

Fetal Medicine Research Center

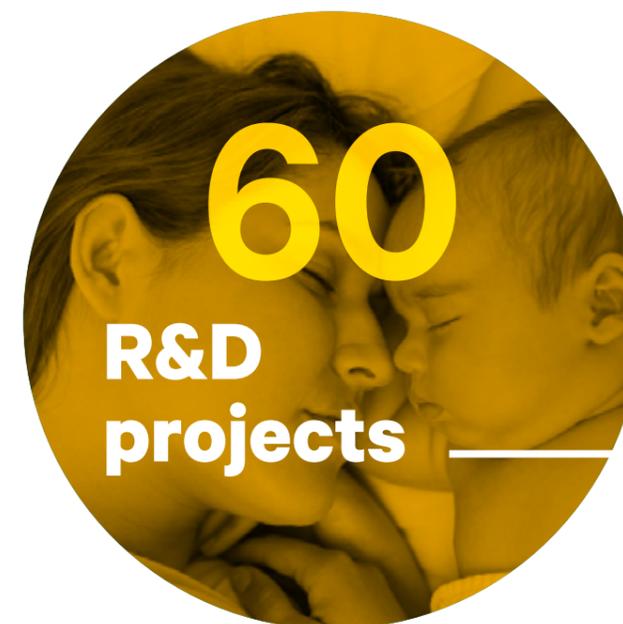
2020



FETAL
MEDICINE
RESEARCH
CENTER



Summary



BCNatal Fetal Medicine Research Center Annual Report 2020

Eduard Gratacós
Director of BCNatal
Fetal Medicine
Research Center



Health begins before birth. Even though it seems like an invisible period of our lives, the prenatal period is the most important one. The quality of life that we will have in childhood and adulthood is programmed during the nine months in the womb. Detecting any anomaly during the development process is a huge opportunity to reverse consequences and improve future health. We have been working with this premise at the BCNatal Fetal Medicine Research Center since its creation, 15 years ago.

During this time we have consolidated a research model of scientific excellence based on efficiency, multidisciplinary and innovation. Today we are the team with the highest number of scientific articles published in the area of fetal medicine. We are trusted and supported by notable promoters such as CELLEX Foundation, Obra Social “la Caixa”, CEREBRA and other funders, friends, and collaborators.

Thanks to them we have ongoing innovative studies that will improve the prognosis of relevant problems such as fetal growth restriction, pre-eclampsia, and prematurity. In recent years we have incorporated new methodologies and approaches to these problems, based on microbiota, machine/deep learning, lung development assessment, and the importance of lifestyle and environmental exposure in fetal programming.

“

This year we started one of our most ambitious projects: the development of an artificial placenta

”

This year, with the exceptionality of the pandemic, in addition to adapting our way of working to comply with preventive measures, some of our projects have focused on clarifying the impact of the SARS-CoV-2 infection on the health of pregnant women and perinatal outcomes. We have published several scientific articles on COVID-19. One of the most prominent is the one that shows that being born with a low weight increases susceptibility to severe COVID-19.

This year, moreover, we have started one of our most ambitious projects for the development of an artificial placenta, thanks to the support of “la Caixa” Foundation. Based on new high-precision technologies and with experts in fetal surgery, cardiovascular physiology, metabolism, intensive support, applying technologies that include new biomaterials, microfluidics, robotics and other areas of bioengineering.

As a bridge between fetal medicine and society, we continue to develop outreach tools and actions. Our main purpose is to develop science of excellence to improve health and, ultimately, people’s lives.



1

Who we are

Purpose

A team of excellence

Nature

Scientific results

Organizational chart

History

Purpose

We defend the integral conception of the fetus and the child as the same patient to diagnose and treat early diseases of childhood and adulthood.

BCNatal Fetal Medicine Research Center is a university and multidisciplinary research center in fetal and perinatal medicine recognized as one of the best in the world in its field. The center is linked to BCNatal (Hospital Clínic and Hospital Sant Joan de Déu in Barcelona) and the University of Barcelona.

OUR MISSION

The main mission of our center is to identify methods of early diagnosis and treatment for diseases of prenatal origin that have an impact on childhood and adult life. In this way, we can reduce the prevalence and severity of certain diseases in adults, especially those that have neurological, cardiovascular and pulmonary consequences of prenatal origin.

**“
We identify methods of early diagnostic and treatment for diseases of prenatal origin
”**

OUR METHODOLOGY

We identified the fetus as a patient to demonstrate and characterize the profound impact that fetal life has on children and their future health. This way we can tackle the same problem from different perspectives to overcome it in an efficient and innovative way. This way of working allows us to integrate prenatal and postnatal care through the services of Maternal-Fetal Medicine and Neonatology.

OUR PROJECTS

Currently we have different ongoing research projects. Among them we would like to highlight the following three projects: a human intervention study that aims to improve the prognosis of fetal growth restriction; the development of new fetal surgery tools that will radically change the future perspectives of fetuses that struggle between life and death; and finally, a study that allows us to advance in the creation of new biomarkers that will detect fetuses at risk.



750 m²

ALLOCATED TO RESEARCH



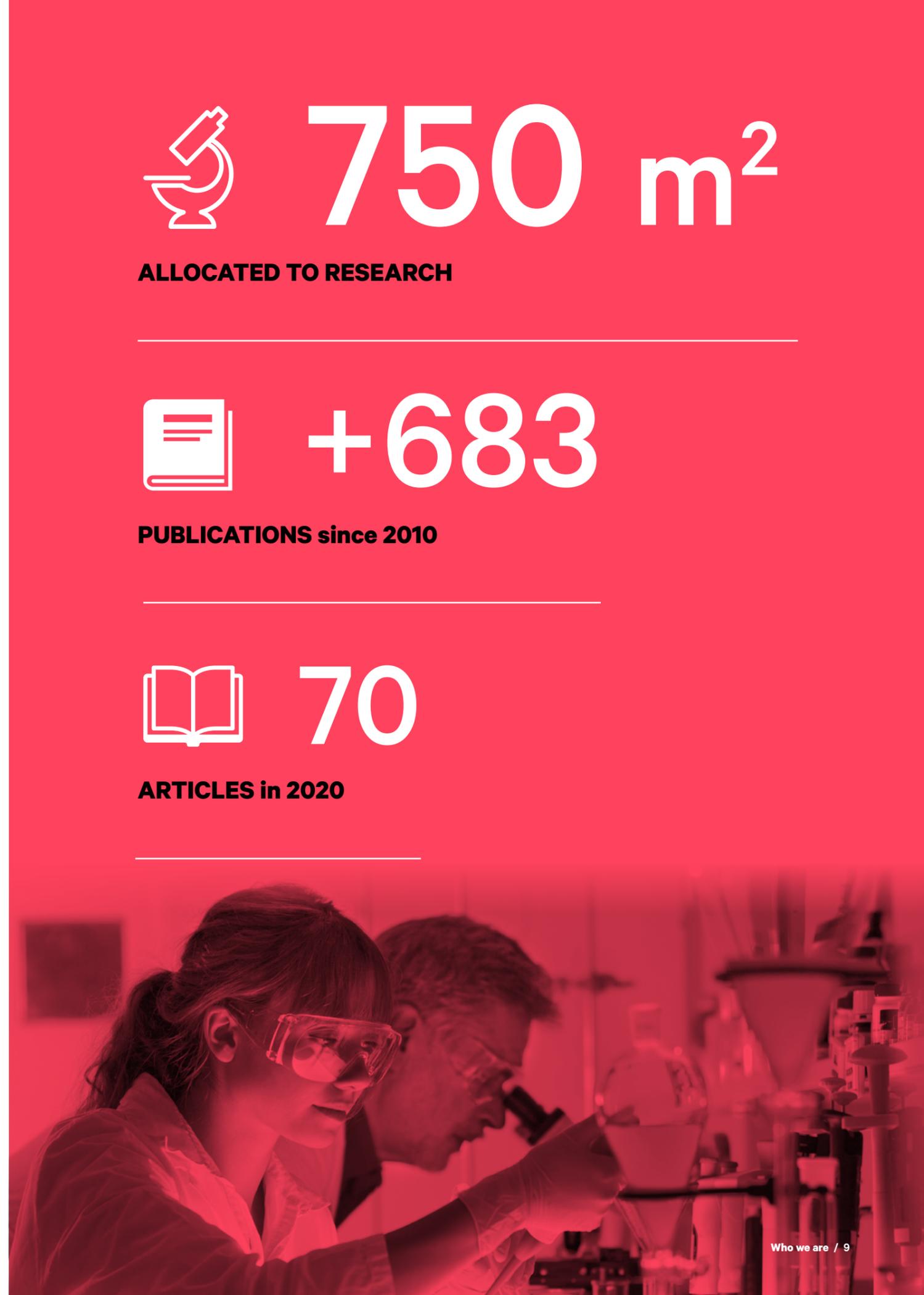
+683

PUBLICATIONS since 2010



70

ARTICLES in 2020



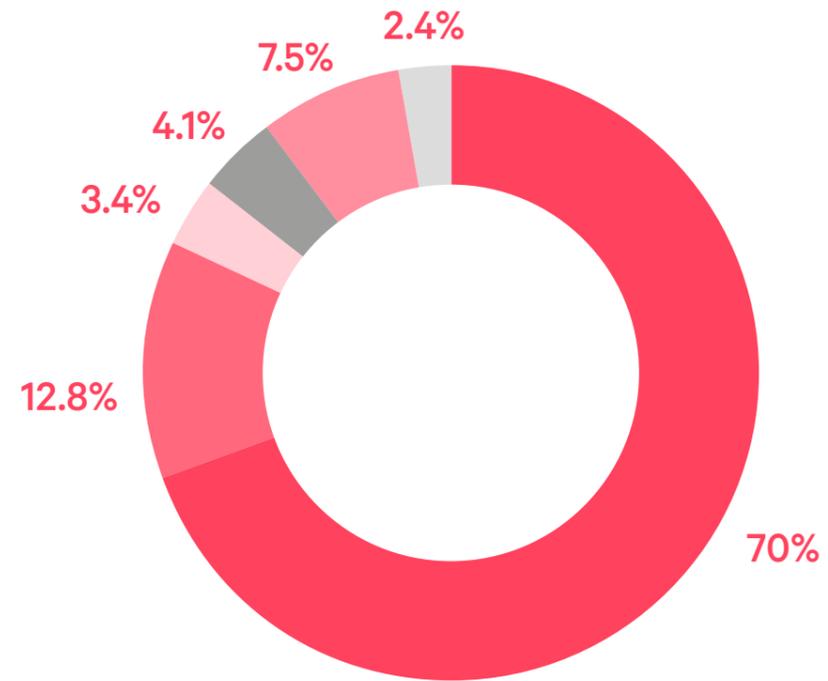
A team of excellence



The center has a high transnational capacity thanks to a multidisciplinary team made up of more than 125 members including specialists in fetal medicine, cardiology, neurodevelopment and reproductive medicine, and also biologists, pharmacists, bioengineers, epidemiologists, and statisticians. Together we aim to achieve highly

competitive research in fetal development, both at a physiological and pathological level. The team is led by Eduard Gratacós, together with Fàtima Crispí as a scientific coordinator. In addition, each research line has its own scientific director and the management of the entire center is carried out by an independent unit.

HR AREAS (%)



82 Clinician

15 Basic

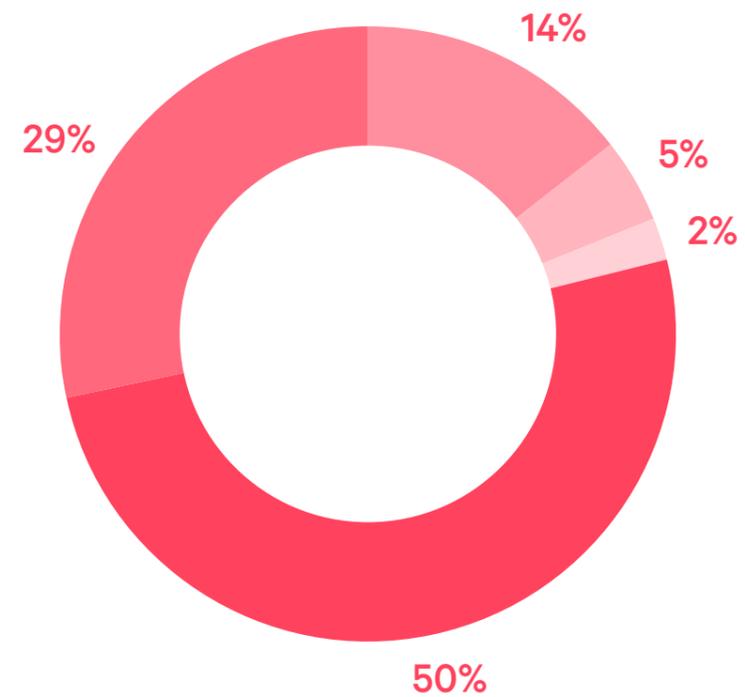
9 STEM

5 Psychology

4 Nursery

3 Management

HR CATEGORIES (%)



38 Doctors

67 4-year Bachelor's degree

3 3-year Bachelor's degree

6 Technicians

19 Students

Nature

“
BCNatal performs 85% of fetal surgeries performed in Spain, many of them to save the fetus' life
”

BCNATAL

Resulting from the integration of Hospital Clínic and Hospital Sant Joan de Déu, BCNatal is one of the largest university centers of maternal-fetal and neonatal medicine in Europe. With more than 7,000 deliveries, 3,500 fetal medicine consultations, 2,000 fetal echocardiograms, 150 fetal surgeries, and more than 500 cases of placental disease per year, the center is positioned as a world leader. BCNatal is specialized in fetal surgery, performing 85% of the interventions performed in Spain, many of them to save the fetus' life. The most common surgery is performed on twins sharing a placenta. The center also receives patients from the rest of the world.

IDIBAPS

BCNatal is part of the Institut d'Investigacions Biomèdiques August Pi i Sunyer, one of the main health research centers in Europe, with an increasing scientific production of more than a thousand articles in international journals. With more than 450 first-level researchers, it is a privileged environment for innovation and clinical transfer.

FUNDACIÓ CLÍNIC & FUNDACIÓ SANT JOAN DE DÉU

The Fundació Clínic per a la Recerca Biomèdica (FCRB) and the Fundació Sant Joan de Déu (FSJD) offer service and support to the BCNatal Fetal Medicine Research Center researchers and to all scientific activities developed. FCRB also provides administrative management to IDIBAPS.

UNIVERSITAT DE BARCELONA

The University of Barcelona (UB) is the main public university in Catalonia, with the greatest number of students and delivering the broadest and most comprehensive offering in higher educational courses. UB coordinates the international doctorate program in fetal medicine, Erasmus FetalMed-PhD, thanks to the links of group researchers and UB.

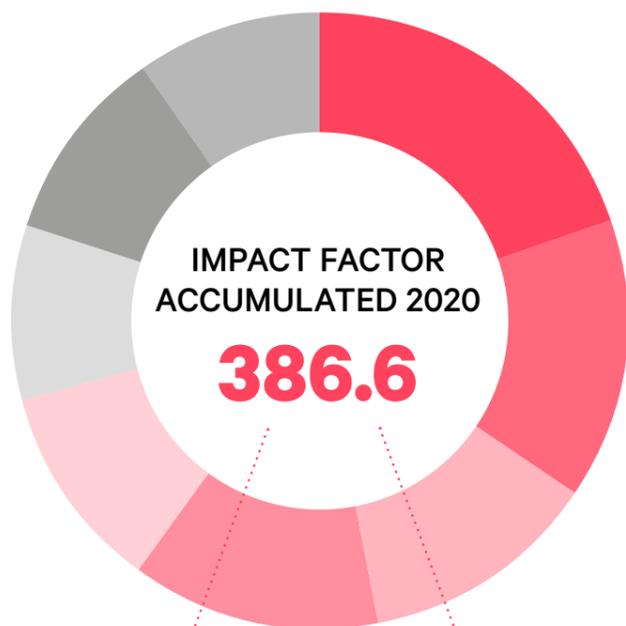


Scientific results

In the last 10 years the group has published more than 500 articles, directed more than 50 doctoral theses and has been awarded more than 60 national and international projects financed by

prestigious institutions such as the CELLEX private foundation, Cerebra Foundation (UK) and the Obra Social "la Caixa".

