
Fetal Medicine Research Center

2019



FETAL
MEDICINE
RESEARCH
CENTER



Summary



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we are



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Fetal Medicine Research Center Annual Report 2019

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, moreover, we are about to close one of our most ambitious projects on new high-precision technologies in fetal medicine and surgery that brings together experts in robotics, photonics, and bioengineering. Some

of its results, such as the intrauterine guidance system, are already being applied to clinical practice.

We do not forget our teaching and social vocations. Our commitment to the scientific community is embodied in the PhD program in Fetal Medicine, FetalMed-PhD, an European reference in the field that will come to its final edition in 2019. As a bridge between fetal medicine and society, we continue to develop tools and carry out outreach actions. Our main purpose is to develop science of excellence to improve health, and, ultimately, people’s lives.

Eduard Gratacós

Director of BCNatal Fetal Medicine Research Center



01

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.

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.



750m²

allocated
to research



+500

PUBLICATIONS
since 2010



76

ARTICLES
published
in 2019

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

Nature

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, concentrating 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 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.



131

PROFESSIONALS
from 20 different
nationalities



101

Women



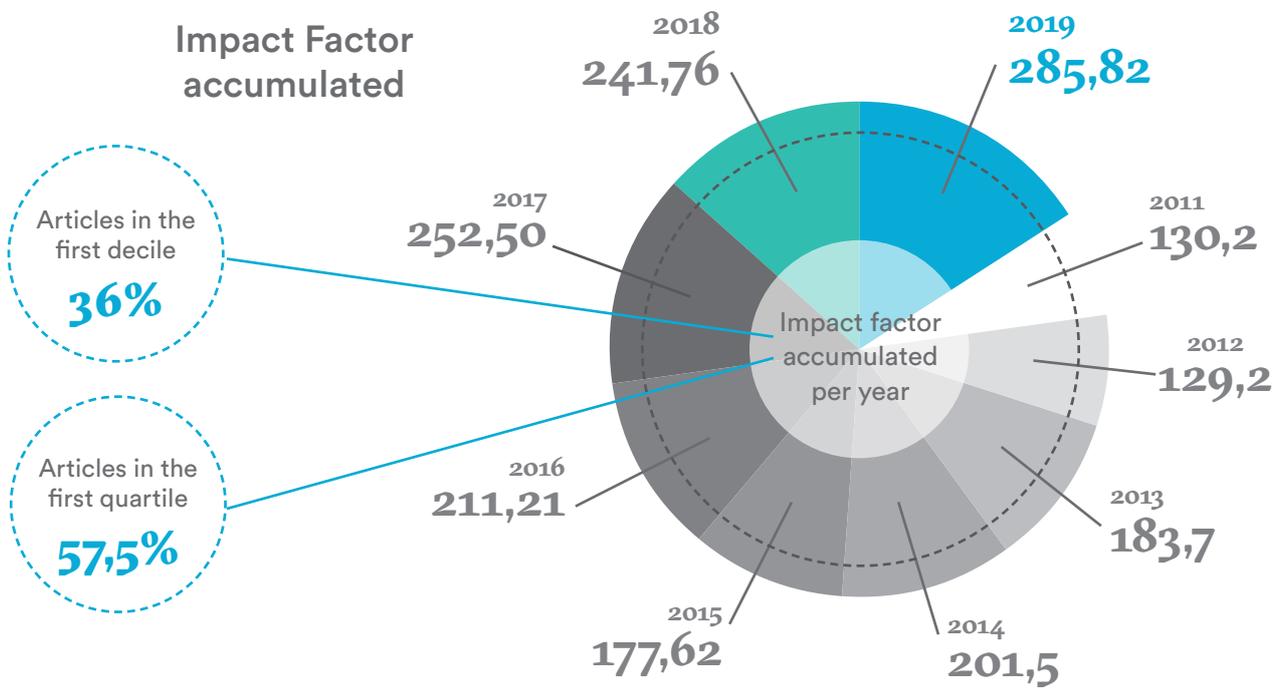
30

Men

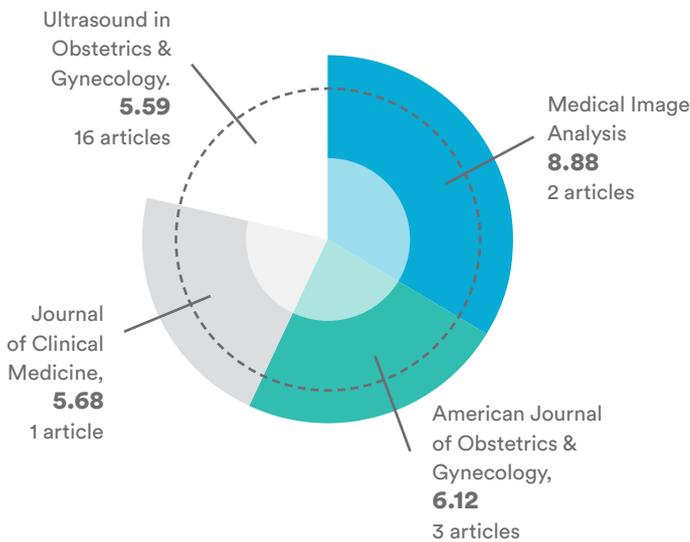
Scientific results

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

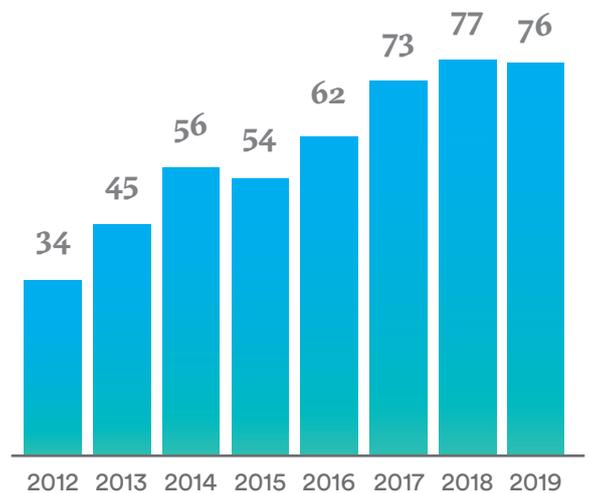
projects financed by prestigious institutions such as the CELLEX private foundation, Cerebra Foundation (UK) and the Obra Social “la Caixa”.



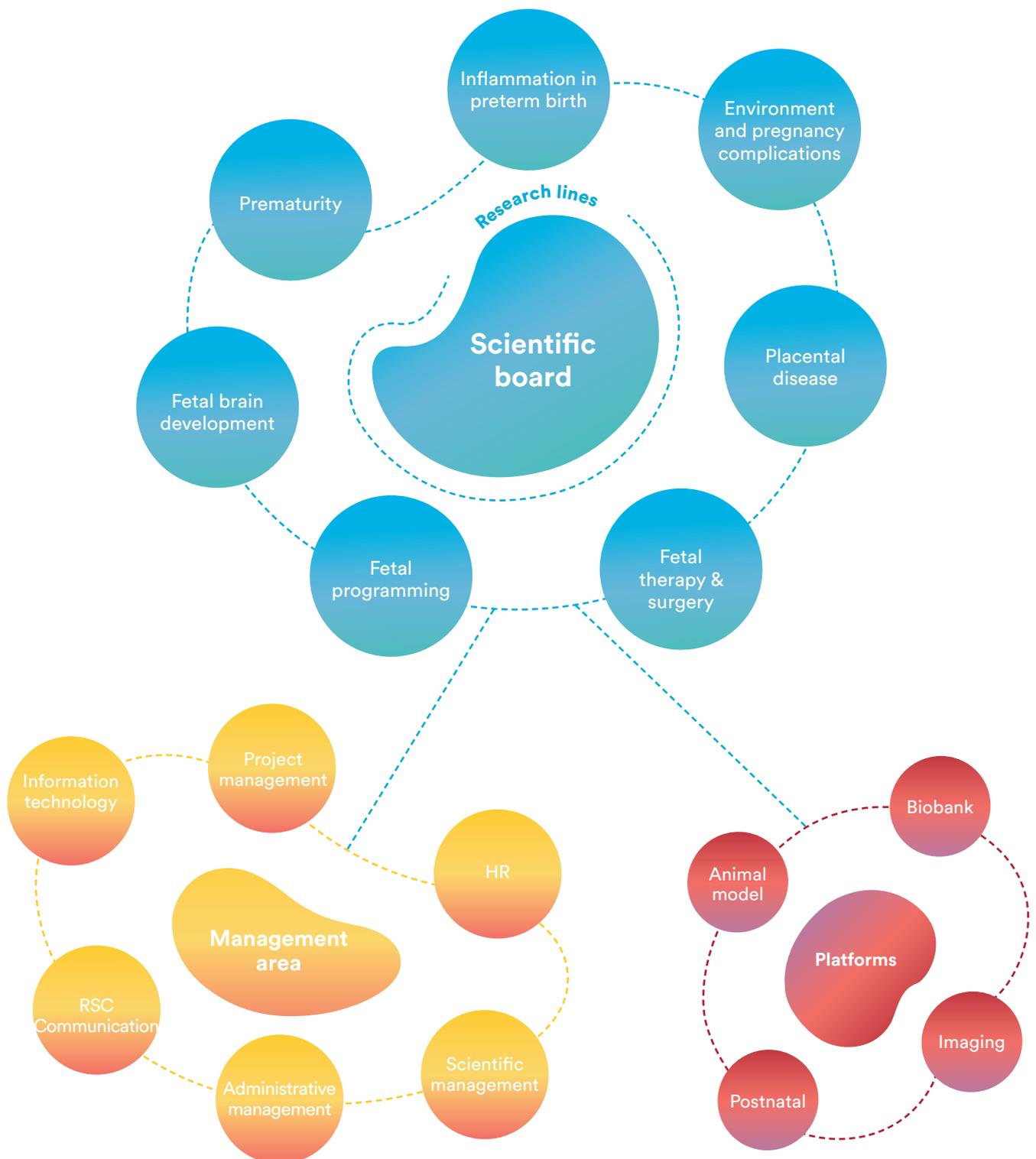
Articles with + impact factor (IF) in the first quartile in 2019



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 Fetal Medicine Research Center, from the beginning to the present.

