# BCNATAL

# FETAL

MEDICINE RESEARCH CENTER













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BCNatal FMRC celebrates another year of activity. Since its inception, we have driven research standards based on excellence and innovation with a multidisciplinary team of professionals. Our constant effort and dedication have positioned us as a reference group, and we have gained an international reputation as a result of our research in the field of Maternal and Fetal Medicine. For all these reasons, we have received national and European funds, only to name a few "la Caixa" Foundation and CEREBRA. We want to acknowledge the invaluable contributions of both funders and collaborators, which are necessary to continue developing our research projects.

I am pleased to share the most relevant milestones of 2022. We have continued working on the results of the IMPACT clinical trial, initially published in 2021. The study shows the implications of a healthy diet and the reduction of maternal stress during pregnancy, leading to a decrease in maternal and fetal complications. Furthermore, we have successfully concluded the first phase of the Artificial Placenta project, which aims at developing a solution for the most extreme prematurity, specifically infants born before 6 months of gestation who face survival challenges and severe associated comorbidities. The solution we propose is highly disruptive and innovative, and it would allow us to improve these adverse effects of prematurity.

Our mission is to continue researching to solutions for provide new problems associated with Maternal and Fetal Medicine and to improve the health of our patients. Additionally, we are dedicated to training future researches in the field of Maternal and Fetal Medicine. In this report, we want to highlight the research areas in which we are working: maternal and fetal complications, neurodevelopment, prematurity, inflammation in prematurity, prevention of major obstetric syndromes, placental disease, fetal heart programming, environment and pregnancy complications, and development of new high-precision therapies and technologies in Fetal Medicine and surgery.



Indeed, it is also important to emphasize our commitment to promoting the importance of prenatal health throughout life. Therefore, we design informative tools and activities that bring Fetal Medicine closer to society.

For all these reasons, we remain committed to pursuing the development of knowledge to have a real impact on maternal and fetal health.

#### **Eduard Gratacós**

Director of BCNatal FMRC

# WHO WE ARE





### OUR MISSION IS TO EARLY DIAGNOSE AND TREAT CHILDHOOD DISEASES THAT IMPACT IN THE ADULT LIVE, WE CONSIDER THE FETUS AND THE BABY AS THE SAME PATIENT

The Fetal Medicine Research Centre BCNatal is а research center associated to the University of Barcelona, we are a multidisciplinary specialized in Fetal and team Perinatal Medicine. We are a wellknown research group associated to Hospital Sant Joan de Déu and Hospital Clínic de Barcelona and our centre is recognized as one of the best centers in Maternal and Fetal Medicine worldwide

#### **Our mission**

Our mission is to achieve an early diagnosis to treat diseases at prenatal stage that will have an impact throughout all life. Thus, we consider the fetus and the baby as the same patient. Our goal is to reduce the severity and prevalence in adults of those conditions associated with neurodevelopment, cardiovascular and lung anomalies originated at fetal life.

#### **Our methodology**

We consider the fetus as our patient to identify that perturbations of fetal health prevail during childhood and future adulthood. We treat fetal pathologies from this innovative point of view. As such, we integrate prenatal and postnatal care in Maternal, Fetal and Neonatology Units.

#### **Our projects**

At the moment, there are multiple research projects ongoing. Of note, we would like to highlight the study to improve the prognosis of fetal growth restriction (FGR), as well as, our research with biomarkers for an early identification of risk factors during pregnancy. In addition, we are developing new fetal surgeries aiming to change the paradigm of such interventions, giving an alternative to conditions that nowadays lead to fetal death.

An early diagnosis allow us to treat diseases at prenatal stage that will have an impact throughout life

750 m<sup>2</sup>

Allocated to research

+ 761

**Publications since 2010** 

**78** 

Scientific publications in 2022

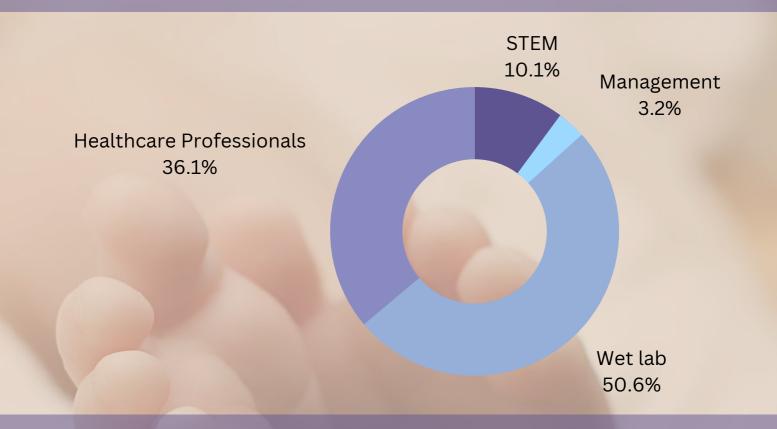
## A TEAM OF EXCELLENCE

The group has a high translational capacity due to our multidisciplinary team composition. Our team is composed by specialist in Maternal and Fetal Medicine, cardiology, and neurodevelopment; in addition to this, biologists, pharmacists, bioengineers, epidemiologists and statisticians. As a result, we have achieved high-quality research in the physiological and pathological study of the fetus.

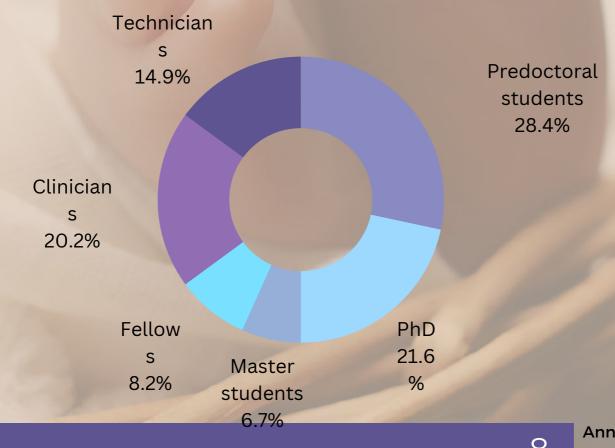
The center is led by Dr. Eduard Gratacós as a director and Dra. Fàtima Crispi as a Scientific coordinator. Indeed, there are multiple lines of research with their own principal investigator and a dedicated management department to the centre.



## HR AREAS %



## **HR CATEGORIES %**



## **OUR NATURE**

#### **BCNATAL FMRC**

The research centre BCNatal FMRC was created after merging Maternal, Fetal and Neonatology Unit at Hospital Sant Joan de Déu and Hospital Clínic de Barcelona, and it is one of the university centers of reference in Europe and worldwide. Each year, there are more than 7,000 deliveries, 3,500 Fetal Medicine consultations, 2,000 fetal echocardiograms, 150 fetal surgeries and more than 400 patients with placental disease. The fetal surgery that we perform represents the 85% of all interventions in Spain, being critical to sustain fetal life. The center also accepts patients from other nationalities.

#### **FCRB-IDIBAPS**

BCNatal FMRC is part of the August Pi i Sunyer Biomedical Research Institute (IDIBAPS), one of the leading Health research centres in Europe with an

outstanding scientific production withmore than 1,000 Scientific articles each year in international peer-review journals. The first-class researchers make IDIBAPS a great center for innovation and catalyze knowledge transference into the clinic.

#### CLÍNIC **FOUNDATION AND** SANT **JOAN DE DÉU FOUNDATION**

Clínic Foundation (FCRB) and Sant (FSJD) Déu Foundation Joan support researchers at BCNatal FMRC and their scientific activities. Indeed, also takes care of administrative tasks at IDIBAPS.

#### **UNIVERSITY OF BARCELONA**

University of Barcelona (UB) reputed public university in Catalonia, with a great number of trainings and courses. Most of our PhD students enroll in doctoral programmes of the UB.

The fetal surgery conducted at BCNatal represents the 85% of all interventions in Spain, being critical to sustain fetal life









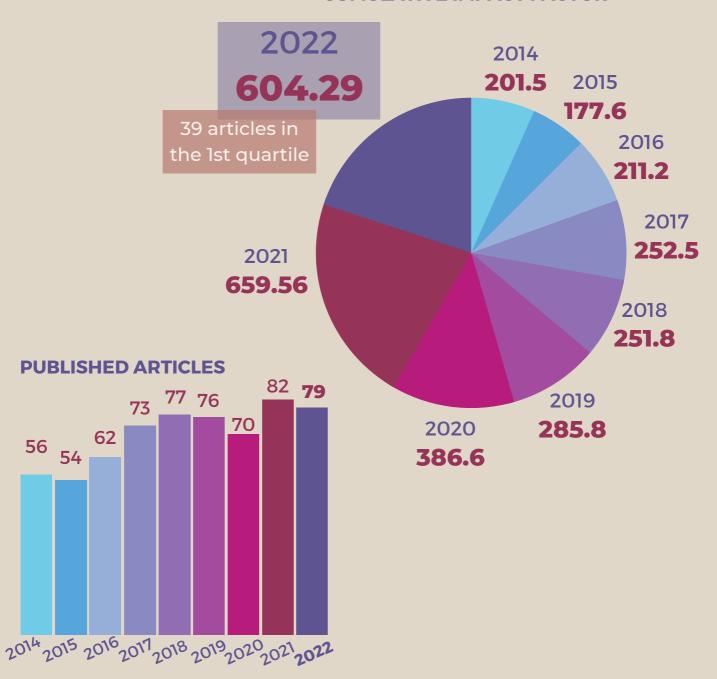




# SCIENTIFIC RESULTS

In the last decade, BCNatal FMRC has published more than 750 scientific papers, led more than 50 doctoral Thesis and it has been awarded with more than 60 national and international projects endorsed by prestigious institutions such as CELLEX, Cerebra Foundation (UK) or Obra Social "la Caixa".