IMPACT FACTOR ACCUMULATED



ARTICLES IN THE FIRST DECIL
61%

ARTICLES IN THE FIRST QUARTILE
42%

IF: 386.6 2020

285.8 2019

241.8 2018

252.5 2017

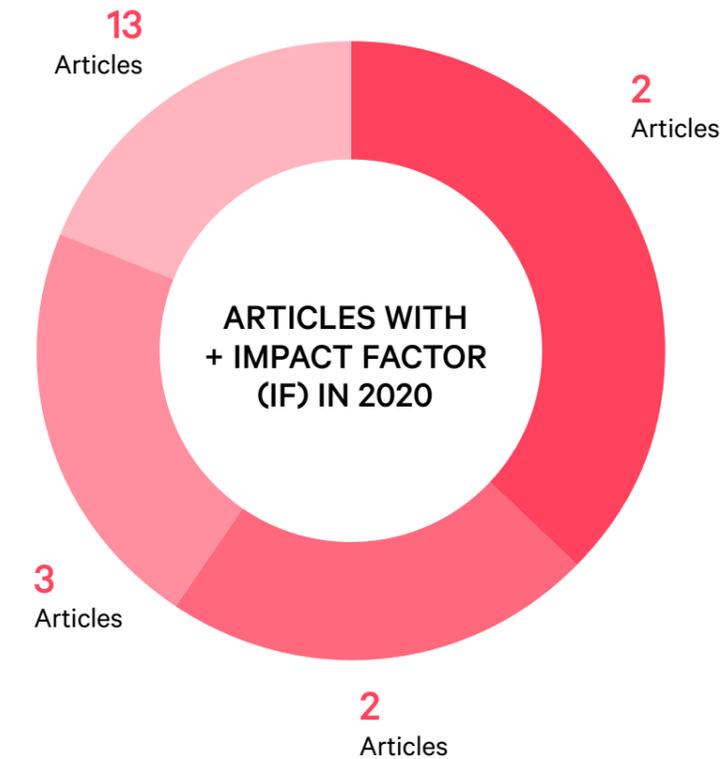
211.2 2016

177.6 2015

201.5 2014

183.7 2013

ARTICLES WITH + IMPACT FACTOR (IF) IN 2020



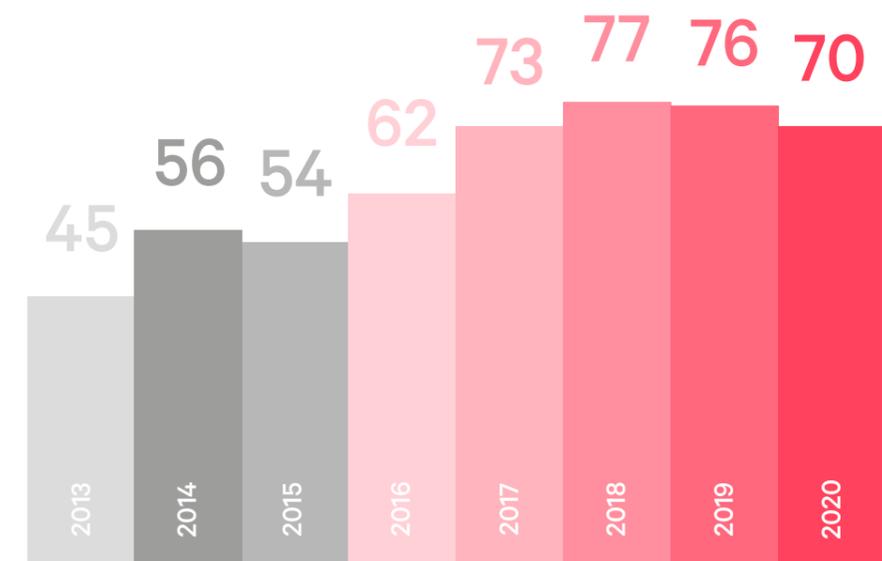
IF: 11.15 Medical Image Analysis

IF: 6.69 IEEE Transactions on Medical Imaging

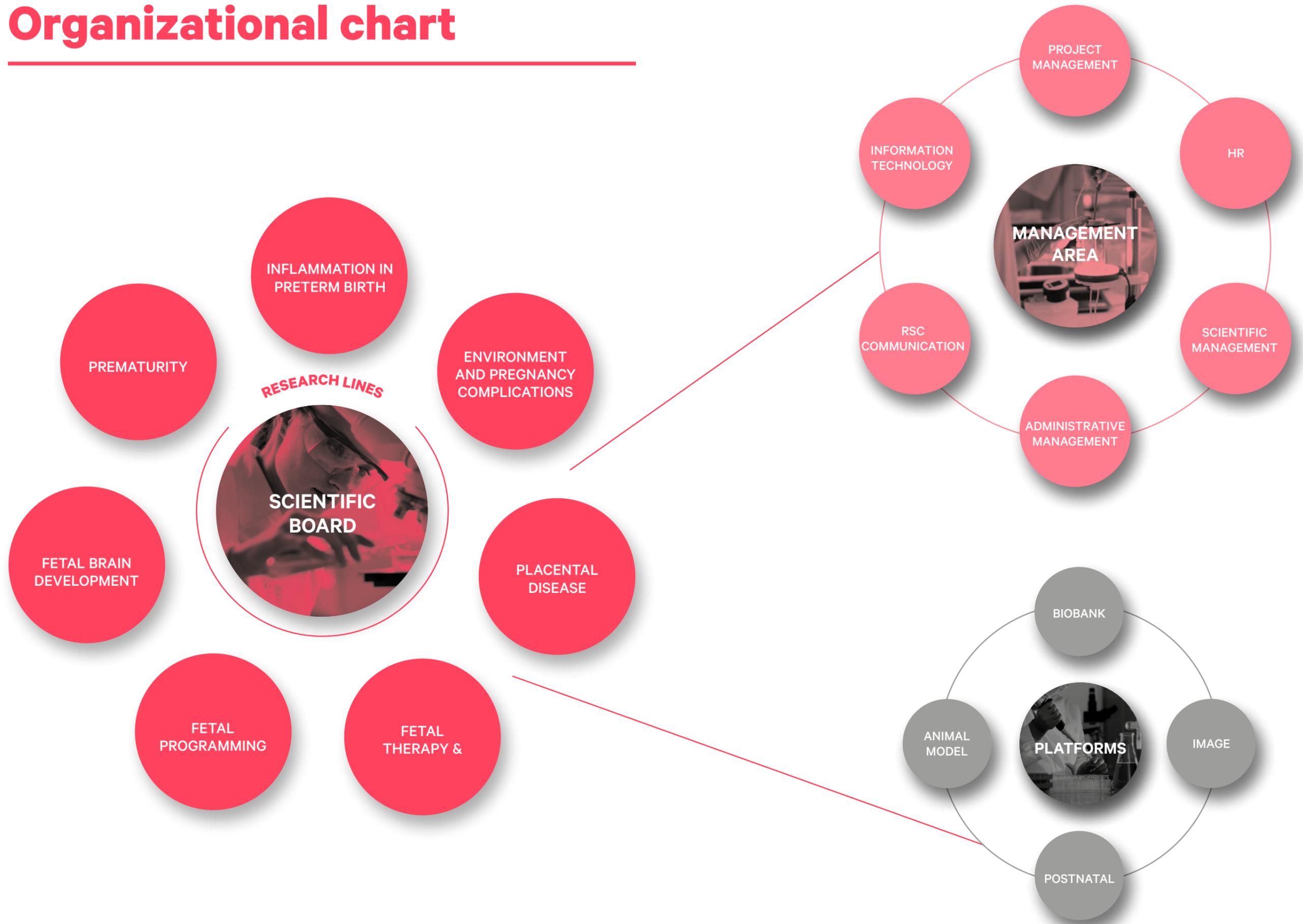
IF: 6.50 American Journal of Obstetrics and Gynecology (AJOG)

IF: 5.58 Ultrasound in Obstetrics & Gynecology

PUBLISHED ARTICLES



Organizational chart



History

Twenty years ago the fetus did not exist as a patient. Today babies are born with a medical history under their arms: we have opened the window of opportunity

to improve their quality of life starting before birth. These are the key dates of the BCNatal Fetal Medicine Research Center, from the beginning to the present.

2005



OUR BEGINNING

Eduard Gratacós creates the research team in Fetal and Perinatal Medicine thanks to the support of the Hospital Clinic and IDIBAPS.

2009



OUR SCIENTIFIC PRODUCTION GROWS

We publish 46 scientific articles in journals specialized in maternal-fetal medicine, achieving the highest impact factor to date: 119.31.

2012



INATAL: THE BRIDGE BETWEEN FETAL MEDICINE AND SOCIETY

We collaborate in the creation of iNatal, a reference website about pregnancy, birth, and the postpartum period, and the first with 100% reliable content. It includes a forum moderated by maternal-fetal medicine specialists.

2015



NEW RESEARCH LINE: FETAL THERAPY AND SURGERY

Thanks to the support of CELLEX, we bring together experts in medical imaging, robotics, biomaterials, and electronic and optical biosensors to develop better technologies in intrauterine interventions.

2017



IMPROVEMENTS IN THE DIAGNOSIS OF FETAL GROWTH RESTRICTION

We publish the RATIO37 protocol, a multicentric study that incorporates a new ultrasound parameter in week 37 to detect low birth weight, and hence, reduce the rate of fetal death and complications in childbirth.

2019



NEW SYSTEM TO IMPROVE FETAL SURGERIES

We developed, together with the Pompeu Fabra University, a three-dimensional personalized pre-surgical planning system for cases with twin-to-twin transfusion syndrome.



FOCUSED ON FETAL CARDIOLOGY AND NEURODEVELOPMENT

We develop innovative technologies that allow us to understand how the brain and heart are reprogrammed in fetal life.

2007



THE FIRST FETAL LUNG SURGERY

The team performs a surgical intervention for the first time on a fetus with a lethal congenital pulmonary disease. The baby girl is called Alaitz -'happiness' in Basque- and becomes news 16 months later.

2010



FIRST SPECIALIZED EUROPEAN DOCTORATE

We start coordinating the first Erasmus Mundus Joint PhD Program in Fetal and Perinatal Medicine in collaboration with the University of Barcelona (Spain), and the Universities of Leuven (Belgium) and Lund (Sweden).

2013



IMPACTBCN, CLINICAL TRIAL IN PREGNANCY

"Improving Mother for a better Prenatal Care Trial" is a broad clinical trial based on interventions of nutrition and emotional well-being of the mother to assess the impact of maternal well-being on the newborn.

2016



INATAL APP, 100% PERSONALIZED AND RIGOROUS

We launch the iNatal app, the first app on pregnancy carried out by experts in maternal-fetal medicine and the only one with personalized plans to improve the nutrition and emotional well-being of pregnant women.

2018



NEW RESEARCH ON THE IMPACT OF COVID ON PREGNANCY AND CHILDHOOD

We participate in the KIDS CORONA study at Hospital Sant Joan de Déu to study the effects of the coronavirus on the fetus, the pregnant woman and the baby: is there vertical transmission? Are breastfeeding and skin-to-skin safe? We also carry out training for patients and health personnel to clarify action protocols.

2020



2

Research

Fetal Programming

Fetal Brain Development

Prematurity

Inflammation in Preterm Birth

Fetal Therapy and Surgery

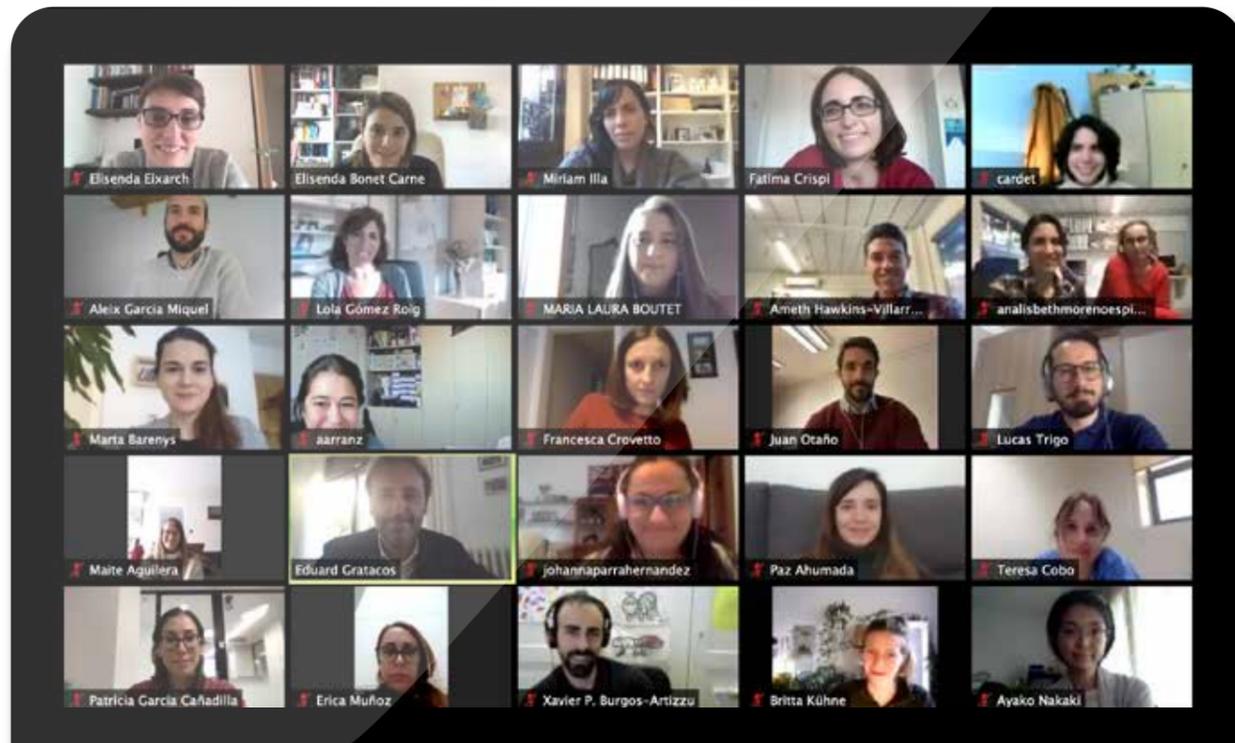
Environment and Pregnancy Complications

Placental Disease

Research platforms

Research Management

Research lines



¡Haz click en este botón para ver toda la galería de fotos!

Our seven research areas are aimed to identify new diagnosis and treatment methods for diseases with prenatal origin that have an impact on childhood and adult life.

THE FETUS AS A PATIENT

In BCNatal Fetal Medicine Research Center we treat the fetus as a patient, whom we can diagnose and certain of whose diseases can be managed while still in the womb in order to minimize or avoid their consequences in the future. Our research

focuses particularly on the heart and brain, given the special importance that fetal programming has on the development of these organs, as well as on the development of new intrauterine treatments that are able to reverse or mitigate certain fetal disorders.

“Our research is organized in 7 lines that allow us to achieve a comprehensive study of the fetus and the mother”



Fetal Programming



Fetal Brain Development



Prematurity



Inflammation in Preterm Birth



Fetal Therapy and Surgery



Placental Disease



Environment and Pregnancy Complications

Fetal Programming



The line brings together a multidisciplinary team of fetal medicine specialists, pediatricians, epidemiologists, biologists and engineers.



Better understanding the effect of pregnancy complications on fetal development will allow us to discover preventive strategies to improve the quality of life of many babies.

What is the impact of the fetal period on our health?

The prenatal period is critical for the development of all organs. An insult during prenatal life such as intrauterine growth restriction, assisted reproduction techniques, exposure to toxic agents or congenital heart diseases may affect this development and have long-term health effects that persist during adult life. How? By affecting the optimal development of the main fetal organs such as the heart, lung, and brain and making us more susceptible to diseases in adult life.

Is it possible to improve the prognosis of babies with fetal complications?

Previous studies have helped us to understand that mother's nutrition and stress level can directly affect the growth and development of fetuses. Now we have started pioneering studies to evaluate whether by improving the mother's diet and reducing her stress level, we can also improve fetal growth and development, as well as microbiota and epigenetics, thereby improving the health of future children and adults.