OUR BEGINNING

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



2005

FOCUSED ON FETAL CARDIOLOGY AND NEURO-DEVELOPMENT

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



2007

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.



2009



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



2011

WE PUBLISH THE FIRST ANNUAL REPORT

For the first time, we collect all our achievements in a report of activities, which features the illustrations of Maria Corte. Since then, we have become one of the few research teams with their own annual report.



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.

2012



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.

DEVOTED TO THE SOCIETY

We organize workshops with patient associations and pregnant women to promote healthy habits in pregnancy. We publish a recipe book for pregnant women together with Michelin star chefs.

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. More than 1,200 pregnant women with a risk of having a baby with growth restriction participate in the trial.

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. A project financed by Obra Social ‘la Caixa’ and developed in collaboration with nutritionists from IDIBAPS and professionals of Mindfulness.

2013



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).

2014



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 in search of high-precision treatments to develop better technologies in intrauterine interventions.

2015



2016



IMPROVEMENTS IN THE DIAGNOSIS OF INTRAUTERINE 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.

2017



2018



FREE DOWNLOAD FOR iOS AND ANDROID

02

Research

Fetal Programming
Fetal Brain Development
Prematurity
Inflammation in Preterm Birth
Fetal Therapy and Surgery
Environment and Pregnancy Complications
Placental Disease
Platforms
Research Management



**Fetal
Programming**



**Fetal Brain
Development**



Prematurity



**Inflammation in
Preterm Birth**



**Fetal Therapy
and Surgery**



**Environment
and Pregnancy
Complications**



**Placental
Disease**

Research areas

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

The fetus as a patient

In BCNatal Fetal Medicine Research Center we treat the fetus as a patient, whom we can diagnose and manage certain diseases 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 areas that allow us to achieve a comprehensive study of the fetus and the mother



Fetal Programming

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



FÀTIMA 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.



Francesca Crovetto
Maternal-Fetal
Medicine specialist



Olga Gómez
Maternal-Fetal
Medicine specialist



Anna Goncé
Maternal-Fetal
Medicine specialist



Marta López
Maternal-Fetal
Medicine specialist



Gemma Casals
Postdoctoral
researcher



Laura García
Postdoctoral
researcher



Mónica Zamora
Postdoctoral
researcher



María Laura Boutet
Predoctoral
researcher

Publications 2019

1. Cardiac and mitochondrial function in HIV-uninfected fetuses exposed to antiretroviral treatment. García-Otero L, López M, Guitart-Mampel M, Morén C, Goncé A, Esteve C, Salazar L, Garrabou G, Crispi F, Gratacós E. *PLoS One*. 2019 Mar 4;14(3):e0213279. doi: 10.1371/journal.pone.0213279.

2. 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 Diagn Ther*. 2019 Jan 4;1-12. doi: 10.1159/000494838.

3. Postnatal persistence of fetal cardiovascular remodelling

associated with assisted reproductive technologies: a cohort study. Valenzuela B, Serafini A, Sepulveda A, Casals G, Rodríguez-López M, Garcia-Otero L, Cruz-Lemini M, Bijmens B, Sitges M, Balasch J, Gratacós E, Crispi F. *BJOG*. 2019 Jan;126(2):291-298. doi: 10.1111/1471-0528.15246.

4. Mitochondrial implications in human pregnancies with



THE LINE BRINGS TOGETHER A MULTIDISCIPLINARY TEAM OF FETAL MEDICINE SPECIALISTS, PEDIATRICIANS, EPIDEMIOLOGISTS, BIOLOGISTS AND ENGINEERS.



Andre Gie
Predoctoral researcher



Grigorios Kalapotharakos
Predoctoral researcher



Mari Kinoshita
Predoctoral researcher



Sergio Quesada
Predoctoral researcher



Álvaro Sepúlveda
Predoctoral researcher



Killain Vellvé
Predoctoral researcher



Lina Youssef
Predoctoral researcher



Annachiara Basso
Clinical researcher



Laura Guirado
Clinical researcher



Ayako Nakaki
Clinical researcher



Laura Salazar
Clinical researcher



Iris Soveral
Clinical researcher



Brenda Valenzuela
Clinical researcher



Tania Freitas
Nutritionist



Karen Castillo
Master's student



Lucía García
Master's student



Silvana Santamaria
Master's student



Marta Dacal
Technician



Marta Gracia
Technician



Laura Segalés
Technician



Marcos Alonso
Student

intrauterine growth restriction and associated cardiac remodelling. Guitart-Mampel M, Juarez-Flores DL, Youssef L, Moren C, Garcia-Otero L, Roca-Agujetas V, Catalan-Garcia M, Gonzalez-Casacuberta I, Tobias E, Milisenda JC, Grau JM, Crispi F, Gratacós E, Cardellach F, Garrabou G. *Journal of Cellular and Molecular Medicine* 2019.

5. **Distinctive patterns of placental lesions in preeclampsia versus fetal growth restriction and their association with fetoplacental Doppler.** Paules C, Youssef L, Rovira C, Crovetto F, Nadal A, Peguero A, Figueras F, Eixarch E, Crispi F, Miranda J, Gratacós E. *Ultrasound in Obstetrics & Gynecology* 2019 Nov;54(5):609-616. doi: 10.1002/uog.20350.

6. **Prenatal adverse environment is associated with epigenetic age deceleration at birth and hypomethylation at the hypoxia-responsive EP300 gene.** Palma-Gudiel H, Eixarch E, Crispi F, Morán S, Zannas AS, Fañanas L. *Clinical Epigenetics* volume 11, Article number: 73 (2019)

7. **Comprehensive Analysis of Animal Models of Cardiovascular Disease**

using Multiscale X-Ray Phase Contrast Tomography. Dejea H, Garcia-Canadilla P, Cook AC, Guasch E, Zamora M, Crispi F, Stampanoni M, Bijmens B, Bonnin A. *Scientific Reports* volume 9, Article number: 6996 (2019)

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9. **Transgenerational transmission of small for gestational age.** Sepúlveda-Martínez Á, Rodríguez-López M, Paz-Y-Miño F, Casu G, Crovetto F, Gratacós E, Crispi F. *Ultrasound in Obstetrics & Gynecology.* 2019 May;53(5):623-629. doi: 10.1002/uog.20119.

10. **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, Sepúlveda-Martínez A, Crovetto F, Gómez O, Gratacós E, Crispi F.

American Journal of Obstetrics and Gynecology. 2020 Jan;222(1):79. e1-79.e9. doi: 10.1016/j.ajog.2019.07.025. Epub 2019 Jul 20.

11. **Blood parameters in fetuses infected with cytomegalovirus according to the severity of brain damage and trimester of pregnancy at cordocentesis.** Hawkins-Villarreal A, Moreno-Espinosa AL, Eixarch E, Marcos MA, Martinez-Portilla RJ, Salazar L, Garcia-Otero L, Lopez M, Borrell A, Figueras F, Goncé A. *Journal of Clinical Virology.* Volume 119, October 2019, Pages 37-43

12. **Determination of the steroid profile in alternative matrices by liquid chromatography tandem mass spectrometry.** Gómez-Gómez A, Miranda J, Feixas G, Arranz Betegon A, Crispi F, Gratacós E, Pozo OJ. *The Journal of Steroid Biochemistry and Molecular Biology* Volume 197, March 2020, 105520

13. **Complement activation and thrombotic microangiopathies.** Palomo M, Blasco M, Molina P, Lozano M, Praga M, Torramade-Moix S, Martinez-Sanchez J, Cid J, Escolar G, Carreras E, Paules C, Crispi F, Quintana LF, Poch E, Rodas

Strategic goals

	Translational research	Experimental research	Computational models and artificial intelligence
Study and develop	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

L, Goma E, Morelle J, Espinosa M, Morales E, Avila A, Cabello V, Ariceta G, Chocron S, Manrique J, Barros X, Martin N, Huerta A, Fraga-Rodriguez GM, Cao M, Martin M, Romera AM, Moreso F, Manonelles A, Gratacós E, Pereira A, Campistol JM, Diaz-Ricart M. **Clin J Am Soc Nephrol.** 2019 Dec 6;14(12):1719-1732. doi: 10.2215/CJN.05830519. Epub 2019 Nov 6.

14. **Exercise-induced cardio-pulmonary remodelling in endurance athletes: Not only the heart adapts.** Domenech-Ximenes B, Garza MS, Prat-González S, Sepúlveda-Martínez Á, Crispí F, Perea RJ, Garcia-Alvarez A, Sitges M. **European Journal of Preventive Cardiology.** 2020 Apr;27(6):651-659. doi: 10.1177/2047487319868545. Epub 2019 Aug 18.

15. **Natural history of atherosclerosis and abdominal aortic intima-media thickness: rationale, evidence, and best practice for detection of atherosclerosis in the young.** Skilton MR, Celermajer DS, Cosmi E, Crispí F, Gidding SS, Raitakari OT, Urbina EM. **Journal of Clinical Medicine.** 2019 Aug 12;8(8). pii: E1201. doi: 10.3390/jcm8081201.

16. **Nomograms of fetal right ventricular fractional area change by 2d echocardiography.** Guirado L, Crispí F, Soveral I, Valenzuela-Alcaraz B, Rodríguez-López M, García-Otero L, Torres X, Sepúlveda-Martínez Á, Escobar-Diaz MC, Martínez JM, Friedberg MK, Gratacós E, Gómez O. **Fetal Diagnosis and Therapy.** 2019 Dec 10:1-12. doi: 10.1159/000503228.

17. **Comparison of 2D versus M-mode echocardiography for assessing**

fetal myocardial wall thickness. Sepúlveda-Martínez A, García-Otero L, Soveral I, Guirado L, Valenzuela-Alcaraz B, Torres X, Rodríguez-Lopez M, Gratacós E, Gómez O, Crispí F. **The Journal of Maternal-Fetal & Neonatal Medicine.** 2019 Jul;32(14):2319-2327. doi: 10.1080/14767058.2018.1432041. Epub 2018 Feb 11.