#### **CUMULATIVE IMPACT FACTOR**



## ORGANIZATIONAL CHART



## **HISTORY**

**2005** OUR

#### **BEGINNING**

Dr. Eduard Gratacós created the research team in Fetal and Perinatal Medicine thanks to the support of Hospital Clínic and IDIBAPS. The fetus was not considered a patient 20 years ago. Today babies are born with a medical record; with this change of paradigm, we offer more opportunities and better care improving the quality of life at prenatal stage. Please, find below key dates at BCNatal FMRC from the past to present days.

#### 2010

### THE FIRST FETAL LUNG SURGERY

Our first surgical intervention on a fetus with a lethal congenital pulmonary disease. The baby is called Alaitz –'happiness' in Basque – and becomes news 16 months later.

2016

#### 2013

### FIRST SPECIALIZED EUROPEAN DOCTORATE

We coordinated the 1st Erasmus Mundus
Joint PhD Program in Fetal and Perinata
Medicine in collaboration with the
University of Barcelona (Spain), and the
Universities of Leuven (Belgium) and
Lund (Sweden).

## IMPACTBCN, CLINICAL TRIAL IN PREGNANCY

"Improving Mother's wellbeing for a better Prenatal Care Trial" It was a comprehensive clinical trial based on interventions in the nutrition and emotional wellbeing of the mother to assess the impact of maternal well-being on the newborn. More than 1,200 pregnant women at risk of having a baby with growth restriction participated in the study.

2015

## NEW RESEARCH LINE: FETAL THERAPY AND SURGERY

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

## **HISTORY**

#### 2020

## NEW RESEARCH ON THE IMPACT OF COVID ON PREGNANCY AND CHILDHOOD

We participated in the KIDS CORONA study at Hospital Sant Joan de Déu to study the effects of SARS-CoV 2 on the fetus, the pregnant woman and the baby: is there vertical transmission? Are breastfeeding and skin-to-skin safe? We also carried out training for patients and health personnel to clarify action protocols.

#### 2021

#### WE DEMONSTRATE THE IMPACT OF PREGNANCY LIFESTYLE ON FETAL HEALTH

The publication of the results of the IMPACT trial in JAMA confirmed that maternal Mediterranean diet and following a stress reduction programme during pregnancy decreases the risk of low birth weight babies.

#### 2019

#### NEW SYSTEM TO IMPROVE

#### **FETAL SURGERIES**

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

#### 2017

## IMPROVEMENTS IN THE DIAGNOSIS OF FETAL GROWTH RESTRICTION

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



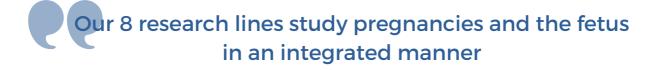


OUR 8 RESEARCH AREAS AT BCNATAL FMRC ARE DEDICATED TO
DEVELOPING DIAGNOSTIC AND TREATMENT METHODS TO ADDRESS
PRENATAL PATHOLOGIES THAT CAN IMPACT THE FUTURE BABY'S LIFE AND
LONG-TERM WELL-BEING INTO ADULTHOOD

#### THE FETUS AS A PATIENT

In BCNatal Fetal Medicine Research Center we treat the fetus as a patient to tackle diseases that can arise at fetal stage and mitigate potential sequelae that could manifest after birth and throughout the adult life. Our research is focused in the heart and brain because fetal programming impacts greatly on the development of these organs. In addition, we investigate new intrauterine treatments that cure or palliate fetal pathologies.





## Fetal Heart Programming

OUR MISSION IS TO COMPREHEND THE IMPACT OF PREGNANCY COMPLICATION IN THE FETAL GROWTH AND DEVELOPMENT AND DESIGN INTERVENTIONS TO IMPROVE FETAL HEALTH AND FUTURE HEALTH THROUGHOUT LIFE

### IS FETAL LIFE DETERMINANT IN OUR FUTURE HEALTH THROUGHOUT LIFE?

The fetal stage is fundamental in the development of our organism. Indeed, pregnancy complications increase the susceptibility of manifesting a disease, therefore, these complications can threaten our health in the future. It is worth mentioning some of the most well-known pregnancy complications; intrauterine growth restriction, assisted reproductive techniques, exposure to toxins or congenital cardiopathies. These can affect the optimal development of organs such as heart, lungs and brain.

### CAN INTERVENTIONS IN PREGNANT WOMEN IMPROVE BABIES' HEALTH?

For years, we have been pioneers proving how an improvement in lifestyle and diet during pregnancy has a positive effect on fetal growth and development. We put efforts to help improve lifestyle of pregnant women in order to improve their health and the health or their future sons and daughters.





Fàtima Crispi
Coordinator of the
research line and the
scientific coordinator of
the group. Maternal-Fetal
Medicine Specialist at
BCNatal

### IN 2022....

- We have described the profile of endothelial and metabolomic dysfunction in preeclampsia.
- We have proposed and validated a new tool for the study of the fetal heart.
- We have described the association of assisted reproductive techniques with changes in fetal neurodevelopment.
- We have provided evidence of the impact of fetal growth restriction in pulmonary health



#### **TEAM MEMBERS**

#### COORDINATOR

Fàtima Crispi

#### SPECIALISTS IN MATERNAL AND FETAL MEDICINE

Olga Gómez, Anna Goncé, Marta López, Gemma Casals

#### POSTDOCTORAL RESEARCHER

Gabriel Bernandino, Sara Castro-Barquero, Mònica Selma-Royo, Laura Guirado, Patricia García Cañadilla, Lina Youssef

#### PREDOCTORAL RESEARCHER

Leticia Benítez, Maria Laura Boutet, Laura Salazar, Katarzyna Darecka, Marta Larroya, Laura Nogué, Kilian Vellvé

#### RESEARCH FELLOWS

Eugenio Denaro, Nuno Simoes, Gerarda Gaeta, Roberta Castellani

#### MASTER STUDENT

Karen Castillo, Víctor Narváez, Caroline David

#### COLLABORATORS

Bart Bijnens, Roger Borràs

#### COLLABORATIONS

#### NATIONAL

- BCN-MedTech, University Pompeu Fabra
- Cardiac Imaging, Hospital Clínic-IDIBAPS
- Biopathology and treatment of cardiac arrythmias, Hospital Clínic-IDIBAPS
- Atherosclerosis, Coronary disease and heart failure, Hospital Clínic-IDIBAPS
  - Centro Nacional de Investigaciones Cardiovasculares (CNIC)
- Inflammation and Repair in Respiratory diseases, Hospital Clinic-IDIBAPS
  - Cardiovascular risk, nutrition and aging, Hospital Clínic-IDIBAPS
    - Bipolar and Depressive Disorders, Hospital Clinic-IDIBAPS
      - Barcelona Endothelium team, Institut Josep Carreras
- Stem cell biology, developmental leukemia and immunotherapy, Institut

  Josep Carreras
- Metabolómica aplicada, Institut Hospital del Mar d'Investigacions Mèdiques

#### INTERNATIONAL

- Oregon Health and Science University, USA
  - University of Lund, Sweden
- SickKids Hospital, University of Toronto, Canada
- Cardiology Care for Children, Pennsylvania, USA
  - Universidad ICESI, Colombia
- Hospital Clínico de la Universidad de Chile, Chile
  - Universidad de Cartagena, Colombia

#### **STRATEGIC GOALS**

	TRANSLATIONAL RESEARCH	EXPERIMENTAL RESEARCH	COMPUTATIONAL MODELS + ARTIFICIAL INTELLIGENCE
UNDERSTAND AND PREVENT	Study fetal cardiovascular and lung development and the factors that influence them.  Develop strategies to improve maternal nutrition and well-being to improve fetal growth and development.	Study fetal cardiovascular development and test new therapies.	Understand hemodynamic changes in fetal pathologies that affect cardiovascular development and test potential therapies.

