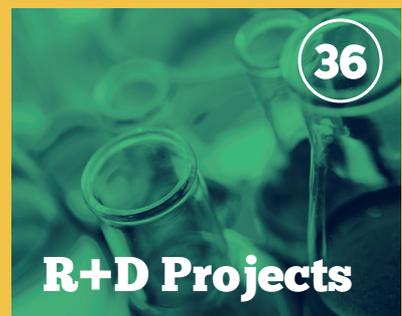




**Fetal  
Medicine  
Research  
Center**  
**2018**

# Summary



# Fetal Medicine Research Center Annual Report 2018

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, pluridisciplinarity and innovation. These three pillars make up our DNA. 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 great promoters such as CELLEX Foundation, Obra Social “la Caixa”, CEREBRA and other funders, friends and collaborators. Without their support and ifunding none of this would be possible.

Thanks to them we have ongoing innovative human intervention studies that will improve the prognosis of fetal growth restriction and we have initiated new studies based on microbiota, machine deep learning, lung development assessment and contamination. 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 the clinical practice..

We do not forget our teaching and social vocation. Our commitment to the scientific community materializes with the PhD programme in Fetal Medicine FetalMed-PhD, a 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 to make everyone aware that “health begins before birth”. At the end, our main purpose is to improve science, health, and the lives of people.



  
Eduard Gratacós

Director of BCNatal Fetal Medicine Research Center



# Who we are

Purpose

A tem of excellence

Nature

Scientific results

Organizational chart

History

# Purpose

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

BCNatal Fetal Medicine Research Center is a 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 (the clinical center: Hospital Clínic de Barcelona and Hospital Sant Joan de Déu) and is affiliated with 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 identify 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, the study that allows us to advance in the creation of new biomarkers that will detect fetuses at risk.

**We identify methods of early diagnosis and treatment for diseases of prenatal origin**

**+450**



**PUBLICATIONS**

since 2010



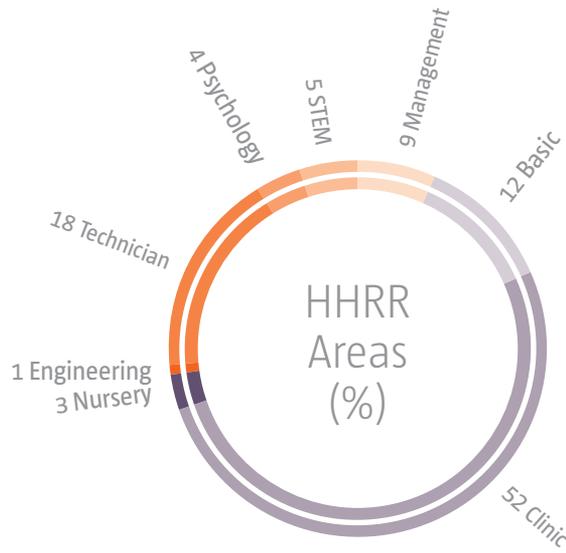
**ARTICLES**

published in 2018 in  
33 different scientific journals

**77**

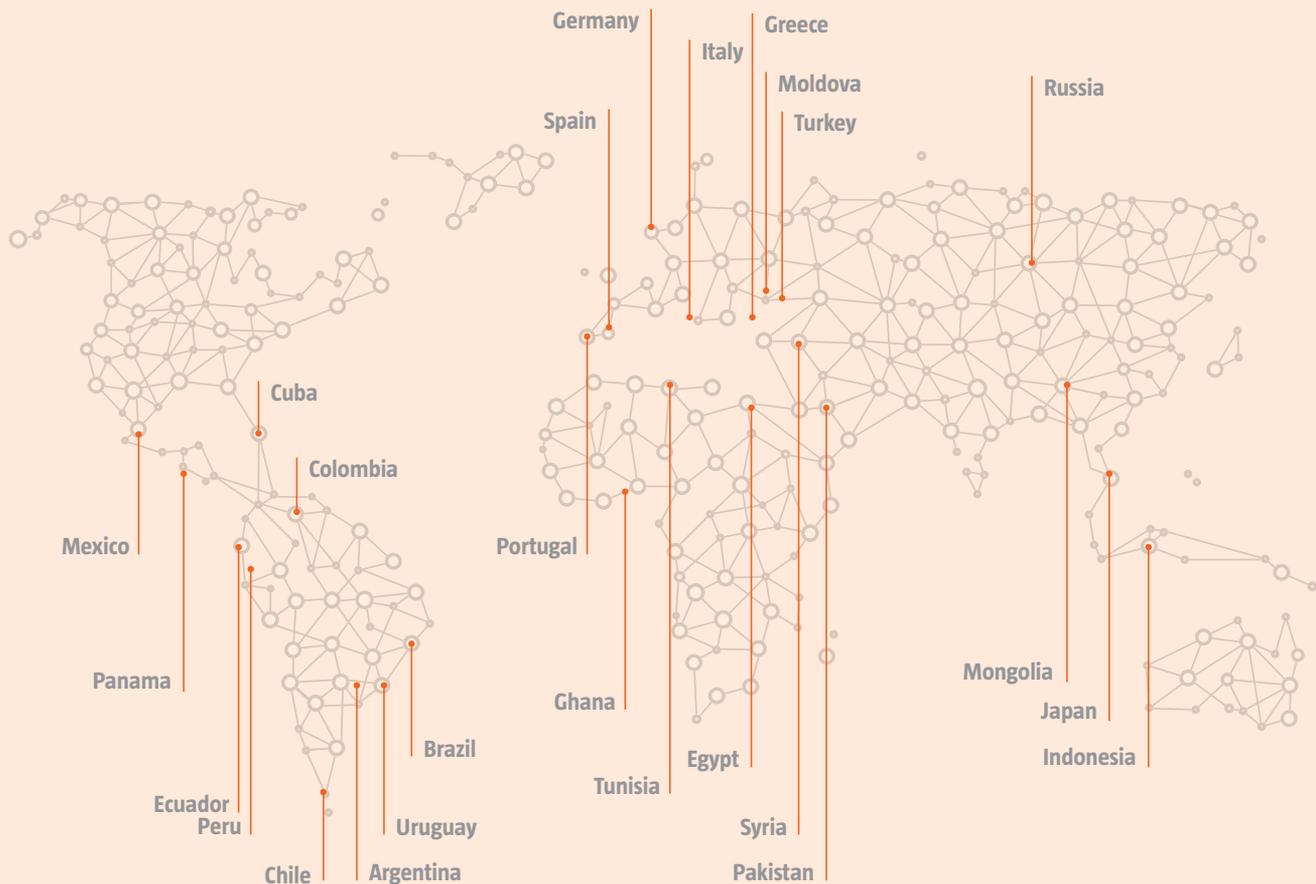
# A team of excellence

The center has a high transnational capacity thanks to a multidisciplinary team made up of more than 100 members including specialists of fetal medicine, cardiology, neurodevelopment and reproductive medicine, and also biologists, pharmacists, bioengineers, epidemiologists and statisticians. Together we aim to achieve highly competitive research in fetal development, both at the physiological and pathological level. The team is led by Eduard Gratacós, together with Fàtima Crispi as the scientific coordinator. In addition, each research line has its own scientific director and the management of the entire center is carried out by an independent unit.



**PROFESSIONALS**  
from different nationalities

**26**



**Multidisciplinary team**

82 Women | 22 Men



# Nature

**BCNATAL**

BCNatal was born as the result of the integration of Hospital Clínic and Hospital Sant Joan de Déu and has become one of the largest university centers for maternal-fetal and neonatal medicine in Europe. With more than 7.000 births, 3.500 consultations in fetal medicine, 2.000 fetal echocardiographies, 150 fetal surgeries and 500 cases of placental disease per year, the center is positioned as a world leader. It is specialized in fetal surgery, concentrating 85% of the interventions performed in Spain, many of them carried out to save the life of the baby. The most common surgery is the one that is done to the twins sharing placenta, which also receives patients from the rest of the world.

**IDIBAPS**

BCNatal Fetal Medicine Research Center is part of the Biomedical Research Institute 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 and more than 450 first-level researchers

that conform a privileged environment for innovation and clinical translation.

**FUNDACIÓ CLÍNIC & FUNDACIÓ SANT JOAN DE DÉU**

The Clinic Foundation for Biomedical Research (FCRB) and Sant Joan de Déu Foundation offer administrative service and support to the researchers of the BCNatal Fetal Medicine Research Center. FCRB also provides administrative management to IDIBAPS.

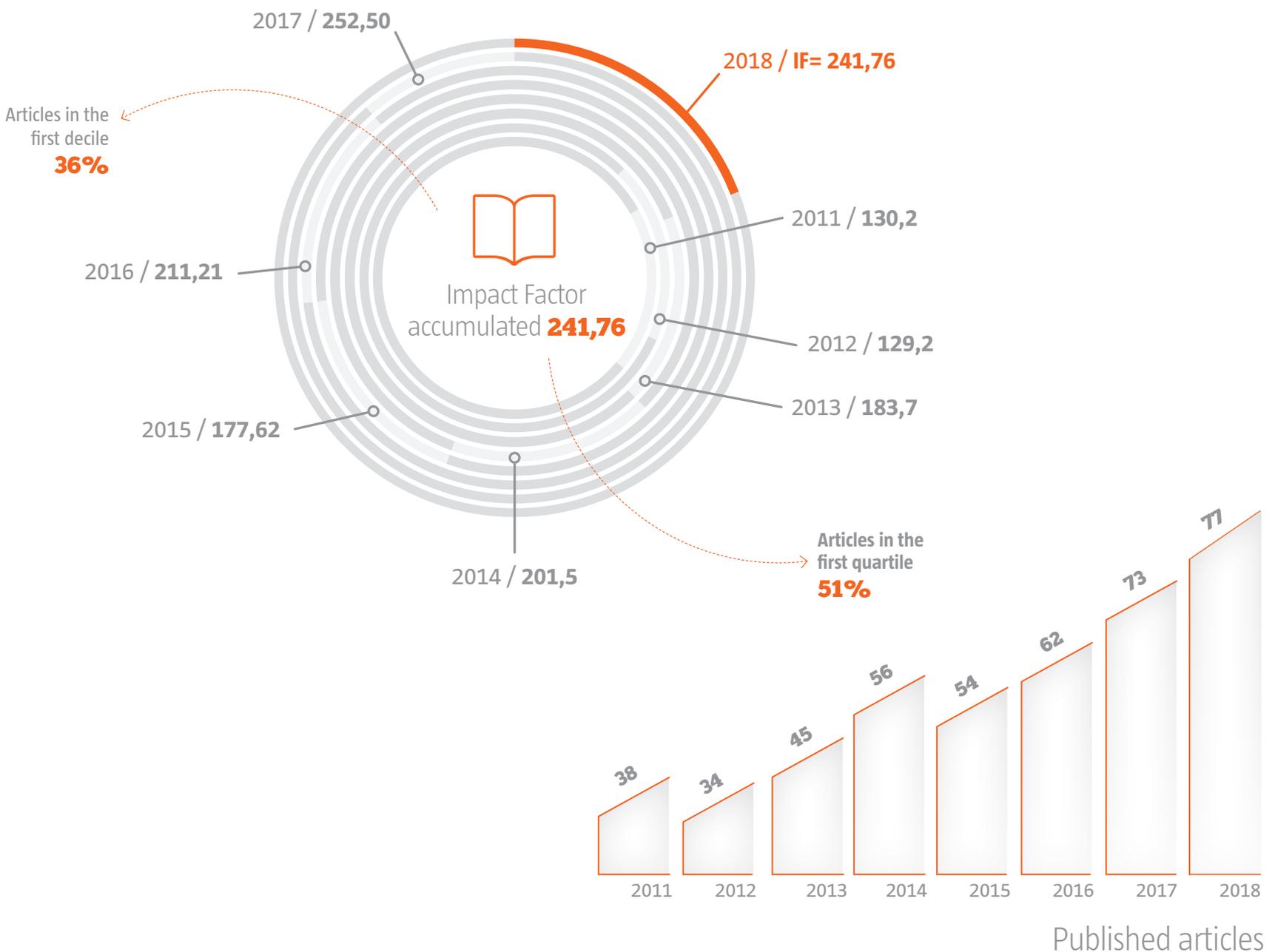
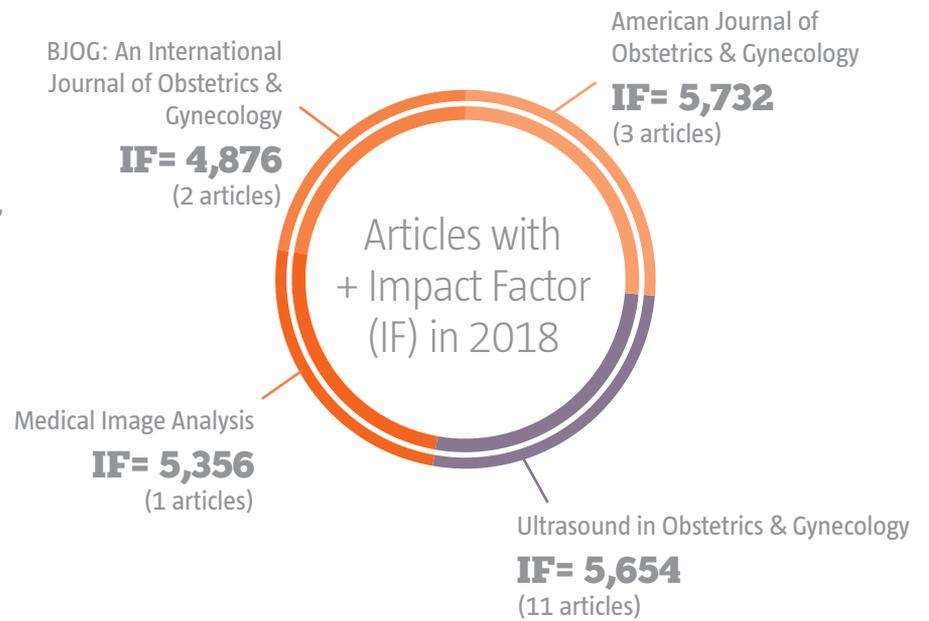
**UNIVERSITAT DE BARCELONA**

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 programme in Fetal Medicine, Erasmus FetalMed-PhD, thanks to the collaborations between the researchers of the group and UB.

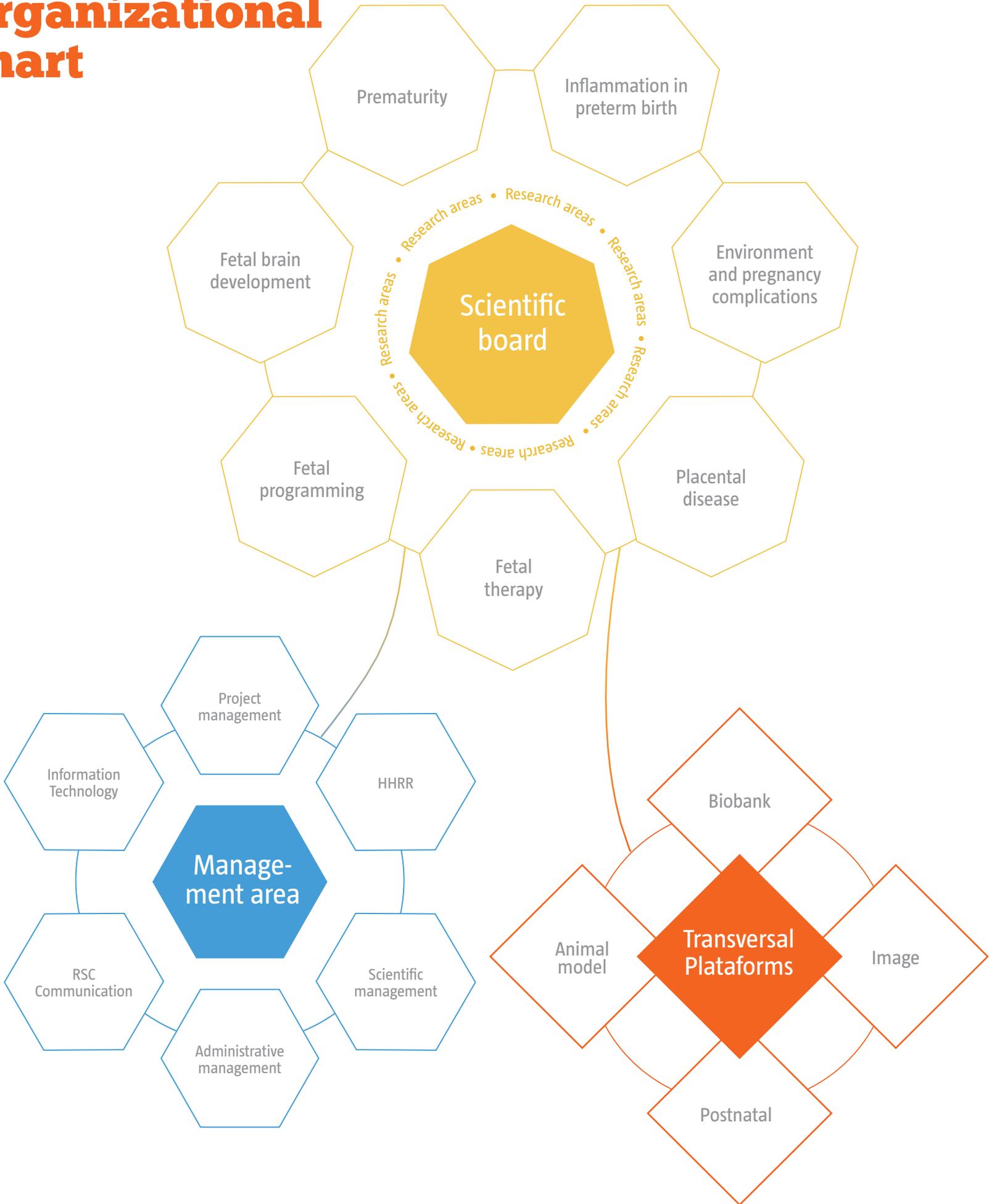


# Scientific results

In the last 10 years the group has published more than 450 articles, directed more than 40 doctoral theses and has been awarded with more than 58 national and international projects, financed by prestigious institutions such as the CELLEX private foundation, Cerebra foundation or the Obra Social "la Caixa".