18. **Premature placental aging in term small-for-gestational-age and fetal-growth-restricted fetuses.** Paules C, Dantas AP, Miranda J, Crovetto F, Eixarch E, Rodríguez-Sureda V, Dominguez C, Casu G, Rovira C, Nadal A, Crispí F, Gratacós E. **Ultrasound in Obstetrics & Gynecology.** 2019 May;53(5):615-622. doi: 10.1002/uog.20103. Epub 2019 Apr 12.

Collaborations

National

- Universitat Pompeu Fabra, Barcelona
- Universidad Rovira i Virgili, Tarragona
- Instituto de Ciencias Fotónicas (ICFO)
- Instituto Aragonés de Ciencias de la Salud (I+CS), Zaragoza
- Hospital Vall d'Hebron de Barcelona
- Hospital del Mar-IMIM, Barcelona
- Parque Tecnológico de Andalucía, Málaga

International

- Oxford University, United Kingdom
- The Labatt Family Heart Center, Division of Cardiology, Hospital for Sick Children and University of Toronto, Canadá
- Division of Pediatric Cardiology, Bronx Lebanon Hospital Center, NY, USA
- Frauenklinik und Poliklinik, Technische Universität München, Munich, Germany
- 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 2019

- We have completed a large cohort study of small fetuses, which has allowed us to identify suboptimal maternal diet and high maternal stress levels as essential factors for adequate fetal growth.
- We have continued 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

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



**THE LINE
GATHERS
FETAL
MEDICINE
SPECIALISTS
AND
ENGINEERS**

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.



Miriam illa
Maternal-Fetal
Medicine specialist



Nadine Hahner
Predoctoral
researcher



Elena Monterde
Predoctoral
researcher



Lucas Trigo
Predoctoral
researcher



Miriam Perez
Maternal-Fetal
Medicine
specialist



Narcis Masoller
Maternal-Fetal
Medicine
specialist

Publications 2019

- 1. Fetal cortical surface atlas parcellation based on growth patterns.** Xia J, Wang F, Benkarim OM, Sanroma G, Piella G, González Ballester MA, Hahner N, Eixarch E, Zhang C, Shen D, Li G. **Human Brain Mapping.** 2019 Sep;40(13):3881-3899. doi: 10.1002/hbm.24637. Epub 2019 May 20.
- 2. Multicenter prospective clinical study to evaluate children short-term neurodevelopmental outcome in congenital heart disease (children NEURO-HEART): study protocol.** Ribera I, Ruiz A, Sánchez O, Eixarch E, Antolín E, Gómez-Montes E, Pérez-Cruz M, Cruz-Lemini M, Sanz-Cortés M, Arévalo S, Ferrer Q, Vázquez E, Vega L, Dolader P, Montoliu A, Boix H, Simões RV, Masoller N, Sánchez-de-Toledo J, Comas M, Bartha JM, Galindo A, Martínez JM, Gómez-Roig L, Crispi F, Gómez O, Carreras E, Cabero L, Gratacós E, Llorba E. **BMC Pediatrics.** 2019 Sep 10;19(1):326. doi: 10.1186/s12887-019-1689-y.
- 3. Blood parameters in fetuses infected with cytomegalovirus according to the severity of brain damage and trimester of pregnancy at cordocentesis.** Hawkins-Villarreal A, Moreno-Espinosa AL, Eixarch E, Marcos MA, Martínez-Portilla RJ, Salazar L, García-Otero L, López M, Borrell A, Figueras F, Goncé A. **Journal of Clinical Virology.** 2019 Oct;119:37-43. doi: 10.1016/j.jcv.2019.08.008. Epub 2019 Aug 20.
- 4. Global and regional changes in cortical development assessed by MRI in fetuses with isolated nonsevere ventriculomegaly correlate with neonatal neurobehavior.** Hahner N, Benkarim OM, Aertsen M, Perez-Cruz M, Piella

G, Sanroma G, Bargallo N, Deprest J, Gonzalez Ballester MA, Gratacos E, Eixarch E. **American Journal of Neuroradiology.** 2019 Sep;40(9):1567-1574. doi: 10.3174/ajnr.A6165.

Collaborations

National

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

International

- University Hospitals Leuven, Belgium
- University of São Paulo, Brazil
- Center for the Developing Brain, King's College, United Kingdom
- Department of Radiology and BRIC, University of North Carolina, USA

In 2019

- We have shown that in cases with ventricular dilation (ventriculomegaly), the degree of prenatal cortical maturation assessed by prenatal magnetic resonance is related to neonatal neurodevelopment. This is the first time that this relationship has been demonstrated and the results have been published in the American Journal of Neuroradiology.
- In collaboration with international engineering groups, we have described a new method to analyze fetal brain images prenatally.

Strategic goals

	Clinical/Basic	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

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 PREMATUREITY?

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 PREMATUREITY?

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.

Team members



MONTSE PALACIO

Coordinator of the research line.
Specialist in Prematurity at BCNatal.
Lecturer in specialized courses of Fetal I+D Education Barcelona.



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Sílvia Ferrero
Postdoctoral
researcher



Xavier Burgos-Artizzu
Postdoctoral
researcher



Laia Grau
Predoctoral
researcher



Núria Lorente
Predoctoral
researcher



Ana Moreno
Predoctoral
researcher



Clara Murillo
Predoctoral
researcher



Álvaro Pérez-Moreno
Predoctoral
researcher

Publications 2019

1. A systematic review and meta-analysis of randomized controlled trials comparing 17-alpha-hydroxyprogesterone caproate versus placebo for the prevention of recurrent preterm birth. Fernandez-Macias R, Martinez-Portilla RJ, Cerrillos L, Figueras F, Palacio M. **International Journal of Gynecology & Obstetrics.** 2019 Aug 11. doi: 10.1002/ijgo.12940.
2. Evaluation of an improved tool for non-invasive prediction of neonatal respiratory morbidity based on fully automated fetal lung ultrasound analysis. Burgos-Artizzu XP, Perez-Moreno A, Coronado-Gutierrez D, Gratacos E, Palacio M. **Scientific Report.** 2019 Feb 13;9(1):1950.
3. Cervical consistency index and risk of cesarean delivery after induction of labor at term. Migliorelli F, Rueda C, Angeles MA, Baños N, Posadas DE, Gratacós E, Palacio M. **Ultrasound in Obstetrics & Gynecology.** 2019 Jun;53(6):798-803
4. Clinical and sonographic model to predict cesarean delivery after induction of labor at term. Migliorelli F, Baños N, Angeles MA, Rueda C, Salazar L, Gratacós E, Palacio M. **Fetal Diagnosis and Therapy.** 2019;46(2):88-96.

5. Clinical feasibility of quantitative ultrasound texture analysis: a robustness study using fetal lung ultrasound images. Perez-Moreno A, Dominguez M, Migliorelli F, Gratacos E, Palacio M, Bonet-Carne E. **J Ultrasound Med.** 2019 Jun;38(6):1459-1476.
6. Should phenotype of previous preterm birth influence management of women with short cervix in subsequent pregnancy? Comparison of vaginal progesterone and Arabin pessary. Care A, Muller-Myhsok B, Olearo E, Todros T, Caradeux J, Goya M, Palacio M, Carreras E, Alfírevic Z. **Ultrasound in Obstetrics & Gynecology.** 2019 Apr;53(4):529-534.
7. Follow-up of asymptomatic high-risk patients with normal cervical length to predict recurrence of preterm birth. Caradeux J, Murillo C, Julià C, Escura S, Ferrero S, Cobo T, Gratacós E, Palacio M. **Fetal Diagnosis and Therapy.** 2019;45(1):50-56.
8. Influence of perinatal inflammation on the neurodevelopmental outcome of premature infants. Rodríguez-Trujillo A, Ríos J, Ángeles MA, Posadas DE, Murillo C, Rueda C, Botet F, Bosch J, Vergara A, Gratacós

E, Palacio M, Cobo T. **The Journal of Maternal-Fetal & Neonatal Medicine.** 2019 Apr;32(7):1069-1077.



In 2019

- We continued to develop prediction tools based on quantitative analysis of lung and cervical texture for screening the risk of preterm birth.
- We investigated markers to predict cesarean delivery in induction cases.

Collaborations

National

- Instituto de Salud Carlos III (ISCIII)

International

- St George's, University of London, UK
- Thomas Jefferson University Hospital, Philadelphia, USA
- Erasmus Mundus Joint Doctorate in Fetal Medicine

Industry

- Transmural Biotech, Spain
- 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	



Julia Ponce
Predoctoral researcher



Claudia Rueda
Predoctoral researcher



Inflammation in preterm birth

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?

Subclinical intra-amniotic infection and the inflammatory response it generates are the most frequent causes of spontaneous preterm delivery, especially at early gestational ages. The main drawback is that its diagnosis requires an amniocentesis, an invasive procedure that limits translationality at the clinical level. For this reason we want to develop new, non-invasive, rapid detection tools that allow better clinical management at the patient's bedside.

DOES INFECTION HAVE A LONG-TERM IMPACT ON THE FETUS AND THE NEWBORN?

We are leading a clinical project in order to study the impact of intrauterine exposure to infection and inflammation at different stages of life. We evaluate changes occurring at the cardiovascular, neurological and neurodevelopmental levels during the fetal stage, at birth at 6 months and 1 year of age. To do this we use technologies such as metabolomics, proteomics of the bacterial microbiome, and photonics.

Team members



TERESA COBO

Coordinator of the research line.
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**Ana Belén
Sánchez**
Technician



Clara Murillo
Predoctoral
researcher



Claudia Rueda
Predoctoral
researcher



Eduardo Herreros
Predoctoral
researcher

THE LINE GATHERS SPECIALISTS IN
MATERNAL-FETAL MEDICINE AND NEONATOLOGY,
BIOCHEMISTS, BIOPHYSICISTS, MICROBIOLOGISTS,
BIOTECHNOLOGY ENGINEERS, BIOLOGISTS,
BIOSTATISTICIANS, AND TECHNICIANS.