#### **PUBLICATIONS IN 2022**

- - 1. Youssef L, Crovetto F, Simoes RV, Miranda J, Paules C, Blasco M, Palomo M, García-Calderó H, Tura-Ceide O, Dantas AP, Hernandez-Gea V, Herrero P, Canela N, Campistol JM, Garcia-Pagan JC, Diaz-Ricart M, Gratacos E, Crispi F. The Interplay between Pathophysiological Pathways in Early-Onset Severe Preeclampsia Unveiled by Metabolomics. Life (Basel). 2022 Jan 7;12(1):86. doi: 10.3390/life12010086.
  - 2. García-Otero L, Walles J, Balcha TT, Merga G, López M, Crispi F, Björkman P. Cardiovascular effects of intrauterine exposure to maternal HIV and antiretroviral therapy in Ethiopian infants followed from fetal life. AIDS. 2022 Jun 1;36(7):941-951. doi: 10.1097/QAD.0000000000003188.
  - 3. Torres X, Bennasar M, Bautista-Rodríguez C, Martínez-Portilla RJ, Gómez O, Micheletti T, Eixarch E, Crispi F, Gratacós E, Martínez JM. The heart after surviving twin-to-twin transfusion syndrome. Am J Obstet Gynecol. 2022 Sep;227(3):502.e1-502.e25. doi: 10.1016/j.ajog.2022.03.049.
- 4. Nogué L, Gómez O, Izquierdo N, Mula C, Masoller N, Martínez JM, Gratacós E, Devore G, Crispi F, Bennasar M. Feasibility of 4D-Spatio Temporal Image Correlation (STIC) in the Comprehensive Assessment of the Fetal Heart Using FetalHQ®. J Clin Med. 2022 Mar 4;11(5):1414. doi: 10.3390/jcm11051414.
- 5. Palomo M, Youssef L, Ramos A, Torramade-Moix S, Moreno-Castaño AB, Martinez-Sanchez J, Bonastre L, Pino M, Gomez-Ramirez P, Martin L, Garcia Mateos E, Sanchez P, Fernandez S, Crovetto F, Escolar G, Carreras E, Castro P, Gratacos E, Crispi F, Diaz-Ricart M. Differences and similarities in endothelial and angiogenic profiles of preeclampsia and COVID-19 in pregnancy. Am J Obstet Gynecol. 2022 277.e1-277.e16. Aug;227(2): 10.1016/j.ajog.2022.03.048.



- 6. Boutet ML, Eixarch E, Ahumada-Droguett P, Nakaki A, Crovetto F, Cívico MS, Borrás A, Manau D, Gratacós E, Crispi F, Casals G. Fetal neurosonography and infant neurobehavior following conception by assisted reproductive technology with fresh or frozen embryo transfer. Ultrasound Obstet Gynecol. 2022 Nov;60(5):646-656. doi: 10.1002/uog.24920.
- 7. Boutet ML, Youssef L, Erlandsson L, Hansson E, Manau D, Crispi F, Casals G, Hansson SR. Maternal and fetal haemopexin and α1microglobulin concentrations in pre-eclamptic IVF pregnancies according to presence of corpus luteum at embryo transfer. Reprod Biomed Online. 2022 Jul;45(1):135-145. doi: 10.1016/j.rbmo.2022.01.005.
- 8. Casas R, Castro-Barquero S, Crovetto F, Larroya M, Ruiz-León AM, Segalés L, Nakaki A, Youssef L, Benitez L, Casanovas-Garriga F, Vieta E, Crispi F, Gratacós E, Estruch R. Maternal Dietary Inflammatory Index during Pregnancy Is Associated with Perinatal Outcomes: Results from the IMPACT BCN Trial. Nutrients. 2022 May 29;14(11):2284. doi: 10.3390/nu14112284.

- 9. Soveral I, Guirado L, Escobar-Diaz MC, Alcaide MJ, Martínez JM, Rodríguez-Sureda V, Bijnens B, Antolin E, Llurba E, Bartha JL, Gómez O, Crispi F. Cord Blood Cardiovascular Biomarkers in Left-Sided Congenital Heart Disease. J Clin Med. 2022 Nov 30;11(23):7119. doi: 10.3390/jcm11237119.
- 10. Rodriguez-Lopez M, Vergara-Sanchez C, Crispi F, Cepeda IL. Sources of heterogeneity when studying the cardiovascular effects of fetal growth restriction: an overview of the issues. J Matern Fetal Neonatal Med. 2022 Apr;35(7):1379-1385. doi: 10.1080/14767058.2020.1749592.
- 11. Spencer RN, Hecher K, Norman G, Marsal K, Deprest J, Flake A, Figueras F, Lees C, Thornton S, Beach K, Powell M, Crispi F, Diemert A, Marlow N, Peebles DM, Westgren M, Gardiner H, Gratacos E, Brodszki J, Batista A, Turier H, Patel M, Power B, Power J, Yaz G, David Development of standard definitions and grading for Maternal and Fetal Adverse Event Terminology. Prenat Diagn. 2022 Jan; 42 (1):15-26. 10.1002/pd.6047.

- 12. Vellvé K, Sepúlveda-Martínez Á, Rodríguez-López M, Crovetto F, Bernardino G, Burgos F, Faner R, Agustí À, Bijnens B, Gratacós E, Crispi F, Blanco I. Lung function in young adults born small for gestational age at term. Respirology. 2023 Feb;28(2):183-186. doi: 10.1111/resp.14361.
- 13. García-Otero L, Walles J, Balcha TT, Merga G, López M, Crispi F, Björkman P Cardiovascular effects of intrauterine exposure to maternal HIV and antiretroviral therapy in Ethiopian infants followed from fetal life. AIDS. 2022 Jun 1;36(7):941-951. doi: 10.1097/QAD.0000000000003188.

This line of research has a multidisciplinary team of fetal medicine specialists, pediatricians, epidemiologists, biologists and engineers

## Fetal Brain Development



WE ASSESS FETAL BRAIN DEVELOPMENT IN PREGNANCY TO DETERMINE OPTIMAL BIOMARKERS AND IDENTIFY BABIES AT HIGHER RISK OF MANIFESTING IMPAIRED NEURODEVELOPMENT

### WHY IS THE ANALYSIS OF FETAL NEURODEVELOPMENT IMPORTANT?

The brain is a complex organ that develops during a long time period. In addition, the brain is susceptible of changes due to multiple factors in pregnancy. As such, a thorough follow up of fetal brain development and growth could identify biomarkers that help us to determine those fetuses at higher risk of suffering alterations in neurodevelopment.

## HOW DO WE SELECT THE BEST BIOMARKERS?

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



Elisenda Eixarch
Coordinator of the
research line. MaternalFetal Medicine Specialist
at BCNatal. Member of
the fetal surgery team.

### IN 2022...

- For the first time, we have shown by ultrasound that fetuses with congenital cardiopathies have a reduced development of corpus callosum, most likely in cases with low blood flow to the brain. These results show that corpus callosum is a great biomarker of prenatal development of the white matter.
- We have shown by magnetic resonance that 50% of fetuses with defects in neural tube and candidates to prenatal reparation have supratentorial anomalies that can compromise their long-term development.
- A precise evaluation of cortical development shows that fetuses infected with Cytomegalovirus, even those without apparent lesions, have a delay in the cortical maturation pattern and it can be related with a higher risk of manifesting anomalies in their development in childhood



#### **TEAM MEMBERS**

#### COORDINATOR

Elisenda Eixarch

#### SPECIALISTS IN MATERNAL AND FETAL MEDICINE

Míriam Illa, Narcís Masoller, Míriam Pérez

#### PREDOCTORAL RESEARCHER

Ameth Hawkins, Elena Monterde, Lucas Trigo

RESEARCH FELLOWS

Iris Calvo, Ron Charach, Yvan Gómez, Laia Grau, Paola Traversi

#### COLLABORATIONS

#### NATIONAL

-Speech, Acquisition & Perception Group, Universitat Pompeu Fabra, Barcelona -Simulation, Imaging and Modelling for Biomedical Systems, Universitat Pompeu Fabra, Barcelona

-CIBERSAM (grupo 8), Universitat de Barcelona

-Unitat de Medicina Fetal, Hospital de la Santa Creu i Sant Pau, Barcelona

#### INTERNATIONAL

-University Hospitals Leuven, Belgium -University of São Paulo, Brazil

-Lausanne University CIBM Center for Biomedical Imaging and Lausanne University Hospital (CHUV), Switzerland

-Aix-Marseille Université Institut de Neurosciences de la Timone (INT), France

-Technischen Universität München Institute for Medical Informatics, Germany

#### **PUBLICATIONS IN 2022**

- 1. Hawkins-Villarreal A, Moreno-Espinosa AL, Castillo K, Hahner N, Picone O, Mandelbrot L, Simon I,Gratacós E, Goncé A, Eixarch E. Cortical maturation assessed by magnetic resonance imaging inunaffected/mildly affected fetuses with cytomegalovirus infection. Ultrasound Obstet Gynecol. 2022Nov 9. doi: 10.1002/uog.26110.
- 2. Boutet ML, Eixarch E, Ahumada-Droguett P, Nakaki A, Crovetto F, Cívico MS, Borrás A, Manau D,Gratacós E, Crispi F, Casals G. Fetal neurosonography andinfant neurobehavior following conceptionby assisted reproductive technology with fresh or frozen embryo transfer. Ultrasound Obstet Gynecol.2022 Nov;60(5):646-656. doi: 10.1002/uog.24920.
- 3. Basso A, Youssef L, NakakiA, Paules C, Miranda J, Casu G, Salazar L, Gratacos E, Eixarch E, CrispiF, Crovetto F. Fetal neurosonography at 31-35 weeks reveals altered cortical development in pre-eclampsia with and without small-for-gestational-age fetus. Ultrasound Obstet Gynecol.2022Jun;59(6):737-746. doi:

  1.1002/uog.24853.
- 4. Trigo L, Eixarch E, Bottura I, Dalaqua M, Barbosa AA, De Catte L, Demaerel P, Dymarkowski S,Deprest J, Lapa DA, Aertsen M, Gratacos E. Prevalence of supratentorial

- anomaliesassessed bymagnetic resonance imaging in fetuses with open spina bifida. Ultrasound Obstet Gynecol. 2022Jun;59(6):804-812. doi: 10.1002/uog.23761.
- 5. Hawkins-Villarreal A, Moreno-Espinosa AL, Martinez-Portilla RJ, Castillo K, Hahner N, Nakaki A, Trigo L, Picone O, Siauve N, Figueras F, Nadal A, Eixarch E, Goncé A. Fetal Liver Volume AssessmentUsing Magnetic Resonance Imaging in Fetuses With Cytomegalovirus Infection † Front Med(Lausanne). 2022 May 16;9:889976. doi: 10.3389/fmed.2022.889976.
- 6. Van der Veeken L, Russo FM, Litwinska E, Gomez O, Emam D, Lewi L, Basurto D, Van der VeekenS, De Catte L, Gratacos E, Eixarch E, Nicolaides K, Deprest J. Prenatal cerebellar growth is altered incongenital diaphragmatic hernia on ultrasound. Prenat Diagn. 2022 ar;42(3):330-337. doi:10.1002/pd.5993.
- 7. Pérez-Cruz M, Gómez O, Gibert M, Masoller N, Marimon E, Lip-Sosa D, Bennasar M, Bonet-CarneE, Gómez-Roig MD, Martínez-Crespo JM, Gratacós E, Eixarch E. Corpus callosum size byneurosonography in fetuses with congenital heart defect and relationship with expected pattern of brainoxygen supply. Ultrasound Obstet Gynecol. 2022 Feb;59(2):220-225. doi: 10.1002/uog.23684.

#### **STRATEGIC GOALS**

		CLINIC	EGINEERING
TO DEVELOP		Normality curves for late gestational age	Develop systems of analysis of cortical development by studying the surface in fetal MRI. Develop systems of automatic segmentation of brain structures in ultrasound.
	TO VALIDATE	Integration of cortical maturation within the evaluation of patients at risk(cardiopathies, growth restrictions, toxics)	Analysis of cortical maturation pattern in clinical studies.

## **Prematurity**

OUR MISSION IS TO IDENTIFY PREGNANT WOMEN WITH A HIGH RISK OF PRETERM DELIVERY AND OFFER THE BEST TREATMENT AVAILABLE

TO PROLONG GESTATION AS MUCH AS POSSIBLE AND IMPROVE THE PROGNOSTIC OF THE BABY

### WHY IS IT IMPORTANT TO INVESTIGATE PREMATURITY?

It is estimated that there are around 15 million babies born premature worldwide every year, these are 1 in 10 deliveries in Spain. Premature deliveries are considered below 37 weeks of gestational age and it is associated with a high perinatal morbimortality. The aim of our line of research is to advance in the current knowledge and improve procedures.



The objective is to extend premature pregnancies. Premature babies would have a better quality of life even if delivery is delayed two weeks. We are investigating multiple non-invasive interventions to improve decision capacity in cases with premature delivery. One of our main tools is the quantitative analysis of lung and cervical textures of ultrasound images. Analysis of lung textures is a practice in the clinic and helps to predict the outcome in induced delivery. Analysis of cervical textures will help to stratify the risk of



Montse Palacio Coordinator of the research line. Specialist in Prematurity at BCNatal.

### IN 2022....

 We have published multiple studies that assess the predicition of fetal lung maturity in particular population and we have shared our experience in the handling of premature membrane break in preterm pregnancies.

prematurity in the general population. In the future, we will investigate the causes of prematurity in multiple pregnancies because it is not well studied.



### TEAM MEMBERS

#### COORDINATOR

Montse Palacio

#### POSTDOCTORAL RESEARCHER

Sílvia Ferrero

#### PREDOCTORAL RESEARCHER

Ana Moreno, Clara Murillo, Julia Ponce, Claudia Rueda

### STRATEGIC GOALS

TO IMPROVE DIAGNOSIS	TO IMPROVE PATIENT MANAGEMENT	
Quantitative analysis of the lung texture to predict the outcome after inducing delivery and risks associated with premature delivery.	Evaluate the effect of pharmaceutical drugs that can delay preterm delivery in patients at risk of premature delivery	CLINIC AN BIOENGINEE
Quantitative analysis of cervical texture in patients at risk of premature delivery		RING

#### **PUBLICATIONS IN 2022**

1.Bhatia A, Palacio M, Wright AM,Yeo GSH. Lower uterine segment scar assessment at 11-14 weeks'gestation to screen for placenta accreta spectrum in women with prior Cesarean delivery. Ultrasound Obstet Gynecol. 2022 Jan;59(1):40-48. doi: 10.1002/uog.23734.

2.Ronzoni S, Cobo T, D'Souza R, Asztalos E, O'Rinn SE, Cao X, Herranz A, Melamed N, Ferrero S,Barrett J, Aldecoa V, Palacio M. Individualized treatment of preterm premature rupture of membranesto prolong the latency period, reduce the rate of preterm birth, and improveneonatal outcomes. Am JObstet Gynecol. 2022 Aug;227(2):296.e1-296.e18. doi: 10.1016/j.ajog.2022.02.037.

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4.Castillo K, Hawkins-Villarreal A, Valdés-Bango M, Guirado L, Scazzocchio E, Porta O, Falguera G,López M, Palacio M, Gratacós E, Figueras F, Goncé A. Congenital Cytomegalovirus Awareness and Knowledge among Health Professionals and Pregnant Women: An Action towards Prevention. Fetal Diagn Ther. 2022;49(5-6):265-272. doi: 10.1159/000525528.



5.Moreno-Espinosa AL, Hawkins-Villarreal A,Coronado-Gutierrez D, Burgos-Artizzu XP, Martínez-Portilla RJ, Peña-Ramirez T, Gallo DM, Hansson SR, Gratacòs E, Palacio M. Prediction of NeonatalRespiratory Morbidity Assessed by Quantitative Ultrasound Lung Texture Analysis in TwinPregnancies. J Clin Med. 2022 Aug 20;11(16):4895. doi: 10.3390/jcm11164895.

6.Baños N, Burgos-Artizzu XP, Valenzuela-Alcaraz B, Coronado-Gutiérrez D, Perez-Moreno Á, PonceJ, Gratacós E, Palacio M. Intra-and interobserver reproducibility of second trimester ultrasound cervicallength measurement in a general population. J Matern Fetal Neonatal Med. 2022 Mar;35(5):999-1002.doi:

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7.Ponce J, Benítez L, Baños N, Goncé A, Bennasar M, Muñoz M, Cobo T, Palacio M. Latency to deliveryin physical examination-indicated cerclage in twins is similar to that in singleton pregnancies. Int JGynaecol Obstet. 2022 Oct;159(1):188-194. doi: 10.1002/ijgo.14070.

## **Inflammation in Prematurity**

OUR OBJECTIVE IS TO IDENTIFY INTRAAMNIOTIC INFECTION AND INFLAMMATION WITH NON-INVASIVE METHODS IN PREGNANT WOMEN WITH RISK OF PRETERM DELIVERY TO OPTIMIZE PROCEDURES

### WHY IS IT RELEVANT TO STUDY INFECTION IN AMNIOTIC LIQUID?

Currently, prediction of preterm delivery is poor. More than 70% of women at high-risk of preterm delivery are hospitalized and will give birth at term. Women with intraamniotic infection and inflammation the 40% of the (around hospitalizations with high-risk of preterm delivery) are the group with higher risk of delivery in the following 7 days. They benefit the most from the existent strategies to improve the prognostic of premature kids (corticoids administration, magnesium sulfate, and antibiotics). Identification of the intraamniotic infection and inflammation allows to select those at higher risk. avoiding unnecessary treatments in those at low risk of intraamniotic infection.

## WHY IS IT REQUIRED TO USE MINIMALLY INVASIVE SAMPLES?

Up until now, amniocentesis was performed to diagnose intraamniotic infection and inflammation. It is a high invasive procedure with limited use. Our objective is to develop new non-invasive technologies able to determine at early stage the risk of intraamniotic infection and inflammation. This way, we can choose the best candidates that would benefit from an amniocentesis to identify or rule out infection.



Teresa Cobo
Coordinator of the
research line. Specialist in
Prematurity at BCNatal.
Cofounder of Compartim,
a support group for
perinatal loss

## WHICH ARE THE SEQUELAE OF INFECTION AND INFLAMMATION IN FETAL LIFE AND LIFETIME?

Our group studies the effects of intrauterine infection and inflammation on growth, cardiovascular and neurological system at prenatal stage, at birth, and the first 6 months of life. Indeed, we perform a follow up of the neurodevelopment in the first year of life.