# 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 from before birth. These are the key dates of the Fetal Medicine Research Center, from the beginning to the present.



**2005**

## Our beginning

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



**2007**

## Focused on fetal cardiology and neurodevelopment

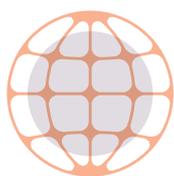
We develop innovative technologies that allow us to understand how the brain and heart are reprogrammed in fetal life.



**2009**

## Our scientific production grows

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



**2013**

## First specialized European doctorate

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



**2013**

## BCNatal, a reference center in pregnancy

The consortium formed by the Hospital Sant Joan de Deu Barcelona and the Hospital Clínic becomes a reference in the attention to mothers and babies and also when there are fetal complications. The coordinated assistance network allows us to respond to these situations quickly and safely.



**2014**

## Devoted to the society

We organize ludic-scientific sessions 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.



# 2018

**iNatal app is born,  
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 'laCaixa' and developed in collaboration with nutritionists from IDIBAPS and professionals from the institute of esMindfulness.

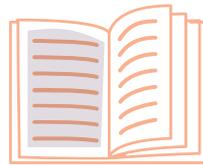
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## 2010

### **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 –means happiness in Basque- and becomes news 16 months later.



## 2011

### **We publish first annual report**

For the first time, we collect all our achievements in a memory 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.



## 2012

### **iNatal: the bridge between fetal medicine and the society**

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



## 2015

### **New research line: fetal therapy and surgery**

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



## 2016

### **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.



## 2017

### **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.



# Research

Fetal programming  
Fetal brain development  
Prematurity  
Inflammation in preterm birth  
Fetal therapy  
Environment and pregnancy complications  
Placental disease  
Platforms  
Research management



# Research areas

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

## The fetus as a patient

In BCNatal Fetal Medicine Research Center we treat the fetus as a patient, to 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 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 6 areas that allow achieving a comprehensive study of the fetus and the mother**



Fetal programming



Fetal brain development



Prematurity



Inflammation in preterm birth



Fetal therapy



Environment and pregnancy complications



Placental disease

# Fetal programming



Understanding better 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.

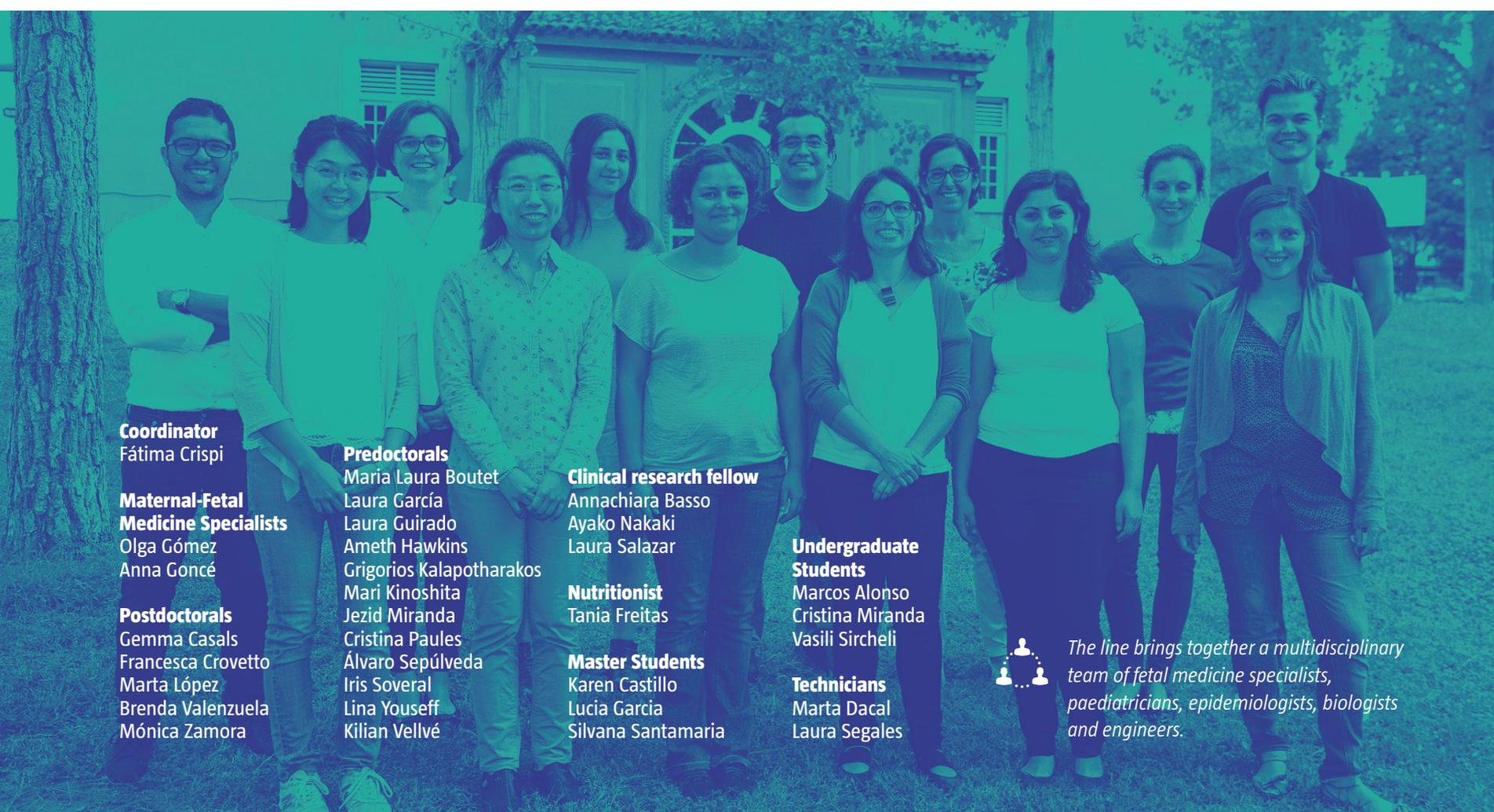
## IS IT POSSIBLE TO IMPROVE THE PROGNOSIS OF BABIES WITH FETAL COMPLICATIONS?

Longitudinal studies, combined with animal and computational models, will allow us to develop new therapies that improve the prognosis of babies who experience some of these complications. For this purpose, we must



### 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.*



**Coordinator**  
Fátima Crispi

**Maternal-Fetal Medicine Specialists**  
Olga Gómez  
Anna Goncé

**Postdoctorals**  
Gemma Casals  
Francesca Croveto  
Marta López  
Brenda Valenzuela  
Mónica Zamora

**Predectorals**  
Maria Laura Boutet  
Laura García  
Laura Guirado  
Ameth Hawkins  
Grigorios Kalapotharakos  
Mari Kinoshita  
Jezid Miranda  
Cristina Paules  
Álvaro Sepúlveda  
Iris Soveral  
Lina Youseff  
Kilian Vellvé

**Clinical research fellow**  
Annachiara Basso  
Ayako Nakaki  
Laura Salazar

**Nutritionist**  
Tania Freitas

**Master Students**  
Karen Castillo  
Lucía García  
Silvana Santamaria

**Undergraduate Students**  
Marcos Alonso  
Cristina Miranda  
Vasili Sircheli

**Technicians**  
Marta Dacal  
Laura Segales



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

characterize the phenotypic variability of small fetuses and understand cardiovascular diseases of prenatal origin in order to develop biomarkers for early diagnosis and monitoring of fetal cardiovascular remodelling, as well as new therapies that improve alterations affecting fetus' life. Today, we know that by improving maternal health we can have an influence on fetal development, thereby improving the prognosis of some fetal diseases.

## ★ IN 2018...

- (1) We have completed a large cohort study of small fetuses and evidenced placental aging and the release of exosomes, as well as altered maternal and fetal lipid profiles in these pregnancies.
- (2) Following previous studies about the effect of assisted reproductive techniques on cardiac function, we have reported their postnatal persistence and implications in twin pregnancies.
- (3) In addition, we have provided evidence of the harmful transgenerational effect of growth retardation.

## COHORT RECRUITMENT

- 1200 IUGR cases with matched controls to characterize phenotypic variability of small fetuses (PHENOMAPPING cohort).
- 500 adult IUGR cases with matched controls for the ADULTHEART study to assess the long-term cardiovascular impact of IUGR.
- We have recruited half of the patients necessary for a large randomized trial IMPACTBCN that studies how the interventions in pregnant women, such as introducing a balanced diet or reducing stress, can improve fetal growth.

## Publications

- ★ (1) **The impact of prenatal insults on the human placental epigenome: A systematic review.** Palma-Gudiel H, Císera F, Crispi F, Eixarch E, Fañanás L. **Neurotoxicology Teratology.** 66:80-93 (2018).
- **Macronutrient and fibre intake of young Spanish children with reference to their in utero growth status: Are they eating a healthy diet?** Nuruddin R, Urpi-Sarda M, Rodriguez-Lopez M, Garcia-Arenas D, Gratacos E, Crispi F, Acosta-Rojas R. **Journal of Paediatrics and Child Health.** 54(5):563-571 (2018).
- ★ (2) **Differential changes in myocardial performance index and its time intervals in donors and recipients of twin-to-twin Transfusion Syndrome before and after laser therapy.** Ortiz JU, Torres X, Eixarch E, Bennasar M, Cruz-Lemini M, Gómez O, Lobmaier SM, Martínez JM, Gratacós E, Crispi F. **Fetal Diagnosis and Therapy.** 44(4):305-310 (2018).
- **Long-term cardiovascular consequences of fetal growth restriction: biology, clinical implications, and opportunities for prevention of adult disease.** Crispi F, Miranda J, Gratacós E. **The American Journal of Obstetrics and Gynecology.** 218(2S):S869-S879 (2018).

- **Comparison of 2D versus M-mode echocardiography for assessing fetal myocardial wall thickness.** Sepúlveda-Martínez A, García-Otero L, Soveral I, Guirado L, Valenzuela B, Torres X, Rodriguez-Lopez M, Gratacos E, Gómez O, Crispi F. **The Journal of Maternal-Fetal & Neonatal Medicine.** 11:1-9 (2018).
- **Cardiac and placental mitochondrial characterization in a rabbit model of intrauterine growth restriction.** Guitart-Mampel M, Gonzalez-Tendero A, Niñerola S, Morén C, Catalán-Garcia M, González-

- Casacuberta I, Juárez-Flores DL, Ugarteburu O, Matalonga L, Cascajo MV, Tort F, Cortés A, Tobias E, Milisenda JC, Grau JM, Crispi F, Gratacós E, Garrabou G, Cardellach F. **Biochimica et Biophysica Acta.** 1862(5):1157-1167 (2018).
- **Remodeling of the cardiovascular circulation in fetuses of mothers with diabetes: A fetal computational model analysis.** Kulkarni A, Garcia-Cañadilla P, Khan A, Lorenzo JM, Beckerman K, Valenzuela-Alcaraz B, Cruz-Lemini M, Gomez O, Gratacos E, Crispi F, Bijmens B. **Placenta.** 63:1-6 (2018).

We want to understand and prevent long-term consequences of prenatal diseases

- **Characterizing cardiac dysfunction in fetuses with left congenital diaphragmatic hernia.** Cruz-Lemini M, Valenzuela-Alcaraz B, Granados-Montiel J, Martínez JM, Crispi F, Gratacós E, Cruz-Martínez R. **Prenatal Diagnosis.** 38(6):422-427 (2018).
  - **Placental exosomes profile in maternal and fetal circulation in intrauterine growth restriction - Liquid biopsies to monitoring fetal growth.** Miranda J, Paules C, Nair S, Lai A, Palma C, Scholz-Romero K, Rice GE, Gratacos E, Crispi F, Salomon C. **Placenta.** 64:34-43 (2018).
- ★ (3) **Premature placental aging in term small-for-gestational-age and fetal-growth-restricted fetuses.** Paules C, Dantas AP, Miranda J, Crovetto F, Eixarch E, Rodriguez-Sureda V, Dominguez C, Casu G, Rovira C, Nadal A, Crispi F, Gratacos E. **Ultrasound in Obstetrics & Gynecology.** 2018

- **Intrauterine growth restriction and later cardiovascular function.** Crispi F, Crovetto F, Gratacos E. **Early Human Development.** 126:23-27 (2018).
  - **Metabolic profiling and targeted lipidomics reveals a disturbed lipid profile in mothers and fetuses with intrauterine growth restriction.** Miranda J, Simões RV, Paules C, Cañueto D, Pardo-Cea MA, García-Martín ML, Crovetto F, Fuertes-Martin R, Domenech M, Gómez-Roig MD, Eixarch E, Estruch R, Hansson SR, Amigó N, Cañellas N, Crispi F, Gratacós E. **Scientific Reports Nature.** 8(1):13614 (2018).
- (3) **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.** [2018 Epub ahead or print].

- **Postnatal persistence of fetal cardiovascular remodeling associated with assisted reproductive technologies: a cohort study.** Valenzuela-Alcaraz B, Serafini A, Sepulveda-Martínez A, Casals G, Rodríguez-López M, Garcia-Otero L, Cruz-Lemini M, Bijmens B, Sitges M, Balasch J, Gratacos E, Crispi F. **BJOG.** 126(2):291-298 (2019).