Publications 2019

1. **Characterization of vaginal microbiota in women with preterm labor with intra-amniotic inflammation.** Cobo T, Vergara A, Collado MC, Casals-Pascuala C, Herreros E, Bosch J, Sánchez-García AB, López-Parellada R, Ponce J, Gratacós E. **Scientific Report. 2019** Dec 12;9(1):18963. doi: 10.1038/s41598-019-55611-y.

Collaborations

National

- Centro de Investigación Príncipe Felipe de Valencia (Antonio Pineda)
- Institut de Ciències Fotòniques (ICFO) (Valerio Pruneri y Romain Quidant)
- Dept. de Bioquímica y Biomedicina Molecular of Universitat de Barcelona (Marta Cascante)
- Dept. de Biotecnología of Instituto de Agroquímica y Tecnología de Alimentos (IATA) of Consejo Superior de Investigaciones Científicas (CSIC)

(M Carmen Collado)

- Plataforma de Bioestadística of IDIBAPS (José Ríos)

International

- Dept. of Metabolism, Digestion and Reproduction. Imperial College, London (David Macintyre)
- Dept. of Obstetrics and Gynecology, Charles University in Prague, Faculty of Medicine Hradec Kralove, Hradec Kralove, Czech Republic (Marian Kacerovsky)
- Dept. of Obstetrics and Gynecology, Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden (Bo Jacobsson)

Industry

- Hologic, USA
- Medix Biochemica, Finland

Intraamniotic inflammation is a risk factor for the neurodevelopment of extremely premature babies



In 2019

- We have observed that women with intra-amniotic infection have a characteristic vaginal metabolic profile.
- Today we know that women with a low bacterial load of *Lactobacillus* spp in their vaginal fluid are at increased risk of perinatal intra-amniotic inflammation, preterm labor, and short latency to labor.
- We continue to collaborate with companies on projects with a high translational component. With HOLOGIC we intend to identify inflammation and/or intra-amniotic infection in women at risk of premature birth by determining proteins in the vaginal discharge through the validation of a non-invasive test.
- With MEDIX Biochemica, we are contributing to the validation of a rapid and effective test to detect the MMP-8 protein. In this way we can diagnose intra-amniotic inflammation at the bedside in order to individualize the clinical management of women at risk of premature birth.

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

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

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 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.

Team members



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ELISENDA EIXARCH

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Laura Pla
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Narcis Masoller
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THE LINE GATHERS MEDICAL
SPECIALISTS IN FETAL
MEDICINE, BIOLOGISTS, AND
RESEARCH TECHNICIANS



Mar Bennasar
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Alexander Engels
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Britta Ana Kühner
Predoctoral
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Molka Kammoum
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Mirza Awais
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Alex Agyemang
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Ximena Torres
Predoctoral
researcher



David Basurto
Predoctoral
researcher



Lennart Van der Veeken
Predoctoral
researcher



Ameth Hawkins
Predoctoral
researcher



Maria Espina
Engineer



Joan Junyent
Engineer



Rocio Lopez
Engineer



Sabrina Gea
Lab technician



Anna Rocabert
Lab technician



Cristina Baques
Student



Mercè Fuentes
Student Neurospheres
Project



Montse Mayol
Student



Paula Vazques
Student



Publications 2019

1. **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;51:61-88. doi: 10.1016/j.media.2018.10.003. Epub 2018 Oct 19. Review
2. **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 MÁ. **Medical Image Analysis.** 2019 May;54:263-279. doi: 10.1016/j.media.2019.03.008. Epub 2019 Mar 28.
3. **Prenatal adverse environment is associated with epigenetic age deceleration at birth and hypomethylation at the hypoxia-responsive EP300 gene.** Palma-Gudiel H, Eixarch E, Crispi F, Morán S, Zannas AS, Fañanás L. **Clinical Epigenetics.** 2019 May 9;11(1):73. doi: 10.1186/s13148-019-0674-5.

Barrena J, Monill N, Piella G, Gratacós E, Eixarch E, Ceresa M, González Ballester MA. **Academic Radiology.** 2019 Dec 23. pii: S1076-6332(19)30575-6. doi: 10.1016/j.acra.2019.11.006.

6. **Vision based robot assistance in TTTS fetal surgery.** Sayols N, Hernansanz A, Parra J, Eixarch E, Gratacos E, Amat J, Casals A. **Conference IEEE Engineering in Medicine and Biology Society.** 2019 Jul;2019:5855-5861. doi: 10.1109/EMBC.2019.8856402.

Collaborations

National

- Unit of Toxicology of Facultat de Farmàcia of the Universitat de Barcelona
- Simulation, Imaging and Modelling for Biomedical Systems, Universitat Pompeu Fabra
- Institut de Ciències Fotòniques (ICFO)

Robotics, photonics and miniaturization will allow us to make a generational leap in fetal surgeries

- Instituto de Bioingeniería de Catalunya (IBEC)
- Institut Químic de Sarrià (IQS)
- Department of Cell Biology, Immunology and Neuroscience of the Universitat de Barcelona

International

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

Strategic goals

	Fetal Therapy	Fetal Surgery
Experimental	Evaluation of cell cultures and neuroprotective therapies Evaluation of the effects, structure and function of new therapeutic strategies	Functional and safety tests for a membrane sealing system
Clinical	Clinical trial in prenatal therapy Fetal Brain Care	Multicenter clinical validation study of a 3D-P three-dimensional personalized pre-surgical planning system Pilot study of a membrane sealing system FET-SEALING



4. **TTTS-GPS: Patient-specific preoperative planning and simulation platform for twin-to-twin transfusion syndrome fetal surgery.** Torrents-Barrena J, López-Velazco R, Piella G, Masoller N, Valenzuela-Alcaraz B, Gratacós E, Eixarch E, Ceresa M, González Ballester MA. **Computer Methods and Programs in Biomedicine.** 2019 Oct;179:104993. doi: 10.1016/j.cmpb.2019.104993. Epub 2019 Jul 24.
5. **Assessment of radiomics and deep learning for the segmentation of fetal and maternal anatomy in Magnetic Resonance imaging and ultrasound.** Torrents-



In 2019

- In collaboration with the research group of the Unit of Toxicology of Facultat de Farmàcia of the Universitat de Barcelona, we have developed the in vitro culture of neurospheres of stem cells derived from the animal model, a pioneering technique for the study of the effects on neurodevelopment in vitro.
- We have identified therapies with a neuroprotective capacity in the animal model, specifically lactoferrin and omega3, which, administered prenatally, prevent damage secondary to intrauterine growth restriction.
- We have developed, in conjunction with Universitat Pompeu Fabra, a personalized three-dimensional presurgical planning system for cases of twin-to-twin transfusion syndrome.
- We have developed a first prototype of a fetal membrane sealing system to be applied after surgery.





Environment and pregnancy complications

Discovering how environmental factors such as exposure to tobacco, alcohol, drugs and environmental toxins influence growth retardation or other pregnancy complications is our purpose.



THE LINE GATHERS FETAL MEDICINE SPECIALISTS, PATHOLOGISTS, BIOLOGISTS AND RESEARCH TECHNICIANS.

WHY IS IT IMPORTANT TO STUDY TOXIC EXPOSURE IN PREGNANCY?

Toxic exposure during pregnancy can have serious effects on fetal growth and neurodevelopment. It is imperative to know the exposure of the mother to substances of abuse (tobacco, alcohol, drugs) and environmental toxins (air pollution, chemicals such as heavy metals, pesticides, and endocrine disruptors) during pregnancy in order to understand their effects on fetal development.

WHAT IS THE MAIN OBJECTIVE OF THE RESEARCH LINE?

Our objective is to characterize the effect of toxic exposures to all these substances during pregnancy to improve our knowledge about them and to predict pregnancy complications related to environmental factors, such as to placental pathology, intrauterine growth restriction, hypertensive states of pregnancy, prematurity, perinatal morbidity, and prenatal and postnatal neurodevelopment.

Team members



LOLA GÓMEZ-ROIG

Coordinator of the research line. Maternal-Fetal Medicine Specialist and Head of the Department at BCNatal-Sant Joan de Déu Hospital. Lecturer in specialized courses of Fetal I+D Education Barcelona.



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Postdoctoral researcher



Miriam Pérez
Postdoctoral researcher



Paz Ahumada
Predoctoral researcher



Laura Almeida
Predoctoral researcher



Marc Cahuana
Predoctoral researcher



Diana Lip
Predoctoral researcher



Mariona Serra
Predoctoral researcher



Giulia Casu
Predoctoral researcher

Publications 2019



1. The frequency-following response (FFR) to speech stimuli: a normative dataset in healthy newborns. Ribas-Prats, T., Almeida, L., Costa-Faidella, J., Plana, M., Corral, M.J., Gómez-Roig, M.D., Escera, C. **Hearing Research** 371, pp. 28 - 39, 2019. ISSN 0378-5955.



2. Associations between neural injury markers of intrauterine growth-restricted infants and neurodevelopment at 2 years of age. Mazarico E, Llurba E, Cabero L, Sánchez O, Valls A, Martín-Ancel A, Cardenas D, Gómez Roig MD. **Journal of maternal-fetal & neonatal medicine. Informa Healthcare.** 32-19, Pp.3197-3203. ISSN 1476-7058. 2019

3. Genetic risk assessment of thrombophilia in patients with adverse obstetric outcomes. Fernández Arias, M., Mazarico, E., Gonzalez, A., Muniesa, M., Molinet, C., Almeida, L., Gómez Roig, M.D. **PLoS One.** 14 – 2. Public Library of Science (PLoS), 2019. ISSN 1932-6203

4. The effects of vegetarian and vegan diet during pregnancy on the health of mothers and offspring. Sebastiani G, Herranz Barbero A, Borrás-Novell C, Alsina Casanova M, Aldecoa-Bilbao V, Andreu-Fernández V, Pascual Tutusaus M, Ferrero Martínez S, Gómez Roig MD, García-Algar O.

Nutrients. Multidisciplinary Digital Publishing Institute (MDPI), 11-3. ISSN 2072-6643. 2019.