We have observed cardiovascular and neurological alterations at fetal stage in prematurity. These alterations are greater in those pregnancies affected with intraamniotic infection and inflammation. It was already known that premature babies have changes in cardiac remodelling. However, we have shown that these changes are produced before birth, in fetal life and it can be detected with an echography or studying biomarkers of cardiac dysfunction in the amniotic liquid.



#### **TEAM MEMBERS**

#### COORDINATOR

Teresa Cobo

**TECHNICIAN** 

Ana Belén Sánchez

PREDOCTORAL RESEARCHER

Clara Murillo, Claudia Rueda

MASTER STUDENT

Catherine Hernández-Mansilla

Over the years we have nurtured collaborations with 'Biotec' companies in our high-translational projects that will improve the current management of patients

#### **COLLABORATIONS**

#### **NATIONALS**

- Dept. de Bioquímica y Biomedicina Molecular de la Universitat de Barcelona
- Dept. de Biotecnología del Instituto de Agroquímica y Tecnología de Alimentos (IATA) del Consejo Superior de Investigaciones Científicas (CSIC)
  - Plataforma de Bioestadística de IDIBAPS
  - Dept. de Genómica de la Universitat Pompeu Fabra
  - Dept. De Ciencias Experimentales y Satlut de la Universitat Pompeu Fabra INTERNATIONALS
  - Dept. of Obstetrics and Gynecology, Charles University in Prague, Faculty of Medicine Hradec Kralove, Hradec Kralove, Czech Republic
    - Dept. of Obstetrics and Gynecology, Sahlgrenska Academy, Gothenburg University, Goteburg, Sweden

#### **COMPANIES**

- Hologic, USA
- Medix Biochemica, Finland
  - Movuntech SI

#### IN 2022....

- We have advanced the diagnosis of intraamniotic infection and inflammation with non-invasive methods. We have integrated *-omics* disciplines such as proteomics, metabolomics and high-throughput sequencing techniques that characterize vaginal microbiome. In addition, we have developed and validated various non-invasive prediction models of intraamniotic infection and inflammation in pregnant women with high-risk of preterm delivery; results are obtained in few hours and can help professionals to handle the patient.
- We have an ongoing multicentric clinical trial that aims at optimizing the current handling of pregnant women with high-risk of preterm delivery by assessing days of hospitalization and corticoid administration for fetal maturation related to the information obtained from amniocentesis.
- Finally, we have finalized two prospective studies in collaboration with the industry (Actim IAI with Medix Biomedica and Scuba Project with Hologic SL), they were also focused in non-invasive diagnostic in intraamniotic infection and inflammation in women with high-risk of preterm delivery and premature membrane break.

#### **PUBLICATIONS 2022**

1. Cobo T, Burgos-Artizzu XP, Collado MC, Andreu-Fernández V, Sanchez-Garcia AB, Filella X, Marin S, Cascante M, Bosch J, Ferrero S, Boada D, Murillo C, Rueda C, Ponce J, Palacio M, Gratacós E. Noninvasive prediction models of intra-amniotic infection in women with preterm labor. Am J Obstet Gynecol. 2023 Jan;228(1):78.e1-78.e13. doi: 10.1016/j.ajog.2022.07.027.





- 3. Ponce J, Benítez L, Baños N, Goncé A, Bennasar M, Muñoz M, Cobo T, Palacio M. Latency to delivery in physical examination-indicated cerclage in twins is similar to that in singleton pregnancies. Int J Gynaecol Obstet. 2022;159(1):188-194. doi:10.1002/ijgo.14070
- 4. Llupià A, Torà I, Lladó A, Cobo T, Sotoca JM, Puig J. Factors related to inhibition of lactation by pharmacological means at birth in a Spanish referral hospital (2011-2017). Gac Sanit. 2022;36(1):6-11. doi:10.1016/j.gaceta.2021.05.001.

#### STRATEGIC GOALS

CLINIC	BASIC	
To prove through a multicentric clinical trial that we can individualize the clinical handling of pregnant women at risk of preterm delivery by studying intraamniotic infection and inflammation to avoid unnecessary treatments in low-risk cases.	To make progress in the development of a non-invasive solution to diagnose intraamniotic infection and inflammation in women at risk of preterm delivery using technologies based on metabolomics, proteomics, microbiome and photonics.	TO IMPROVE DI
To evaluate the impact of intraamniotic infection and inflammation in fetal growth, cardiovascular and neurological development.		DIAGNOSIS

# PREVENTING THE GREAT OBSTETRICAL SYNDROMES

WE STUDY FACTORS THAT CAN BE MODIFIED IN PREGNANCY AND CAN IMPACT ON THE GREAT OBSTETRICAL SYNDROMES: INTRAUTERINE GROWTH RESTRICITION, PREECLAMPSIA AND PRETERM DELIVERY

### DOES THE LIFESTYLE IN PREGNANCY HAVE EFFECTS ON THE FETUS?

Obstetric complications usually arise from multiple causes. Among them, maternal nutrition and stress level in pregnancy can affect the fetal growth and development. As such, we study whether a structured nutrition, stress reduction, emotional well-being, sleep quality and gut microbiome in pregnant women can improve the well-being of the fetus.

## CAN WE CONSIDER A MEDICINE AN IMPROVEMENT OF THE LIFESTYLE IN PREGNANCY?

A few years ago, we started the study IMPACT Barcelona (2017-2020), it is a randomized clinical trial in which 1,200 pregnant women with high-risk of having a baby with low weight at birth were recruited. The stydy had 3 groups randomly divided; the first group followed a nutritional programme based Mediterranean diet supplemented with olive oil and nuts, with the collaboration of Cardiovascular risk, Nutrition and Aging group at FRCB-IDIBAPS, led by Ramon Estruch; the second group followed a stress reduction programme with mindfulness techniques and it was coordinated by Bipolar and Depressive disorders group at



Francesca Crovetto
Coordinator of the
research line.
Maternal-Fetal
Medicine Specialist at
BCNatal.

FRCB-IDIBAPS, led by Eduard Vieta and professionals at etMindfulness Institute; the third group did not follow any intervention, they were only assessed with routinary checkups. This study showed that Mediterranean diet or mindfulness has a positive effect in pregnancy, reducing between 29% and 36% the risk of having a baby with low weight. Indeed, this study has also proven that great obstetrical complications were also reduced.

## IS IT POSSIBLE TO ENHANCE MATERNAL AND FETAL HEALTH WITHOUT MEDICATION?

Results from our study show that it is possible, with both interventions, we have been able to reduce the risk of low birth weight newborns by 30%. Currently, we are interested in understanding how diet and stress reduction affect fetal development and what is the biological mechanism behind. In addition, our clinical trial can inspire other groups to develop other non-pharmacological interventions.



#### **TEAM MEMBERS**

#### COORDINATOR

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Fàtima Crispi, Laura Guirado

#### PREDOCTORAL RESEARCHERS

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#### POSTDOCTORAL RESEARCHERS

Lina Youssef, Ángela Arranz, Sara Castro

#### **RESEARCH FELLOWS**

Katarzya Darecka, Roberta Castellani

#### CLINICAL RESEARCHER

Mireia Pascual

NUTRICIONIST

Tania Freitas

#### **COLLABORATORS**

#### **NATIONALS**

- Traslational Computing in Cardiology, IDIBAPS, Barcelona
- Grupo de Riesgo cardiovascular, nutrición y envejecimiento, Hospital Clínic de Barcelona
  - Instituto Clínic de Psiquiatría, Hospital Clínic de Barcelona
  - Institute of Agrochemistry and Food Technology (IATA), CSIC, Valencia
    - Applied Metabolomics Research Group (LIMA), IMIM, Barcelona
      - Grupo Miguel Angel, Universidad Pompeu Fabra

#### **INTERNATIONALS**

- The Boden Institute of Obesity, Nutrition, Exercise & Eating Disorders, The University of Sydney, Camperdown, NSW, Australia

#### COMPANIES

- Instituto esMinfulness

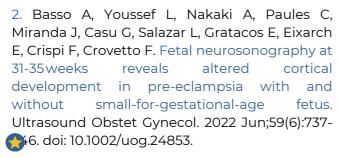
We study how interventions in maternal lifestyle improve fetal growth

#### STRATEGIC GOALS

CLINIC	BASIC	
Study the physiopathological mechanisms of non-pharmacological therapies in pregnancy to improve the results.  Study of maternal and neonatal intestinal microbiota using non-pharmacological therapies in pregnancy.	Developing strategies to improve nutrition and maternal well-being in pregnancy.  Evaluate whether an optimal maternal lifestyle in pregnancy improves fetal growth and development.  Study fetal and neonatal neurodevelopment (with imaging and functional tests) applying nonpharmacological therapies in pregnancy.	COMPRENHEND AND PREVENT

#### **PUBLICATIONS IN 2022**

1. Crovetto F, Selma-Royo M, Crispi F, Carbonetto B, Pascal R, Larroya M, Casas I, Tortajada M, Escudero N, Muñoz-Almagro C, Gomez-Roig MD, González-Torres P, Collado MC, Gratacos E. Nasopharyngeal microbiota profiling of pregnant women with SARS-CoV-2 infection. Sci Rep. 2022 Aug 4;12(1):13404. doi: 10.1038/s41598-022-17542-z.