TEAM MEMBERS

FÁTIMA CRISPI

Coordinator of the research line and the scientific coordinator of the group. Maternal-Fetal Medicine Specialist at BCNatal. Lecturer in specialized courses of Fetal I+D Education Barcelona.

MATERNAL-FETAL MEDICINE SPECIALIST

Gemma Casals, Francesca Crovetto, Olga Gómez, Anna Goncé, Marta López

POSTDOCTORAL RESEARCHERS

Laura García, Patricia García Cañadilla, Brenda Valenzuela, Lina Youssef, Mónica Zamora,

PREDOCTORAL RESEARCHERS

Ayako Nakaki, Leticia Benítez, Maria Laura Boutet, Irene Casas, Álvaro Sepúlveda, Andre Gie, Laura Guirado, Grigorios Kalapotharakos, Mari Kinoshita, Marta Larroya, Laura Nogué, Rosalia Pascal, Laura Salazar, Iris Soveral, Kilian Vellvé

MASTER'S STUDENTS

Karen Castillo, Lucía García, Nuria Ribas

RESEARCH ASSISTANTS

Marta Dacal, Marta Garcia, Laura Segalés

STUDENT

Ismael Ilyana

NUTRITIONIST

Tania Freitas

COLLABORATOR

Roger Borràs

PUBLICATIONS 2020

1. **Early cardiac remodeling in aortic coarctation: insights from fetal and neonatal functional and structural assessment.** Soveral I, Crispi F, Walter C, Guirado L, García-Cañadilla P, Cook A, Bonnin A, Dejea H, Rovira-Zurriaga C, Sánchez de Toledo J, Gratacós E, Martínez JM, Bijmens B, Gómez O. *Ultrasound in Obstetrics & Gynecology*, 2020. doi: 10.1002/uog.21970
- ★ 2. **Main Patterns of Fetal Cardiac Remodeling.** Crispi F, Sepúlveda-Martínez Á, Crovetto F, Gómez O, Bijmens B, Gratacós E. *Fetal Diagnosis and Therapy*, 2020. doi: 10.1159/000506047
3. **Maternal and Fetal Cardiovascular Adaptations in Preeclampsia and/or Fetal Growth Restriction.** Youssef L, Crispi F. *American Journal of Obstetrics and Gynecology*, 2020. doi: 10.1016/j.ajog.2019.12.003
4. **Three-dimensional Regional Bi-Ventricular Shape Remodeling Is Associated With Exercise Capacity in Endurance Athletes.** Bernardino G, Sanz de la Garza M, Domenech-Ximenes B, Prat-González S, Perea R J, Blanco I, Burgos F, Sepúlveda-Martínez A, Rodríguez-Lopez M, Crispi F, Butakoff C, González Ballester M A, De Craene M, Sitges M, Bijmens B. *European Journal of Applied Physiology*, 2020. doi: 10.1007/s00421-020-04335-3.
5. **Fetal cardiac filling and ejection time fractions by pulsed Doppler: fetal nomograms and potential clinical application.** Soveral I, Crispi F, Guirado L, García-Otero L, Torres X, Bennasar M, Sepúlveda-Martínez Á, Nogué L, Gratacós E, Martínez J M, Bijmens B, Friedberg M, Gómez O. *Ultrasound in Obstetrics & Gynecology*, 2020. doi: 10.1002/uog.22152
- ★ 6. **Seroprevalence and presentation of SARS-CoV-2 in pregnancy.** Crovetto F, Crispi F, Llurba E, Figueras F, Gómez-Roig MD, Gratacós E. *The Lancet*, 2020. doi: 10.1016/j.lancet.2020.07.003
7. **Hemopexin and 1-microglobulin heme scavengers with differential involvement in preeclampsia and fetal growth restriction.** Youssef L, Erlandsson L, Åkerström B, Miranda J, Paules C, Crovetto F, Crispi F, Gratacós E, Hansson S R. *PLoS One*, 2020. doi: 10.1371/journal.pone.0239030
8. **Reference ranges for fetal cardiac, ventricular and atrial relative size, sphericity, ventricular dominance, wall asymmetry and relative wall thickness from 18 to 41 weeks of gestation.** García-Otero L, Soveral I, Sepúlveda-Martínez Á, Rodríguez-López M, Torres X, Guirado L, Nogué L, Valenzuela-Alcaraz B, Martínez J M, Gratacós E, Gómez O, Crispi F. *Ultrasound in Obstetrics & Gynecology*, 2020. doi: 10.1002/uog.23127
9. **Uncomplicated Monochorionic Twins: Two Normal Hearts Sharing One Placenta.** Torres X, Bennasar M, García-Otero L, Martínez-Portilla R J, Valenzuela-Alcaraz B, Crispi F, Goncé A, Gratacós E, Figueras F, Martínez J M. *Journal of Clinical Medicine*, 2020. doi: 10.3390/jcm9113602
10. **Exercise-induced cardiopulmonary remodelling in endurance athletes: Not only the heart adapts.** Domenech-Ximenes B, Sanz-de la Garza M, Prat-González S, Sepúlveda-Martínez Á, Crispi F, Perea R J, Garcia-Alvarez A, Sitges M. *European Journal of Preventive Cardiology*, 2020. doi: 10.1177/2047487319868545
- ★ 11. **Machine Learning in Fetal Cardiology: What to Expect.** Garcia-Canadilla P, Sanchez-Martinez S, Crispi F, Bijmens B. *Fetal Diagnosis and Therapy*, 2020. doi: 10.1159/000505021
12. **Handling confounding variables in statistical shape analysis-application to cardiac remodelling.** Bernardino G, Benkarim O, Sanz-de la Garza M, Prat-González S, Sepúlveda-Martínez A, Crispi F, Sitges M, Butakoff C, De Craene M, Bijmens B, González Ballester MA. *Medical Image Analysis*, 2020. doi: 10.1016/j.media.2020.101792
13. **Prevalence and pattern of cardiovascular magnetic resonance late gadolinium enhancement in highly trained endurance athletes.** Domenech-Ximenes B, Sanz-de la Garza M, Prat-González S, Sepúlveda-Martínez A, Crispi F, Duran-Fernandez K, Perea R J, Bijmens B, Sitges M. *Journal of Cardiovascular Magnetic Resonance*, 2020. doi: 10.1186/s12968-020-00660-w
14. **The protective effect of fibroblast growth factor-21 in alcoholic cardiomyopathy: a role in protecting cardiac mitochondrial function.** Ferrer-Curriu G, Guitart-Mampel M, Rupérez C, Zamora M, Crispi F, Villarroya F, Fernández-Solà J, Garrabou G, Planavila A. *The Journal of Pathology*, 2020. doi: 10.1002/path.5573
15. **Maternal proteomic profiling reveals alterations in lipid metabolism in late-onset fetal growth restriction.** Paules C, Youssef L, Miranda J, Crovetto F, Maria Estanyol J, Fernandez G, Crispi F, Gratacós E. *Scientific Reports*, 2020. doi: 10.1038/s41598-020-78207-3
16. **Prediction of Perinatal Mortality in Ebstein's Anomaly Diagnosed in the Second Trimester of Pregnancy.** Masoller N, Gómez O, Herraiz I, Gómez-Montes E, Soveral I, Pérez-Cruz M, Martínez-Biosques C, Granados MA, Bennasar M, Escobar-Diaz MC, María Martínez J, Galindo A. *Fetal Diagnosis and Therapy*, 2020. doi: 10.1159/000504979
17. **Nomograms of Fetal Right Ventricular Fractional Area Change by 2D Echocardiography.** L Guirado, F Crispi, I Soveral, B Valenzuela, M Rodriguez-López, L García-Otero, X Torres, Á Sepúlveda-Martínez, MC Escobar-Diaz, J M Martínez, M K Friedberg, E Gratacós, O Gómez. *Fetal Diagnosis and Therapy*, 2020. doi: 10.1159/000503228
18. **Determination of the steroid profile in alternative matrices by liquid chromatography tandem mass spectrometry.** A Gomez-Gomez, J Miranda, G Feixas, A Arranz, F Crispi, Ed Gratacós, O J Pozo. *Journal of Steroid Biochemistry and Molecular Biology*, 2020. doi: 10.1016/j.jsbmb.2019.105520

★
Click here to read the Fetal Cardiology special on Karger!

★ 19. **Fetal cardiac remodeling and dysfunction is associated with both preeclampsia and fetal growth restriction.** Youssef L, Miranda J, Paules C, Garcia-Otero L, Vellvé K, Kalapotharakos G, Sepulveda-Martinez A, Crovetto F, Gomez O, Gratacós E, Crispi F. *American Journal of Obstetrics & Gynecology*, 2020. doi: 10.1016/j.ajog.2019.07.025

★ 20. **Nomograms of Fetal Cardiac Dimensions at 18-41 Weeks of Gestation.** García-Otero L, Gómez O, Rodríguez-López M, Torres X, Soveral I, Sepúlveda-Martínez Á, Guirado L, Valenzuela-Alcaraz B, López M, Martínez JM, Gratacós E, Crispi F. *Fetal Diagnosis and Therapy*, 2020. doi: 10.1159/000494838

In 2020, we have led a special issue of *Fetal Cardiology in the journal Fetal Diagnosis and Therapy* made up of several review and original articles that provide normalities of various cardiac function parameters.

STRATEGIC GOALS

	TRANSLATIONAL RESEARCH	EXPERIMENTAL RESEARCH	COMPUTATIONAL MODELS AND ARTIFICIAL INTELLIGENCE
UNDERSTAND AND PREVENT	1. Study fetal cardiovascular and lung development, as well as the factors that influence it 2. Develop strategies to improve maternal nutrition and well-being to improve fetal growth and development	3. Study fetal cardiovascular development and test new therapies	4. Understand the hemodynamic changes that take place in fetal pathologies that affect cardiovascular development and test possible therapies

COLLABORATIONS

Nationals

- Hospital Clínic (Institut Clínic Cardiovascular)
- Hospital Clínic (Institut Clínic Respiratory)
- IDIBAPS (Traslational Computing in Cardiology)
- Hospital Clínic (Cardiovascular risk, nutrition and aging)
- Hospital Clínic (Institut Clínic Psychiatry)
- Hospital Clínic (Hemotherapy and Hemostasis)
- Hospital Sant Joan de Déu (Pediatric Cardiology)
- Institut Josep Carreras (Barcelona Endothelium Team)
- Institut Josep Carreras (Stem

- cells, mesenchymal cancer and development Group)
- IMIM (Applied Metabolomics)
- IATA-CSIC (Food Biotechnology), Valencia
- Universidad de Zaragoza (Biomedical Signal Interpretation & Computational Simulation – BSICoS- Group)

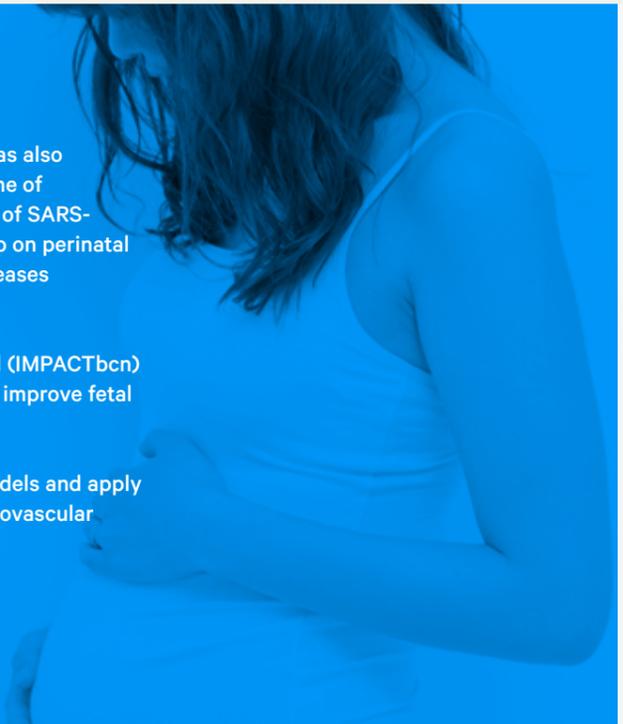
Internationals

- University of Lyon (CREATIS), France
- University of Lund (Obstetrics)
- University of Lund (CMR), Sweden
- University of Oregon, USA

- Fetal Medicine Mexico, Universidad Nacional Autónoma de México, Campus Juriquilla, Querétaro, Mexico
- Monash Newborn, Monash Children's Hospital, Monash University, Melbourne, Australia
- The Boden Institute of Obesity, Nutrition, Exercise & Eating Disorders, The University of Sydney, Camperdown, NSW, Australia
- European Synchrotron Radiation Facility, Grenoble, France
- University of Lund, Sweden
- UQ Centre for Clinical Research and University of Queensland, Australia

In 2020...

- During the exceptional nature of the pandemic, our line has also investigated in this area, following the principles of our line of investigation. In this respect, we have studied the impact of SARS-CoV-2 infection on the health of pregnant women and also on perinatal outcomes. We have also shown that low birth weight increases susceptibility to severe COVID-19.
- We have successfully completed a pioneering clinical trial (IMPACTbcn) that aims to improve maternal nutrition and well-being to improve fetal growth.
- We have continued working to develop computational models and apply artificial intelligence techniques to understand fetal cardiovascular development and test new therapies.





Fetal Brain Development



The line gathers fetal medicine specialists and engineers.

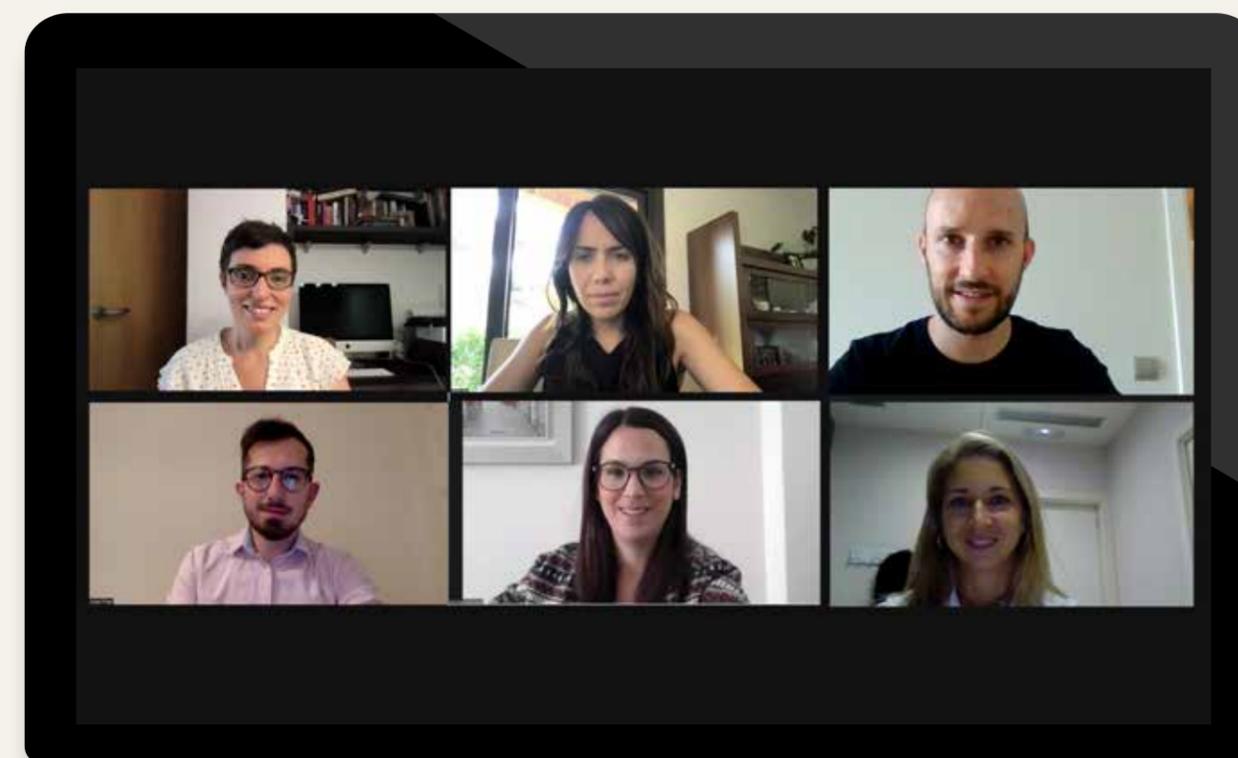
We evaluate prenatal brain development in the most detailed way in order to select the best biomarkers that will identify babies with greater risk of suffering neurological alterations

Why is it important to study the brain development of a fetus?