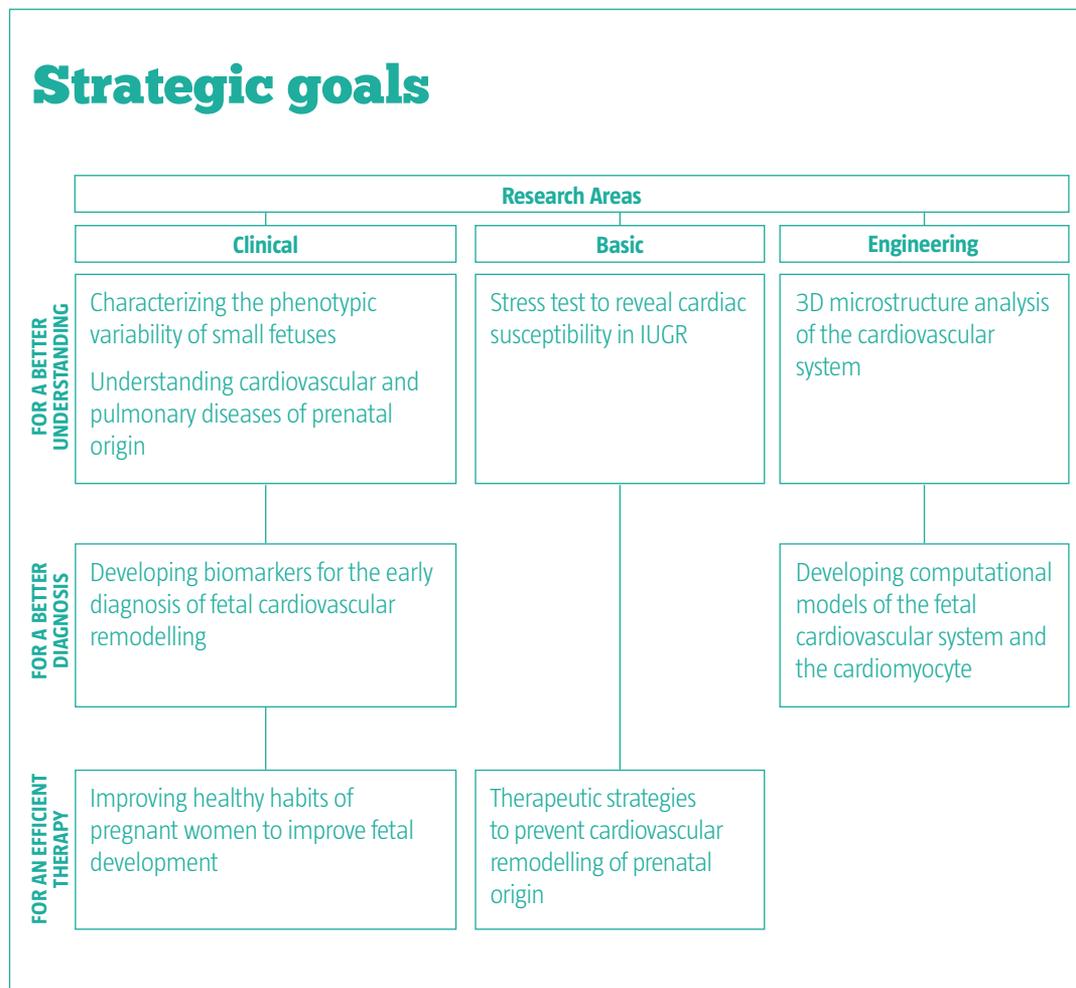
## Collaborations

### Nationals

- Universitat de Barcelona
- Universitat Pompeu Fabra
- IDIBAPS, Barcelona
- Universidad Rovira i Virgili, Tarragona
- 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

### Internationals

- Oxford University, UK
- The Labatt Family Heart Center, Division of Cardiology, Hospital for Sick Children and University of Toronto, Toronto, Canada
- Division of Pediatric Cardiology, Bronx Lebanon Hospital Center, Bronx, NY, USA
- Frauenklinik und Poliklinik, Technische Universität München, Munich, Germany
- Fetal Medicine Mexico, Universidad Nacional Autónoma de México (UNAM), Campus Juriquilla, Querétaro, Mexico
- Neonatologist, Monash Newborn, Monash Children’s Hospital, Monash University, Melbourne, VIC, 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





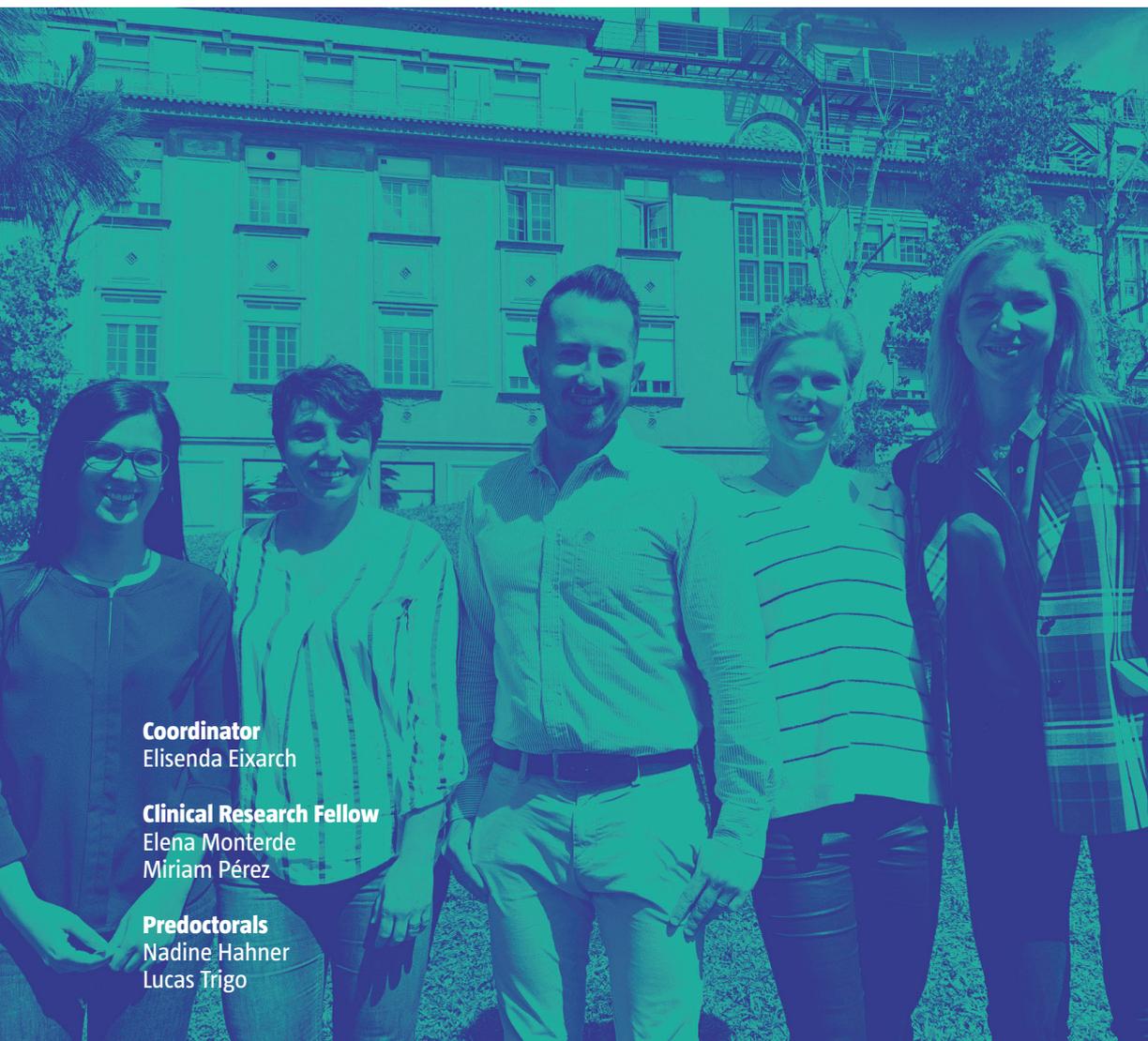
# Fetal brain development

We evaluate the 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.



**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.*



**Coordinator**  
Elisenda Eixarch

**Clinical Research Fellow**  
Elena Monterde  
Miriam Pérez

**Predotorials**  
Nadine Hahner  
Lucas Trigo

**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. Among them we can mention 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 situations such as intrauterine growth restriction, congenital heart diseases and ventriculomegaly, a condition in which the size of one or both lateral ventricles increase.



*In the line we gather fetal medicine specialists and engineers.*

## ★ IN 2018...

(1) We have shown that ventricular dilation may be related to the worst neurodevelopmental outcomes. Today we know that babies with ventriculomegaly have a lower cortical development during pregnancy. This finding, the result of the application of advanced ultrasound analysis in fetuses with isolated non-severe

ventriculomegaly, was published in 'Prenatal Diagnosis Journal'.

(2) Today we also know that it is possible to perform an automatic analysis of the cortical development during pregnancy by applying advanced 3D reconstruction techniques of the fetal brain, which will allow us to advance in this research.

## Publications

★ (1) **Cortical folding alterations in fetuses with isolated non-severe ventriculomegaly.** Benkarim OM, Hahner N, Piella G, Gratacos E, González Ballester MA, Eixarch E, Sanroma G. **Neuroimage Clinical.** 18:103-114 (2018).

★ (2) **Altered cortical development in fetuses with isolated non-severe ventriculomegaly assessed by neurosonography.** Hahner N, Puerto B, Perez-Cruz M, Policiano C, Monterde E, Crispi F, Gratacos E, Eixarch E. **Prenatal Diagnosis.** 38(5):365-375 (2018).

• **Learning to combine complementary segmentation methods for fetal and 6-month infant brain MRI segmentation.** Sanroma G, Benkarim OM, Piella G, Lekadir K, Hahner N, Eixarch E, González Ballester MA. **Computerized Medical Imaging and Graphics.** 69:52-59 (2018).

• **Fetal cortical parcellation based on growth patterns.** Xia J, Zhang C, Wang F, Benkarim OM, Sanroma G, Piella G, González Ballester MA, Hahner N, Eixarch E, Shen D, Li G. **Proceedings IEEE International Symposium on Biomedical Imaging (ISBI).** 2018:696-699 (2018).

• **Patch spaces and fusion strategies in patch-based label fusion.** Benkarim OM, Piella G, Hahner N, Eixarch E, González Ballester MA, Sanroma G. **Computerized Medical Imaging and Graphics.** 71:79-89 (2019).

## Collaborations

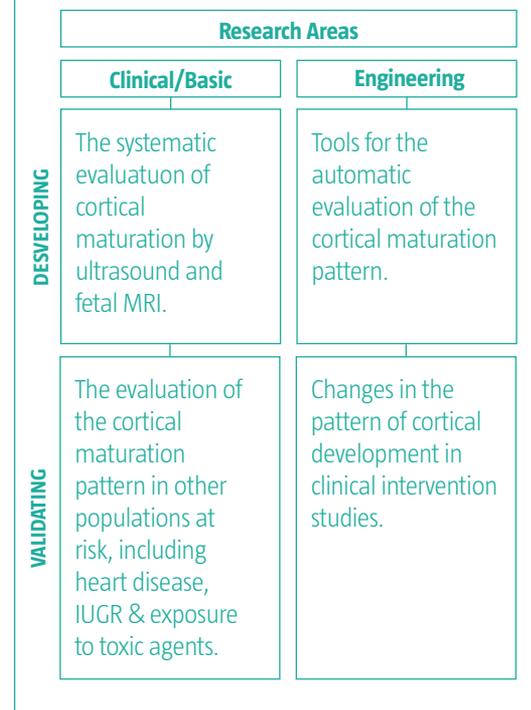
### Nationals

- Speech, Acquisition & Perception Group, Universitat Pompeu Fabra
- Simulation, Imaging and Modelling for Biomedical Systems, Universitat Pompeu Fabra
- CIBERSAM (grupo 8), Universitat de Barcelona

### Internationals

- Center for the Developing Brain, King's College, UK
- Ecole Polytechnique Federal, Laussane, Switzerland
- Hospital Universitaire Geneve, Switzerland

## Strategic goals



**We want to develop imaging biomarkers to identify the fetuses with neurodevelopmental alterations**

# Prematurity



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



## MONTSERRAT PALACIO

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

## 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 in their knowledge as well as in the improvement of their management, two of the main objectives of this line. Any progress that allows us to extend preterm pregnancies only two or three weeks more, would let us change the lives of hundred thousands of families.

## WHAT ADVANCES WOULD ALLOW TO REDUCE IT?

The line investigates non-invasive interventions that improve the decision-making capacity of professionals against the risk of premature 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 one is already applicable to the clinical practice and is also useful to better predict the outcome of labor induction. As for the second one, today we know that cervical texture may be of great help as a screening tool for the risk of prematurity in the general population.

**Coordinator**  
Montserrat Palacio

**Predotorals**  
Núria Lorente  
Ana Moreno  
Àlvaro Pérez

**Postdoctorals**  
Núria Baños



*The research line brings together fetal medicine specialists, as well as bioengineers and research technicians.*

## Publications

- ★ (1) **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. **Journal of Ultrasound in Medicine.** [2018 Epub ahead or print].
- ★ (2) **Quantitative analysis of cervical texture by ultrasound in mid-pregnancy and association with spontaneous preterm birth.** Baños N, Perez-Moreno A, Julià C, Murillo-Bravo C, Coronado D, Gratacós E, Deprest J, Palacio M. **Ultrasound in Obstetrics & Gynecology.** 51(5):637-643 (2018).
- **Mid-Trimester cervical consistency index and cervical length to predict spontaneous preterm birth in a high-risk population.** Baños N, Julià C, Lorente N, Ferrero S, Cobo T, Gratacos E, Palacio M. **AJP Reports.** 8(1):e43-e50 (2018).
- **Should previous preterm birth classification influence treatment of short cervix in a 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, Alfirevic Z. **Ultrasound in Obstetrics & Gynecology.** [2018 Epub ahead or print].
- **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.** [2018 Epub ahead or print].
- **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.** [2018 Epub ahead or print].
- **Use of hydrotherapy during labour: Assessment of pain, use of analgesia and neonatal safety.** KMallen-Perez L, Roé-Justiniano MT, Colomé Ochoa N, Ferre Colomat A, Palacio M, Terré-Rull C. **Enfermería Clínica.** 28(5):309-315 (2018).
- **Uterine cervical length measurement to reduce length of stay in patients admitted for**

## IN 2018...

- **We continued to develop prediction tools based on the quantitative analysis of lung and cervical texture:**

(1) The tool used for the analysis of fetal lung texture is being automated and has been shown to be robust.

(2) Today we know that cervical texture may be useful as a screening tool for the risk of prematurity in the general population..

- The multicentric clinical trial on the impact of the detection and early treatment of asymptomatic carriers of bacterial vaginosis on the preterm delivery rate has been cancelled as a result of the publication of the PREMEVA study, which demonstrates that the screening of vaginosis is not beneficial.

**threatened preterm labor: a randomized trial.** Palacio M, Caradeux J, Sánchez M, Cobo T, Figueras F, Coll O, Gratacós E, Cararach V. **Fetal Diagnosis and Therapy.** 43(3):184-190 (2018).

- **Cervical Alpha-Actinin-4 Is upregulated in women with threatened preterm labor and microbial invasion of the amniotic cavity.** Cobo T, Palacio M, Grande M, Sánchez-García AB, Estanyol JM, López M, Bosch J, Martí C, Gratacós E. **Fetal Diagnosis and Therapy.** 44(1):36-43 (2018).
- **Contribution of amniotic fluid along gestation to the prediction of perinatal mortality in women with early preterm premature rupture of membranes.** Cobo T, Munrós J, Ríos J, Ferreri J, Migliorelli F, Baños N, Gratacós E, Palacio M. **Fetal Diagnosis and Therapy.** 43(2):105-112 (2018).
- **Mid-trimester sonographic cervical consistency index to predict spontaneous preterm birth in a**

**low-risk population.** Baños N, Murillo-Bravo C, Julià C, Migliorelli F, Perez-Moreno A, Ríos J, Gratacós E, Valentin L, Palacio M. **Ultrasound in Obstetrics & Gynecology.** 51(5):629-636 (2018).