- 3. Crovetto F, Crispi F, Gratacós E. Mediterranean Diet or Mindfulness-Based Stress Reduction and Prevention of Small-for-Gestational-Age Birth Weights in Newborns-Reply. JAMA. 2022 Apr 5;327(13):1293-1294. doi: 10.1001/jama.2022.2167.
- 4. Casas R, Castro-Barquero S, Crovetto F, Larroya M, Ruiz-León AM, Segalés L, Nakaki A, Youssef Y, Benitez L, Casanovas-Garriga F, Vieta E, Crispi E, Gratacos E, Estruch R. Maternal Dietary Inflammatory Index during Pregnancy Is Associated with Perinatal Outcomes: Results from the IMPACT BCN Trial. Nutrients. 2022 May 29;14(11):2284. doi: 10.3390/nu14112284.
- 5. Trilla C, Mora J, Crovetto F, Crispi F, Gratacós E, LLurba E, KidsCorona Pregnancy COVID-19 group. First-trimester SARS-CoV-2 infection: clinical presentation, inflammatory markers and obstetric outcomes. Fetal Diagn Ther. 2022;49(3):67-76. doi: 10.1159/000523974.
- 6. Pascal R, Crovetto F, Casas I, Youssef L, Trilla C, Larroya M, Cahuana A, Boada D, Foraster M, Llurba E, Sunyer J, Crispi F, Gratacos E, Gómez-Roig MD. Impact of the COVID-19 Pandemic on Maternal Well-Being during Pregnancy. J Clin Med. 2022 Apr 15;11(8):2212. doi: 10.3390/jcm11082212.



7. Bäuerl C, Randazzo W, Sánchez G, Selma-Royo M, García Verdevio E, Martínez L, Parra-Llorca A, Lerin C, Fumadó V, Crovetto F, Crispi F, Pérez-Cano FJ, Rodríguez G, Ruiz-Redondo G, Campoy C, Martínez-Costa C, Collado MC; MilkCORONA study team. SARS-CoV-2 RNA and antibody detection in breast milk from a prospective multicentre study in Spain. Arch Dis Child Fetal Neonatal Ed. 2022 Mar;107(2):216-221. doi: 10.1136/archdischild-2021-322463.

8. Smith ER, Oakley E, Grandner GW, Rukundo G, Farooq F, Ferguson K, Baumann S, Waldorf KA, Afshar Y, Ahlberg M, Ahmadzia H, Akelo V, Aldrovandi G, Bevilacqua E, Bracero N, Brandt JS, Broutet N, Carrillo J, Conry J, Cosmi E, Crispi F, Crovetto F, Gil MDM, Delgado-López C, Divakar H, Driscoll AJ, Favre G, Buhigas IF, Flaherman V, Gale C, Godwin CL, Gottlieb S, Gratacós E, He S, Hernandez O, Jones S, Joshi S, Kalafat E, Khagayi S, Knight M, Kotloff K, Lanzone A, Longo VL, Le Doare K, Lees C, Litman E, Lokken EM, Madhi SA, Magee LA, Martinez-Portilla RJ, Metz TD, Miller ES, Money D, Moungmaithong S, Mullins E, Nachega JB, Nunes MC, Onyango D, Panchaud A, Poon LC, Raiten D, Regan L, Sahota D, Sakowicz A, Sanin-Blair J, Stephansson O, Temmerman M, Thorson A, Thwin SS, Tippett Barr BA, Tolosa JE, Tug N, Valencia-Prado M, Visentin S, von Dadelszen P, Whitehead C, Wood M, Yang H, Zavala R, Tielsch JM. Clinical risk factors of adverse outcomes women with COVID-19 in among pregnancy and postpartum period: sequential, prospective meta-analysis. Am J Obstet Gynecol. 2022 Aug 23:S0002-9378(22)00680-9. doi: 10.1016/j.ajog.2022.08.038.

### IN 2022....

- We have greatly disseminated our publication of the clinical trial IMPACT BCN that
  was published in the prestigious scientific journal JAMA (Crovetto et al., JAMA 2021).
  This work has been presented in 8 national and international congresses and 35 oral
  communications. This publication has had great impact in various communication
  channels and social network platforms.
- In addition, we have been awarded with 4 congress awards in 2022, it is worth mentioning the best abstract awarded in ISUOG World Congress (London 2022).
- Dr. Crovetto has been granted competitive funding from Instituto de Salud Carlos III to study the microbiome of participants in the clinical trial IMPACT BCN.
- We are pleased to announce that Dra. Sara Castro has joined the group, she has a Margarita Salas postdoctoral grant.
- In 2022 we have published multiple scientific articles related with COVID-19 and its impact in pregnancy.
- We are pleased to communicate that in 2022 we received multiple awards:
  - Best Oral Communication. XII Congress of Mediterranean diet, Barcelona, Spain, 7-8 April 2022. Casas I, Genero M, Nakaki A, Benitez L, Larroya M, Youssef L, Pascal R, Martinez-Aran AI, Pozo OJ, Vieta E, Crispi F, Gomez-Roig MD, Gratacós E, Crovetto F. The IMPACT BCN trial: effects of an intervention during pregnancy based on Mediterranean diet on maternal stress, well-being, and sleep quality throughout gestation. The IMPACT BCN trial.
  - Best Oral Communication. XIII Workshop of the "Sociedad Española de Microbiota, Probióticos y Prebióticos-SEMiPyP", Valencia, Spain, 7-9 June 2022. Crovetto F, Selma-Royo M, Crispi F, Youssef L, Nakaki A, Paules C, Benítez L, Larroya M, Casas I, Castro-Barquero S, Casas R, Vieta E, Estruch R, Gratacós E, Collado MC. Effects of a Mediterranean diet intervention or a Stress Reduction program during pregnancy on maternal gut microbiota. The IMPACT BCN trial.
  - Oral Communication for the Best Abstract. 32nd World Congress on Ultrasound in Obstetrics and Gynecology, London, UK, 15-17 September 2022. Crovetto F, Crispi F, Borras R, Youssef L, Nakaki A, Paules C, Benítez L, Larroya M, Casas I, Castro-Barquero S, Casas R, Vieta E, Estruch R, Gratacós E; on behalf of the IMPACT BCN. Effects of a Mediterranean diet or a Stress Reduction intervention during pregnancy on the incidence of early-late preeclampsia. The IMPACT BCN trial.
  - Best Oral Communication. Mexico, 9 November 2022. Arranz A, Crovetto F, Crispi F, Gratacós E. Ensayo clínico Aleatorio IMPACT BCN. Sociedad Iberoamericana de neonatología (SIBEN).

# FETAL THERAPY AND SURGERY

WE INVESTIGATE NEW THERAPEUTIC LINES AND TREATMENTS TO MITIGATE THE MAIN COMPLICATIONS IN FETAL AND PERINATAL MEDICINE TO OVERCOME CURRENT LIMITATIONS IN FETAL SURGERIES



### HOW DO WE DEVELOP NEW THERAPIES AND FETAL SURGERIES?

Our goal is to prevent and treat pathologies of fetal origin. Thus, we develop surgical procedures to improve fetal survival and reduce long-term sequelae. In addition, we design therapies that are beneficial for an optimal fetal neurodevelopment.

## HOW CAN BE ACHIEVED THE CREATION OF AN ARTIFICIAL PLACENTA SYSTEM?

The aim is to extend the gestational stage up until 4 weeks in an artificial environment to increase the fetal survival and reduce sequelae associated to extreme prematurity. We use an animal model in sheep to prove the viability and safety of our system. As such, it is required to mirror all the conditions that allow fetal survival outside maternal uterus. This project is very complex, thus, it is essential to build a multidisciplinary team composed by specialized doctors in Fetal Medicine, pediatricians, intensivists, engineers, and specialized nurses.



Elisenda Eixarch
Coordinator of the
research line. MaternalFetal Medicine Specialist
at BCNatal. Member of
the fetal surgery team.

Míriam Illa
Coordinators of the
research line.
Maternal-Fetal
Medicine Specialist at
BCNatal.



## IN WHICH THERAPIES ARE YOU INVESTIGATING TO IMPROVE FETAL DEVELOPMENT?

The Fetal Medicine group at BCNatal is been working on experimental models of intrauterine growth restriction for years. In this models, we have proven that supplementation with docosahexaenoic acid, melatonin and lactoferrin can palliate the adverse effects of growth restriction in neurodevelopment.