The brain is an organ with a long and complex development process that is susceptible to different conditions that may occur throughout the pregnancy. Evaluating this development process in a detailed way during the pregnancy, that is, during the fetal period, allows us to select biomarkers that help us identify children with a risk of suffering neurodevelopmental alterations.

How do we perform the search for these biomarkers?

To discover these biomarkers we apply different advanced technologies: the evaluation of cortical development by ultrasound and resonance imaging; the evaluation of brain microstructure by means of spectroscopy and diffusion techniques; and the analysis of brain connectivity by magnetic resonance in different conditions such as intrauterine growth restriction, congenital heart diseases, and ventriculomegaly.



TEAM MEMBERS

ELISENDA EIXARCH

Coordinator of the research line. Maternal-Fetal Medicine Specialist at BCNatal. Member of the fetal surgery team. Lecturer in specialized courses of Fetal I+D Education Barcelona.

PREDOCTORAL RESEARCHERS

Nadine Hahner, Elena Monterde, Lucas Trigo

MATERNAL-FETAL MEDICINE SPECIALIST

Miriam Illa, Míriam Pérez, Narcís Masoller

In 2020...

- We have shown, applying an innovative methodology in the analysis of fetal brain images, that in cases with ventricular dilatation (ventriculomegaly) the degree and location of ventricular dilatation correlates with regional changes at in cortical development.





We evaluated cortical development, microstructure and brain connections in fetuses with complications



PUBLICATIONS 2020

- ★ 1. **A novel approach to multiple anatomical shape analysis: Application to fetal ventriculomegaly.**
 Benkarim O, Piella G, Rekik I, Hahner N, Eixarch E, Shen D, Li G, González Ballester MA, Sanroma G. **Medical Image Analysis, 2020 Aug; 64:101750.**
 doi: 10.1016/j.media.2020.101750. Epub 2020 Jun 10.

COLLABORATIONS

Nationals

- Speech, Acquisition & Perception Group, Universitat Pompeu Fabra, Barcelona
- Simulation, Imaging and Modelling for Biomedical Systems, UPF
- CIBERSAM (grupo 8), Universitat de Barcelona
- Unitat de Medicina Fetal de Hospital de la Santa Creu y Sant Pau

Internationals

- University Hospital Leuven, Belgium
- Universidad de São Paulo, Brazil
- Center for the Developing Brain, King's College, UK

STRATEGIC GOALS

	CLINICAL	ENGINEERING
DEVELOPING	<p>New imaging biomarkers based on the assessment of the corpus callosum</p> <p>Normality curves for late gestational ages</p>	<p>Automatic analysis of fetal central nervous system images to identify key structures</p>
VALIDATING	<p>Integration of cortical maturation within the evaluation of patients at risk (heart disease, growth restriction, toxicant...)</p>	<p>Cortical maturation pattern analysis in clinical studies</p>



Prematurity



Physicians in fetal medicine, biologists, epidemiologists and technical support meet on the line.

Our aim is to detect patients with a real risk of preterm birth to optimize their treatment and prolong pregnancy as long as possible, and thus to improve neonatal prognosis.

Why is it important to study prematurity?

Preterm birth is the most frequent cause of perinatal morbidity and mortality. Each year 15 million babies in the world are born prematurely, that is, before 37 weeks of gestation. In Spain, this ratio is one in ten. For this reason, it is crucial to advance knowledge and improve management of such cases, two of the main objectives of this line. Any progress that allows us to extend preterm pregnancies even only two or three weeks more would allow us to change the lives of hundreds of thousands of families.

What advances would reduce the incidence of prematurity?

The line investigates non-invasive interventions that improve the decision-making capacity of

professionals against the risk of preterm birth. One of the main research tools of the Prematurity line is the quantitative analysis of the pulmonary and cervical textures through images obtained by ultrasound.

The first is already applied in the clinical practice and is also useful to better predict the outcome of labor induction. As for the second, today we know that cervical texture may be of great help as a screening tool for the risk of prematurity in the general population.



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POSTDOCTORAL RESEARCHERS

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PREDOCTORAL RESEARCHERS

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PUBLICATIONS 2020

- 1. Coronavirus Disease 2019 in Pregnancy: A Clinical Management Protocol and Considerations for Practice.** López M, Gonce A, Meler E, Plaza A, Hernández S, Martínez-Portilla RJ, Cobo T, García F, Gómez Roig MD, Gratacós E, Palacio M, Figueras F; on behalf of the COVID Collaborative Group. *Fetal Diagnosis and Therapy*, 2020. doi: 10.1159/000508487.
- 2. The Predictive Value of the Cervical Consistency Index to Predict Spontaneous Preterm Birth in Asymptomatic Twin Pregnancies at the Second-Trimester Ultrasound Scan: A Prospective Cohort Study.** van der Merwe J, Couck I, Russo F, Burgos-Artizzu XP, Deprest J, Palacio M, Lewi L. *Journal of Clinical Medicine*, 2020. doi: 10.3390/jcm9061784.
- 3. Vaginal metabolome: towards a minimally invasive diagnosis of microbial invasion of the amniotic cavity in women with preterm labor.** Vicente-Muñoz S, Cobo T, Puchades-Carrasco L, Sánchez-García AB, Agustí N, Palacio M, Pineda-Lucena A, Gratacós E. *Scientific Reports*, 2020. doi: 10.1038/s41598-020-62542-6.
- 4. Intra- and interobserver reproducibility of second trimester ultrasound cervical length measurement in a general population.** Baños N, Burgos-Artizzu XP, Valenzuela-Alcaraz B, Coronado-Gutiérrez D, Perez-Moreno Á, Ponce J, Gratacós E, Palacio M. *Journal of Maternal-Fetal & Neonatal Medicine*, 2020. doi: 10.1080/14767058.2020.1733516.
- 5. Development and validation of a multivariable prediction model of spontaneous preterm delivery and microbial invasion of the amniotic cavity in women with preterm labor.** Cobo T, Aldecoa V, Figueras F, Herranz A, Ferrero S, Izquierdo M, Murillo C, Amoedo R, Rueda C, Bosch J, Martínez-Portilla RJ, Gratacós E, Palacio M. *American Journal of Obstetrics and Gynecology*. 2020 Sep. doi: 10.1016/j.ajog.2020.02.049.

COLLABORATIONS

Nationals

- Instituto de Salud Carlos III (ISCIII)

Hospital, Philadelphia, USA
- Erasmus Mundus Joint Doctorate in Fetal Medicine

Internationals

- St George University, London
- Thomas Jefferson University

Industry

- Laboratorio Reig-Jofre, Spain

STRATEGIC GOALS

	FOR A BETTER DIAGNOSIS	FOR AN IMPROVED PATIENT MANAGEMENT
CLINICAL & BIOENGINEERING	Quantitative analysis of lung texture to predict the outcome of labor induction and the risk of preterm delivery	Evaluation of the effect of drugs that may delay preterm delivery in patients at risk of preterm birth
	Quantitative analysis of cervical texture in patients at risk of preterm birth	

In 2020...

- We continued to develop prediction tools based on quantitative analysis of lung and cervical texture for screening for the risk of preterm birth.
- We investigated markers to predict cesarean delivery in induction cases.
- During the pandemic, our line has also investigated in this area, participating in the creation of a clinical management protocol for coronavirus during pregnancy and considerations for clinical practice.

Inflammation in Preterm Birth

“

We can detect women who will end up having a preterm birth, who are the ones who really benefit from antenatal management with corticosteroids and tocolysis.

”

We want to predict intra-amniotic infection or inflammation in women at risk of preterm labor using rapid and non-invasive diagnostic tools, and also to evaluate the impact of intrauterine exposure to an infectious or inflammatory environment to the fetal, neonatal, and long-term level.

Why do we study infection of the amniotic liquid?

One in 10 pregnant women will have a premature birth. Current clinical management is very inefficient: only 10% of those admitted with threatened preterm labor (TPP) will have it, while 70% will give birth at term. The current criteria that we use to define PPA does not identify the most severe cases, associated with intra-amniotic infection and inflammation, present in 40% of pregnant women. These are the ones that present a shorter latency to delivery, of a few days, unlike the group without infection or inflammation, whose latency to delivery is an average of 50 days. Despite being groups with different perinatal prognoses, current management is similar. Discriminating the high from the low

risk of infection and/or intra-amniotic inflammation makes it possible to identify the group that benefits from antenatal strategies that improve the prognosis of premature infants (corticosteroids, magnesium sulfate, antibiotics) and avoid unnecessary overtreatment in low-risk infants.

Why investigate in minimally invasive samples?

Despite the relevance of the clinical problem, the main drawback in the diagnosis of intra-amniotic infection and inflammation is that amniocentesis is required, an invasive procedure that limits clinical translation. Our line develops tools based on new technologies, which are minimally invasive, are at the patient's bedside, are fast and improve clinical management.

What is the impact of that infection on the fetus?

To find out the impact of intrauterine exposure to infection and inflammation on the fetus and newborn, we lead two clinical projects that evaluate the influence on fetal and neonatal growth; their cardiovascular system and their neurodevelopment during the fetal stage, at birth and at 6 months of life. We also study the impact on neurodevelopment at one year of life.



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In 2020...

- We have observed that women with intra-amniotic infection have a characteristic vaginal metabolic profile. Women with a low bacterial load of *Lactobacillus* spp in vaginal fluid are at increased risk of perinatal intraamniotic inflammation, preterm labor, and short latency to delivery.
- We have observed metabolic changes in vaginal fluid in women with intra-amniotic infection that indicate activation of glycolysis in situations of hypoxia as a consequence of bacterial infection.
- We are able to discriminate women with threatened preterm labor who will actually deliver preterm in the following days with the information on intra-amniotic infection and inflammation provided by amniocentesis.
- We collaborate with companies on projects with a high translational component. With HOLOGIC we will contribute to improving the detection of the risk of inflammation and/or intra-amniotic infection in women with threat of preterm birth through the validation of a non-invasive test based on determining proteins in vaginal fluid.
- With Medix Biochemica, we will validate a rapid and effective test that detects the MMP-8 protein to diagnose intra-amniotic inflammation at the patient's bedside with the aim of individualizing the clinical management of these women.
- We develop intra-amniotic infection prediction models that integrate information on proteomics, metabolomics and microbiome in minimally invasive samples such as vaginal mucus.

PUBLICATIONS 2020

1. **Risk factors for spontaneous preterm delivery.** Cobo T, Kacerovsky M, Jacobsson B. *International Journal of Gynecology & Obstetrics*, 2020 Jul; doi: 10.1002/ijgo.13184
2. **Bacteremia and intramniotic infection due to *Burkholderia cenocepacia*.** Fidalgo B, Bosch J, Cobo T, Ribera L, Casals C, Almela M. *Clinical Microbiology and Infection*, 2020 Nov; 26(11):1564-1565.
3. **Commentary on a combined approach to the problem of developing biomarkers for the prediction of spontaneous preterm labor that leads to preterm birth.** Lamont RF, Richardson LS, Boniface JJ, Cobo T, Exner MM, Christensen IB, Forslund SK, Gaba A, Helmer H, Jørgensen JS, Khan RN, McElrath TF, Petro K, Rasmussen M, Singh R, Tribe RM, Vink JS, Vinter CA, Zhong N, Menon R. *Placenta*. 2020 Sep 1; doi: 10.1016/j.placenta.2020.05.007
4. **Vaginal metabolome: towards a minimally invasive diagnosis of microbial invasion of the amniotic cavity in women with preterm labor.** Vicente-Muñoz S, Cobo T, Puchades-Carrasco L, Sánchez-García AB, Agustí N, Palacio M, Pineda-Lucena A, Gratacós E. *Scientific Report*, 2020 Mar 25; doi: 10.1038/s41598-020-62542-6
5. **Development and validation of a multivariable prediction model of spontaneous preterm delivery and microbial invasion of the amniotic cavity in women with preterm labor.** Cobo T, Aldecoa V, Figueras F, Herranz A, Ferrero S, Izquierdo M, Murillo C, Amoedo R, Rueda C, Bosch J, Martínez-Portilla RJ, Gratacós E, Palacio M. *American Journal of Obstetrics and Gynecology*, 2020 Sep. doi: 10.1016/j.ajog.2020.02.049.

COLLABORATIONS

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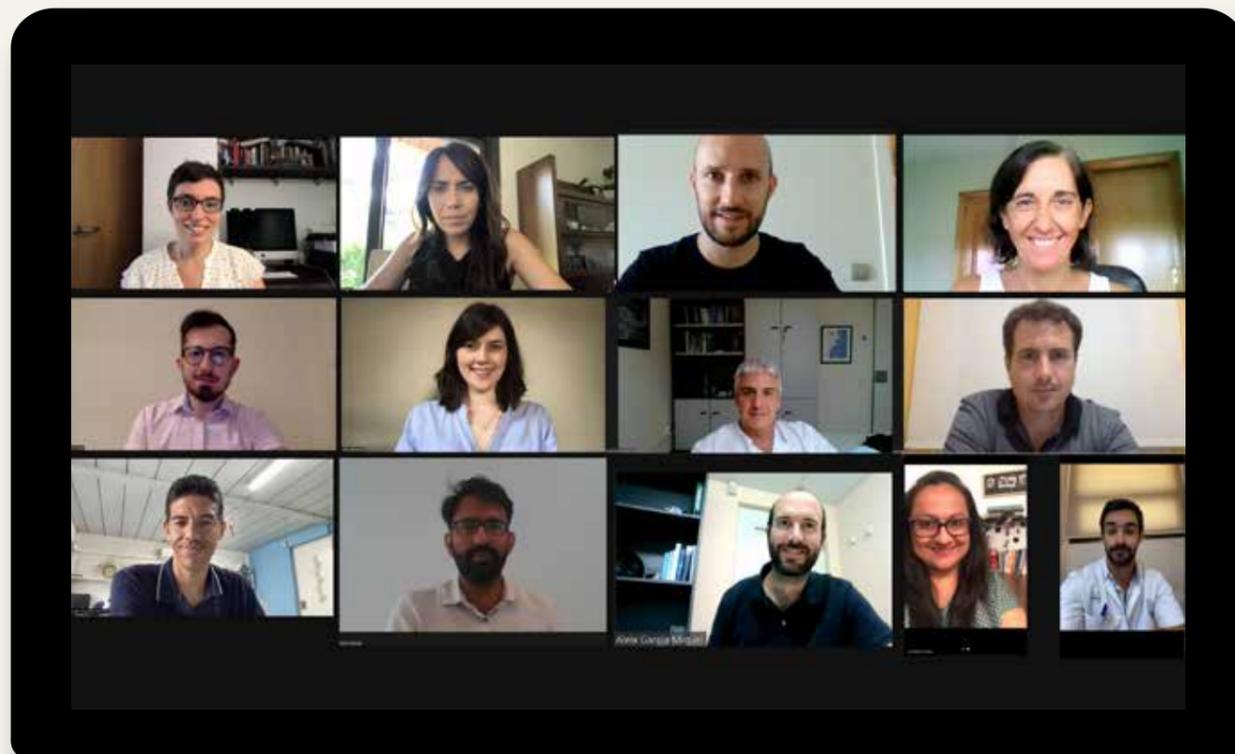
- Hologic, USA
- Medix Biochemica, Finland
- Transmural Biotech, Spain

STRATEGIC GOALS

	CLINICAL	BASIC
FOR A BETTER DIAGNOSIS	To individualize the clinical management of women at risk of preterm birth by studying intra-amniotic infection/inflammation	To advance in the development of a non-invasive clinical solution to diagnose intra-amniotic infection/inflammation in women at risk of premature delivery using technologies based on metabolomics, proteomics, bacterial microbiome and photonics
	To evaluate the impact of intrauterine exposure to intra-amniotic infection/inflammation at the cardiovascular, neurological and neurodevelopmental levels, in the fetus and newborn at 6 months and 1 year of life	

Fetal Therapy and Surgery

“
Robotics, photonics and miniaturization will allow us to take a generational leap in fetal surgery.
 ”



We want to develop new therapies and intrauterine treatments that overcome the limitations that have existed up to now in fetal surgeries.

will allow us to improve the results of the fetal surgeries that we currently perform and create new treatments for as yet unsolved problems.