5. Multicenter prospective clinical study to evaluate children short-term neurodevelopmental outcome in congenital heart disease (children NEURO-HEART): study protocol. Ribera I, Ruiz A, Sánchez O, Eixarch E, Antolín E, Gómez-Montes E, Pérez-Cruz M, Cruz-Lemini M, Sanz-Cortés M, Arévalo S, Ferrer Q, Vázquez E, Vega L, Dolader P, Montoliu A, Boix H, Simões RV, Masoller N, Sánchez-de-Toledo J, Comas M, Bartha JM, Galindo A, Martínez JM, Gómez-Roig L, Crispí F, Gómez O, Carreras E, Cabero L, Gratacós E, Llurba E. **BMC Pediatrics. Biomed Central LTD.** 19-1, pp.326-326. ISSN 1471-2431. 2019

Collaborations

National

- Hospital de Sant Pau, Barcelona
- Instituto de Salud Global (IsGlobal), Barcelona
- Red de Salud materno-infantil 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



In 2019

- The intervention study to reduce alcohol consumption in pregnant women (EMOTIVE) has finished its recruitment phase with more than 400 participants.
- 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 will participate in the ATHLETE study (Advancing Tools for Human Early Lifecourse Exposome Research and Translation) to develop tools for the study of the exposome. A prospective exposure cohort will be studied to quantify the effects of environmental risk factors on mental health, cardiometabolic, respiratory and associated biological pathways during the first two decades of life.

Strategic goals



Marta Muniesa
Predoctoral
researcher



Erica Muñoz
Lab
technician

	Studying	Predicting
Clinical	The effect of exposure to environmental toxins in pregnancy	The risk of pregnancy complications due to environmental factors
Basic	Exposure to toxins and metabolites in pregnancy	



Placental disease

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 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 cause of maternal death in the world. Today, thanks to research, its diagnosis is predictable and we continue to study it to determine possible causes, such as its supposed relationship with oocyte donation.

Team members



FRANCESC FIGUERAS

Coordinator of the research line. Maternal-Fetal Medicine Specialist and Head of the Department at BCNatal-Hospital Clinic. Lecturer in specialized courses of Fetal I+D Education Barcelona.



Ekaterina Nedopekina
Predoctoral researcher



Raigam Martínez
Predoctoral researcher



Marta Rial
Predoctoral researcher



Mariella Giannone
Clinical Research Fellow



Fernanda Paz y Miño
Clinical Research Fellow



Santiago Castelazo
Clinical Research Fellow

Publications 2019

1. **Third-trimester uterine-artery Doppler for prediction of adverse outcome in late small-for-gestational-age fetuses: systematic review and meta-analysis.** Martinez-Portilla RJ, Caradeux J, Meler E, Lip-Sosa DL, Sotiriadis A, Figueras F. **Ultrasound in Obstetrics & Gynecology.** 2019 Nov 30. doi: 10.1002/uog.21940.
2. **Plasma levels of free fatty acids in women with gestational diabetes and its intrinsic and extrinsic determinants: systematic review and meta-analysis.** Villafan-Bernal JR, Acevedo-Alba M, Reyes-Pavon R, Diaz-Parra GA, Lip-Sosa DL, Vazquez-Delfin HI, Hernandez-Muñoz M, Bravo-Aguirre DE, Figueras F, Martinez-Portilla RJ. **Journal of Diabetes Research.** 2019 Aug 18;2019:7098470. doi: 10.1155/2019/7098470.
3. **Heparin therapy in placental insufficiency: Systematic review**



Giulia Benedetto
Clinical Research
Fellow

and meta-analysis. Mazarico E, Molinet-Coll C, Martinez-Portilla RJ, Figueras F. **Acta Obstetrica et Gynecologica Scandinavica.** 2020 Feb;99(2):167-174. doi: 10.1111/aogs.13730. Epub 2019 Oct 8. Review.

4. **Association of plasma lactate concentration at admission of severe preeclampsia to maternal complications.** Peguero A, Parra RA, Carrillo SP, Rojas-Suarez J, Figueras F. **Pregnancy Hypertension.** 2019 Jul;17:89-93. doi: 10.1016/j.preghy.2019.05.003.
5. **Blood parameters in fetuses infected with cytomegalovirus according to the severity of brain damage and trimester of pregnancy at cordocentesis.** Hawkins-Villarreal A, Moreno-Espinosa AL, Eixarch E, Marcos MA, Martinez-Portilla RJ, Salazar L, Garcia-Otero L, Lopez M, Borrell A, Figueras F, Goncá A. **Journal of Clinical Virology.** 2019 Oct;119:37-43. doi: 10.1016/j.jcv.2019.08.008. Epub 2019 Aug 20.



Diagnosing IUGR allows us to implement preventive measures during pregnancy, childbirth and early childhood



In 2019

- We continue to investigate the role of longitudinal growth assessment in predicting fetal growth restriction and its consequences, leading to various publications in indexed journals that include original articles and reviews for the field.
- We advance in the study of the causes of preeclampsia and its complications.
- We continue working on the RATIO37 clinical trial, which studies the incorporation of a new ultrasound parameter at 37 weeks' gestation with the aim of reducing the rate of fetal death and complications during delivery.

- 6. Diagnostic performance of third-trimester ultrasound for the prediction of late-onset fetal growth restriction: a systematic review and meta-analysis.** Caradeux J, Martinez-Portilla RJ, Peguero A, Sotiriadis A, Figueras F. *American Journal of Obstetrics and Gynecology*. 2019 May;220(5):449-459.e19. doi: 10.1016/j.ajog.2018.09.043. Epub 2019 Jan 8.
- 7. A systematic review and meta-analysis of randomized controlled trials comparing 17-alpha-hydroxyprogesterone caproate versus placebo for the prevention of recurrent preterm birth.** Fernandez-Macias R, Martinez-Portilla RJ, Cerrillos L, Figueras F, Palacio M. *International Journal of Gynecology & Obstetrics*. 2019 Nov;147(2):156-164. doi: 10.1002/ijgo.12940. Epub 2019 Aug 28.
- 8. Unravelling the link among growth restriction, placental disorders, and stillbirth.** Figueras F. *Paediatr Perinat Epidemiol*. 2019 Jul;33(4):284-285. doi: 10.1111/ppe.12566. Epub 2019 Jul 9.
- 9. Evaluation of the quality and reliability of middle cerebral artery and umbilical artery Doppler images within an international randomized controlled trial.** Rial-Crestelo M, Morales-Roselló J, Hernández-Andrade E, Prefumo F, Oros D, Caffici D, Sotiriadis A, Zohav E, Cruz-Martinez R, Parra-Cordero M, Lubuski M, Kacerovsky M, Figueras F. *Ultrasound in Obstetrics & Gynecology*. 2019 Jun 10. doi: 10.1002/uog.20370.
- 10. ISUOG Practice Guidelines: ultrasound assessment of fetal biometry and growth.** Salomon LJ, Alfirevic Z, Da Silva Costa F, Deter RL, Figueras F, Ghi T, Glanc P, Khalil A, Lee W, Napolitano R, Papageorgiou A, Sotiriadis A, Stirnemann J, Toi A, Yeo G. *Ultrasound in Obstetrics & Gynecology*. 2019 Jun;53(6):715-723. doi: 10.1002/uog.20272.
- 11. Distinctive patterns of placental lesions in pre-eclampsia vs small-for-gestational age and their association with fetoplacental Doppler.** Paules C, Youssef L, Rovira C, Crovetto F, Nadal A, Peguero A, Figueras F, Eixarch E, Crispi F, Miranda J, Gratacós E. *Ultrasound in Obstetrics & Gynecology*. 2019 Nov;54(5):609-616. doi: 10.1002/uog.20350. Epub 2019 Oct 14.
- 12. Sildenafil therapy in early-onset fetal growth restriction: waiting for the individual patient data meta-analysis.** Figueras F. *BJOG*. 2019 Jul;126(8):1007. doi: 10.1111/1471-0528.15753. Epub 2019 Apr 24.
- 13. Maternal and perinatal outcomes after elective induction of labor at 39 weeks in uncomplicated singleton pregnancy: a meta-analysis.** Sotiriadis A, Petousis S, Thilaganathan B, Figueras F, Martins WP, Odibo AO, Dinas K, Hyett J. *Ultrasound in Obstetrics & Gynecology*.
- 14. Performance of fetal middle cerebral artery peak systolic velocity for prediction of anemia in untransfused and transfused fetuses: systematic review and meta-analysis.** Martinez-Portilla RJ, Lopez-Felix J, Hawkins-Villareal A, Villafan-Bernal JR, Paz Y Miño F, Figueras F, Borrell A. *Ultrasound in Obstetrics & Gynecology*. 2019 Dec;54(6):722-731. doi: 10.1002/uog.20273. Review.
- 15. Osteocalcin Serum Levels in Gestational Diabetes Mellitus and Their Intrinsic and Extrinsic Determinants: Systematic Review and Meta-Analysis.** Martinez-Portilla RJ, Villafan-Bernal JR, Lip-Sosa DL, Meler E, Clotet J, Serna-Vela FJ, Velazquez-García S, Serrano-Díaz LC, Figueras F. *Journal of Diabetes Research*. 2018 Dec 30;2018:4986735. doi: 10.1155/2018/4986735. eCollection 2018. Review.
- 16. Achieving orphan designation for placental insufficiency: annual incidence estimations in Europe.** Spencer R, Rossi C, Lees M, Peebles D, Brocklehurst P, Martin J, Hansson SR, Hecher K, Marsal K, Figueras F, Gratacos E, David AL; EVERREST Consortium. *BJOG*. 2019 Aug;126(9):1157-1167. doi: 10.1111/1471-0528.15590. Epub 2019 Feb 6.
- 17. Added value of chromosomal microarray analysis over conventional karyotyping in**