# **TEAM MEMBERS**

### **COORDINATORS**

Elisenda Eixarch y Miriam Illa

# SPECIALISTS IN MATERNAL AND FETAL MEDICINE

Mar Bennasar, Josep M. Martínez, Narcís Masoller

### **NURSES**

Helena Martí, Patricia Galdeano, Olga Coronel, Erika Sánchez, Ángela Arranz

### POSTDOCTORAL RESEARCHERS

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## PREDOCTORAL RESEARCHERS

Britta Ana Kühner, Johanna Parra, Paula Randanne, Ximena Torres, Lucas Trigo, Ameth Hawkins, Miguel Ángel Morán, Elena Monterde

## **MASTER STUDENTS**

Mercè Fuentes, Daniel Sanin, Víctor Narvaez, María Fernanda Hernández

**TFM STUDENTS** 

David Vizcarro

**UNDERGRAD STUDENTS** 

Anna Ventura

### **TECHNICIANS**

Daniela Aguilar, Sara Barra, Daniele Mariani, Anna Oliveira, Iolanda Campos, Sofia Aledo, Jéssica Ortiz

#### SPECIALIZED NURSES

Marina Chorda, Mireia Gispert, Victor Gómez, Maite Mata

### **RESEARCH FELLOWS**

Ron Charach, Yvan Gómez, Juan Otaño

**RESEARCH ASSISTANT** 

Santiago López

**BIOLOGIST** 

Raquel Fucho

SPECIALIST IN CARDIOVASCULAR SURGERY

Kambiz Rezaei

SPECIALIST IN PEDIATRIC INTENSIVE CARE

Sara Bobillo, Ruth del Río, María del Mar Velilla

**ENGINEERS** 

Yolanda de Roo, Aleix Garcia, Juan Medina, Marc Gallego

RESIDENT PHYSICIAN

Uxía Barba

MANAGEMENT

Elisenda Bonet-Carne, Marco Lescano

### **COLLABORATORS**

#### NATIONAL

- Unidad de Toxicología de la Facultad de Farmacia, Universidad de Barcelona (UB)
  - Simulation, Imaging and Modelling for Biomedical Systems, Universitat

    Pompeu Fabra (UPF), Barcelona
- Research group on Intelligent Robotics and Systems, Universitat Politècnica de Catalunya (UPC)
  - Instituto de Bioingeniería de Cataluña (IBEC), Barcelona
    - Institut Químic de Sarrià (IQS), Barcelona
  - Departamento Biología Celular, Inmunología y Neurociencias de la UB,

Barcelona

#### INTERNATIONAL

- University Hospitals Leuven, Belgium
  - University of São Paulo, Brazil

## **PUBLICATIONS IN 2022**

- 1. Pla L, Kühne BA, Guardia-Escote L, Vázquez-Aristizabal P, Loreiro C, Flick B, Gratacós E, Barenys M, Illa M. Protocols for the Evaluation of Neurodevelopmental Alterations in Rabbit Models In Vitro and In Vivo. Front Toxicol. 2022 Jul 22;4:918520. doi: 10.3389/ftox.2022.918520.
- 2. Micheletti T, Eixarch E, Febas G, Berdun S, Parra J, Hernansanz A, Borrós S, Gratacos E. Intraamniotic sealing of fetoscopic membrane defects in ex vivo and in vivo sheep models using an integrated semirigid bioadhesive patch. Am J Obstet Gynecol MFM. 2022 May;4(3):100593. doi: 10.1016/j.ajogmf.2022. 100593.
- 3. Kühne BA, Vázquez-Aristizabal P, Fuentes-Amell M, Pla L, Loreiro C, Gómez-Catalán J, Gratacós E, Illa M, Barenys M. Docosahexaenoic Acid and Melatonin Prevent Impaired Oligodendrogenesis Induced by Intrauterine Growth Restriction (IUGR). Biomedicines. 2022 May 23;10(5):1205. doi: 10.3390/biomedicines10051205.
- 4. Kühne BA, Teixidó E, Ettcheto M, Puig T, Planas M, Feliu L, Pla L, Campuzano V, Gratacós E, Fritsche E, Illa M, Barenys M. Application of the adverse outcome pathway to identify molecular changes in prenatal brain programming induced by IUGR: Discoveries after EGCG exposure. Food Chem Toxicol. 2022 Dec;170:113506. doi: 10.1016/j.fct.2022.113506.

# IN 2022....

- We have achieved a 7-day survival in an Artificial Placenta system.
- We have developed a sealed system for the Artificial Placenta.
- We have proven that docosahexaenoic acid, melatonin and lactoferrin have a neuroprotector role in fetuses with intrauterine restriction growth.
- We have developed a sealing system of fetal membranes that could be used after fetal surgeries to reduce premature break of membranes.

### STRATEGIC GOALS

THERAPY	SURGERY	
Clinical trial in prenatal therapy in pregnancies with growth restriction (FetalBrainCare).	Pilot study with a membrane sealing system to be used in fetal surgeries.	CLINIC
Evaluation of new therapeutic strategies (neuroprotection) in cell cultures.  Evaluation of new therapeutic strategies (neuroprotection) in animal models.	Functional and safety tests to improve a membrane sealing system. Artificial Placenta: technic improvements; study of the effects in neurodevelopment; study of the effects in cardiovascular system;study of the optimal nutritional and hormonal profile.	EXPERIMENTAL

# **PLACENTAL DISEASE**

WE HAVE IMPROVED THE DIAGNOSTIC AND HANDLING OF PREGNANCIES WITH GROWTH RESTRICTION TO REDUCE DISORDERS IN NEURODEVELOPMENT

# WHAT IS THE IMPACT OF INTRAUTERINE GROWTH RESTRICTION?

Prenatal and after birth complications are higher in intrauterine growth restriction cases. As such, babies can develop multiple grades of dysfunctional neurodevelopment; even mild, these can affect family dynamics and integration in society.

# WHAT IS THE KEY OF PREVENTION AND IMPROVE BIOMARKERS?

Following-up intrauterine growth helps to predict future fetal growth restriction. Diagnosis allows to develop therapies and design preventive measures in pregnancy, giving birth, and infancy.

# WHY IS RELEVANT TO STUDY PREECLAMPSIA?

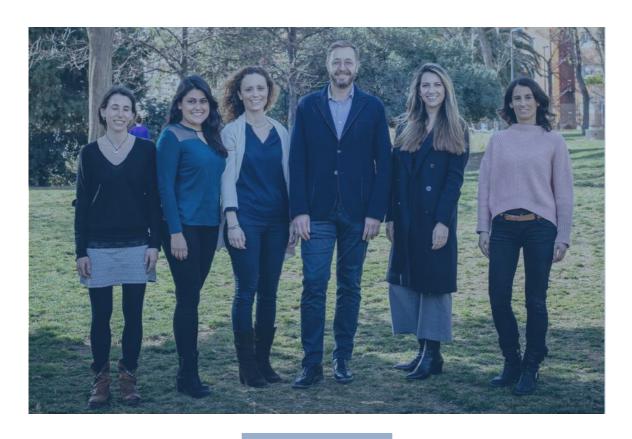
Preeclampsia is the second cause of maternal death worldwide. Currently, preeclampsia can be predicted since the first trimester preventing the majority of extreme cases. Preeclampsia is associated with many complications that compromise fetal life, once diagnosed, it is critical to determine what is the optimal time to induce delivery. For this reason, we study what are the best biochemical markers of preeclampsia to measure the severity.



Francesc Figueras
Coordinator of the
research line. MaternalFetal Medicine Specialist
and Head of the
Department at BCNatalHospital Clínic.

# IN 2022....

- We have completed the patient recruitment in Ratio37 study, more than 10,000 randomized pregnant women have had an echography in the third trimester with or without brain Doppler.
- We have started the PE37 multicentric recruitment that aims at assessing whether termination of pregnancies at term with high risk of preeclampsia reduces this disease.
- We have completed the randomized study TRACIP, aims at proving that heparin of low molecular weight can extend pregnancy in cases of early placental insufficiency.
- Finally, we have completed the cohort DG1st in which a predictive model of gestational diabetes will be implemented in the first trimester of pregnancy.



# **TEAM MEMBERS**

### COORDINATOR

Francesc Figueras

## PREDOCTORAL RESEARCHERS

Analisa Cancemi. Raigam Martínez, Marta Rial, Alba González, Rosa Hernández Cruz

## POSTDOCTORAL RESEARCHERS

Edurne Mazarico

**MASTER STUDENTS** 

Maria Fernanda López

**CLINICAL RESEARCHERS** 

Aleida Castellanos, Juan Otaño, Leila Cabral, Paula Zauzogoitia, Arce Ronald

# STRATEGIC GOALS

	CLINIC
THERAPY	Develop methods to early predict FGR: new definition and prediction of brain injury.
DIAGNOSTIC	Clinical assays to prevent preeclampsia and FGR.