What will technological advances allow in fetal surgery?

Research on new surgical procedures in the fetal environment will allow us to save more lives before birth and improve the prognosis of babies with more serious conditions. The use of ex vivo and experimental models before applying these therapies in clinical practice is key to achieving our goals.

What kind of fetal therapies do we develop?

The main raison d'être of our research team is to prevent or treat pathologies of fetal origin. To this end, we evaluate specific therapeutic strategies with a potential neuroprotective effect that could be useful in certain diseases of fetal origin, such as intrauterine growth restriction. For this, we focus our work on developing technological advances through robotics, photonics, miniaturization, and the use of sensors. Uniting all these disciplines

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PROJECT MANAGER

Aleix Garcia

PUBLICATIONS 2020

- Structural Brain Changes during the Neonatal Period in a Rabbit Model of Intrauterine Growth Restriction.** Pla L, Illa M, Loreiro C, Lopez MC, Vázquez-Aristizabal P, Kühne BA, Barenys M, Eixarch E, Gratacós E. **Developmental Neuroscience, 2020.** doi: 10.1159/000512948.
- ★ **Ex-vivo mechanical sealing properties and toxicity of a bioadhesive patch as sealing system for fetal membrane iatrogenic defects.** Micheletti T, Eixarch E, Berdun S, Febas G, Mazza E, Borrós S, Gratacos E. **Scientific Reports, 2020 Oct.** doi: 10.1038/s41598-020-75242-y.
- ★ **Rabbit neurospheres as a novel in vitro tool for studying neurodevelopmental effects induced by intrauterine growth restriction.** Barenys, M; Illa, M; Hofrichter, M; Loreiro, C; Pla, L; Klose, J; Kühne, AB; Gómez-Catalán, J; Matthias Braun, J; Crispí, J; Gratacós, E; Fritsche, E. **STEM CELLS Translational Medicine** doi: 10.1002/sctm.20-0223
- Segmentation of the placenta and its vascular tree in Doppler ultrasound for fetal surgery planning.** Perera-Bel E, Ceresa M, Torrents-Barrena J, Masoller N, Valenzuela-Alcaraz B, Gratacós E, Eixarch E, González Ballester MA. **International Journal for Computer Assisted Radiology and Surgery, 2020 Nov;** doi: 10.1007/s11548-020-02256-2.
- TTTS-STgan: Stacked Generative Adversarial Networks for TTTS Fetal Surgery Planning Based on 3D Ultrasound.** Torrents-Barrena J, Piella G, Valenzuela-Alcaraz B, Gratacos E, Eixarch E, Ceresa M, Gonzalez Ballester MA. **IEEE Transactions on Medical Imaging, 2020 Nov;** doi: 10.1109/TMI.2020.3001028. Epub 2020 Oct 28.n.
- Deep Q-CapsNet Reinforcement Learning Framework for Intrauterine Cavity Segmentation in TTTS Fetal Surgery Planning.** Torrents-Barrena J, Piella G, Gratacos E, Eixarch E, Ceresa M, Gonzalez Ballester MA. **IEEE Transactions on Medical Imaging. 2020 Oct.** doi: 10.1109/TMI.2020.2987981.
- Micro-needle implantable electrochemical oxygen sensor: ex-vivo and in-vivo studies.** Rivas L, Dulay S, Miserere S, Pla L, Marin SB, Parra J, Eixarch E, Gratacós E, Illa M, Mir M, Samitier J. **Biosensors & Bioelectronic. 2020 Apr.** doi: 10.1016/j.bios.2020.112028.
- Segmentation and classification in MRI and US fetal imaging: Recent trends and future prospects.** Torrents-Barrena J, Piella G, Masoller N, Gratacós E, Eixarch E, Ceresa M, González Ballester MA. **Medical Image Analysis, 2019 Jan.** doi: 10.1016/j.media.2018.10.003.
- Fully automatic 3D reconstruction of the placenta and its peripheral vasculature in intrauterine fetal MRI.** Torrents-Barrena J, Piella G, Masoller N, Gratacós E, Eixarch E, Ceresa M, González Ballester M. **Medical Image Analysis, 2019 May.** doi: 10.1016/j.media.2019.03.008.

COLLABORATIONS

Nationals

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- Instituto de Ciencias Fotónicas (ICFO)
- Instituto de Bioingeniería de Cataluña (IBEC)

- Institut Químic de Sarrià (IQS)
- Dept Biología Celular, Inmunología y Neurociencias de la UB

Internationals

- University Hospitals Leuven, Belgium
- Institute of Mechanical Systems, Switzerland
- University of São Paulo, Brazil

STRATEGIC GOALS

	THERAPY	SURGERY
EXPERIMENTAL	<p>Evaluation of cell cultures and neuroprotective therapies</p> <p>Evaluation of the effects, structure and function of new therapeutic strategies</p>	<p>Functional and safety tests for a membrane sealing system</p>
CLINICAL	<p>Clinical trial in prenatal therapy FETAL BRAIN CARE</p>	<p>Multicenter clinical validation study of a 3D-P three-dimensional personalized pre-surgical planning system</p> <p>Pilot study of a membrane sealing system FET-SEALING</p>

In 2020...

- We demonstrated in experimental models that the developed fetal membrane sealing system is capable of preventing fluid loss through the hole created after surgery. This system can be inserted through the same hole without the need to make more incisions.
- In conjunction with Universitat Pompeu Fabra, we continue to improve a three-dimensional personalized pre-surgical planning system for cases of twin-to-twin transfusion syndrome with improvements in image processing and reconstruction.
- We demonstrate for the first time how the in vitro culture of neural stem cells obtained from an animal model of intrauterine growth restriction reproduces the structural changes previously identified in conventional histological models. This finding positions in vitro culture as a novel technique to continue characterizing neuronal damage secondary to intrauterine growth restriction and to be able to test potential neuroprotective therapies.
- We are working on the development of an artificial placenta system that will be one of the great projects of the coming years.

Placental Disease

“
Diagnosing intrauterine growth restriction allows preventive measures to be implemented in pregnancy, childbirth and early childhood
”

We improve the diagnosis and management of pregnancies with growth restriction to avoid possible neurodevelopmental alterations.

What is the impact of intrauterine growth restriction iugr on babies?

Babies with Intrauterine Growth Restriction (IUGR) have an increased risk of complications before and after birth. But that is not all; additionally they may present neurodevelopmental alterations.

These, although they may be mild and may not have important sequelae, are more and more frequently recognized as family and social problems.

Why is prevention so important?

The evaluation of longitudinal growth in pregnancy is key to making an accurate prediction of fetal growth restriction and its consequences. The correct definition and diagnosis of IUGR is especially important for fetal medicine, since

it will allow the implementation of preventive measures during pregnancy and childbirth, as well as therapies during early childhood.

What is the relevance of studying preeclampsia?

Preeclampsia is the second leading cause of maternal death in the world. Today, thanks to research, its diagnosis is very predictable already in the first trimester, which opens up the opportunity to prevent most severe cases. Once preeclampsia is diagnosed, the clinical challenge is to determine the optimal time to induce delivery in a way that maximizes maternal and neonatal benefits. A very active research focus is the role of biochemical markers of preeclampsia severity in guiding this decision.



TEAM MEMBERS

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CLINICAL RESEARCHERS

Giulia Benedetto, Aleida Castellanos, Judith Martínez, Fernanda Paz y Miño

PUBLICATIONS 2020

- 1. First-trimester prediction of small-for-gestational age in women at false-positive high and intermediate risk for aneuploidy.** Yarygina TA, Bataeva RS, Benitez L, Figueras F. *Ultrasound in Obstetrics & Gynecology*, 2020; doi: 10.1002/uog.21965
- 2. A Spanish-translated clinical algorithm for management of suspected SARS-CoV-2 infection in pregnant women.** Martinez-Portilla RJ, Gonc e A, Hawkins-Villarreal A, Figueras F. *The Lancet Infectious Diseases*, 2020; doi: 10.1016/S1473-3099(20)30285-1.
- 3. Quality assessment of fetal middle cerebral and umbilical artery Doppler images using an objective scale within an international randomized controlled trial.** M Rial, J Morales, E Hern andez-Andrade, F Prefumo, D Oros, D Caffici, A Sotiriadis, E Zohav, R Cruz-Martinez, M Parra, M Lubusky, M Kacerovsky, F Figueras. *Ultrasound in Obstetrics & Gynecology*, 2020. doi: 10.1002/uog.20370
- 4. ISUOG Practice Guidelines: diagnosis and management of small-for-gestational-age fetus and fetal growth restriction.** C C Lees, T Stampalija, A Baschat, F da Silva Costa, E Ferrazzi, F Figueras, K Hecher, J Kingdom, L C Poon, L J Salomon, J Unterscheider. *Ultrasound in Obstetrics & Gynecology*, 2020. doi: 10.1002/uog.22134.
- 5. A clinical management protocol for COVID-19 infection in pregnant women.** M Vald es-Bango, E Meler, T Cobo, S Hern andez, A Caballero, F Garc a, L Ribera, L Guirado, P Ferrer 1, D Salvia, F Figueras, M Palacio, A Gonc e, M L pez. *Clinica e Investigacion en Ginecologia y Obstetricia*, 2020. doi: 10.1016/j.gine.2020.06.014.
- 6. Pregnant women with SARS-CoV-2 infection are at higher risk of death and severe**

- pneumonia: propensity score-matched analysis of a nationwide prospective cohort study (COV19Mx).** R J Martinez-Portilla, A Sotiriadis, C Chatzakis, J Torres-Torres, S Espino Y Sosa, K Sandoval-Mandujano, D A Castro-Bernabe, V Medina-Jimenez, J C Monarrez-Martin, F Figueras, L C Poon. *Ultrasound in Obstetrics & Gynecology*, 2020. doi: 10.1002/uog.23575
- 8. Incidence of pre-eclampsia and other perinatal complications among women with congenital heart diseases: systematic review and meta-analysis.** R J Martinez-Portilla, L C Poon, L Benitez-Quintanilla, A Sotiriadis, M Lopez, D L Lip-Sosa, F Figueras. *Ultrasound in Obstetrics & Gynecology*, 2020. doi: 10.1002/uog.22174
- 9. Heparin therapy in placental insufficiency: Systematic review and meta-analysis.** Mazarico E, Molinet-Coll C, Martinez-Portilla RJ, Figueras F. *Acta Obstetrica et Gynecologica Scandinavica*, 2020. doi: 10.1111/aogs.13730

COLLABORATIONS

Nationals

– EUGIN Clinic, Barcelona

Internationals

– Aristotle University Medical School, Thessaloniki, Grecia
 – Lund University Hospital, Lund, Sweden

STRATEGIC GOALS

	CLINICAL
DIAGNOSIS	Development of early detection methods for growth restriction for a new definition and prediction of brain
THERAPIES	Clinical trials to prevent preeclampsia and growth restriction

In 2020...

- We continue to investigate the role of growth assessment in predicting fetal growth restriction and its consequences. In this regard, we have published our 10-year experience in the management of late forms of growth retardation.
- We advance in the study of the causes of preeclampsia and its complications, and in particular in the value of its biochemical markers of severity:
- On the one hand, we have shown that the progression of maternal levels of angiogenic factors (the biochemical signature of preeclampsia) predicts the risk of complication. In this way we add a clinical criterion that helps us in making decisions about the moment of delivery of these severe forms.
- On the other hand, in mild forms of preeclampsia we have published the first clinical trial (the highest level of scientific evidence) that shows that the incorporation of angiogenic factors in decision-making about the time of delivery decreases up to 5 times the maternal risk without increasing the risk to the neonates.
- We continue to work on the RATIO37 clinical trial, which studies the incorporation of a new ultrasound parameter at week 37 of pregnancy with the aim of reducing the rate of fetal death and complications in childbirth.
- We have incorporated a gestational diabetes prediction project in the first trimester into the line. Once you have a good predictive tool, the possibility of studying different preventive strategies opens up.

Environment and Pregnancy Complications



The line gathers fetal medicine specialists, pathologists, biologists and research technicians.

Our raison d'être is to discover how environmental factors such as exposure to tobacco, alcohol, drugs and environmental toxins influence fetal development and other pregnancy complications.

What is your research based on?

Our objective is to characterize the effect of exposure during pregnancy to all toxins in order to improve our knowledge about them and to be able to predict pregnancy complications related to environmental factors such as placental pathology, intrauterine growth restriction, hypertensive states of pregnancy, prematurity, perinatal morbidity and prenatal and postnatal neurodevelopment.

We also seek prenatal intervention measures to reduce the consumption of toxic substances such as alcohol and thus improve gestational, perinatal and postnatal outcomes.

What are the effects of alcohol exposure during pregnancy? Is it possible to reverse it?

Exposure to alcohol affects fetal growth as well as neurodevelopment. We are studying the effectiveness of a structured prenatal intervention to reduce its deleterious effects on prenatal and postnatal consequences in newborns exposed to alcohol during pregnancy.

What other toxins affect pregnancy?

The negative effect of air pollution and endocrine disruptors such as chemical exposure on fetal development is well known. Increasing knowledge of these effects and their postnatal consequences will allow us to invest in preventive public health measures in the pregnant population.



TEAM MEMBERS

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BIOTECHNOLOGIST/BIOBANK MANAGER

Érica Muñoz

PUBLICATIONS 2020

- Study of the fetal and maternal microbiota in pregnant women with intrauterine growth restriction and its relationship with inflammatory biomarkers: A case-control study protocol (SPIRIT compliant).** Fernandez S, Ortiz O, Joan Galiot Torrecillas EIX Soluciones G, Pérez M, Chueca N, Gómez Roig MD, Gómez C. *Medicine (Baltimore)*, 2020 Nov 13. doi: 10.1097/MD.00000000000022722
- Exposure to greenspace and birth weight in a middle-income country.** Torres M, Miri M, Alonso L, Gómez MD, Foraster M, Dadvand P. *Environmental Research*, 2020. doi: 109866-109866.
- Perceptions and Attitudes of Gynecologic and Pediatric Professionals Regarding Dietary Exposure to Chemical Pollutants.** Arrebola JP, Muñoz A, Ferrero SI, Larrea C. *International Journal of Environmental Research and Public Health*, 2020, Jun. doi: 10.3390/ijerph17113946.
- Bioavailability of Epigallocatechin Gallate administered with different nutritional strategies in healthy volunteers.** Fernández VA, Almeida L, Pizarro N, Tapia EN, Gómez Roig MD, De la Torre R, García Ó. *Antioxidants (Basel)*, 2020. doi: 10.3390/antiox9050440
- The Evolving Microbiome from Pregnancy to Early Infancy: A Comprehensive Review.** Mesa MD, Loureiro B, Iglesia I, Fernandez S, Llurba E, García O, Solana MJ, Cabero MJ, Sainz T, Martinez L, Escuder D, Parra A, Sánchez M, Rodriguez G, Gómez Roig MD, Perez M, Andreu V, Clotet J, Sailer S, Iglesias I, López J, Aras R, Pallás C, de Pipaon MS, Vento M, Gormaz M, Larqué E, Calvo C, Cabañas F. *Nutrients*, 2020. doi: 10.3390/nu12010133.
- Murine Models for the Study of Fetal Alcohol Spectrum Disorders: An Overview.** Almeida L, Andreu V, Navarro E, Aras R, Serra M, Martínez L, García O, Gómez MD. *Frontiers in Pediatrics*, 2020. doi.org/10.3389/fped.2020.00359
- Eating Disorders During Gestation: Implications for Mother's Health, Fetal Outcomes, and Epigenetic Changes.** Sebastiani G, Andreu V, Herranz A, Aldecoa V, Miracle X, Meler E, Balada A, Astals M, Ferrero S, Gómez Roig MD, García O. *Frontiers in Pediatrics*, 2020. doi: org/10.3389/fped.2020.00587
- Early Prophylactic Enoxaparin for the Prevention of Preeclampsia and Intrauterine Growth Restriction: A Randomized Trial.** Llurba E, Bella M, Burgos J, Mazarico E, Gómez Roig MD, Raul de Diego B, Martínez T, Alijotas J, Sánchez MÁ, Sánchez O, Carreras E, Cabero L. *Fetal Diagnosis and Therapy*, 2020. doi: 10.1159/000509662
- Prenatal selection of cord blood donors according to the estimated fetal weight percentile and new approaches; results of a prospective cohort study.** Xinxin L, Crovetto F, González A, Cuadras D, Sanchez M, Azqueta C, Farssac E, Torradabella M, Querol S, Gomez-Roig MD. *Transfusion*. 2021 Apr. doi: 10.1111/trf.16215.