## Collaborations

### Nationals

- Doctorats Industrials
- Instituto de Salud Carlos III (ISCIII)

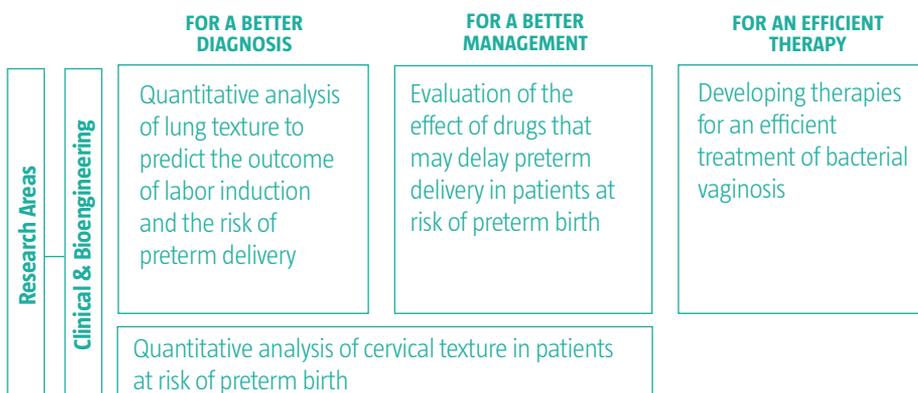
### Internationals

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

### Companies:

- Transmural Biotech, Spain
- Laboratorio Reig-Jofre, Spain

## Strategic goals



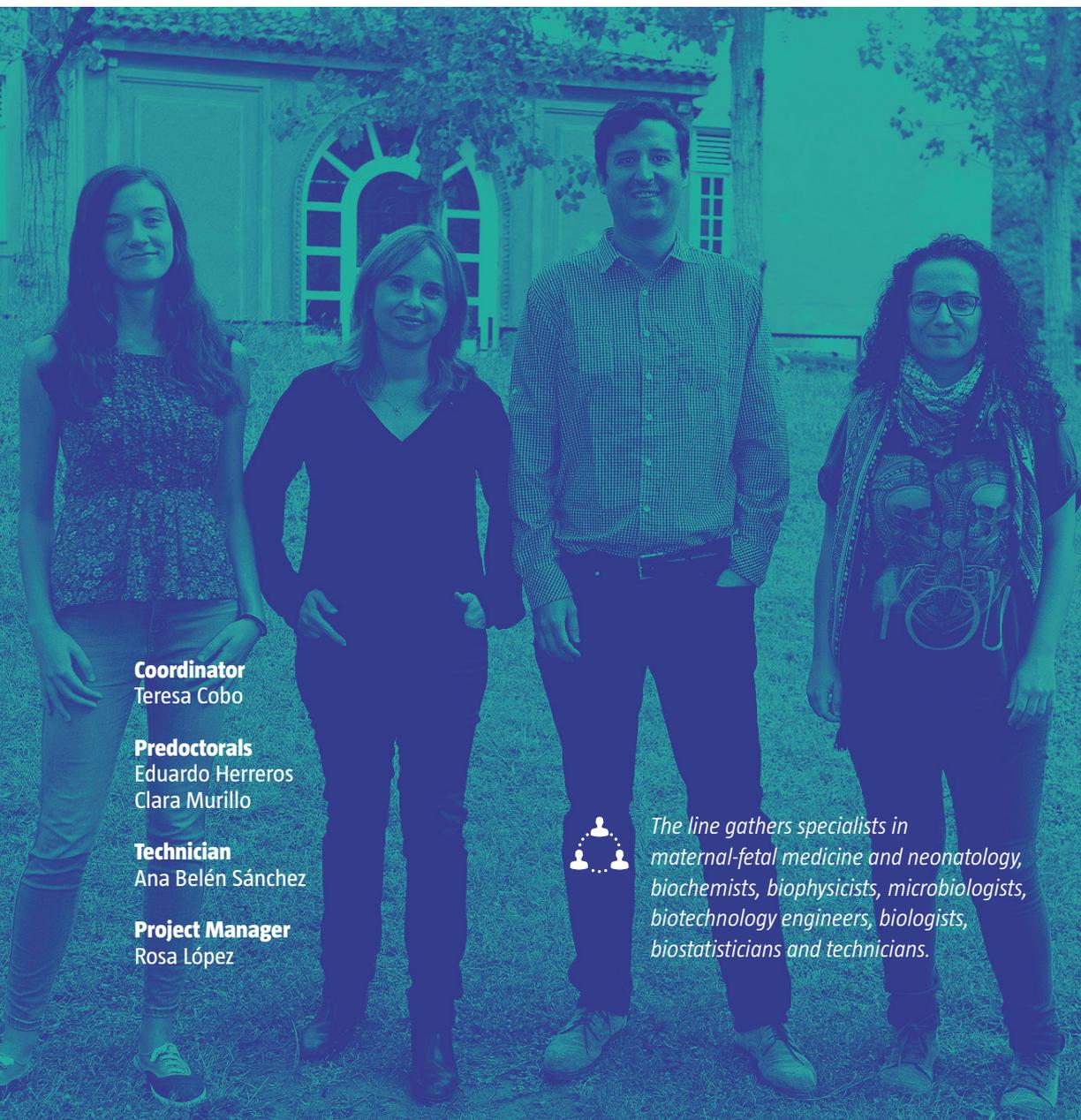
# Inflammation in preterm birth

We want to predict intraamniotic infection or inflammation in women at risk of preterm labor using rapid and non-invasive diagnostic tools to minimize the impact on the newborn.



## TERESA COBO

*Coordinator of the research line. Specialist in Prematurity at BCNatal. Cofounder of Compartim, support group for perinatal loss. Lecturer in specialized courses of Fetal I+D Education Barcelona.*



**Coordinator**  
Teresa Cobo

**Predotorials**  
Eduardo Herreros  
Clara Murillo

**Technician**  
Ana Belén Sánchez

**Project Manager**  
Rosa López



*The line gathers specialists in maternal-fetal medicine and neonatology, biochemists, biophysicists, microbiologists, biotechnology engineers, biologists, biostatisticians and technicians.*

## WHY DO WE STUDY THE INFECTION OF THE AMNIOTIC LIQUID?

Subclinical intraamniotic 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 (through samples such as the cervicovaginal fluid) that allow a better clinical management at the patient's bedside.

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

In fact, we lead 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, or photonics.

## We have observed that intraamniotic inflammation is a risk factor for the neurodevelopment of extreme premature

### Publications

★ **Interleukin-6 measured using the automated electrochemiluminescence immunoassay method for the identification of intra-amniotic inflammation in preterm prelabor rupture of membranes.** Musilova I, Andrys C, Holeckova M, Kolarova V, Pliskova L, Drahosova M, Bolehovska R, Pilka R, Huml K, Cobo T, Jacobsson B, Kacerovsky M. **The Journal of Maternal-Fetal & Neonatal Medicine.** [2018 Epub ahead of print].

★ **The association between selected mid-trimester amniotic fluid candidate proteins and spontaneous preterm delivery.** Hallingström M, Cobo T, Kacerovsky M, Skogstrand K, Hougaard DM, Holst RM, Tsiartas P, Bullarbo M, Carlsson Y, Nilsson S, Jacobsson B. **The Journal of Maternal-Fetal & Neonatal Medicine.** 10:1-10 (2018).

• **Noninvasive sampling of the intrauterine environment in women with preterm labor and intact membranes.** Cobo T, Kacerovsky M, Jacobsson B. **Fetal Diagnosis and Therapy.** 43(4):241-249 (2018).

### Collaborations

#### Nationals

- Centro de Investigación Príncipe Felipe de Valencia (Antonio Pineda)
- Instituto de Ciencias Fotónicas (ICFO) (Valerio Pruneri / Romain Quidant)
- Departamento de Bioquímica y Biomedicina Molecular de la Universidad de Barcelona (Marta Cascante)
- Departamento de Biotecnología del Instituto de Agroquímica y Tecnología de Alimentos (IATA) perteneciente a la Agencia Estatal Consejo Superior de Investigaciones Científicas (CSIC) (M. Carmen Collado)
- Plataforma de Bioestadística del IDIBAPS (José Ríos)

#### Internationals

- University of Gothenburg, Sweden (Bo Jacobsson)
- University Hospital Hradec Kralove, Czech Republic (Marian Kacerovsky)

#### Companies

- Hologic, USA
- Medix Biochemica, Finland

### ★ IN 2018...

- We have strengthened our collaboration with other research groups to deepen the development of a robust, non-invasive diagnostic tool applicable in any sanitary environment (hospital or not) to detect intraamniotic infection/inflammation in vaginal discharge in women at risk of premature birth.
- We have collaborated with companies, such as HOLOGIC in the 'SCUBA' clinical project that aims to identify intraamniotic infection/inflammation in women at risk of premature birth by determining proteins in the vaginal discharge. Likewise, we signed an agreement with the MEDIX Biochemica Industry to test a rapid device that measures the MMP-8 protein (intraamniotic inflammation marker) in the amniotic fluid in women at risk of premature birth.
- Thanks to an agreement with the Department of Biochemistry of Hospital Clínic, we have carried out the necessary experiments to implement the use of IL-6 in amniotic fluid at the clinical level in women at risk of premature birth, scheduled for 2019. This will allow the personalization of patient management (hospital admission, antibiotics, etc.).

## Strategic goals

		Research Areas	
		Clinical	Basic
FOR A BETTER DIAGNOSIS		To individualize the clinical management of women at risk of preterm birth by studying intraamniotic infection/inflammation.	To advance in the development of a non-invasive clinical solution to diagnose intraamniotic 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 intraamniotic infection/inflammation at the cardiovascular, neurological and neurodevelopmental levels, in the fetus, newborn, 6 months and 1 year of life.	

### "AJUDAS JOSEP FONT" AWARD FROM HOSPITAL CLÍNIC

- The project "Impact of the threat of premature birth and premature rupture of membranes on fetal and neonatal neurodevelopment and cardiovascular system. Influence of intraamniotic inflammation", that is developed by Clara Murillo, has received the "Ajudas Josep Font" award from Hospital Clínic.

# Fetal therapy



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 reason 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 (IUGR). Before applying these therapies to clinical practice, we evaluate their effects in animal models of IUGR.

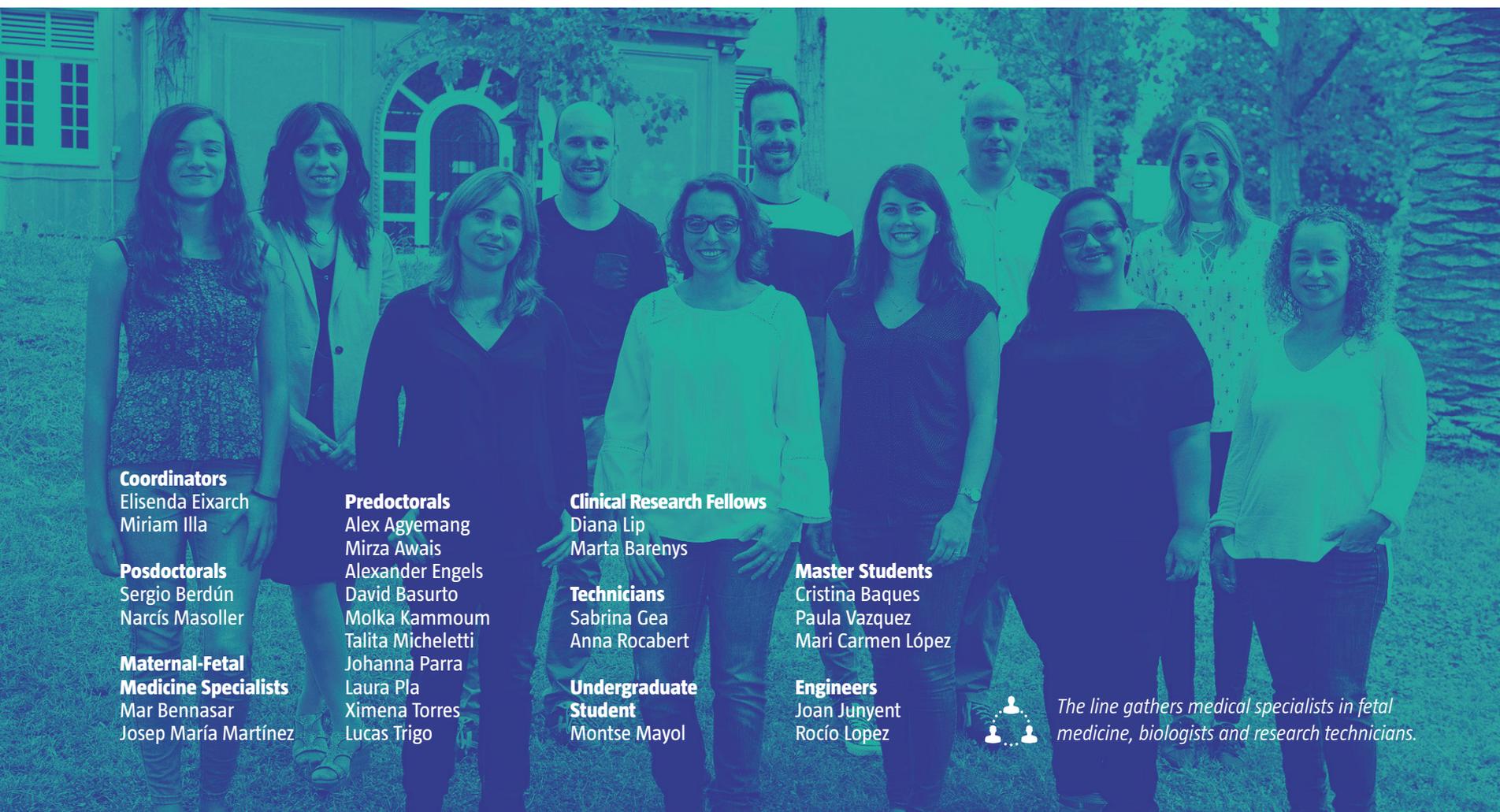
## WHAT WILL TECHNOLOGICAL ADVANCES ALLOW IN FETAL SURGERY?

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. 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 the problems that have no solution at the moment. The use of ex vivo and experimental models is key to achieving our objectives.



### ELISENDA EIXARCH Y MIRIAM ILLA

*Coordinators of the research line. Maternal-Fetal Medicine Specialists at BCNatal. Lecturers in specialized courses of Fetal I+D Education Barcelona.*



#### Coordinators

Elisenda Eixarch  
Miriam Illa

#### Postdoctorals

Sergio Berdún  
Narcís Masoller

#### Maternal-Fetal Medicine Specialists

Mar Bennasar  
Josep María Martínez

#### Predotorals

Alex Agyemang  
Mirza Awais  
Alexander Engels  
David Basurto  
Molka Kammoum  
Talita Micheletti  
Johanna Parra  
Laura Pla  
Ximena Torres  
Lucas Trigo

#### Clinical Research Fellows

Diana Lip  
Marta Barenys

#### Technicians

Sabrina Gea  
Anna Rocabert

#### Undergraduate Student

Montse Mayol

#### Master Students

Cristina Baques  
Paula Vazquez  
Mari Carmen López

#### Engineers

Joan Junyent  
Rocío Lopez



*The line gathers medical specialists in fetal medicine, biologists and research technicians.*

## Publications

- ★ **Early environmental enrichment enhances abnormal brain connectivity in a rabbit model of Intrauterine Growth Restriction.** Illa M, Brito V, Pla L, Eixarch E, Arbat A, Batallé D, Muñoz-Moreno E, Crispí F, Udina E, Figueras F, Ginés S, Gratacós E. *Fetal Diagnosis and Therapy*. 44(3):184-193 (2018).
- ★ **Nutritional intra-amniotic therapy increases survival in a rabbit model of fetal growth restriction.** Gümüs HG, Illa M, Pla L, Zamora M, Crispí F, Gratacós E. *PLoS One*. 13(2):e0193240 (2018).
- **Genetic profile of isolated congenital diaphragmatic hernia revealed by targeted next generation sequencing.** Kammoun M, Souche E, Brady P, Ding J, Cosemans N, Gratacós E, Devriendt K, Eixarch E, Deprest J, Vermeesch JR. *Prenatal Diagnosis*. 38(9):654-663 (2018).
- **Assessment of prenatal cerebral and cardiac metabolic changes in a rabbit model of fetal growth restriction based on 13C-labelled substrate infusions and ex vivo multinuclear HRMAS.** Simões RV, Cabañas ME, Loreiro C, Illa M, Crispí F, Gratacós E. *PLoS One*. 13(12):e0208784 (2018).
- **Fetal MRI Synthesis via balanced auto-encoder based generative adversarial networks.** Torrents J, Piella G, Masoller N, Gratacós E, Eixarch E, Ceresa M, Ballester MAG. *Conference proceedings: IEEE Engineering in Medicine and Biology Society*. 2018:2599-2602 (2018).
- **Segmentation and classification in MRI and US fetal imaging: Recent trends and future prospects.** Torrents J, Piella G, Masoller N, Gratacós E, Eixarch E, Ceresa M, Ballester. *Medical Image Analysis*. 51:61-88 (2019).
- **Consensus definition and essential reporting parameters of selective fetal growth restriction in twin pregnancy: a Delphi procedure.** Khalil A, Beune I, Hecher K, Wynia K, Ganzevoort W, Reed K, Lewi L, Oepkes D, Gratacós E, Thilaganathan B, Gordijn SJ. *Ultrasound in Obstetrics & Gynecology*. 53(1):47-54 (2018).
- **Fetoscopic endoluminal tracheal occlusion and reestablishment of fetal airways for congenital**

## ★ IN 2018...

- We have shown that the administration of Lactoferrin and DHA during gestation and lactation reduces the negative effects on brain development, secondary effects of IUGR, in animal models.
- We have described, for the first time in an experimental setting, the positive effects of postnatal stimulation both on cerebral structure and function.
- We have developed a surgical planning system based on 3D reconstruction that allows us to improve the accuracy of the surgeries in twin-to-twin transfusion syndrome.
- We have developed the first prototype of the membrane sealing system that has proven to work well in ex vivo models.