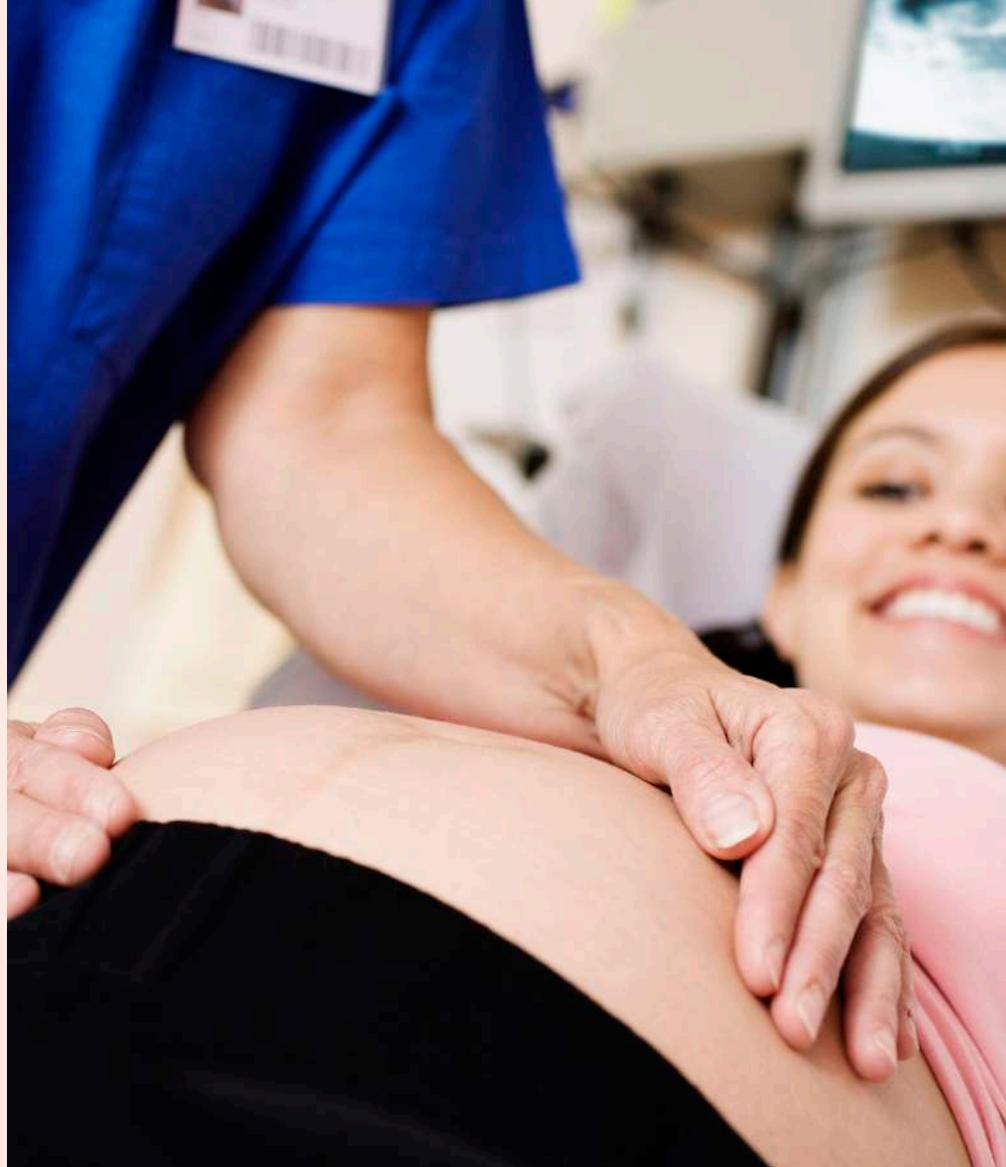
New studies suggest that the risk of preeclampsia may be associated with pregnancies resulting from oocytes donation

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19. Essential variables for reporting research studies on fetal growth restriction: a Delphi consensus. Khalil A, Gordijn SJ, Beune IM, Wynia K, Ganzevoort W, Figueras F, Kingdom J, Marlow N, Papageorghiou AT, Sebire N, Zeitlin J, Baschat AA. **Ultrasound in Obstetrics & Gynecology.** 2019 May;53(5):609-614. doi: 10.1002/uog.19196.

 **20. First-trimester and combined first- and second-trimester prediction of small-for-gestational age and late fetal growth restriction.** Sotiriadis A, Figueras F, Eleftheriades M, Papaioannou GK, Chorozioglou G, Dinas K, Papantoniou N. **Ultrasound in Obstetrics & Gynecology.** 2019 Jan;53(1):55-61. doi: 10.1002/uog.19055.



Collaborations

National

- EUGIN Clinic, Barcelona, Spain

International

- Aristotle University Medical School, Thessaloniki, Greece

- Lund University Hospital, Lund, Sweden



THIS LINE GATHERS FETAL MEDICINE SPECIALISTS, PSYCHOLOGISTS AND RESEARCH TECHNICIANS

Strategic goals

	Clinical research
Diagnosis	Development of early detection methods for growth restriction for a new definition and prediction of brain damage.
Therapies	Clinical trials to prevent preeclampsia and growth restriction.

Platforms



Biobank

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



WHAT DO WE DO?

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.



[BCNATALRESEARCH.ORG/
BIOBANK](https://bcnatalresearch.org/biobank)

Scientific Coordinator: Fàtima Crispí **Technical Coordinator:** Miriam Osorio
Research Technicians: Cristina Miranda, Erica Muñoz, Núria Rierola, Vasili Sircheli



Animal model

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

WHAT DO WE DO?

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





Postnatal

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

WHAT DO WE DO?

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 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
Technical support: Alba Camacho, Aitor Molina, Paula Navarro, Nadia Rojas, Natalia Torrico, Mireia Pascual
Psychologists: Juana Cajiao, Maite Mañosa, Marta Bello, Marta Ros
Assistant nursing care technician: Sara Aceña, M. Rosa García, Sandra León, Mercedes Madeiros, Manuela Mancebo



Imaging

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.



WHAT DO WE DO?

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, Brenda Valenzuela, Cora Roig Blay, Claudia Gracia

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 CSR. One of its highest priorities is the professional development of the researchers of the group. In this sense, different learning and networking actions are carried out, such as the Journal Club, the Personal Career Development Plan, 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.

PERSONAL CAREER DEVELOPMENT PLAN

Another tool we have available to help researchers evaluate their skills and interests is the Personal Career Development Plan. This plan allows them to trace what their professional career trajectory will be, define their (and their supervisor's) profile and adapt the training and education program according to their learning and development objectives in the short-, medium-, and long-term.

The teamwork of the specialists in economy, communication and new technologies is the key for the excellent research performed at the group

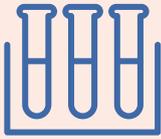


In 2019

Among the invited speakers at the 2019 Journal Club, eminent researchers from different fields of health, biomedical research and maternal-fetal medicine stand out.

- **Mark Friedberg**, a pediatric cardiologist at Toronto's Hospital for Sick Children, explained the unique hemodynamics of the right ventricle from fetal to postnatal life.
- **Jana Hutter**, of the Center for the Developing Brain at King's College, London, where she studies functional MRI of the placenta in fetuses with IUGR.
- **Emilio Herrera**, from the Institute of Biomedical Sciences (ICBM), University of Chile, presented experimental models to evaluate fetal cardiovascular programming due to hypoxia.
- **Daniela Prayer**, from the Medical University of Vienna, explained the use of advanced MRI in fetal brain abnormalities.

Fields of action



RESEARCH SUPPORT

Supporting the scientific activity of the researchers of the group and promoting excellent research in fetal medicine



PROFESSIONAL DEVELOPMENT

Contributing to the professional development of the team members to encourage motivation in the workplace and ensure their future employability



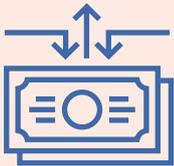
COORDINATION

Coordinating different research projects in order to ensure maximum efficiency and innovation in all of them



GOOD PRACTISES

Ensuring ethics and the application of ethical principles in research



FINANCIAL MANAGEMENT

Managing efficiently the funds that finance research activities and ensuring the efficient use of resources and infrastructure



KNOWLEDGE TRANSFER

Promoting the translation of results and providing the knowledge of the progress made to society, the scientific community and the economic system

Team members



Elisenda Bonet
Scientific manager



Ester Cardet
Project manager



Iris Uribesalgo
Scientific writer



Isil Tekeli
Scientific writer



Maite Aguilera
HR Coordinator



Merche Alonso
Purchasing and administrative



Pere Lorente
Communication CSR



Alba Bellot
Scientific Writer



**THE GROUP
GATHER EXPERTS
IN ECONOMICS,
HUMAN RESOURCES,
COMMUNICATION
AND NEW
TECHNOLOGIES**



03

R&D Projects

Research projects and grants 2019

Clinical transfer

Obra Social 'la Caixa' Project

CEREBRA Project

CELLEX Project

Research projects and grants

Ongoing in 2019

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

Eduard Gratacós

European Commission. Erasmus +
► 01/08/2013 - 31/10/2021

FIRST Project. New high-precision technologies for fetal surgery and medicine.

Eduard Gratacós
Fundación privada CELLEX
► 04/01/2016 - 30/06/2019

Towards a real impact on prenatal brain damage, a multidisciplinary research programme for the evaluation of diagnostic techniques and intervention measures for prenatal brain damage using growth restriction as a model.

Eduard Gratacós

CEREBRA Foundation
► 01/01/2014-31/12/2019

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 - 31/11/2020

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 - 31/12/2020

Tratamiento del CIR precoz con heparina de bajo peso molecular (TRACIP): Ensayo Clínico Randomizado.

Eduarne Mazarico

Instituto de Salud Carlos III (ISCIII)
► 01/01/2017 - 31/12/2019

Maternal prenatal stress and HPA axis sensitization mediated by 11-HSD2 gene epigenetic signatures and its interplay with childhood psychosocial stress in explaining risk for psychopathology in adolescence.

Lourdes Fañanás, Elisenda Eixarch, Fàtima Crispi

CIBERSAM (CIBERER)
► 01/01/2017 - 31/12/2019

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 - 31/12/2020

Prevenió de les conseqüències neurològiques i cardiovasculars de les patologies fetals.