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- Instituto de Salud Global (ISGlobal), Barcelona
- Red de Salud maternoinfantil y del desarrollo. Instituto de Salud Carlos III (ISCIII), Madrid
- Institut de Recerca Sant Joan de Déu, Barcelona
- Cognitive Neuroscience Department, Brainlab, Universitat de Barcelona (UB)

STRATEGIC GOALS

	STUDYING	PREDICTING
BASIC	The effect of exposure to environmental toxins in pregnancy	The risk of pregnancy complications due to environmental factors
CLINICAL	Exposure to toxins and metabolites in pregnancy	

In 2020...

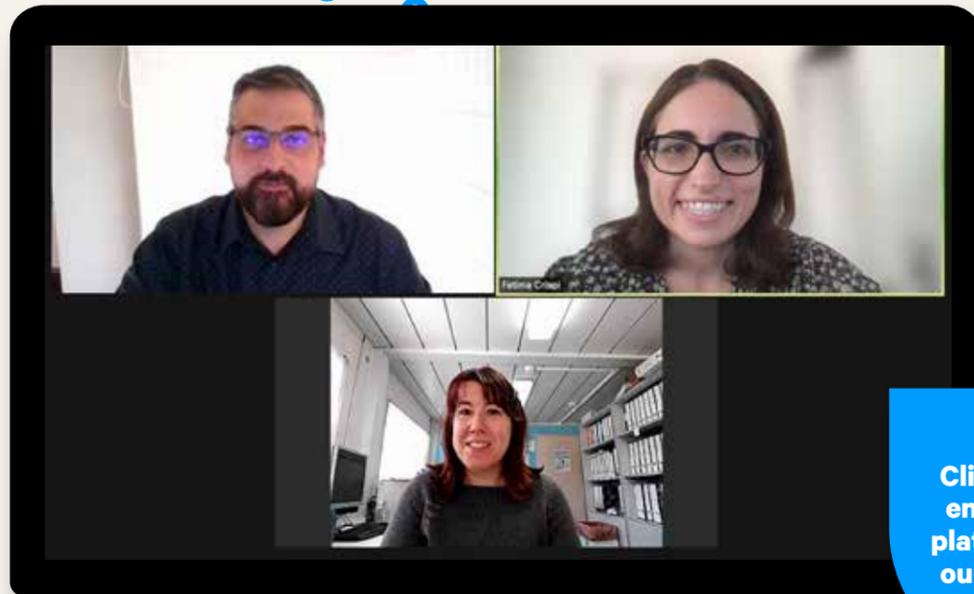
- The intervention study to reduce alcohol consumption in pregnant women (EMOTIVE) is ongoing to study the effectiveness of a structured prenatal intervention to reduce the effects of alcohol during pregnancy.
- We participated in the 'BiSC' (Barcelona Life Study Cohort) study to understand the effect of contamination on placental function and fetal cardiovascular and brain development. We performed ultrasounds on 600 volunteers from the metropolitan area of Barcelona.
- We started a study to validate the brain response of the baby's auditory system (frequency tracking response) and its relation to language development.
- We participated in the ATHLETE study (Advancing Tools for Human Early Lifecourse Exposome Research and Translation) to develop tools for the study of the exposome. We are recruiting a prospective exposure cohort to quantify the effects of environmental risk factors on mental health, cardiometabolic, respiratory, and associated biological pathways during the first two decades of life.

Research platforms

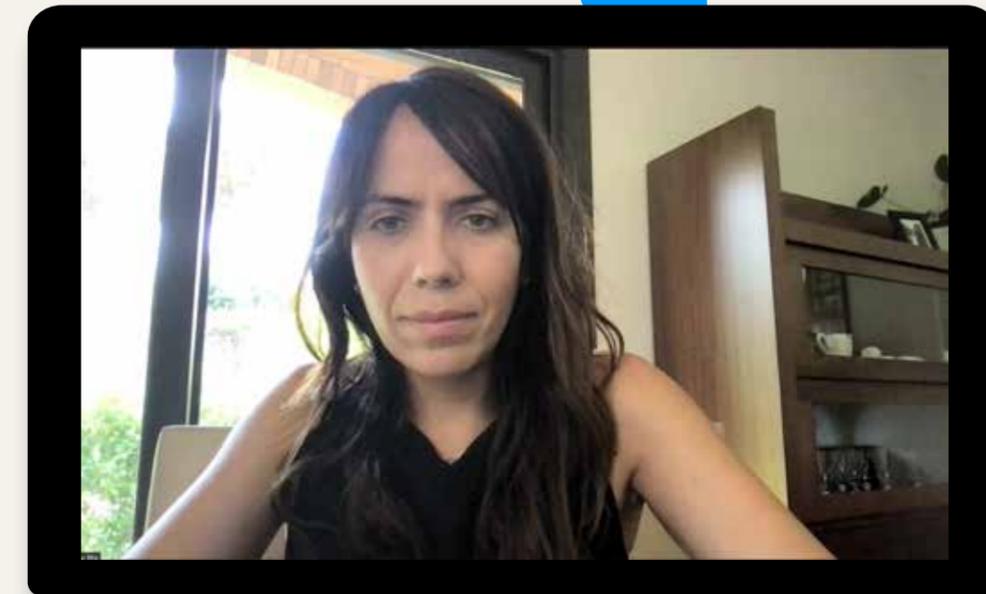
“
The biobank and the animal model are key platforms to advance our research
”

BIOBANK

ANIMAL MODEL



Click here to enter to the platform from our biobank!



Our mission is to collect, process and, make available to the scientific community maternal-fetal and neonatal biological samples.

The project, framed within the Biobank of the Hospital Clínic-IDIBAPS and the Biobank of the Sant Joan de Déu Hospital for Research (BHSJDI), combines biological samples obtained from a wide range of pathologies during pregnancy (twin-to-twin transfusion, IUGR, preeclampsia, etc) and postnatally to support different maternal-fetal research studies. Working with

these samples allows us to advance our knowledge about pregnancy pathologies and to improve diagnostic possibilities and future therapies.

Scientific Coordinator:
Fàtima Crispí
Technician:
Laura González
Postdoctoral biologist:
Víctor Rodríguez

We manage the projects of the group that require animal research and coordinate with the animal facility platform of the Universitat de Barcelona.

In addition to managing different workspaces, coordinating procedures and providing administrative, technical, and scientific support, we ensure animal wellness by supervising them periodically and by revising the protocols for animal experimentation according to the current ethical committee.

Scientific Coordinator:
Miriam Illa
Research Technician:
Carla Loreiro

“

In the postnatal platform we identify methods of diagnosis and early treatment of diseases of prenatal origin

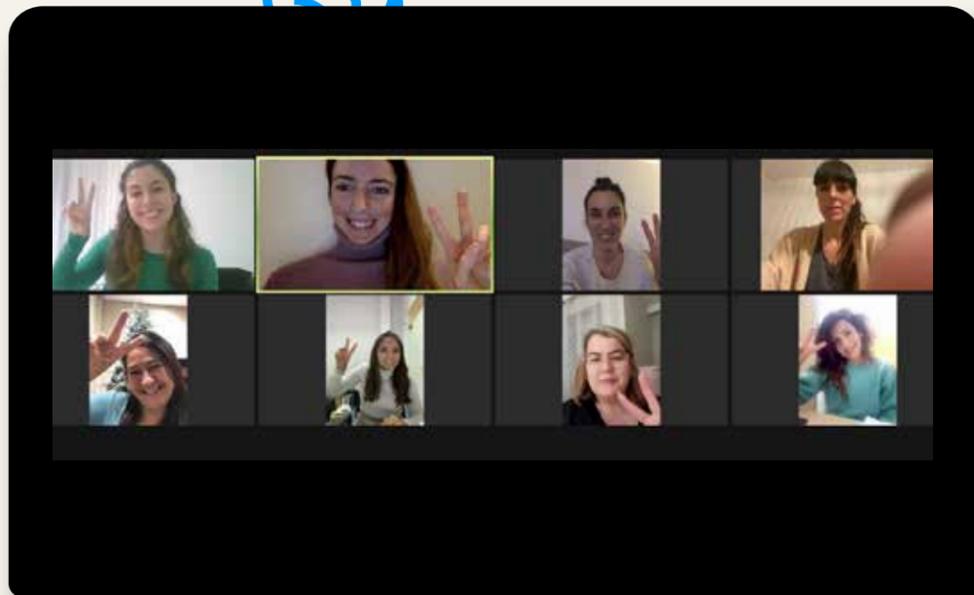
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“

Through artificial intelligence we will be able to analyze the ultrasound images to improve the diagnosis

”

POSTNATAL



Our priority is to guarantee the best neonatal follow-up of all patients participating in the various research projects of the group.

Our nurses and psychologists are experts in neurodevelopment and they are specialized in carrying out a follow-up of the patients and their babies that is personalized throughout. Once the baby is born, they accompany families during magnetic resonance procedures or the assessments of children's capabilities using the Brazelton or Bayley and Wisc tests. These tests allow early identification of

neurodevelopmental delays in order to act as early as possible by applying the appropriate treatment in each case.

Scientific Coordinator and Head Nurse of BCNatal: Ángela Arranz
Nurses: Mireia Pascual, Nadia Rojas, Natalia Torrico, Maira Rodríguez
Psychologists: Alba Camacho, Paula Navarro
Assistant nursing care technician: Mireia Marín, Carolina Cruz, Nerea González

IMAGE



We enter the new technological era to improve the diagnosis and patient care through the application of Artificial Intelligence techniques that are able to see things that are not visible to the naked eye.

We gather the ultrasound images taken during the routine pregnancy follow-up of all of our patients (mothers and babies) at BCNatal hospitals. We classify and order them by type and relate them to the clinical data by strictly complying with the data protection regulations that are currently in force. Thanks to the high volume of patients we receive, we hope to build a large database of ultrasound images that will allow us to study Artificial

Intelligence techniques. This will open new possibilities for us to expand our knowledge about pregnancy pathologies and improve their diagnosis.

Scientific Coordinator: Xavier P. Burgos
Research Support: David Coronado

Research management

The departments of project management, purchasing, human resources, IT, communication, and CSR, business development and internationalization work together to facilitate the good functioning of the research group.

The BCNatal Fetal Medicine Research Center has its own independent management department whose lines of action range from economic management and logistics of various projects to communication and Corporate Social Responsibility. One of its highest priorities is the professional development of the researchers of the group. In this

In 2020...

Among the invited speakers at the Journal Club

- Ferran Prados, from the UOC and University College London, who explained the translation of advances in medical imaging, specifically neuroimaging, to clinical practice and to improving the life of the patient.
- Stefan Verlohren, from the Charité University Medicine, Berlin, who spoke about the role of angiogenic factors in preeclampsia.
- Dafnis Batallé, from King's College London, who spoke about the developing human connectome project.

regard, different learning and networking actions are carried out, such as the Journal Club, workshops and Christmas and summer events.

JOURNAL CLUB

From the team's beginnings, in 2005, we wanted to create a space to present and debate among researchers the issues related to the projects that are being carried out. This is how the Journal Club was born, a space for weekly discussions to see the progress of the group, and occasionally, to welcome external researchers or experts in maternal-fetal medicine to discuss topics of general interest.

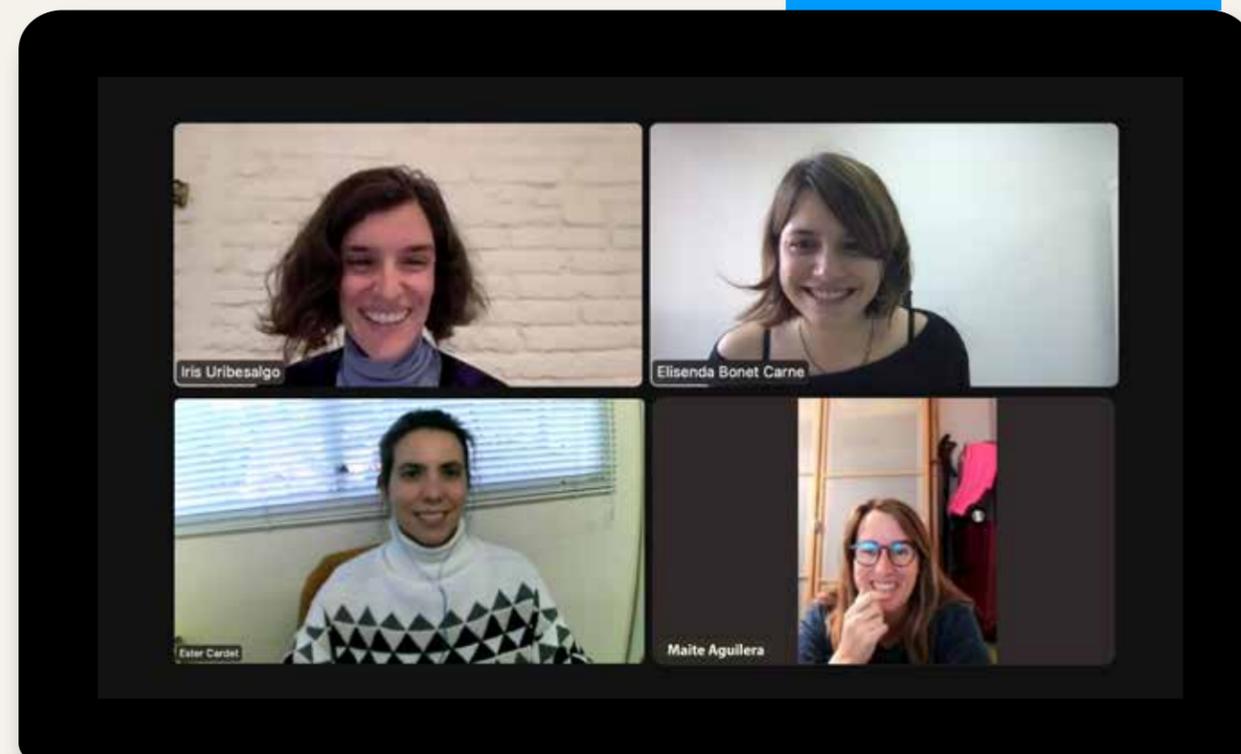
COVID PANDEMIC

Due to the pandemic and the reorganization that COVID-19 prevention measures have meant for researchers, the management team has tried to adapt all events to digital format. The Journal Clubs, for example, have been carried out by streaming videoconference. In addition, acts of group cohesion have also been maintained, such as the celebration of a virtual Tea Time coinciding with each Journal Club.

Scientific Manager: Elisenda Bonet-Carne
Project Manager: Ester Cardet
Scientific Writer: Iris Uribesalgo
HR Coordinator: Maite Aguilera
Purchasing and Administrative: Mercedes Alonso

FIELDS OF ACTION

- RESEARCH SUPPORT**
Supporting the scientific activity of the researchers of the group and promoting excellent research in fetal medicine
- COORDINATION**
Coordinating different research projects in order to ensure maximum efficiency and innovation in all of them
- FINANCIAL MANAGEMENT**
Managing efficiently the funds that finance research activities and ensuring the efficient use of resources and infrastructure
- PROFESSIONAL DEVELOPMENT**
Contributing to the professional development of the team members to encourage motivation in the workplace and ensure their future employability
- GOOD PRACTISES**
Ensuring ethics and the application of ethical principles in research
- KNOWLEDGE TRANSFER**
Promoting the translation of results and providing the knowledge of the progress made to society, the scientific community and the economic system





3

R&D Projects

Research projects and grants

Clinical transfer

Obra Social 'la Caixa' Project

CEREBRA Project

CELLEX Project

BCNatal CaixaResearch Artificial Placenta Project

Research projects and grants

ONGOING IN 2020

Erasmus Mundus Joint Doctorate in Fetal and Perinatal Medicine. FetalMed-PhD.