**diaphragmatic hernia.** Van der Veecken L, Russo FM, De Catte L, Gratacós E, Benachi A, Ville Y, Nicolaidis K, Berg C, Gardener G, Persico N, Bagolan P, Ryan G, Belfort MA, Deprest J. *Gynecological Surgery*. 15(1):9 (2018).

## Collaborations

### Nationals:

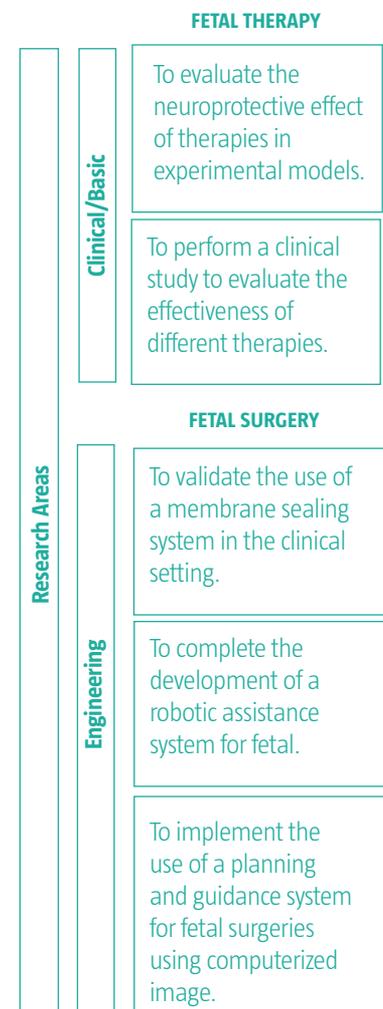
- Universitat Pompeu Fabra
- Instituto de Ciencias Fotónicas (ICFO)
- Instituto de Bioingeniería de Cataluña (IBEC)
- Institut Químic de Sarrià (IQS)
- Departamento de Biología Celular, Inmunología y Neurociencias de la Universitat de Barcelona (UB)

### Internationals

- University Hospitals Leuven, Belgium
- Institute of Mechanical Systems, Switzerland
- Leibniz Research Institute for Environmental Medicine, Germany
- University of São Paulo, Brazil

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

## Strategic goals



# 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.



**LOLA GÓMEZ-ROIG**

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

**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.



**Coordinator**  
Lola Gómez-Roig

**Postdoctorals**  
Silvia Ferrero  
Edurne Mazarico  
Miriam Perez

**Predocorals**  
Laura Almeida  
Marc Cahuana  
Paz Ahumada

**Clinical Research Fellow**  
Giulia Casu  
Marta Muniesa

**Technician**  
Erica Muñoz Sanz



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

### 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 IUGR.

### SPECIAL ATTENTION IS PAID TO THE EFFECTS OF ALCOHOL CONSUMPTION DURING PREGNANCY, WHAT ARE THE NEXT STEPS?

Our previous research indicates an incipient alcohol consumption in pregnant women. That is why we are carrying out a study to evaluate the effectiveness of an intervention program based on motivational interviewing during pregnancy. Our objective? Decreasing alcohol consumption during pregnancy, as well as the deleterious effects on perinatal and infant health associated with prenatal alcohol exposure.

### ★ IN 2018...

- (1) We have published an article evidencing the serious problem of alcohol consumption during pregnancy. In this study, we detected the presence of ETG (a metabolite of alcohol) in the hair of a significant number of pregnant women. For this reason, in 2018 we initiated an intervention study in order to reduce alcohol consumption in pregnant women.
- We have participated in the “BiSC” (Barcelona Life Study Cohort) study, a collaborative project of ISGlobal (Barcelona Institute for Global Health), BCNatal and Hospital de Sant Pau to understand the effect of air pollution on placental function, fetal growth, and the cardiovascular and cerebral development of the fetus. Currently, the group is in the recruitment phase of 600 volunteers who live in Barcelona and are in the first trimester of the pregnancy.

## Studying the influence of the environment on pregnancy will help us to reduce its effects in the prenatal and postnatal stages of the baby

### Publications

- ★ (1) **Differential correlations between maternal hair levels of tobacco and alcohol with fetal growth restriction clinical subtypes.** Sabra S, Malmqvist E, Almeida L, Gratacos E, Gomez Roig MD. *Alcohol*. 70:43-49 (2018).
- ★ **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. *The Journal of Maternal-Fetal & Neonatal Medicine*. 18:1-7 (2018).
- Maternal hair and neonatal meconium to assess gestational consumption and prenatal exposure to drugs of abuse and psychoactive drugs.** Cortes L, Almeida L, Sabra S, Muniesa M, Busardo FP, Garcia-Algar O, Gomez-Roig MD. *Current Pharmaceutical Biotechnology*. 19(2):136-143 (2018).
- Estimated fetal weight percentile as a tool to predict collection of cord blood units with higher cellular content: implications for prenatal selection of cord blood donors.** Lin X, Torrabadella M, Amat L, Gómez S, Azqueta C, Sánchez M, Cuadras D, Martínez Lorenzo MJ, Brull JM, Gayà A, Cemborain A, Pérez Garcia C, Arroyo J, Querol S, Gómez Roig MD. *Transfusion*. 58(7):1732-1738 (2018).
- The effects of alcohol and drugs of abuse on maternal nutritional profile during pregnancy.** Sebastiani G, Borrás-Novell C, Casanova MA, Pascual Tutusaus M, Ferrero Martínez S, Gómez Roig MD, García-Algar O. *Nutrients*. 10(8) (2018).
- 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 MJ, Gómez-Roig MD, Escera C. *Hearing Research*. Epub 2018 Nov 9.

### Collaborations

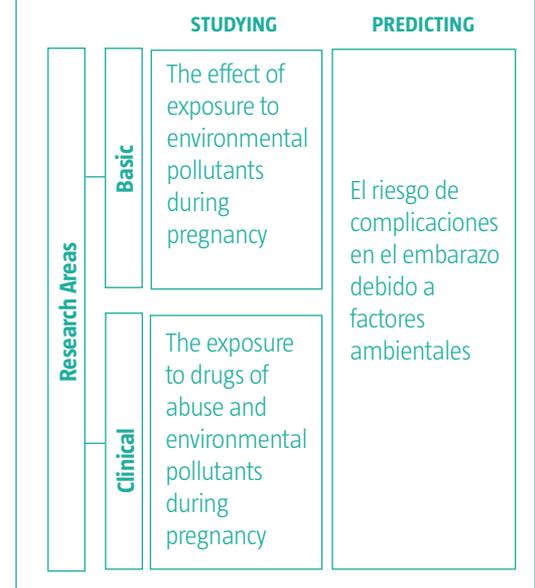
#### Internationals

- Icahn School of Medicine, Mount Sinai Hospital, New York, USA

#### Nationals

- Hospital de la Santa Creu i Sant Pau de Barcelona
- Instituto de Salud Global de Barcelona (ISGlobal)
- Instituto de Salud Carlos III (ISCIII)
- RD16/0022/0014, Red de Salud materno-infantil y del desarrollo, Instituto de Salud Carlos III (ISCIII)
- Institut de Recerca Sant Joan de Déu (IRSJD)
- Cognitive Neuroscience Department, Brainlab, University of Barcelona

### Strategic goals



# Placental disease

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



**FRANCESC FIGUERAS**

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



**Coordinator**  
Francesc Figueras

**Predotorals**  
Tri Rahmat Basuki  
Raigam Martínez  
Katerina Nedopekina  
Anna Peguero  
Marta Rial

**Clinical Research Fellow**  
Annalisa Cancemi  
Javier Caradeux  
Santiago Castelazo  
Javiera Alejandra Fuenzalida  
Fernanda Paz y Miño



*This line gathers fetal medicine specialists, psychologists and research technicians..*

**WHAT IS THE IMPACT OF THE INTRAUTERINE GROWTH RESTRICTION ON BABIES?**

Babies with IUGR have an increased risk of complications before and after birth. But that is not all; in addition, they may present neurodevelopmental alterations. These, although may be mild and may not have important sequelae, are more and more frequently recognized as family and social problems.

**WHY IS PREVENTION IMPORTANT?**

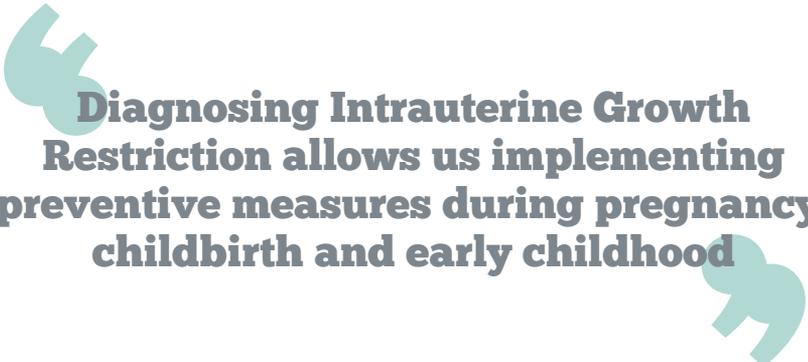
The evaluation of the longitudinal growth in pregnancy is key to making an accurate prediction of fetal growth restriction and its consequences. The correct definition and diagnosis of IUGR is especially important for fetal medicine, since it will allow implementing preventive measures during pregnancy and childbirth, as well as therapies during early childhood.

**ANOTHER AREA OF THIS LINE RESEARCH FOCUSES ON PREECLAMPSIA, ARE THERE NEW DEVELOPMENTS?**

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.

## ★ IN 2018...

- (1) We have mainly investigated the role of longitudinal growth assessment in the prediction of IUGR and its consequences, which led to the publication of 5 studies in indexed journals (which summarize 17 impact factor points) and the defense of 2 doctoral theses.
- (2) In addition, the research about the relationship between oocyte donation and preeclampsia has resulted in a doctoral thesis and the publication of 2 additional studies.

 **Diagnosing Intrauterine Growth Restriction allows us implementing preventive measures during pregnancy, childbirth and early childhood**

## Publications

- ★ (1) Longitudinal growth assessment for prediction of adverse perinatal outcome in fetuses suspected to be small-for-gestational age. Caradeux J, Eixarch E, Mazarico E, Basuki TR, Gratacos E, Figueras F. **Ultrasound in Obstetrics & Gynecology.** 52(3):325-331 (2018).
- ★ (2) Risk of fetal death in growth-restricted fetuses with umbilical and/or ductus venosus absent or reversed end-diastolic velocities before 34 weeks of gestation: a systematic review and meta-analysis. Caradeux J, Martinez-Portilla RJ, Basuki TR, Kiserud T, Figueras F. **American Journal of Obstetrics & Gynecology.** 218(2S):S774-S782.e21 (2018).
- Longitudinal assessment of abdominal circumference versus estimated fetal weight in the detection of late Fetal Growth Restriction. Basuki TR, Caradeux J, Eixarch E, Gratacós E, Figueras F. **Fetal Diagnosis and Therapy.** [2018 Epub ahead or print].
- Diagnosis and surveillance of late-onset fetal growth restriction. Figueras F, Caradeux J, Crispi F, Eixarch E, Peguero A, Gratacos E. **American Journal of Obstetrics & Gynecology.** 218(2S):S790-S802.e1 (2018).
- Evidence-based national guidelines for the management of suspected fetal growth restriction: comparison, consensus, and controversy. McCowan LM, Figueras F, Anderson NH. **American Journal of Obstetrics & Gynecology.** 218(2S):S855-S868 (2018).
- Added value of cerebro-placental ratio and uterine artery Doppler at routine third trimester screening as a predictor of SGA and FGR in nonselected pregnancies. Rial-Crestelo M, Martinez-Portilla RJ, Cancemi A, Caradeux J, Fernandez L, Peguero A, Gratacos E, Figueras F. **The Journal of Maternal-Fetal & Neonatal Medicine.** 4:1-7 (2018).
- Risk of pre-eclampsia after fresh or frozen embryo transfer in patients undergoing oocyte donation. Blazquez A, García D, Vassena R, Figueras F, Rodriguez A. **European Journal of Obstetrics & Gynecology and Reproductive Biology.** 227:27-31 (2018).
- Cerebroplacental ratio assessment in early labor in uncomplicated term pregnancy and prediction of adverse perinatal outcome: prospective multicenter study. Dall'Asta A, Ghi T, Rizzo G, Cancemi A, Aloisio F, Arduini D, Pedrazzi G, Figueras F, Frusca T. **Ultrasound in Obstetrics & Gynecology.** 53(4):481-487 (2019).
- Using cerebroplacental ratio in non-SGA infants to predict adverse perinatal outcome: caution is required. Kumar S, Figueras F, Ganzevoort W, Turner J, McCowan L. **Ultrasound in Obstetrics & Gynecology.** 52(4):427-429 (2018).
- 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; Fetal Growth Restriction Minimum Reporting Set Working Group. **Ultrasound in Obstetrics & Gynecology.** [2018 Epub ahead or print].
- Risk of preeclampsia in pregnancies resulting from double gamete donation and from oocyte donation alone. Blazquez A, García D, Vassena R, Figueras F, Rodriguez A. **Pregnancy Hypertension.** 13:133-137 (2018).
- Maternal and perinatal outcomes after elective labor induction at 39 weeks in uncomplicated singleton pregnancies: a meta-analysis. Sotiradis A, Petousis S, Thilaganathan B,

Figueras F, Martins WP, Odibo AO, Dinas K, Hyett J. **Ultrasound in Obstetrics & Gynecology.** 53(1):26-35 (2018).

- **Study protocol for a randomised controlled trial: treatment of early intrauterine growth restriction with low molecular weight heparin (TRACIP).** Mazarico E, Peguero A, Camprubí M, Rovira C, Gomez Roig MD, Oros D, Ibáñez-Burillo P, Schoorlemmer J, Masoller N, Tàssies MD, Figueras F. **BMJ Open.** 8(10): e020501 (2018).
- **First-trimester and combined first- and second-trimester prediction of small-for-gestational age and fetuses with late growth restriction.** Sotiriadis A, Figueras F, Eleftheriades M, Papaioannou GK, Chorozioglou G, Dinas K, Papantoniou N. **Ultrasound in Obstetrics & Gynecology.** 53(1):55-61 (2019).
- **First trimester screening for early and late preeclampsia based on maternal characteristics, biophysical parameters, and angiogenic factors.** Figueras F. **Prenatal Diagnosis.** 8(11):892 (2018).
- **Added value of chromosomal microarray analysis above conventional karyotyping in stillbirth work-up: a systematic review and meta-analysis. Review.** Martinez-Portilla RJ, Pauta M, Hawkins-Villarreal A, Rial-Crestelo M, Paz Y Miño F, Madrigal I, Figueras F, Borrell A. **Ultrasound in Obstetrics & Gynecology.** [2018 Epub ahead or print].
- **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. **BJOG.** [2018 Epub ahead or print].
- **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-Garcia S, Serrano-Diaz LC, Figueras F. **Journal of Diabetes Research.** 2018:4986735 (2018).

## Collaborations

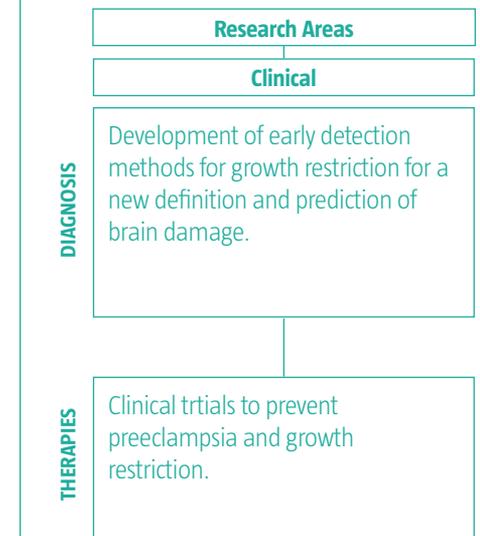
### Nationals

- EUGIN Clinic, Barcelona, Spain

### Internationales

- Aristotle University Medical School, Thessaloniki, Greece
- Lund University Hospital, 221 85 Lund, Sweden

## Strategic goals



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



# Platforms



**Scientific Coordinator**  
Fàtima Crispí

**Technical Coordinator**  
Miriam Osorio

**Research Technicians**  
Cristina Miranda  
Erica Muñoz  
Núria Rierola

## 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...) 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 the diagnostic possibilities and future therapies.