Eduard Gratacós

Fundació "la Caixa"
► 01/01/2015 - 31/12/2019

Validación de biomarcadores proteómicos y metabólicos de inflamación intraamniótica en el parto prematuro en muestras cervico-vaginales y desarrollo de algoritmos clínicos predictores.

Tere Cobo

Instituto de Salud Carlos III (ISCIII)
► 01/01/2016 - 31/12/2019

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

Started in 2019

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

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

Eduard Gratacós

Obra Social 'la Caixa'

► 01/01/2019 - 31/12/2022

MIIFI - Multimodality Integrated Imaging for Fetal Intervention.

Eduard Gratacós

European Commission

► 25/04/2019 - 31/07/2020

Awarded in 2019

Desarrollo y validación de una herramienta diagnóstica no-invasiva de infección intra-amniótica en flujo vaginal basada en la integración de metabólica y microbioma.

Teresa Cobo

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

La restricción de crecimiento fetal predispone en la vida adulta a una respuesta a estrés cardíaco defectuosa: papel de la cardioquina FGF21.

Mónica Zamora

Instituto de Salud Carlos III (ISCIII)

► 01/01/2020 - 31/12/2022

Clinical transfer: guidelines and protocols

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 practise of maternal-fetal and neonatology medicine units, optimizing patient care and promoting the application of certain preventive measures and treatments in healthcare.

19

ONGOING
RESEARCH
projects and grants

1.8

MILLION EUROS
invested in research
projects in maternal-fetal
medicine

26

CLINICAL GUIDES
developed for
health services
since 2015

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 OBJETIVE?

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.

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

 fetalmedbarcelona.org/lacaixa

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.

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.

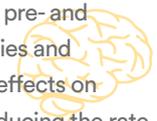
NEW BIOMARKERS

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

Fundació Privada
CELLEX

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 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

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.

 **upf.** Universitat
Pompeu Fabra
Barcelona

 **IBEC**
Institute for Bioengineering of Catalonia

 **ICFO**
Institut
de Ciències
Fotòniques

 **IQS**
PERSONA CIÈNCIA EMPRESA
UNIVERSITAT RAMON LLULL



04

Scientific results

National and international congresses and courses

Participation in congresses

Academic output

National and international congresses and courses

SMFM's 39th Annual Pregnancy Meeting SMFM **11-16 February**

1. Las Vegas, Nevada, USA

12th Annual Meeting of CIBERER **12-14 March**

2. Madrid, Spain

2nd World Congress on Maternal fetal Neonatal Medicine EFCNI **4-6 April**

3. London, United Kingdom

15th ISUOG International Symposium ISUOG **12-14 April 4. Sao Paulo, Brazil**

Joined meeting of CardioNet and CIBERER working team

"Salut Cardiovascular en Malalties Rares" CardioNet, Societat Catalana de Cardiologia, CIBERER, BCNatal Fetal Medicine Research Center

24 April 5. Barcelona, Spain

EuroMedLab 2019 **19-23 May**

6. Barcelona, Spain

18th World Congress in Fetal Medicine FMF **25-29 June**

7. Alicante, Spain

2019 EuroISSHP Conference International society for the study of hypertension in pregnancy **2-4 October**

8. Lund, Sweden

8th International Conference on Fetal Growth **9-11 October**

9. Berlin, Germany

29th World Congress on Ultrasound in Obstetrics and Gynecology ISUOG

12-16 October 10. Berlin, Germany

FMF Advances Course The fetal medicine foundation **7-8 December**

11. London, United Kingdom

20th International Congress of the The Egyptian Society of Gynecology & Obstetrics **9-10 February**

12. Cairo, Egypt

ISMRM 27th Annual Meeting & Exhibition International Society for Magnetic Resonance in Medicine (ISMRM) **11-16**

May 13. Montreal, Canada

CDMRI 2019 - MICCAI 2019 International Workshop on Computational Diffusion MRI **17**

October 14. Shenzhen, China

Open Day Summer School 2019 FetalMedPhd BCNatal Fetal Medicine

Research Center **19 September**

15. Barcelona, Spain

Avengers for Better Science

29-1 October-November

16. Leiden, The Netherlands

XXVII Congreso de Neonatología y Medicina Perinatal, VII Congreso de Enfermería Neonatal **2-4 October**

17. Madrid, Spain

45%
National

50%
International



Participation in congresses

Invited talks

RESEARCHER	TITLE	CONGRESS
Fàtima Crispi	Evaluation of the intrinsic function of the fetal heart	ISUOG 2019
	Cardiovascular consequences following FGR – DOHaD	SMFM's 39th Annual Pregnancy Meeting
Eduard Gratacós	Fetal Interventions in Monochorionic twins	ISUOG 2019
	Management of early growth restriction: The European view.	
	Consensus definition of fetal growth restriction	15th ISUOG International Symposium
	Fetal surveillance and timing of delivery	
	Lessons from the TRUFFLE trial	
	Management of fetal growth restriction in practice	
	Selective intrauterine growth restriction	
Francesc Figueras	Management of fetal growth restriction	20th International Congress of the Egyptian Society of Gynecology & Obstetrics
	Update on fetal therapy and surgery	
Francesc Figueras	Early and late SGA management	Advances in Fetal Medicine Course
	Late FGR: management	18th World Congress in Fetal Medicine
Elisenda Eixarch	A sealing system for fetoscopic defects & Patient-specific planning platform for TTTS surgery.	18th World Congress in Fetal Medicine
	Patient-specific planning platform for TTTS surgery	
Teresa Cobo	Prediction of preterm birth and intraamniotic infection	18th World Congress in Fetal Medicine
Lola Gomez-Roig	Environmental impact on pregnancy	2019 EuroISSHP Conference
Lina Youssef	Metabolomics approach to understand the pathophysiology of preeclampsia and fetal growth restriction	2019 EuroISSHP Conference

Oral Communications

RESEARCHER	TITLE
Fetal Growth Congress 2019	
Francesc Figueras	Fetal size vs growth in predicting outcome
Lola Gomez-Roig	Identification of phenotypes of FGR using a network-based clustering approach
Jezip Miranda	Identification of phenotypes of FGR using a network-based clustering approach
ISUOG 2019	
Elena Monterde	Assessment of the Corpus Callosum in fetuses with isolated non-severe ventriculomegaly
Ximena Torres	Cardiac morphometry in uncomplicated monochorionic diamniotic twins: a comparison to singletons
Clara Murillo Bravo	Contribution of the amniocentesis for the ultrasound prediction of spontaneous preterm delivery in women with preterm labor
Elisenda Eixarch	Differential effect in corpus callosum development in fetuses with congenital heart defect
Nadine Hahner	Differential regional distribution of ventricular volumes in fetuses with isolated non-severe ventriculomegaly is associated with poor neurodevelopmental outcome
Talita Micheletti	Mechanical properties and toxicity of different bioadhesives as sealing system for fetal membranes
Lina Youssef	Metabolomic profiling of paired maternal and cord blood in preeclampsia and fetal growth restriction
SMFM's 39th Annual Pregnancy Meeting	
Jezip Miranda	Maternal Stress and Placental RNA Expression and Methylation of the HSD11B2 Gene in Fetal Growth Restriction

Oral Presentations

RESEARCHER	TITLE
2nd World Congress on Maternal-fetal Neonatal Medicine	
Lola Gomez-Roig	Presentation on prenatal exposure to endocrine disruptors
18th World Congress in Fetal Medicine	
Francesca Crovetto	Cortical development in PE and FGR
Miriam Perez	Differential effect in Corpus Callosum development in fetuses with Congenital Heart Defect assessed by ultrasound
Fàtima Crispi	Identification of different phenotypes of FGR & Cardiac dysfunction and hypoxia in SGA fetuses & Core concepts in fetal cardiac function
Nadine Hahner	Isolated non-severe ventriculomegaly: neurodevelopment
Raigam Martinez	Maternal congenital heart disease and PE
Lina Youssef	Proteomics, metabolomics and lipidomics in early PE & Fetal cardiac remodeling and dysfunction in PE and FGR

RESEARCHER	TITLE
12th Annual Meeting of CIBERER	
Fàtima Crispi	Papel de la actuación del complemento en la fisiopatología de la preeclampsia grave y síndrome de HELLP
EuroMedLab 2019	
Fàtima Crispi	Evolving role of biomarkers in prenatal care: preeclampsia
ISUOG 2019	
Lina Youssef	Alpha-1 microglobulin involvement in maternal and fetal blood in pre-eclampsia and/or fetal growth restriction
Francesca Crovetto	Angiogenic factors and fetoplacental Doppler for the prediction of adverse perinatal outcome among suspected small-for-gestational-age fetuses
	Patterns of cortical development assessed by neurosonography in pregnancies complicated by pre-eclampsia with or without fetal growth restriction
	Placental perfusion assessed by MR IVIM model and its correlation with placental volume in pregnancies at term complicated by fetal growth restriction
Elisenda Eixarch	Automatic classification of fetal ultrasound images: a remarkable application of deep learning technology for fetal medicine
Miriam Illa	Brain reorganisation at neonatal period in a rabbit model of IUGR
	Using sFlt-1/PIGF in IUGR
Raigam Martinez	Prediction of small for gestational age: added contribution of second to third trimester growth velocity
Lucas Trigo	Prevalence of severe CNS abnormalities assessed by fetal MR among candidates for spina bifida prenatal surgery



29

ORAL COMMUNICATIONS
in national and
international
congresses



17

COURSES AND CONGRESSES
national and international
in which we have participated
in 2019