Eduard Gratacós

European Commission. Erasmus +
► 01/08/2013 - 31/10/2022

Papel del factor de crecimiento placentario en el manejo de la preeclampsia no severa: estudio aleatorizado (Estudio MAP).

Francesc Figueras

Instituto de Salud Carlos III (ISCIII)
► 01/01/2016 - 31/12/2020

Targeting endothelial dysfunction in highly prevalent diseases: characterization and validation of prognostic biomarkers and identification of potential therapeutic strategies.

Eduard Gratacós, Fàtima Crispi

Instituto de Salud Carlos III (ISCIII)
► 01/01/2016 - 31/11/2020

Desarrollo de herramientas predictivas para la identificación precoz de las alteraciones del neurodesarrollo de origen prenatal basadas en el estudio del desarrollo cortical fetal.

Elisenda Eixarch

Instituto de Salud Carlos III (ISCIII)

► 01/01/2017 - 30/06/2021

Grup de Medicina Maternofetal i Neonatal mixte Hospital Clínic de Barcelona i Hospital Sant Joan de Déu

Eduard Gratacós

Generalitat de Catalunya - Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR)

► 01/01/2017 - 30/09/2021

Impacto de técnicas de reproducción asistida en la programación cardiovascular fetal, resultado perinatal y epigenética fetal

Fàtima Crispi

Instituto de Salud Carlos III (ISCIII)

► 01/01/2018 - 31/12/2021

Impacto de la detección y tratamiento precoz de las gestantes portadoras asintomáticas de vaginosis bacteriana, en la tasa de parto pretérmino (VB-PREM): ensayo clínico multicéntrico.

Montse Palacio

Instituto de Salud Carlos III (ISCIII)

► 01/01/2018 - 31/12/2020

Clasificación fenotípica para una nueva clasificación clínica de la restricción de crecimiento fetal.

Eduard Gratacós

Instituto de Salud Carlos III (ISCIII)

► 01/01/2019 - 31/12/2021

Evaluación in vitro e in vivo de terapias neuroprotectoras en un modelo animal de restricción de crecimiento intraútero

Miriam Illa

Instituto de Salud Carlos III (ISCIII)

► 01/01/2019 - 31/12/2021

Desenvolupament de noves eines diagnòstiques i terapèutiques personalitzades per prevenir i tractar les malalties fetals i les seves conseqüències en la salut.

Eduard Gratacós

Fundació "la Caixa"

► 01/01/2019 - 31/12/2020

MIFI - Multimodality Integrated Imaging for Fetal Intervention.

Eduard Gratacós

European Commission

► 25/04/2019 - 31/07/2020

STARTED IN 2020

Desarrollo y validación de una herramienta diagnóstica no-invasiva de infección intra-amniótica en flujo vaginal

Clinical transfer: guidelines

One of the main objectives of our research is the translation of results to the medical community through the improvement of clinical practice in maternal-fetal medicine. Therefore, an important contribution of the team is the development of clinical guidelines and protocols.

This activity allows us to integrate some of our research results into the clinical practice of maternal-fetal and neonatology medicine units, optimizing patient care and promoting the application of certain preventive measures and treatments in healthcare.

26

CLINICAL GUIDES developed for health services since 2015

20

ONGOING RESEARCH projects and grants

1.8

MILLION EUROS invested in research projects in maternal-fetal medicine

basada en la integración de metabólica y microbioma.

Teresa Gobo

Instituto de Salud Carlos III (ISCIII)

► 01/01/2020 - 31/12/2022

FetalBrainCare: Tratamiento para la mejora del neurodesarrollo en el crecimiento intrauterino restringido.

Elisenda Eixarch

Instituto de Salud Carlos III (ISCIII)

► 01/01/2020 - 31/12/2022

Preventing prenatal brain damage with new tools for improved risk identification and therapy.

Eduard Gratacós

Fundación CEREBRA

► 01/01/2020 - 28/02/2024

Impacto de la dieta mediterránea durante la gestación en la microbiota del neonato

Francesca Crovetto

Fundació Agrupació

► 01/01/2020-30/04/2021

ATHLETE: Advancing Tools for Human Early Lifecourse Exposome research and Translation

Lola Gómez-Roig

European Commission

► 01/01/2020-28/02/2024

AWARDED IN 2020

Placenta Artificial

Eduard Gratacós

Fundació "la Caixa"

► 03/12/2020 - 02/07/2023

Impacto del crecimiento intrauterino restringido sobre el desarrollo pulmonar

Fàtima Crispi

Instituto de Salud Carlos III (ISCIII)

► 01/01/2021 - 31/12/2023

Impacto de un programa de intervención prenatal estructurado, de disminución de consumo de alcohol en los resultados perinatales y de neurodesarrollo

Lola Gómez-Roig

Instituto de Salud Carlos III (ISCIII)

► 01/01/2021 - 31/12/2023

Desarrollo del modelo multiparamétrico de predicción de diabetes gestacional en el primer trimestre del embarazo

Francesc Figueras

Instituto de Salud Carlos III (ISCIII)

► 01/01/2021 - 31/12/2023

FET-SEAL: Sistema integrado de sellado de membranas fetales para cirugía fetal fetoscópica

Elisenda Eixarch

Instituto de Salud Carlos III (ISCIII)

► 01/01/2021 - 31/12/2023

Obra Social 'la Caixa' Project

Under the title 'Preventing the neurological and cardiovascular consequences of fetal diseases', this research program aims to improve neurodevelopment and cardiovascular health from the earliest stages of life.

WHAT IS THE OBJECTIVE?

The main objective of this project –realized thanks to the financial support of Obra Social 'la Caixa'– is to develop tools that allow us to diagnose and prevent brain and cardiovascular development diseases from the prenatal stage.

HOW WE DO THIS?

For this purpose, we have designed a broad research program that includes randomized clinical trials



to test possible treatments, observational intervention studies in pregnant women with high-risk pregnancies and experimental studies with animal and computer models that allow new therapies to be developed. In addition, we also have a program of scientific education and one of diffusion to society.

fetalmedbarcelona.org/lacaixa

“
We have launched the only pregnancy app developed by fetal medicine experts
”

FIELDS OF ACTION

FETAL NEURODEVELOPMENT

Our goal is to develop biomarkers that allow us to detect those fetuses with brain developmental problems using non-invasive imaging techniques such as ultrasound or magnetic resonance imaging. In addition, we have identified potential beneficial treatments for the fetal brain that we are testing in various clinical trials based on improving the nutrition and lifestyle of the pregnant woman.

TRAINING

Offering a multidisciplinary training program in maternal-fetal medicine based on innovation and excellence, and linked to the Erasmus Mundus European Doctorate program in fetal medicine supported by the European Commission and coordinated by our group.

CARDIOVASCULAR HEALTH

We intend to carry out a large epidemiological study to identify prenatal problems that condition a higher cardiovascular risk in adult life, and thus be able to apply preventive treatments that can improve the heart development of these fetuses and future children and adults.

ACTIONS FOR SOCIETY

We have developed a dissemination and social participation program that includes informative events for the society, communication and an intense media presence. We have created iNatal, the only pregnancy application with personalized plans to improve the nutrition and emotional well-being of pregnant women.

Cerebra Project

In most children with neurodevelopmental problems, their brain injury occurs in prenatal life. Diagnosing and acting at that time prevents and reduces its long-term impact.

WHAT IS THE OBJECTIVE?

The possibility of diagnosing abnormal brain development in fetuses and newborns and implementing interventions to prevent or reduce their impact would represent a great advance in global public health. The main objective of this research program, and the main expected impact, is to reduce the prevalence and severity



of neurodevelopmental problems of fetal origin.

HOW WE DO THIS?

The research is carried out using IUGR as a disease model, although the findings will be applicable to other conditions.

fetalmedbarcelona.org/cerebra

“

With Cerebra we work to reduce the prevalence and severity of neurodevelopmental problems of fetal origin

”

FIELDS OF ACTION

DETECTION OF FETUSES AT RISK

We devote all our efforts to develop a new set of diagnostic criteria to substantially increase the detection of fetuses that suffer growth restriction in the uterus.

NEW BIOMARKERS

Developing new biomarkers of abnormal neurodevelopment using state-of-the-art technologies, such as the evaluation of the cortical development by ultrasound imaging, the evaluation of the microstructure by means of spectroscopy and diffusion MRI, and the analysis of brain connectomics by means of magnetic resonance.

NEW THERAPIES

Developing new pre- and postnatal therapies and evaluating their effects on preventing or reducing the rate of adverse outcomes of the brain injury.

CELLEX Project

We use **bioengineering, miniaturization, photonic sciences and robotics** to develop **high precision technologies** that permit **new interventions in fetal medicine and surgery.**

WHAT IS THE OBJECTIVE?

In the last twenty years, the application of fetal surgery has created the opportunity to treat fetal anomalies that would be lethal without treatment. The objective of this project is to improve the available tools and develop a new set of solutions that will allow new interventions in fetal medicine and surgery.

HOW WE DO THIS?

We have gathered scientists from the best research centers in bioengineering, robotics, miniaturization, imaging, chemistry

Fundació Privada CELLEX



and photonic sciences to reduce the invasiveness of the procedures, to help the surgeon in the guidance, to increase the efficiency and accuracy of fetal surgeries and to be able to control the evolution of the fetus at all times.

THE VISION OF PERE MIR

A pioneering project funded thanks to Pere Mir (Cellex Foundation), one of the most visionary people and who has helped the most to the development of Catalan and Spanish science in the last 25 years. His confidence in our group was the key to achieving advances that would have been impossible without his strong support.

fetalmedbarcelona.org/cellex


A pioneering project financed thanks to the trust and vision of the philanthropist Pere Mir

“
We want to improve the tools available to be able to carry out new interventions in fetal medicine and surgery
”

FIELDS OF ACTION

MEDICAL IMAGING

Developing a planning and guidance system for high-precision fetal surgeries. A surgical GPS that helps the surgeon to guide in the operating room by pointing out the entry point, the exact location of the umbilical cord and the blood vessels of the placenta in order to complete the surgery successfully.

ROBOTICS AND ELECTRONIC BIOSENSORS

Developing a system of fetal biosensors that can monitor the biological parameters of the fetus and transmit them to the outside, as well as a robotic assistance system to improve the surgeon's accuracy during fetal surgeries.

OPTICAL BIOSENSORS

Through photonics we will have a faster and less invasive diagnosis of fetal diseases -thanks to a microchip we will be able to, for example, detect infections in the amniotic fluid- and better monitor the fetus thanks to optical probes that interact with the fetus to control its blood supply and the level of oxygenation.

BIOMATERIALS

Creating an integrated and automatic system that allows the sealing and fixation of membranes in fetal surgeries through the use of new biomaterials that will minimize the risks of fetal surgery and open up new opportunities.

BCNatal CaixaResearch Artificial Placenta Project

The artificial placenta will significantly decrease complications from extreme prematurity (and other fetal conditions), increasing survival and reducing morbidity.



WHAT IS THE OBJECTIVE?

The objective of this ambitious project, financed by the “la Caixa” Foundation, is the development of an artificial placenta for extremely premature babies, which will allow the fetus to be kept outside the mother’s womb in an environment as similar as possible to it and thus minimize the risk of sequelae. “The artificial placenta is a unique project in Europe, a medical and technological challenge to find a transformative solution that offers an opportunity to the 25,000 babies born with six months or less of gestation per year in Europe”, explained Eduard Gratacós in the presentation of the project. And he added: “When they are born so prematurely, their body is not prepared to breathe and eat

like full-term babies. With the artificial placenta, we are going in favor of their nature, providing them with a medium that is natural for them”.

HOW WE DO THIS?

Through collaborations with other technological centers of excellence, we want to bring together the knowledge and resources necessary for the development, safety and quality validation, and transfer to clinical practice of an artificial placenta.

bcnatalresearch.org/es/proyectos-id/placenta-artificial/

“

We will gather the knowledge and resources necessary for the development of an artificial placenta

”

1
2
3

FIELDS OF ACTION

DEVELOPMENT OF THE ARTIFICIAL PLACENTA SYSTEM

Development, integration and monitoring of the different components of the artificial placenta with the aim to provide the fetus with the environmental conditions, nutrients and oxygen necessary for proper fetal development.

FETAL DEVELOPMENT AND PROGRAMMING

To study the safety of the artificial placental system during fetal development and its short- and long-term structural and functional consequences on the brain, cardiovascular system, respiratory system, and hormonal, digestive, and metabolic systems.

PRE-CLINICAL AND CLINICAL STUDIES

During the pre-clinical stage, various activities will be carried out to enhance the interaction of patients and society in the process of creating the artificial placenta and its implications. During the clinical stage, the artificial placenta will be transferred to a clinical setting where protocols and procedures will be developed to carry out a pilot study.



Scientific results

National and international congresses and courses
Participation in congresses
Academic output

National and international congresses and courses

FACE-TO-FACE

In-Utero MRI 2020 The Royal College of Radiologist **7-10 January Oxford (UK)**

Fetal Neonatal Heart - Implication for adult life European Congenital Cytomegalovirus Initiative (ECCI) **23-25 April Paris (France)**



ONLINE

Webinar COVID-19 y Embarazo. Inatal. **27 April**

2020 OHBM ANNUAL MEETING The Organization for Human Brain Mapping (OHBM) **20 June-3 July**

ESHRE Annual Meeting European Society of Human Reproduction and Embryology **5-8 July**

ISUOG 2020 **16-18 October**



ORAL COMMUNICATIONS

RESEARCHER	TITLE
Virtual World Congress on Ultrasound in Obstetrics and Gynecology	
Elena Monterde	Significance of anterior horn dilatation at diagnosis in mild ventricular abnormalities
	Structural changes in corpus callosum are associated with abnormal neurodevelopment in fetuses with isolated non-severe ventriculomegaly
ESHRE Annual Meeting 2020	
María Laura Boutet	Cardiac remodeling in fetuses conceived by assisted reproductive technologies following fresh versus frozen embryo transfer
ISUOG 2020	
Talita Micheletti	Intra-amniotic sealing system for fetal membrane defects after fetoscopic surgery
Lina Youssef	Metabolomic profiling of pathophysiological pathways in early-onset severe preeclampsia
30th World Congress on Ultrasound in Obstetrics and Gynecology	
Eduard Gratacós	The current state of the art and potential future for fetal surgery
Francesca Crovetto	Placental perfusion assessed by MRI IVIM model and its correlation with placental volume in near term pregnancies complicated by fetal growth restriction
	Placental assessment with T2* sequence in fetuses with fetal growth restriction
In Utero MRI 2020	
Francesca Crovetto	COVID19 in pregnancy: seroprevalence, clinical spectrum, impact on pregnancy outcomes, and influence of microbiota in clinical severity. A population-based study in Spain
	Improving Mothers for a better Prenatal Care Trial Barcelona (IMPACT BCN): randomised controlled trial study protocol
World Congress in Perinatal Medicine	
Fàtima Crispi	Machine learning in Fetal Medicine
26th Annual Meeting of the Organization for Human Brain Mapping (OHBM)	
Elisenda Bonet	Corpus Callosum length and area measurements, an open source software for ultrasound and MR images
Webinar Inatal COVID-19 y Embarazo	
Francesca Crovetto	Charla "Dieta, ejercicio y Mindfulness durante el confinamiento"
Eduard Gratacós	Bienvenida. Qué es el Sars-COV2 y efectos sobre el embarazo. Discusión
Jezid Miranda	Cómo protegernos de la infección y medidas de aislamiento. Discusión
Francisc Figueras	Organización del trabajo en los hospitales. Discusión

59

COMMUNICATIONS
in national and
international
congresses



6

COURSES AND CONGRESSES
national and international

21

POSTERS
at national and
international
conferences

INVITED TALKS

RESEARCHER	TITLE
In-Utero MRI 2020	
Ayako Nakaki	Placental perfusion assessed by MRI IVIM model and its correlation with placental volume in near term pregnancies complicated by fetal growth restriction
Killian Vellvé	Placental assessment with T2* sequence in fetuses with FGR
ISUOG 2020	
Miriam Illa	In vivo and In vitro neurodevelopmental effects of Docosahexaenoic acid in an IUGR animal model
Elisenda Eixarch	Use of exome sequencing in fetuses with complex central nervous system anomalies
Johanna Parra	Face validity evaluation of a fetoscopic laser surgery simulator
Talita Micheletti	Intraamniotic sealing system for fetal membrane defects after fetoscopic surgery
Patricia Garcia	Metabolomic profiling of pathophysiological pathways in early-onset severe preeclampsia
Maria Laura Boutet	Cardiac remodeling in fetuses conceived by assisted reproductive technologies following fresh versus frozen embryo transfer