### ONLINE

At [fetalmedbarcelona.org/biobank](http://fetalmedbarcelona.org/biobank) you can order valuable maternal, placental and fetal samples that would otherwise be costly to obtain both economically and time wise.

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



## Animal model

**Scientific Coordinator**  
Miriam Illa

**Research Technician**  
Carla Loreiro



### WHAT DO WE DO?

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

**We give support to any research in fetal medicine requiring animal model experimentation**



**Scientific Coordinator and Head Nurse of BCNatal**  
Ángela Arranz

Mercedes Medeiros  
Rosa García  
Sandra León  
Sara Aceño  
Julia Prieto

**Technical support**  
Alba Camacho  
Paula Navarro  
Nadia Rojas  
Nathalia Torrico  
Manuela Mancebo

**Psychologists**  
Juana Cajiao  
Maite Mañosa  
Marta Bello  
Marta Ros

# Postnatal



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

**Postnatal support maintains the insight of quality and excellence**

**WHAT DO WE DO?**

Our nurses and psychologists are experts in neurodevelopment and they are specialized in carrying out a personalized follow-up of the patients and their babies at all times. Once the baby is born, they accompany families during magnetic resonance procedures or the

assessments of children’s capabilities using the Brazelton or Bayleys tests. These tests allow early identification of neurodevelopment delays in order to act as early as possible by applying the appropriate treatment in each case.

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



**Scientific Coordinator**  
Xavier Paolo Burgos

**Research Support**  
David Coronado  
Brenda Valenzuela  
Cora Roig Blay  
Claudia Gracia

# Image



**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.

# 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.



**LUIS ENCISO**  
Executive director



**MAITE AGUILERA**  
HHRR  
Coordinator



**MERCEDES ALONSO**  
Purchasing and administrative management



**ESTEFANIA CALLADO**  
Project Manager



**PERE LORENTE**  
Communication  
CSR



**ISIL TEKELI**  
Scientific  
Writer



**ESTER CARDET**  
Project  
Manager



**IDOIA BERAZA**  
Information  
Technology



**RAÚL BELLAHIZAD**  
Logistics

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

## Fields of action



### RESEARCH SUPPORT

Supporting the scientific activity of the researchers of the group and promote 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



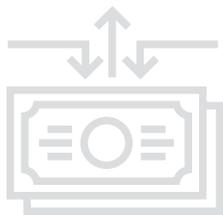
### COORDINATION

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



### GOOD PRACTICES

Ensuring ethics and the application of ethical principles in research



### FINANCE 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 into the society, the scientific community and the economic system

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 Carrier Development Plan, workshops and Christmas and summer events.

### JOURNAL CLUB

From the beginning of the team, 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, weekly discussions to see the progress of the group, and occasionally, to receive external researchers or experts in maternal-fetal medicine to discuss topics of general interest.

### PERSONAL CARRIER DEVELOPMENT PLAN

Another tool we have available to help researchers

evaluate their skills and interests is the Personal Carrier 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.

## IN 2018...

Among the invited speakers at the 2018 Journal Club, eminences from different fields of health, biomedical research and maternal-fetal medicine stand out.

- **Ignasi Labastida**, member of the Steering Committee of Info and Open Access Policy Group in LERU, vice president of the SPARC Europe Board and member of the Working Group on Open Science at CRUE. He came to explain the new Open Acces policy,

one of the strategic objectives of the H2020 Program of the European Community.

- **Thomas McElrath**, director of the Brigham & Women's Preterm Prevention Clinic in Boston (USA).

- **Liona Poon**, maternal-fetal medicine specialist at Imperial College Healthcare NHS Trust and King's College Hospital NHS Foundation Trust with professor KH Nicolaides as supervisor.

# R+D Projects

Research projects and grants 2018

Clinical transfer

Obra Social “la Caixa” Project

CEREBRA Project

CELLEX Project

# Research projects and grants

## ONGOING IN 2018

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

**Eduard Gratacós**

European Commission. Erasmus +

► 01/08/2013 - 31/10/2021

EVERREST - Does vascular endothelial growth factor gene therapy safely improve outcome in severe early-onset fetal growth restriction?

**Eduard Gratacós**

European Commission

► 01/01/2013 - 31/12/2018

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

**Eduard Gratacós**

Fundación privada CELLEX

► 04/01/2016 - 30/06/2019

Preventing the neurological and cardiovascular consequences of fetal diseases.

**Eduard Gratacós**

Obra Social 'la Caixa'

► 01/01/2015-31/12/2018

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**

Fundación CEREBRA

► 01/01/2014-31/12/2019

Impacto de la restricción de crecimiento intrauterino en la dinámica del remodelado cardiovascular en las diferentes etapas de la vida.

**Fàtima Crispi**

Instituto de Salud Carlos III (ISCIII)

► 01/01/2015 - 31/12/2018

Identificación de moduladores y dianas terapéuticas en el remodelado y enfermedad cardiovascular del adulto asociada a retraso de crecimiento intrauterino.

**Eduard Gratacós**

Instituto de Salud Carlos III (ISCIII)

► 01/01/2016 - 31/12/2018

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

**Francesc Figueras**

Instituto de Salud Carlos III (ISCIII)

► 01/01/2016 - 31/12/2018

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

**Teresa Cobo**

Instituto de Salud Carlos III (ISCIII)

► 01/01/2016 - 31/12/2018

Evaluación pronóstica de las cardiopatías congénitas desde la etapa prenatal mediante ecocardiografía avanzada y biomarcadores plasmáticos.

**Olga Gómez**

Instituto de Salud Carlos III (ISCIII)

► 01/01/2016 - 31/12/2018

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 - 31/12/2018

Valoración de la exposición prenatal a sustancias de abuso y tóxicos ambientales en fetos con retraso de crecimiento intrauterino y su

influencia en la patología placentaria.

**Maria Dolores Gómez-Roig, Laura Almeida**

Hospital Sant Joan de Déu - Esplugues HSJD

► 01/10/2015 - 30/09/2018

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 - 31/12/2019

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 - 31/12/2019

Beques Daniel Bravo per a estades curtes d'investigació biomèdica a l'estranger.

**Laura García**

Fundació Daniel Bravo

► 01/01/2018 - 31/12/2018

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**ONGOING RESEARCH**  
projects and grants

**MILIONS**  
euros invested in research  
projects in maternal-fetal  
medicine

1,8

## STARTED IN 2018

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

**Fàtima Crispi**

Instituto de Salud Carlos III (ISCIII)

► 01/01/2018 - 31/12/2021

Efectividad de la entrevista motivacional repetida durante el embarazo en el abandono del consumo de alcohol.

**Maria Dolores Gómez-Roig**

Instituto de Salud Carlos III (ISCIII)

► 01/01/2018 - 31/12/2020

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

## AWARDED IN 2018

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

**Eduard Gratacós**

Instituto de Salud Carlos III (ISCIII)

► 01/01/2019 - 31/12/2021

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

**Miriam Illa**

Instituto de Salud Carlos III (ISCIII)

► 01/01/2019 - 31/12/2021

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

**Eduard Gratacós**

Obra Social "LaCaixa"

► 01/01/2019 - 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 and that goes through the improvement of clinical practice in maternal-fetal medicine. Therefore, an important contribution of the team is the development of clinical guidelines and protocols. This activity allows us to integrate some of our research results into the clinical practice of maternal-fetal and neonatology medicine units, optimizing patient care and promoting the application of certain preventive measures and treatments in the healthcare.



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**CLINICAL GUIDES**

developed for health services since 2015

# Obra Social “LaCaixa” Project

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

## WHAT IS THE OBJECTIVE?

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

## HOW DO 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.



Obra Social “la Caixa”



[fetalmedbarcelona.org/lacaixa](http://fetalmedbarcelona.org/lacaixa)

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

## Fields of action



### FETAL NEURODEVELOPMENT

Our goal is to develop biomarkers that allow us to detect those fetuses with a brain development problem 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 programme 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 THE SOCIETY

We have developed a dissemination and social participation programme 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, brain injury occurs in prenatal life. Diagnosing and acting at that time, prevents and reduces its long-term impact.

## WHAT IS THE OBJECTIVE?

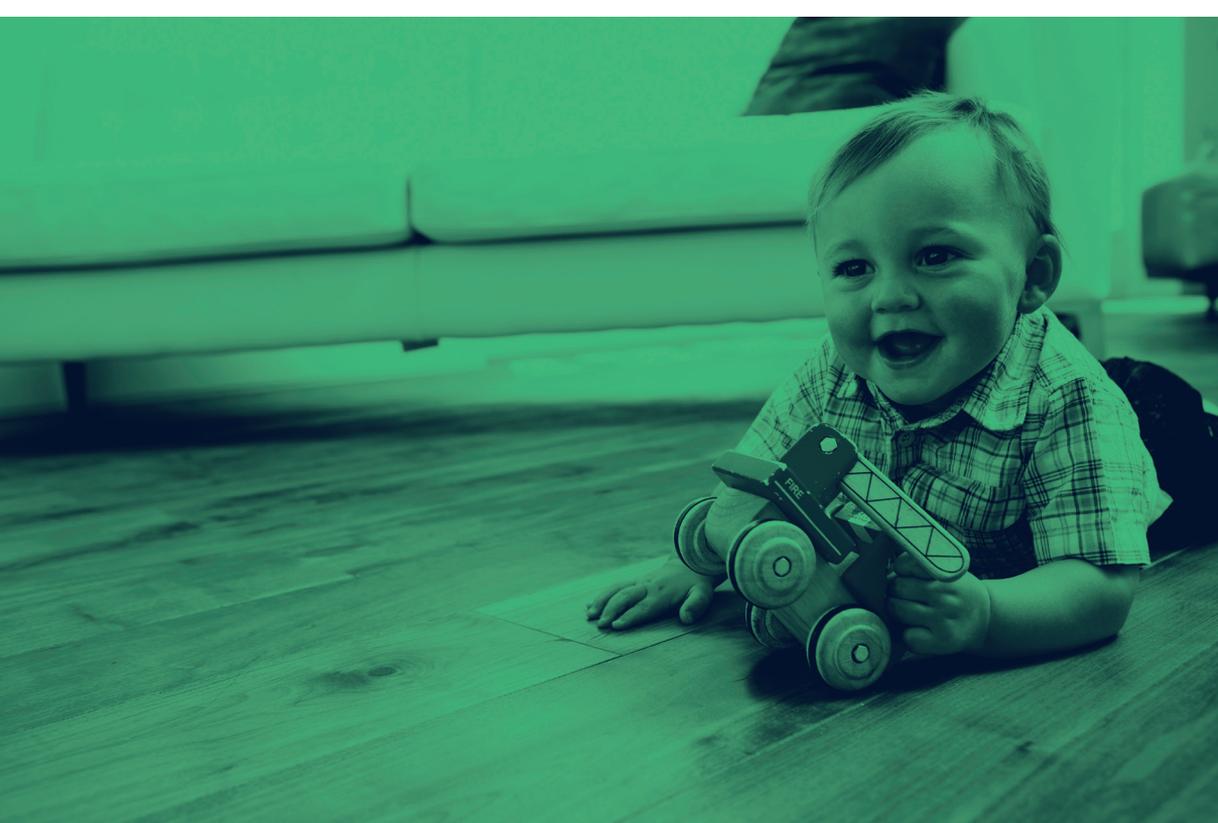
The possibility of diagnosing abnormal brain development in fetuses and newborns and implementing interventions to prevent or reduce their impact would represent a great advance in global public health. The main objective of this research program, and the main expected impact, is to reduce the prevalence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

## HOW DO WE DO THIS?

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



[fetalmedbarcelona.org/cerebra](http://fetalmedbarcelona.org/cerebra)



## 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 undergo growth restriction in the uterus.



### NEW BIOMARKERS

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



### NEW THERAPIES

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

# CELLEX project

We use bioengineering, miniaturization, photonic sciences and robotics to develop high precision technologies that allow making 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 DO WE DO THIS?

We have gathered scientist 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 Mr. 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 for achieving advances that would have been impossible without his strong support.

Fundació Privada  
**CELLEX**



[fetalmedbarcelona.org/cellex](http://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.



### 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.



### 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.



### 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.



# Scientific results

National and international congresses and courses  
Participation in congresses  
Academic output

# National and international congresses and courses



**Barcelona, Spain.** Scientific Session at Societat Catalana D'Obstetricia i Ginecologia. **January.** Organized by Societat Catalana D'Obstetricia i Ginecologia.

**Cairo, Egypt.** 4th Annual International Conference of Egyptian Fetal Medicine Foundation (AICFM 2018). **8-9 February.** Organized by EFMF.



**NATIONALS 50%**  
**INTERNATIONALS 50%**

**Lloret de Mar, Spain.** Advanced Maternal-Fetal Medicine Course. **4-9 March.** Organized by FMFB.

**Castelldefels, Spain.** 11th Annual CIBERER Meeting. **12-14 March.** Organized by CIBERER.

**Barcelona, Spain.** Curso Perfeccionamiento en Neonatología. **17-18 April.** Organized by SJD.

**Barcelona, Spain.** Course on Placental insufficiency and Prematurity. **3-4 May.** Organized by Vall d'Hebron.

**Edinburgh, Scotland.** 3rd European Spontaneous Preterm Birth Congress. **16-18 May.** Organized by University of Edinburgh.

**Murcia, Spain.** 26º Congreso Nacional de la Sección de Medicina Perinatal de la Sociedad Española de Ginecología y Obstetría. **24-26 May.** Organized by SEGO.

**Barcelona, Spain.** International Meeting of Congenital Diaphragmatic Hernia. **2-3 June.** Organized by La vida con HDC.

**Athens, Greece.** 17th World Congress in Fetal Medicine. **24-28 June.** Organized by FMF.

**Berlín, Germany.** 11th FENS Forum of Neuroscience. **7-11 July.** Organized by FENS.

**Barcelona, Spain.** 7th Workshop on Clinical Image-based Procedures: Translational Research in Medical Imaging (CLIP). **16 September.**

**Barcelona, Spain.** 3rd International Workshop on Reconstruction and Analysis of Moving Body Organs (RAMBO). **16 September.**

**Cartagena, Colombia.** International Congress in Maternal-Fetal Medicine. **20-24 September.** Organized by FMFB.

**Paris, France.** Ultrasound meets Magnetic Resonance. **27-29 September.** Organized by MCA.

**Milan, Italy.** 7th International Conference on Fetal Growth. **1-3 October.** Organized by Perinatal Institute & Lobardy Society of Obstetrics and Gynaecology.

**Palermo, Italy.** Curso "First Trimester, Fetal Heart, IUGR". **12-13 October.** Organized by SIEOG (Società Italiana Ecografia Ostetricia e Ginecologia).

**Singapore, Singapore Republic.** 28th World Congress on Ultrasound in Obstetrics and Gynecology. **20-24 October.** Organized by ISUOG.

**Mazatlán, Mexico.** 68 Congreso Mexicano de Obstetricia y Ginecología Femecog 2018. **11-15 November.** Organized by FEMECOG.

**Barcelona, Spain.** Course on Biomedical Research on Reproductive and Maternal-Fetal Medicine. **23 November.** Organized by FMFB.