12

POSTERS
presented in 2019 at
national and international
conferences

Posters and oral posters

RESEARCHER	TITLE
Fetal Growth Congress 2019	
Edurne Mazarico	Neonatal mortality and morbidity of extreme premature neonates with growth restriction
Marta Rial	Prescriptive reference standards of third-trimester cerebroplacental ratio and its physiological determinants
ISUOG 2019	
Lina Youssef	A prospective study of aortic isthmus Doppler changes in appropriately-grown and small-for-gestational-age fetuses and establishing the threshold of aortic isthmus values for prediction of adverse perinatal outcome: a prospective cohort study
Elisenda Eixarch	Added value of fetal brain magnetic resonance after a systematic neurosonography in congenital heart defects
Miriam Illa	Obstetric risk factors for levator avulsion: a meta-analysis and systematic review
Nadine Hahner	Pattern of cortical development in fetuses with isolated non-severe ventriculomegaly is associated with poorer neurodevelopmental performance at early infancy
SMFM's 39th Annual Pregnancy Meeting	
Tere Cobo	Targeting pregnancy management according to information of intra-amniotic infection/inflammation in women with preterm labor
Eduardo Herreros	Influence of vaginal microbiota on the pathophysiology of intra-amniotic inflammation in women with preterm labor
Tere Cobo	Targeting pregnancy management according to information of intra-amniotic infection/inflammation in women with preterm labor
XXVII Congreso de Neonatología y Medicina Perinatal, VII Congreso de Enfermería Neonatal	
Ángela Arranz	Impacto de la lactancia materna en el neurodesarrollo del recién nacido con bajo peso para edad gestacional
Ángela Arranz	Uso de la bayley scale of infant development-third edition (bsid-iii) como instrumento predictor del riesgo de autismo
Ángela Arranz	Evaluación del vínculo de la madre durante la infancia y efecto en la percepción de los cuidados a su bebé

Academic output

Completed doctoral theses

RESEARCHER	TITLE	DIRECTORS	UNIVERSITY	DATE
Molka Kammoum	Genomic analysis of congenital diaphragmatic hernia	Elisenda Eixarch Joris Vermeesch	Katholieke Universiteit Leuven	24/01/2019
Alex Agyemang	Brain damage and neurological impairment in preterm infants with intraventricular hemorrhage	Míriam Illa David Ley	Lund University	15/03/2019
Álvaro Pérez	Quantitative ultrasound texture analysis for its use on prematurity	Elisenda Bonet Montse Palacio Jan Deprest	Universitat de Barcelona	25/03/2019
Federico Migliorelli	Evaluación de los factores clínicos y ecográficos predictivos del resultado de la inducción del parto en gestaciones únicas	Montse Palacio	Universitat de Barcelona	11/07/2019
Álvaro Sepúlveda	Impact of fetal growth restriction on cardiovascular structure and function across life course	Eduard Gratacós Fàtima Crispi Erik Hedström	Universitat de Barcelona	21/10/2019
Nadine Hahner	Assessment of cortical development in fetuses with isolated non-severe ventriculomegaly and its correlation with neurodevelopmental outcome	Elisenda Eixarch Eduard Gratacós Jan Deprest	Universitat de Barcelona	18/12/2019
Grigorios Kalapotharakos	Preeclampsia, a cardiovascular risk factor	Stefan Hansson Fàtima Crispi	Lund University	21/12/2019

Research Grants

RESEARCHER	TITLE	CONGRESS
Ayako Nakaki	Beca predoctoral "INPhINIT Retaining"	Obra Social "la Caixa"
Elisenda Eixarch	Intensificació de professionals de la Salut, programa PERIS	Generalitat de Catalunya
Tere Cobo	Intensificació de professionals de la Salut, programa PERIS	Generalitat de Catalunya



Awards

RESEARCHER	AWARD	TITLE	AWARDED BY
Francesca Crovetto	Premi Extraordinari de Doctorat	Development of combined screening test for the prediction of preeclampsia and intrauterine growth restriction in the first trimester of pregnancy	Universitat de Barcelona
	Premios Infancia	Impacto de la dieta mediterránea durante la gestación en la microbiota del neonato	Fundació Agrupació
Jezid Miranda	Best oral presentation	Human Fetal Growth Restriction is Influenced Mainly by Maternal Socioeconomic Status: An Ecological Study Within a City from a Developing Country	8th International Conference on Fetal Growth
Raigam Jafet Martínez-Portilla	Best short oral presentation: "Fetal Growth: Normal and Abnormal" category	Prediction of small-for-gestational-age: added contribution of second-to-third trimester growth velocity	ISUOG 2019
Lucas Trigo	Best short oral presentation: "Fetal brain and CNS anomalies" category	Prevalence of severe CNS abnormalities assessed by fetal MR among candidates for Spina bifida prenatal surgery	ISUOG 2019
	TOP 5- 4th place obstetrician oral presentation	Diagnóstico US de microcefalia: uma comparação entre três curvas de referência e o diagnóstico pós-natal	SOGESP
	Clinical Research Scholar Award	Outstanding performance and participation in the Principles and Practice of Clinical Research 2019	Harvard Medical School
Lina Youssef	Poster Award Presentation. Best 2 top abstracts of 5	Fetal cardiac remodeling and dysfunction in preeclampsia and fetal growth restriction	2019 EuroISSHP
Lola Gómez-Roig	Premio Academia Kronos	International prize for the environment and climate	Reproductive and Developmental Environmental Health Committee of FIGO



Research Fellowships

RESEARCHER	UNIVERSITY / COUNTRY
Lina Youssef	Lund University, Sweden
Mari Kinoshita	Lund University, Sweden
Lucas Trigo	Sao Paulo, Brazil



05

Education

Training in Maternal-Fetal Medicine
FetalMed PhD Summer School

Training in Maternal-Fetal Medicine

In 2019 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).



40

DOCTORATES have been awarded thanks to the FetalMed PhD Erasmus Mundus Joint Doctorate

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 from.





Master's and Undergraduate Thesis Projects

RESEARCHER	TITLE	UNIVERSITY / SUPERVISOR
Montse Mayol (Undergraduate)	Anàlisi del dany neurològic i identificació de possibles teràpies neuroprotectores en un model animal de restricció de creixement intrauterí	Facultat de Biologia UB Miriam Illa, Fàtima Crispi
Marcos Alonso (Undergraduate)	Caracterització del remodelat cardiovascular fetal en resposta a isoproterenol en un model animal de restricció del creixement intrauterí	Facultat de Biologia UB Monica Zamora, Fàtima Crispi
Lucía García (Master)	Revealing higher susceptibility to cardiovascular diseases in adult rats with intrauterine growth restriction	Facultat de Medicina UB Monica Zamora, Fàtima Crispi
Paula Vázquez (Undergraduate)	Evaluation of neuroprotective therapies in a neurosphere model of IUGR	Facultat de Medicina UB Marta Barenys, Miriam Illa



Ongoing Doctoral Theses

RESEARCHER	TITLE	UNIVERSITY / COUNTRY
Ayako Nakaki	Impact of maternal life-style on fetal and maternal brain	UB / Japan
Britta Kühne	Safety and efficacy investigations for new prenatal neuroprotective therapies. Applications in a model of intrauterine growth restriction (IUGR)	UB / Germany
Clara Murillo	Impacto de la amenaza de parto prematuro y la rotura prematura de membranas sobre neurodesarrollo y el sistema cardiovascular fetal y neonatal	UB / Spain
David Coronado	Evaluation of Deep Learning techniques for automatic diagnosis from medical ultrasound	UB / Spain
Diana Lip	Correlation between fetal brain structures and frequency-following response (FFR) for early evaluation of language acquisition	UB / Spain
Raigam Martínez	Developing an effective model for the prediction of gestational diabetes in the first trimester of pregnancy (GD1sT)	UB / Mexico

FetalMed PhD Summer School

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

In 2019, the fourth Erasmus Mundus FetalMed-PhD Summer School was held in Barcelona. The extensive program of this latest event was designed with the aim, as always, of providing researchers-in-training with new tools and knowledge that can improve their ongoing research projects and increase their research skills.

With this event we intended to expand the network of students contacts thinking about their future incorporation into the work

world, whether in the research environment, industry or academia. To make it possible we organized an Open Day with international expert speakers in the areas 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.



06

Media

Under the spotlight
The team on the Internet

Under the spotlight

In 2019, 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.



WE PUBLISH A STUDY ON ALCOHOL CONSUMPTION IN PREGNANCY

► The study, financed by 'la Caixa', shows that 42% of pregnant women consume alcohol to a greater or lesser dose, despite the fact that any consumption can negatively affect fetal growth and its neurodevelopment. This study, led by our researcher Lola Gómez-Roig and published in the journal "Alcohol", includes 153 women who had their children at BCNatal, and shows that only between 2 and 3% of pregnant women are aware that they consume alcohol. These conclusions reflect maternal ignorance of alcohol's negative influences on fetal well-being. Thanks to this, the group appeared on television, radio, newspapers, and social media.

'la Caixa'
La Razón
La Vanguardia
20 minutos
Canal 324 / TV3

INTRODUCING A WORLD-PIONEERING SURGICAL NAVIGATION SYSTEM FOR FETAL SURGERY

► A new tool for fetal surgery developed in collaboration with BCN Med Tech-UPF Barcelona and BCNatal was presented at a press conference in November. It is a kind of GPS that reconstructs the placenta of a pregnant woman from an MRI and ultrasound images. It enables preoperative planning of surgery

and intraoperative navigation, improving precision, surgical time, and associated risks. We are currently using this navigation system successfully for twin-to-twin transfusion cases. This news was widely covered in the media: the group appeared on television, radio, and more than 40 print and digital media networks.

We are reference interlocutors in reports and news about maternity and the fetal stage

La Vanguardia / ABC / El Punt Avui / El Periódico

CELEBRATING 20 YEARS OF THE FIRST FETAL SURGERY IN SPAIN

► In June 1999 Eduard Gratacós performed the first surgery on a fetus inside the mother's uterus. The pregnancy was affected by twin-to-twin transfusion, a characteristic complication of twins who share a placenta that can be fatal. Today, 20 years later, fetal medicine is a specialty that saves lives every day. The press covered the news and El País Semanal dedicated an extensive report to our work.



El País Semanal / iNatal

The team on the Internet

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.

We want to raise awareness about the importance of research in maternal-fetal medicine to improve public health

Social media



1386

FOLLOWERS
@BCNatalResearch



1220

FOLLOWERS
BCNatal Fetal
Medicine Research



614

FOLLOWERS
@fetalmedbcn



915

MEMBERS
BCNatal Fetal Medicine
Research

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.



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