POSTERS AND ORAL POSTERS

RESEARCHER	TITLE
ISUOG 2020	
Paz Ahumada	Corpus callosum as an imaging biomarker of neurodevelopmental effects of prenatal ethanol exposure Effects of metal exposure during pregnancy on corpus callosum development
David Coronado	Automatic classification of fetal axial brain planes from ultrasound images via deep learning
Elisenda Eixarch	MR-based patient-specific planning platform for twin-to-twin transfusion syndrome surgery
Ameth Hawkins	Cortical maturation assessed by magnetic resonance imaging in unaffected/mildly affected fetuses with cytomegalovirus infection Fetal sonographic follow-up after maternal COVID-19 infection. Is there a matter of concern
Miriam Illa	Cavum septi pellucidi: prenatal diagnosis and outcomes Anomalies of cavum septi pellucidi in routine prenatal ultrasound screening
Diana Lip	Reliability of corpus callosum-fastigium and tectal length measurements in the third trimester
Mónica Pérez Cruz	Sylvian fissure evaluation in axial plane as marker of Malformation of Cortical Development
Elena Monterde	Significance of anterior horn dilatation at diagnosis in mild ventricular abnormalities
Lucas Trigo	Central Nervous System anomalies in fetuses with open spina bifida fetoscopic repair in late gestational age Neurological outcomes of children with open spina bifida fetoscopic repair at late gestational age
Lina Youssef	Maternal proteomic profiling reveals alterations in lipid metabolism in late-onset fetal growth restriction Angiogenic factors profile in preeclampsia and/or fetal growth restriction and its correlation with alpha-1-microglobulin
Claudia Rueda	Fetal growth in a cohort of pregnancies complicated by preterm labor or preterm prelabor rupture of membranes
Ana Moreno	Risk of neonatal respiratory morbidity (NRM) by QuantusFLM® in twin vs singleton pregnancies Agreement on the risk of neonatal respiratory morbidity (NRM) by QuantusFLM® in twin pregnancies
Mar Bennasar	Perinatal outcome after selective termination in discordant dichorionic twins



Academic output

COMPLETED DOCTORAL THESES

RESEARCHER	TITLE	DIRECTORS	UNIVERSITY	DATA
Lina Youssef	Omics approach to characterize different phenotypes of preeclampsia and fetal growth restriction	Eduard Gratacos Fatima Crispi	Universitat de Barcelona	30/01/2020
Laura Guirado	Cardiopatías con obstrucción del tracto de salida del ventrículo derecho: estudio del remodelado cardiovascular fetal mediante ecocardiografía	Olga Gómez Fatima Crispi	Universitat de Barcelona	09/10/2020
Andre Gie	The influence of mechanical stretch on the structure and function of the developing lung	Monica Zamora	Leuven University Universitat de Barcelona	03/09/2020
Míreia Fernández Arias	Estudio genético de trombofilias en pacientes con antecedentes obstétricos desfavorables	Lola Gómez Roig Eduarne Mazarico	Universitat de Barcelona	20/11/2020
Laura Cortés	Valoración de la exposición prenatal a antidepresivos y ansiolíticos mediante su determinación en matrices biológicas alternativas	Lola Gómez Roig Oscar Garcia Algar	Universitat de Barcelona	20/11/2020

AWARDS

RESEARCHER	AWARD	TITLE	AWARDED BY
Patricia Garcia	Best Oral Abstract	Machine-learning based phenogrouping of echocardiographic data can predict the risk of death or heart transplant in pediatric dilated cardiomyopathy	AEPC 2020



RESEARCH GRANTS

RESEARCHER	TITLE	AWARDED BY	DATE
Eduard Gratacós	Preventing Prenatal Brain damage with tools for improving risk identification and therapy	CEREBRA Foundation	01/01/2020-28/02/2024
	Programa Interdisciplinar para el desarrollo de un prototipo experimental de placenta artificial y evaluación de aplicación clínica	La Caixa Foundation	03/12/2020-02/07/2023



RESEARCH FELLOWSHIPS

RESEARCHER	UNIVERSITY / COUNTRY
Patricia Garcia	Zayed Centre for Research into Rare Disease in Children / United Kingdom
Ana Moreno	Lund University, Sweden
Maria Laura Boutet	Lund University, Sweden
Paz Ahumada	Lund University, Sweden



Education

Training in Maternal-Fetal Medicine
FetalMed PhD Summer School
Academic output

Training in Maternal-Fetal Medicine

In 2020 the work of FetalMed PhD, the first internationally recognized doctorate in Fetal and Perinatal Medicine coordinated by our team, has been strengthened. Today, the program already has 40 researchers, 6 of whom have defended their doctoral thesis this year.

WHAT IS FETALMED PHD?

It is the first interdisciplinary doctoral program in Fetal and Perinatal Medicine carried out in collaboration with three of the best European universities and research centers in the field: the BCNatal Fetal Medicine Research Center (Universitat de Barcelona, Spain) and the universities of Leuven (Belgium) and Lund (Sweden).



DOCTORATES

have been awarded thanks to the FetalMed PhD Erasmus Mundus Joint



MAIN GOALS

1

To train professionals capable of tackling and providing effective and comprehensive solutions to maternal-fetal health problems. And, at the same time, to promote the development of new products and processes for different sections of society.

2

To strengthen the research center and the capacity of institutions and people in different countries around the world. This is achieved by promoting international networks and collaborative projects between the entities coordinating the program and their countries, and the universities and training centers from which the participating researchers come.

FetalMed PhD Summer School

Erasmus Mundus facilitates the training of professionals capable of solving maternal-fetal health problems.

The Erasmus Mundus FetalMed PhD Summer School is an initiative organized by the group that has been ongoing since the start of the program. Not only is a great opportunity for students to do networking activities but it also allows them to discover new techniques or knowledge that can help with their research activities.

The main aim of the Summer School is to connect students with the latest advances in their fields and motivate them to question and research about new upcoming topics. Since 2015 there has been only two occasions in which the Summer School could not be held, in 2017, due to organizational reasons, and in 2020, due to the Covid19 pandemic.

2019

The fourth Erasmus Mundus FetalMed-PhD Summer School was held in Barcelona, Spain. We organized an Open Day with international expert speakers in the areas of interest of the researchers-in-training. This day was attended by around 100 researchers from different organizations, which led to an exchange of experiences between all the attendees and speakers that gave rise to scientific discussions that will contribute relevant added value to the projects and future of training researchers of the program.

2018

The third edition of the FetalMed PhD Summer School was held in Athens, coinciding with the 17th World Congress in Fetal Medicine, one of the most important fetal medicine congresses in the world. It is a unique opportunity for our predoctoral researchers, which contributes to improving their ongoing research projects and their research skills. The event gathers the leading experts and interesting debates on how to advance within the field of maternal-fetal medicine.

2016

This year, the second edition of Erasmus Mundus FetalMed PhD Summer School took place under one of the most important conferences of fetal medicine in the world, the 15th World Congress in Fetal Medicine in Mallorca, Spain. This event counted with interesting discussions on how to advance within the field of maternal-fetal medicine, more than 2,000 attendees and participation of fetal i+D.

2015

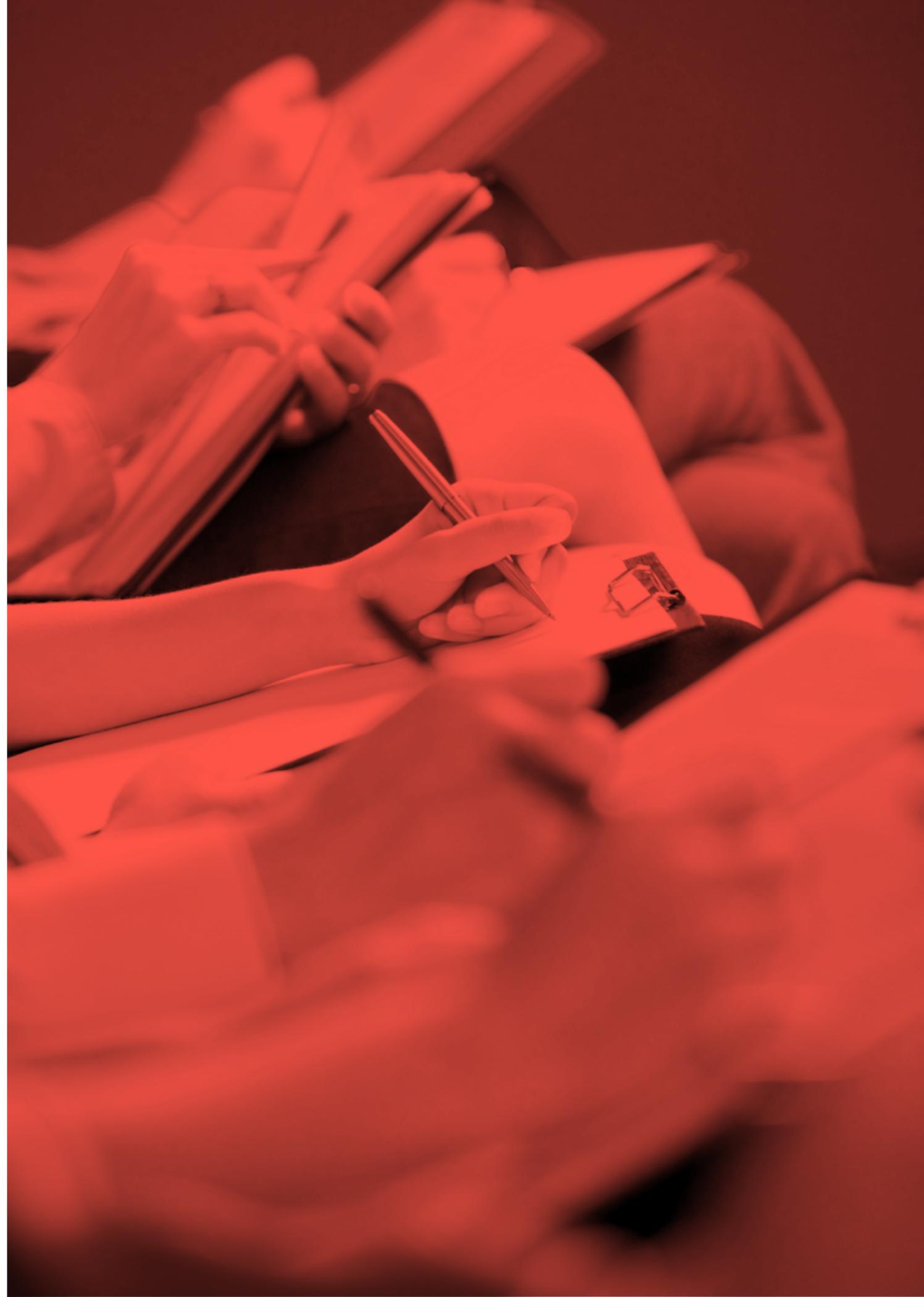
The first edition of the Summer School took place under two of the most important conferences of fetal medicine in the world, the 14th World Congress in Fetal Medicine and the 34th Annual Meeting of the International Fetal Medicine and Surgery Society. Both counted with interesting discussions on how to advance within the field of maternal-fetal medicine, more than 2,000 attendees and participation of fetal i+D.



Academic output

ONGOING DOCTORAL THESES

RESEARCHER	TITLE	DIRECTORS	UNIVERSITY
Laura Almeida	Modelo de síndrome alcohólico fetal en ratón según dos patrones de consumo humano y el papel de la epigallocatequina galato en su prevención. Estudio de biodisponibilidad de la epigallocatequina galato en humanos	Lola Gómez Roig Dr Andreu	Universitat de Barcelona
Anna Peguero	Third-trimester biochemical markers for the prediction and prognosis of preeclampsia	Francesc Figueras	Universitat de Barcelona
Yolanda Giménez	Depresión posparto, vínculo materno-filial y lactancia materna en gestantes con preeclampsia	Francesc Figueras	Universitat de Barcelona
Marta Rial	Developing an effective model for the prediction studio of gestational diabetes in the first trimester of pregnancy	Francesc Figueras	Universitat de Barcelona
Clara Murillo	Impacto de la amenaza de parto prematuro y de la rotura prematura de membranas sobre el neurodesarrollo y el sistema cardiovascular a nivel fetal y neonatal e influencia del origen inflamatorio	Montse Palacio Teresa Cobo	Universitat de Barcelona





Media

Under the spotlight

The team on the Internet

Under the spotlight

In 2020, the group has been in the headlines of many national and international media. This is how we position ourselves as a national and international reference in the fields of fetal medicine research, fetal therapy, and surgery.

Outreach in fetal medicine is essential to give value to a field of health that is still unknown to many sectors of society. Twenty years ago the fetus did not exist as a patient. Today, more and more babies come with a medical record under their arm. The dissemination of

these advances in maternal-fetal medicine allows us to continue advancing. What habits of the pregnant woman affect fetal growth? Can one operate on an unborn baby with maximum precision? In the media we respond to all these concerns.



“
The presentation of the artificial placenta project, unique in Europe, receives great coverage by media around the world
”



1

We participate in studies and training on the effects of COVID-19 on pregnancy and childhood

In June 2020, the first results of the Kids Corona research platform, created by Hospital Sant Joan de Déu in March 2020 and in which we collaborate, are published. Gratacós explains to the media the evidence extracted from the pregnant women analyzed, 14% of whom tested positive for COVID-19, differentiating the incidence in the first and third trimesters of pregnancy. New data appears in July, from which it follows that skin-to-skin and breastfeeding are safe even if the mother has COVID-19, since perinatal transmission of the virus is unlikely.

Media:
La Vanguardia, La Razón



2

We present a pioneer project in the world: the artificial placenta

Eduard Gratacós announces the first major European research project to create an artificial placenta. Promoted by “la Caixa”, this placenta prototype will increase the survival of extremely premature infants, minimize neurological sequelae and improve their quality of life. “Essentially we have to take the fetus from its mother’s womb and transfer it to a liquid environment. Connected through their umbilical cord to an organ they need to survive, an artificial placenta.” This news had great coverage in the media and the group appeared on television channels, radio and more than 40 print and digital media.

Media:
La Vanguardia, El Periódico, Antena 3, TV3, El economista



3

We are leaders in innovation

Thanks to the world’s first surgical navigation system that we presented in 2019, developed in collaboration with BCN Med TechUPF Barcelona, we continue to make headlines. UPF echoes the first scientific results, published in IEEE Transactions on Medical Imaging, which present the first automatic method for detecting and segmenting the intrauterine cavity through the three views (axial, sagittal and coronal) of magnetic resonance imaging using artificial intelligence and deep learning techniques.

Media: UPF



4

We report on how toxins and lifestyle influence pregnancy

Specifically, how exposure to endocrine disruptors during pregnancy, such as parabens, increases the risk of overweight and obesity during childhood. Following the results of this German study, the press interviewed Eduard Gratacós, who gave his point of view on the impact of parabens, and also of alcohol, whose consequences are much more serious and, even so, “25% of pregnant women drink”. With statements like this we promote quality information for pregnant women and their families.

Media: La Vanguardia

SOCIAL MEDIA



1,386

FOLLOWERS @BCNatalResearch



1,220

FOLLOWERS BCNatal Fetal Medicine Research



915

MEMBERS BCNatal Fetal Medicine Research



614

FOLLOWERS @fetalmedbcn

The team on the internet

“

In Ibero-America we are a benchmark in Fetal Medicine at the media level with more than 150 appearances in the press, radio, television and online media”

In addition to the scientific objectives, our team is committed to promoting and disseminating our research results. To this end, in addition to regular press releases and press conferences, we share our daily progresses with the medical community and the society online. We do this through our website, a quarterly newsletter and an active participation in social media and networks. Thus, we generate awareness of the importance of maternal-fetal medicine research to improve public health.

Our relaunched website

bcnatalresearch.org allows access to the different research areas and projects of the group, as well as to the personnel directory and the historical list of scientific articles.



Edited by:

socialMED:
communication