**Londres, United Kingdom.** FMF Advances Course. **1-2 December.** Organized by FMF.

# Participation in congresses

## INVITED TALKS

RESEARCHER	TITLE	CONGRESS
Teresa Cobo	Infección e inflamación intraamniótica: ¿por qué identificarlas?	Scientific Session at Societat Catalana D'Obstetrícia i Ginecologia
	Rotura prematura de membranes, infecció i inflamació	Curso Perfeccionamiento en Neonatología
	Progesterona en la prevención del parto pretérmino	Curso Insuficiencia placentaria y prematuridad
Fàtima Crispi	FGR: Cardiovascular changes from fetal to adult life	17th World Congress in Fetal Medicine
Francesc Figueras	FGR: prediction and management	FMF Advances Course
Elisenda Eixarch	Advanced imaging and image analysis in fetal medicine	21st International Conference on Medical Image Computing & Computer Assisted Interventions
Eduard Gratacós	Systematic approach on mono-chorionic twins Updates on FG	4th Annual International Conference of Egyptian Fetal Medicine Foundation
	Fetal cystoscopy Lung maturity: Automated measurement	17th World Congress in Fetal Medicine
	Anomalías pulmonares Algoritmo diagnóstico de la patología monocorial Hernia diafragmática. ¿Qué hacer y cuándo? Consecuencias cardiovasculares a largo plazo de la RCIU Tratamiento de la RCIU: conceptos actuales ¿Deben administrarse corticosteroides en prematuridad tardía?	68 Congreso Mexicano de Obstetrícia y Ginecología Femecog 2018

## ORAL PRESENTATIONS

RESEARCHER	TITLE
11th Annual CIBERER Meeting	
Francesca Crovetto	The fetoscopic surgery for the prenatal treatment of Spina Bífida.
26º Congreso Nacional de la Sección de Medicina Perinatal de la Sociedad Española de Ginecología y Obstetrícia	
Teresa Cobo	Inflamation and Prematurity
17th World Congress in Fetal Medicine	
Miriam Illa	FGR: Treatment by maternal docosahexaenoic acid and lactoferrin



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**INVITED TALKS**

in national and international congresses

**COURSES AND CONGRESSES**

We have participated in 21 national and international congresses and

21

RESEARCHER	TITLE
Jezid Miranda	FGR: Metabolic profiling and targeted lipidomics
Lina Youssef	FGR: Fetoplacental Doppler and placental histology
Nadine Hahner	Cortical development in fetuses with ventriculomegaly
Talita Micheletti	MCDAs twins: ROM after cord occlusion
Laura García-Otero	Normograms of cardiac dimensions with gestation
Iris Soveral	CHD: Cardiac remodelling in CoA
Laura Guirado	CHD: Cardiac remodelling in TOF
Mar Bannasar	TTTS fetoscopic laser: Outcome for procedures <17 and ≥17
Amet Hawkins	CMV infection: Cordocentesis in prediction of adverse outcome
Ultrasound meets Magnetic Resonance	
Amet Hawkins	Fetal liver volume assessment using magnetic resonance imaging in fetuses with CMV infection
Nadine Hahner	Altered cortical development in fetuses with isolated nonsevere ventriculomegaly is associated with neonatal neurobehaviour
Ayako Nakaki	Placental volume assessed by MR in near term fetal growth restriction
	Placental perfusion assessed by MR IVIM model in near term fetal growth restriction
7th International Conference on Fetal Growth	
Francesc Figueras	Early onset FGR - baseline medical and obstetric characteristics: 6 year prospective study
Raigam Jafet Martinez-Portilla	Performance of third trimester ultrasound for the prediction of smallness-for-gestational age: a diagnostic test accuracy meta-analysis
28th World Congress on Ultrasound in Obstetrics and Gynecology	
Raigam Jafet Martinez-Portilla	17α-hydroxyprogesterone caproate for the prevention of recurrent preterm birth: systematic review and metaanalysis (OC10.07)
Lina Youssef	Fetal cardiac remodelling in pregnancies complicated by preeclampsia with and without fetal growth restriction (OC13.04)

**72**

**POSTERS**

Posters and oral communications

**20**

**ORAL  
PRESENTATIONS**

20 oral presentations in national and international congresses

**26**

**POSTERS IN  
INTERNATIONAL  
CONGRESSES**

We have presented 26 posters in international congresses

## ORAL POSTERS

RESEARCHER	TITLE
7th International Conference on Fetal Growth	
Raigam Jafet Martinez-Portilla	Higher-risk of adverse perinatal outcome in adequate-for-gestational age fetuses with abnormal cerebro-placental ratio
Marta Rial-Crestelo	Evaluation of the quality and reliability of middle cerebral artery (MCA) and umbilical artery (UA) doppler images in a randomized controlled trial
28th World Congress on Ultrasound in Obstetrics and Gynecology	
Raigam Jafet Martinez-Portilla	Diagnostic performance of ultrasound for the prediction of late smallness-for-gestational age: a systematic review and meta-analysis (OP19.01)
	Added value of chromosomal microarray analysis above conventional karyotyping in stillbirth work-up: systematic review and meta-analysis (OP21.11)
Lina Youssef	Fetoplacental Doppler association with placental pathology in pre-eclampsia and fetal growth restriction

## POSTERS

RESEARCHER	TITLE
17th World Congress in Fetal Medicine	
Mar Bennasar	Perinatal outcome of fetoscopic laser surgery for twin-to-twin transfusion syndrome in early gestation
Laura García-Otero	Cardiac and mitochondrial function in HIV-uninfected fetuses exposed to antiretroviral treatment
Nadine Hahner	Automatic evaluation of cortical folding pattern in isolated ventriculomegaly
Amet Hawkins	Blood parameters at cordocentesis in cytomegalovirus infected fetuses based on gestational age and severity of affection
Eduardo Herreros	Vaginal microbiota in women with preterm labor and intact membranes
Miriam Illa	Survival and neurodevelopmental effects of Docosahexaenoic acid and Lactoferrin in an IUGR animal model
Mari Kinoshita	Fetal cardiovascular characterization in a rabbit model of intrauterine growth restriction
Talita Micheletti	Predictors of iatrogenic preterm prelabor rupture of membranes and outcomes after cord occlusion in monochorionic diamniotic pregnancies
Jezid Miranda	Metabolic profiling and targeted lipidomics in small for gestational age and fetal growth restriction
	Prenatal stress modifies RNA expression of HSD11 $\beta$ 2 and the hypothalamic-pituitary-adrenocortical axis in fetal growth restriction
L Nogué	Muscular ventricular septal defects in fetal life: pattern of cardiovascular remodeling by echocardiography in the third trimester of pregnancy
Cristina Paules	Patterns of placental stromal-vascular lesions in preeclampsia and fetal growth restriction
	Placental ageing in term small for gestational age and growth restricted fetuses
Marta Rial-Crestelo	Evaluation of the quality and reliability of middle cerebral artery and umbilical artery Doppler images in a randomized controlled trial
Iris Soveral	Fetal right cardiac dominance in coarctation of the aorta: understanding its origin
Ximena Torres	Cardiac function in uncomplicated monochorionic diamniotic twins. Is normal really normal?
Lina Youssef	Association of feto-placental Doppler with placental histopathology in fetal growth restriction and preeclampsia
7th International Conference on Fetal Growth	
Eduarne Mazarico	Birth weight and nutritional indices prediction using fractional limb volume and estimated fetal weight

# Academic output



## COMPLETED DOCTORAL THESES

RESEARCHER	TITLE	DIRECTORS	UNIVERSITY	DATE
Javier Caradeaux	Longitudinal assessment for the prediction of abnormal fetal growth	Francesc Figueras	Universitat de Barcelona	18/01/2018
Sally Sabra	Maternal Heavy Metals and Toxins Exposure and their influences on Fetal Growth Restriction Clinical Subtypes	Lola Gómez-Roig Eduard Gratacos Ebba Malmqvist	Universitat de Barcelona	22/01/2018
Tri Rahmat Basuki	Longitudinal Study of Fetal Growth in Low-Risk Population	Francesc Figueras Eduard Gratacós Stefan Hansson	Universitat de Barcelona	22/02/2018
Hatice Gülçin Gümüs	Intrauterine Therapy for Fetal Growth Restriction	Fàtima Crispí Eduard Gratacós David Ley	Universitat de Barcelona	11/04/2018
Laura García Otero	Fetal cardiovascular remodelling in HIV pregnancies	Fàtima Crispí Marta López Per Björkman	Universitat de Barcelona	13/12/2018
Jeziel Miranda Quintero	Phenomapping of Fetal Growth Restriction	Fàtima Crispí Eduard Gratacós Stefan Hansson	Universitat de Barcelona	17/12/2018



## RESEARCH GRANTS

RESEARCHER	TITLE	AWARDED BY
Iris Soveral	Evaluación pronóstica de las cardiopatías congénitas desde la etapa prenatal mediante ecocardiografía avanzada y biomarcadores plasmáticos.	Hospital Clínico y Provincial de Barcelona Premio Joan Font
Laura García-Otero	Understanding and preventing fetal cardiovascular remodeling in HIV-infected pregnancies.	Generalitat de Catalunya, AGAUR Beca recursos humanos de Doctorado
Àlvaro Pérez	Anàlisi quantitatiu de la textura del coll de l'úter en embarassades (cèrvix): nova eina per la predicció de l'èxit en la inducció del part i el risc de part prematur.	Generalitat de Catalunya, AGAUR Beca Doctorat Industrial
Cristina Paules	Ayudas para Contratos post Formación Sanitaria Especializada Río Hortega.	Instituto de Salud Carlos III (ISCIII)
Miriam Osorio	Incorporació de tecnòlegs programa PERIS	Generalitat de Catalunya
Fàtima Crispí	Perfil angiogénico en gestantes infectadas por VIH y su asociación con patología placentaria.	Hospital Clínico y Provincial de Barcelona Premio Fi de Residència Emili Letang

8

**RESEARCH GRANTS**

awarded for research in fetal medicine

**AWARDS**  
for the research done by 3  
of our researchers in 2018

3

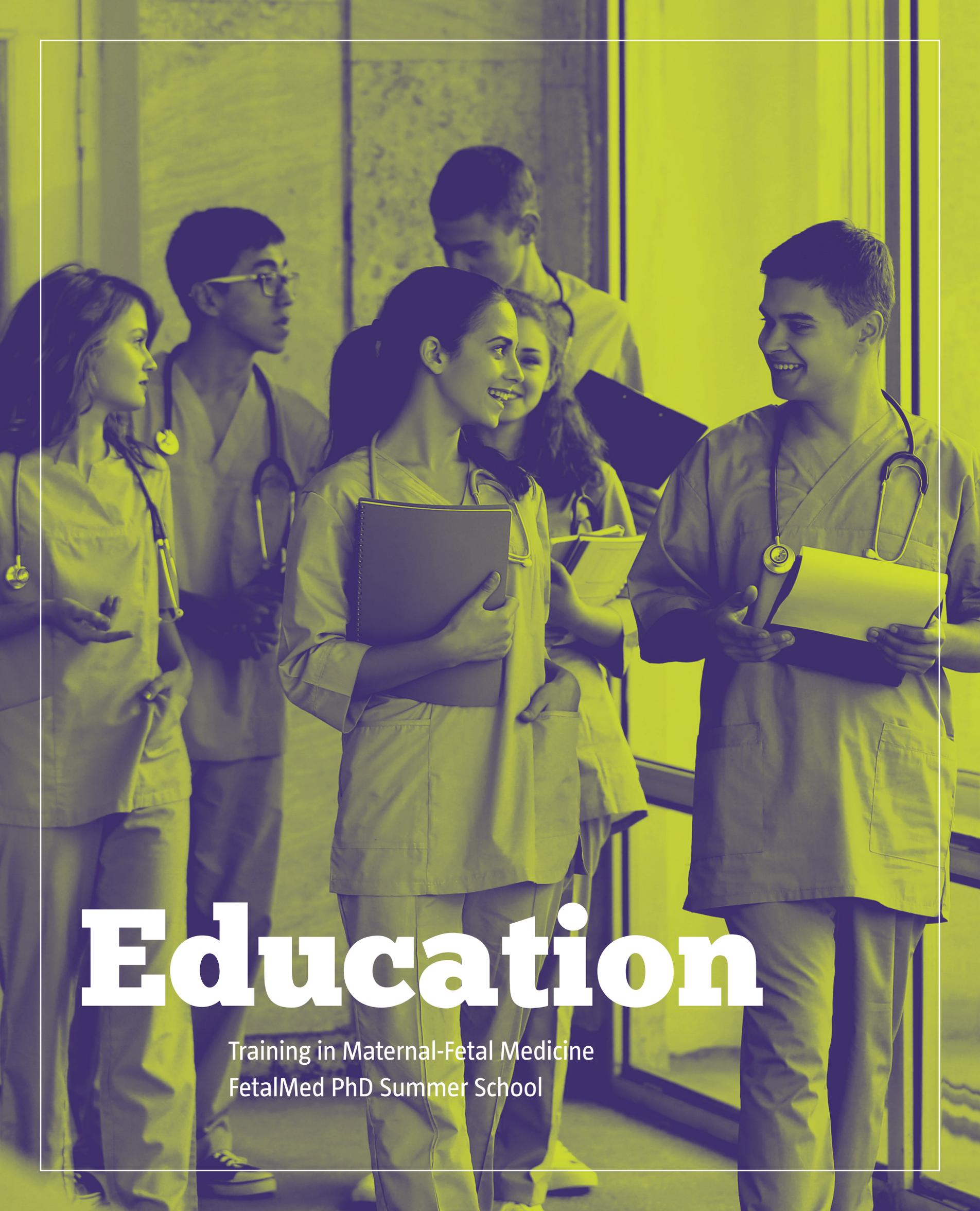
RESEARCHER	TITLE	AWARDED BY
Kilian Vellvé	Impacto del crecimiento intrauterino restringido sobre el desarrollo pulmonar.	Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS)
Cristina Paules	Caracterización de diversos fenotipos de crecimiento intrauterino restringido: neurodesarrollo y metabólica fetal.	Fundación Dexeus Salud de la Mujer, Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS)


**AWARDS**

RESEARCHER	PREMIO	TITLE	CONGRESS/AWARDED BY
Clara Murillo	Ajut a la Recerca Josep Font	Impacto de la amenaza de parto prematuro y la rotura prematura de membranas sobre el neurodesarrollo y el sistema cardiovascular fetal y neonatal. Influencia de la inflamación intraamniótica	Hospital Clínic de Barcelona
Jezid Miranda	Invitación a la SMFM Fast-Track Submission	Targeted lipidomics of maternal and cord blood in term gestations with suboptimal fetal growth	38th SFMF Meeting
Raigam Jafet Martínez-Portilla	Mejor presentación oral corta (Obstetrics)	Prenatal Stress Modifies RNA Expression of HSD11-2 and the Hypothalamic-Pituitary-Adrenocortical Axis in Fetal Growth Restriction	29th ISUOG World Congress


**RESEARCH FELLOWSHIPS**

RESEARCHER	UNIVERSITY/COUNTRY
Laura García-Otero	University of Adama, Ethiopia
Laura Pla Codina	Department of Physiology Development & Neuroscience, Cambridge, UK
Cristina Paules	Leeds Institute of Cancer & Pathology, Leeds, UK
Lina Youssef	Lund University, Sweden



# Education

Training in Maternal-Fetal Medicine  
FetalMed PhD Summer School

# Training in Maternal-Fetal Medicine

In 2018 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 has already 34 researchers, 4 of which have defended their doctoral thesis this year.

## WHAT IS FETALMED PHD?

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



**DOCTORATES**

have been trained thanks to the FetalMed PhD Erasmus Mundus Joint Doctorate

**34**

## 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 the society.
2. To strengthen the research centres 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 of which the participating researchers come from.

