure and unexplained infertility."

- **H-ART-US (Hysteroscopy, ART and Ultrasound)**; Rome, Italy. April. "Embryo vs Uterus."

- **ESHRE Course – The Microbiome in Reproduction**; Stockholm, Sweden. May. "The receptive endometrium: what role does the microbiome play?"

- **21st World Congress of the International Society of Gynecological Endocrinology (ISGE)**; Florence, Italy. May. "The endometrial microbiome – a window into reproductive health."

- **International Symposium on Patient-Friendly IVF Solutions.** CHA Bio Complex, South Korea. May. "Virtual Speaker: The impact of endometrial dysbiosis in recurrent implantation failure."

- **Midwest Reproductive Symposium International (MRSi)**; Chicago, USA. June. "The clinical impact of the reproductive microbiome."

- **ESHRE Annual Meeting**; Amsterdam, Netherlands. July. 2 oral communications and 3 posters.

- **Next Fertility Spain**; Valencia, Spain. September. "Clinical relevance of the endometrial microbiome in assisted reproduction techniques."

- **II National Congress of the SEISEGO (Spanish Society of Gynecology and Obstetrics – Infertility Section)**; Alicante, Spain. September. "Keynote: The role of the microbiome in fertility and ART."

- **ASRM Annual Meeting Precongress Course**; Denver, USA. October. "Introduction to Precision Reproductive Medicine", "Genotypes in endometrial receptivity assessment." 1 oral communication and 3 posters.

- **Vitrolife Symposium at ASRM**; Denver, USA. October. “Unveiling the impact of the endometrial microbiome: why testing reproductive tract microbiota is crucial in infertility treatment.”

- **Keynote Lecture, Middle East Fertility Society (MEFS) 31st Annual Scientific Meeting**; Doha, Qatar. November. “Asherman Syndrome: Decoding its origin at single-cell level and designing advanced cell therapy.”

- **CIRA Congress on Assisted Reproduction**; Lima, Peru. November. “The future of reproductive medicine”, “Asherman’s Syndrome.”

Prepared by: María Lloret (Project Manager), Rut Campos (Grants Specialist), Adrián González (Marketing & Communication Specialist). Approved by: Dr. Carlos Simon.
Last reviewed: May 13, 2025