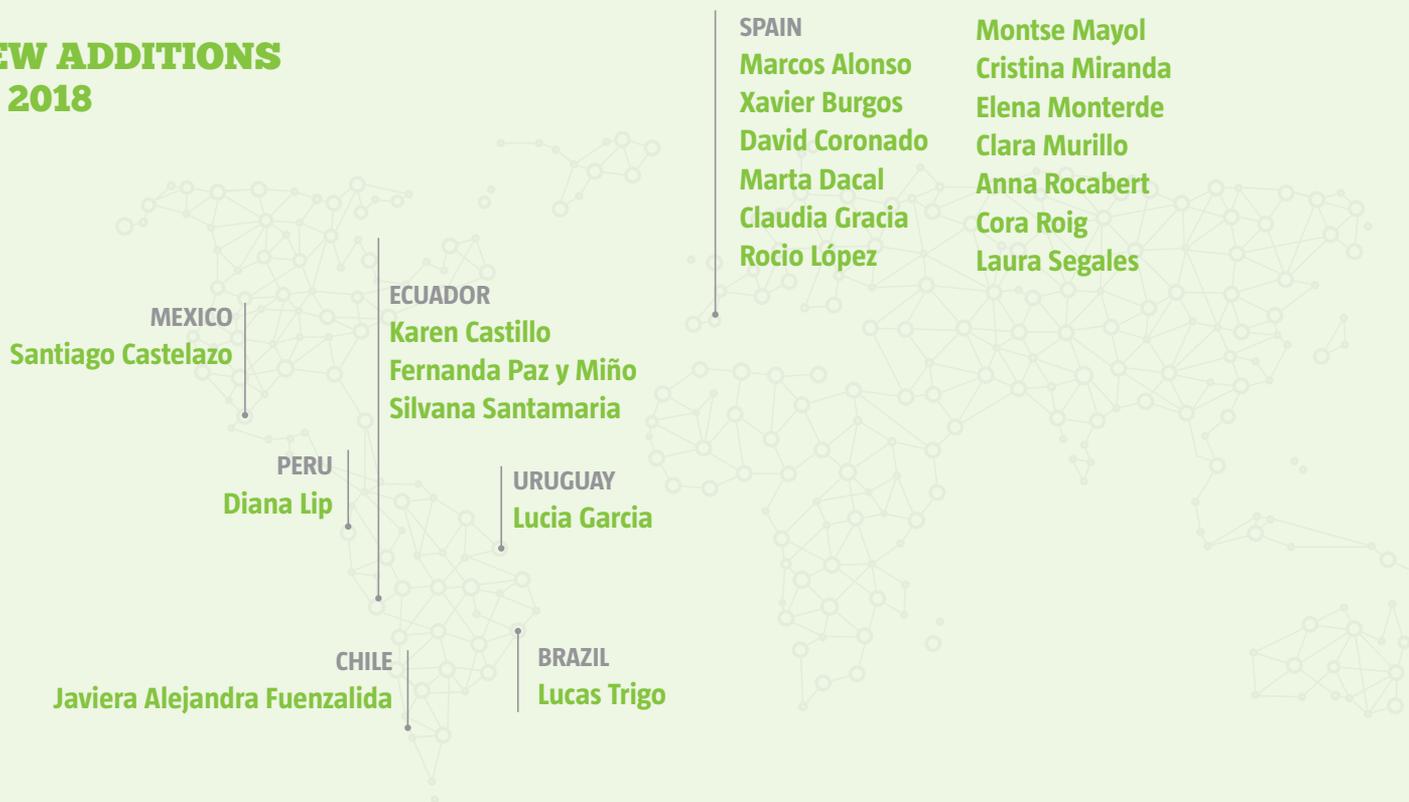


**KU LEUVEN**



Co-funded by the Erasmus+ Programme of the European Union

## NEW ADDITIONS IN 2018



## MASTERS AND UNDERGRADUATE THESIS PROJECTS

RESEARCHER	TITLE	UNIVERSITY/ SUPERVISOR
Cristina Miranda (UNDERGRADUATE)	Avaluació del dany neurològic i identificació de teràpies neuroprotectores en un model animal de restricció de creixement intrauterí.	Universitat de Barcelona / Miriam Illa
Alicia Urbiego (UNDERGRADUATE)	Estudi sobre la susceptibilitat latent a malalties cardiovasculars en vida adulta en fetus de rata amb restricció de creixement intrauterí.	Universitat de Barcelona / Mónica Zamora
Vasili Sircheli (UNDERGRADUATE)	Estudi sobre la susceptibilitat latent a malalties cardiovasculars en vida adulta en fetus de rata amb restricció de creixement intrauterí.	Universitat de Barcelona / Mónica Zamora
Mari Carmen López (MASTER)	Structural evaluation of brain damage in an animal model of Intrauterine Growth Restriction.	Universitat de Barcelona / Miriam Illa



## ONGOING DOCTORAL THESES

RESEARCHER	TITLE	COUNTRY
David Basurto	Novel interventions for congenital diaphragmatic hernia	Mexico
Lucas Trigo	Structural and Function Brain Effects of prenatal Spina bifida	Brazil
Maria Laura Boutet	Fetal programming in assisted reproductive technologies	Argentina
Kilian Vellvé	Impact of FGR on lung development	Spain
Yumjirmaa Mandakh	The effect of air pollution on the risk of preeclampsia and low birth weight	Mongolia
Mirza Awais	Single Orifice and Robotic Solutions for Fetal and Gynecologic Surgery	Pakistan
Paz Ahumada	Effectiveness of repeated motivational intervention sessions during pregnancy to stop ethanol use	Chile

# FetalMed PhD Summer School

**Erasmus Mundus facilitates the training of professionals who are able to address and give comprehensive solutions to maternal-fetal health problems**

The Erasmus Mundus Fetalmed-PhD Summer School takes place within the framework of one of the most important fetal medicine congresses in the world, the World Congress in Fetal Medicine. It is a unique opportunity for our predoctoral researchers, which contributes to improving their ongoing research projects and their research skills. The event gathers the leading experts and interesting debates on how to advance within the field of maternal-fetal medicine. A unique environment that helps us to program ad hoc complementary activities for our

researchers to exchange experiences in an international environment.

## ★ IN 2018...

The third edition of FetalMed PhD Summer School was held in Athens, on 23-28 June 2018, coinciding with the 17th World Congress in Fetal Medicine.





# Media

Under the spotlight  
The team on the Internet

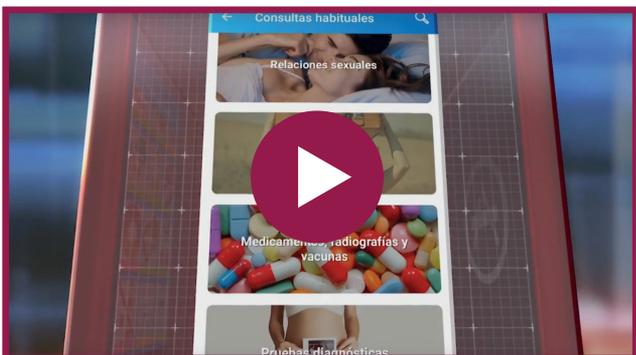
# Under the spotlight

In 2018, the group has been in the headlines of many national and international media, and has participated in important social events. This is how we have been positioned as a national and international reference in the fields of fetal medicine research, fetal therapy and surgery.

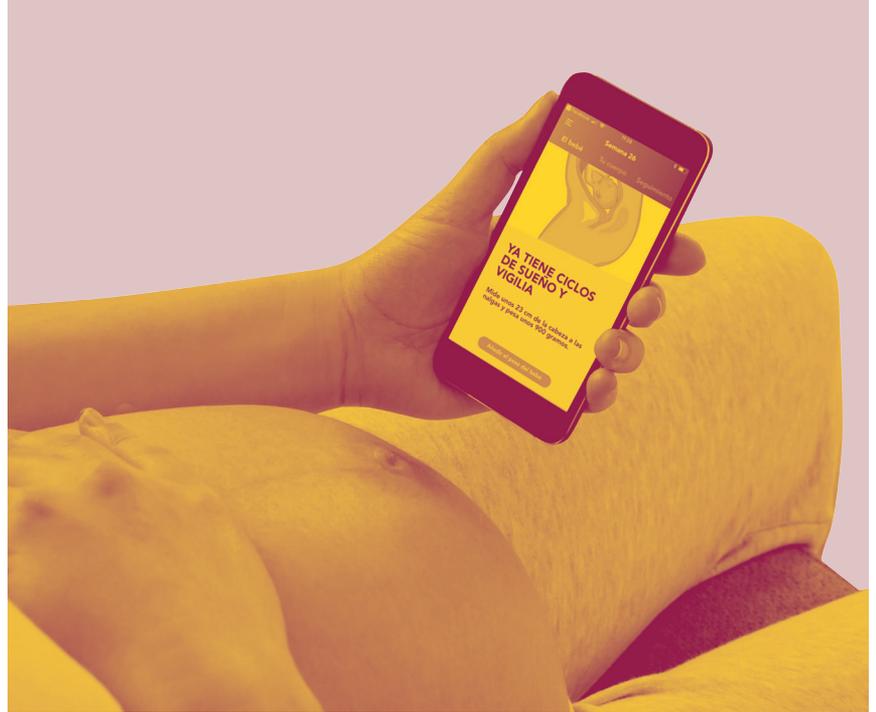
Fetal medicine advances at giant steps. Twenty years ago the fetus did not exist as a patient. Today, more and more babies come with a medical record under their arm. Outreach in this field, as well as dissemination by the media, is essential. What do fetuses do before they are born? Do in vitro babies have more cardiovascular problems during adulthood? We, as a team, always respond to fetal medicine related concerns.



Informatiu migdia (La 2 de TVE)



Espai Internet (TV3)



## WE LAUNCH THE INATAL APP THANKS TO OBRE SOCIAL 'LA CAIXA'

After becoming the most recommended pregnancy website by the Spanish-speaking medical community, inatal.org becomes the first mobile application endorsed by maternal-fetal medicine specialists. Developed in collaboration with Obra Social 'la Caixa', the app is totally customizable and it is the only one that offers personalized plans for emotional well-being and nutrition, two aspects that are key for the correct development of the fetus. It was presented at the Palau Macaya in Barcelona in March and, thanks to this, the group appeared on television, radio, newspapers and social networks from March to June 2018.



La Vanguardia

El Periódico

Diario Médico

La Razón

El Plural

Siete Días Médicos

## WE PRESENT A NEW PROJECT ON THE POLLUTION AND THE PREGNANCY

How does atmospheric pollution affect the neurological and cardiovascular development of the fetus? The BiSC project, carried out in collaboration with ISGlobal, BCNatal and Hospital de Sant Pau, will be responsible for determining the impact of contamination on pregnancy. It was presented at the end of the year, thanks to the support of Obra Social 'la Caixa', and it became news on television, newspapers, and the digital media.



14/11/2018 Se buscan 1.200 embarazadas para estudiar los efectos de la contaminación desde la placenta | Ciencia | EL PAÍS

**CONFIRMACIÓN ATMOSFÉRICA**  
**Se buscan 1.200 embarazadas para estudiar los efectos de la contaminación desde la placenta**

Investigadores de Barcelona quieren analizar el impacto de la polución en la salud desde antes de nacer

ACCESIA MEDICAL QUANTUM

Barcelona - 6 NOV 2018 - 14:28 CET

GETTY IMAGES

Se buscan 1.200 embarazadas en Barcelona. A poder ser, que estén dentro del primer trimestre de embarazo. La salud de los niños del futuro les va en ello. La Organización Mundial de la Salud (OMS) alertó la semana pasada de que el 90% de los niños del mundo respiran diariamente aire tóxico. La contaminación es un problema de primer orden para las autoridades sanitarias y su impacto en la salud no entiende de edades. Es por ello que un grupo de investigadores de varios hospitales de Barcelona han lanzado

El País // 06/11

sostenible

Diputació de Barcelona #DibaOberta

**1.200 dones embarassades participaran a Barcelona a un dels majors estudis sobre contaminació atmosfèrica i gestació**

Font: ISGlobal

08/11/2018 - 15:33

Aquest 6 de novembre s'ha presentat el projecte BiSC (Barcelona Life Study Cohort), un dels estudis més complets realitzats fins la data per entendre com afecta la contaminació atmosfèrica a la salut dels bebès i al seu desenvolupament cerebral fins i tot des d'abans del naixement. BiSC es portarà a terme a la ciutat de Barcelona sota la coordinació de l'Institut de Salut Global de Barcelona (ISGlobal), un centre impulsat per la Fundació Bancària "la Caixa", en col·laboració amb el centre BCNatal (Hospitals Sant Joan de Déu, Hospital Clínic i Universitat de Barcelona) i l'Hospital de la Santa Creu i Sant Pau.

Sostenible.cat (Diputació de Barcelona) // 08/11

**Estudi únic al món sobre l'impacte de la contaminació en embarassades i fetus**

Investigació pionera de l'Institut Global de Salut i els hospitals Sant Joan de Déu i Sant Pau de Barcelona

Begoña Grigelmo  
 06/11/2018 - 16:33 | Actualitzat: 07/11/2018 - 06:45

TEMA: SALUT

324 (TV3) // 06/11

## EDUARD GRATACÓS TALKS ABOUT FETAL MEDICINE RESEARCH AND FETAL SURGERY

National newspapers (La Vanguardia, La Razón, El Periódico ...) and international newspapers (Europapress), as well as other health-related media, including ConSalud, DiarioMedico and Siete Días Médicos, have dedicated interviews to Eduard Gratacós and the group to discuss fetal medicine research and advances in fetal surgery. In La 2 of TVE we were able to follow an operation of the fetofetal transfusion syndrome.

DR. EDUARD GRATACÓS  
 Director BCNatal: Hospital Clínic de Barcelona, Hospital Sant Joan de Déu y UB

-Medicina fetal es todo aquello que afecta a la salud del feto.

TP 2

La ciencia de la salud. Vivir en femenino. (La 2 de TVE) // 03/06

## WE INCREASE AWARENESS ABOUT FETAL LIFE AND THE IMPORTANCE OF FOLLOWING HEALTHY HABITS IN PREGNANCY

In the fetal period a third of our intelligence is determined, and also, the bases of our future health are established. That is why it is important to diagnose any alteration that may happen during that period. In this context, the publication of new biomarkers to detect neurodevelopmental diseases and the dissemination of perinatal infections such as cytomegalovirus are very significant.

HOME > PACIENTES > AVANCES

NUEVO DESCUBRIMIENTO

### Identifican un biomarcador fetal para el pronóstico de alteraciones neurológicas

Un estudio sobre la ventriculomegalia ha revelado que las regiones corticales con plegamiento alterado podrían constituir buenos biomarcadores para prevenir este tipo de alteraciones.



La ventriculomegalia es una afección que implica el aumento del tamaño de uno de los dos ventrículos laterales del cerebro

Con Salud // 15/02

### Desvelan un biomarcador fetal para el pronóstico de alteración neurológica

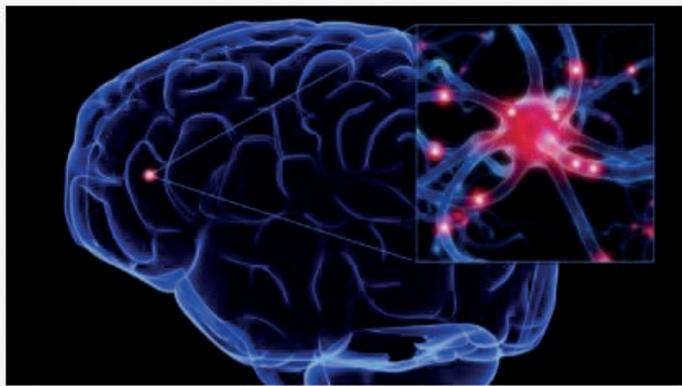
La ventriculomegalia, una afección relacionada con la aparición de alteraciones neurológicas a largo plazo, y su relación con el plegamiento cortical cerebral podrían ser marcadores de alteraciones neurológicas.

Redacción | 15/02/2018 15:18

compartir Compartir Like 0 Twitlear

★★★★☆ ¡vota! comentarios

imprimir tamaño



Cerebro. (DM)

Díario Médico // 15/02

CITOMEGALOVIRUS >

### La ignorada enfermedad del hermano mayor

El citomegalovirus infecta a 1.960 recién nacidos al año en España, el 0,5% de los embarazos

MANUEL ANSEDE

14 SEP 2018 - 13:46 CEST



Leticia Zarza, Inmaculada López y Elena Fernández, con sus hijos afectados por el citomegalovirus. LUIS SEVILLANO

El País // 14/09

In Iberoamerica we are referents in fetal medicine with more than 150 appearances on newspapers, radio, television and digital media

**If you want to contact us, write to:**

**Pere Lorente.**  
Head of Communication  
plorente@clinic.cat  
T. +34 932 279 333



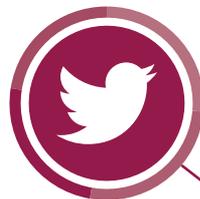
# The team on the Internet

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 through internet. We do it through our website, a quarterly newsletter and an active participation in social media and networks. Thus, we generate awareness and impact on the importance of maternal-fetal medicine research to improve public health.

**We want to create awareness on the importance of maternal-fetal medicine research to improve public health**

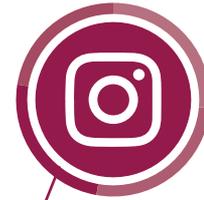
**Our main website fetalmedbarcelona.org allows the access to different research areas of the group and holds the Certificate of Health and the Hon Web Interest Code, as well as the accreditation by the College of Physicians of Barcelona.**

## Social Media



@BCNatalResearch

**909**  
followers



@fetalmedbcn

**317**  
followers



BCNatalFetalMedicineResearch

**631**  
likes



BCNatal Fetal Medicine Research Center

**729**  
members