## **COLLABORATORS**

#### NATIONAL

- EUGIN Clinic, Barcelona

#### INTERNATIONAL

- Instituto Nacional de Perinatología, Mexico
- Lis Hospital for Women, Tel Aviv University, Tel Aviv, Israel
- Institute for the care of mother and child, Third Faculty of Medicine, Charles University, Prague, Czech Republic
- Departmente of Obstetrics and Gynecology, Palacky University Olomouc, Faculty of Medicine and Dentistry, University Hospital Olomouc, Olomouc, Czech Republic -Unidad de Investigación en Medicina y Cirugía Fetal, Hospital de Especialidades del Niño y la Mujer de Querétaro. Unidad de Investigación en Neurodesarrollo, Instituto de Neurobiología, Universidad Nacional Autónoma de México (UNAM) campus Juriquilla, Querétaro, Mexico
  - -Department of Obstetrics and Gynecology, Fetal Medicine Unit, University of Chile Hospital, Santiago, Chile

### **PUBLICATIONS IN 2022**

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- Morales-Prieto DM, Schleußner E, pregnancies with systemic lupus erythematosus: A narrative review. Front 10.1111/1471-0528.17181. Immunol. 2022 Aug 17;13:941586. doi: 10.3389/fimmu.2022.941586.
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- Meler E, Mazarico E, Peguero A, Gonzalez A, Martinez J, Boada D, Vellvé K, 2. Castellanos Gutierrez AS, Figueras F, Arca G, Gómez-Roig MD, Gratacós E, Figueras F. Death and severe morbidity in Espinosa G, Baños N. Placental damage in isolated periviable small-for-gestational-age fetuses. BJOG. 2022 Apr 19. doi:

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- 12. Fernández-Alba JJ, Castillo Lara M, 7. Figueras F, Meler E. Fetal growth patterns Sánchez Mera R, Aragón Baizán S, González Jimenez Heras JM, Moreno Corral LJ, Figueras F. INTERGROWTH-21st versus a customized method for the prediction of 8. Hawkins-Villarreal A, Moreno-Espinosa AL, neonatal nutritional status in hypertensive Feb 19;22(1):136. doi: 10.1186/s12884-022-
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# ENVIRONMENT AND PREGNANCY COMPLICATIONS

OUR LINE OF RESEARCH STUDIES ENVIRONMENTAL FACTORS THAT CAUSE COMPLICATIONS DURING PREGNANCY AND THAT CAN AFFECT FETAL DEVELOPMENT SUCH AS TOBACCO, ALCOHOL, CHEMICAL TOXINS AND AIR POLLUTION



# WHAT IS THE FOUNDATION OF OUR RESEARCH LINE?

Our objective is to define which are the toxins that affect the fetus and anticipate possible complications such as placental pathology, intrauterine growth restriction, hypertension, prematurity, perinatal morbidity, heart function and neurodevelopment prenatally and after birth. As such, we aim at developing interventions to reduce alcohol consumption and other drugs to protect fetal development.

# WHAT ARE THE EFFECTS OF ALCOHOL AT FETAL STAGE? ARE THEY REVERSIBLE?

Alcohol consumption in pregnancy impacts in the fetal growth and fetal neurodevelopment. We have designed a prenatal intervention to assess whether it is possible to reduce the toxic effects of alcohol in fetus and after birth.



Lola Gómez-Roig
Coordinator of the
research line. MaternalFetal Medicine Specialist
and Head of the
Department at BCNatalSant Joan de Déu
Hospital.

# WHAT OTHER TOXINS AFFECT THE FETUS IN PREGNANCY?

Air pollution, exposure to toxic chemical substances and endocrine disruptors are examples of toxic factors that affect the fetus. We continue investigating to identify and determine what are the effects in babies to take action and prevent toxic exposure in pregnancy.

# IN 2022....

- This year we have finished the recruitment of the BISC cohort with a total of 1,100 pregnant women.
- This cohort is also part of the ATHLETE project along with other international cohorts to create and Exposome that will compile environmental risks.
- Our group is part of RICOR: Primary care interventions to prevent maternal and child chronic diseaes of perinatal and developmental origin del Instituto de Salud Carlos III (RD21/0012/0003).



# **TEAM MEMBERS**

### COORDINATOR

Lola Gómez-Roig

### POSTDOCTORAL RESEARCHERS

Edurne Mazarico, Miriam Pérez, Laura Almeida, Silvia Ferrero, Joan Sabrià, Natalia Gorina

# PREDOCTORAL RESEARCHERS

Marc Cahuana, Pilar Duarte, Diana Lip, Marta Muniesa, Rosalía Pascal, Laia Grau

# **COLLABORATORS**

### NATIONAL

- Hospital de Sant Pau, Barcelona
- Instituto de Salud Global (IsGlobal), Barcelona
- Red de Salud maternoinfantil y del desarrollo. Instituto de Salud Carlos III (ISCIII), Madrid
  - Institut de Recerca Sant Joan de Déu, Barcelona
  - Cognitive Neuroscience Department, Brainlab, Universidad de Barcelona (UB)
  - Primary Care Interventions to Prevent Maternal and Child Chronic Diseases of Perinatal and Development Origin, Instituto de Salud Carlos III, Madrid

### **PUBLICATIONS IN 2022**

- 1. Cahuana-Bartra MJ, Mazarico-Gallego E, Cahuana-Bartra AJ, Pascal R, Alonso-Garcia L, Targa J, Muñoz-Lozano C, Dadvand P, Gómez-Roig MD. Maternal short-term exposure to NO2 during pregnancy and its relationship with Doppler markers of placental function. Environ Res. 2022 Nov;214(Pt 1):113813. doi: 10.1016/j.envres.2022.113813.
- 2. Torres Toda M, Miri M, Heydari H, Lari Najafi AM, Gómez-Roig MD, Llurba E, Foraster M, EDadvand P. A study on exposure to Regreenspace during pregnancy and lipid Coprofile in cord blood samples. Environ Res. 2022 Nov;214(Pt 1):113732. doi: 10.1016/j.envres.2022.113732.
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- 7. Ribas-Prats T, Arenillas-Alcón S, Lip-Sosa DL, Costa-Faidella J, Mazarico E, Gómez-Roig MD, Escera C. Deficient neural encoding of speech sounds in term neonates born after fetal growth restriction. Dev Sci. 2022 May;25(3):e13189. doi: 10.1111/desc.13189.
- 8. Rubio R, Aguilar R, Bustamante M, Muñoz E, Vázquez-Santiago M, Santano R, Vidal M, Melero NR, Parras D, Serra P, Santamaria P, Carolis C, Izquierdo L, Gómez-Roig MD, Dobaño C, Moncunill G, Mazarico E. Maternal and neonatal immune response to SARS-CoV-2, IgG transplacental transfer and cytokine profile. Front Immunol. 2022 Sep 27;13:999136. doi: 10.3389/fimmu.2022.999136.

## **STRATEGIC GOALS**

STUDYING	PREDICTING	
The effect of exposure to toxins in pregnancy.	The risk of complications in pregnancy	BASIC
Exposure of toxins and metabolites in pregnancy.	and fetal development due to environmental factors.	CLINIC

# Platforms

BCNATAL FMRC HAS TRANSVERSAL PLATFORMS THAT GIVE SUPPORT TO THE 8
RESEARCH LINES BY A BIOBANK SERVICE, ANIMAL HUSBANDRY, POSTNATAL
SUPPORT AND AI DATA ANALYSIS



# **Biobank**

OUR MISSION IS TO COLLECT AND STORE THE BEST WAY POSSIBLE MATERNAL, FETAL AND NEONATAL BIOLOGICAL SAMPLES AND MAKE THEM AVAILABLE TO THE SCIENTIFIC COMMUNITY WHEN NEEDED

The Maternal and Fetal Biobank is part of the Biobank at the Hospital Clínic-IDIBAPS and the Biobank at Hospital Sant Joan de Déu for clinical Research (BHSJDI). We have collected a great number of biological samples from a variety of pathologies associated to pregnancy such as twin-to-twin transfusion, fetal growth restriction (FGR) and preeclampsia. Thanks to these samples we can make progress with our research and improve diagnosis and future therapies

Scientific coordinator: Fàtima Crispi
Postdoctoral Biologist: Víctor Rodríguez

Technician: Laura González, Noelia Rodríguez





# **Animal Model**

WE MANAGE PROJECTS WITH ANIMAL EXPERIMENTATION AND COORDINATE THE ANIMAL FACILITY PLATFORM AT THE UB

We provide administrative, technical and scientific support to make sure that all procedures run smoothly and to set up an optimal workspace. To ensure animal welfare, we perform regular check-ups and supervision of the experimental protocols to follow guidelines approved by the ethical committee.

Scientific Coordinator: Miriam Illa



# **Postnatal**

WE GUARANTEE THE BEST CHECK-UPS TO NEWBORNS AND PREGNANT WOMEN THAT PARTICIPATE
IN OUR RESEARCH PROJECTS

Our team is composed by nurses and psychologist specialized in neonatology to offer the best medical care to mothers and their babies. We give company to the families in the procedures such as magnetic resonance and we evaluate the baby's capabilities by Brazelton, Bayley or Wisc tests aiming to an early detection of neurodevelopment impairment and rapidly initiate treatment.

Scientific coordinator: Ángela Arranz

**Psychologists:** Alba Camacho y Paula Navarro

**Nurses:** Mireia Pascual, Nadia Rojas, Natalia Torrico y Maira Rodríguez

Assistant nursing care technician: Nerea González



# **Image**

WE ARE IMPROVING DIAGNOSIS BY APPLYING AI TECHNIQUES TO IDINTIFY, PROCESS AND INTERPRET CLINICAL DATA

We classify echografies from pregnant patients to be associated with clinical data while preserving the privacy of their data. The participation of a vast number of patients in our medical visits helped us to generate a large data. All is speeding up the knowledge of pathologies associated to pregnancy and development of better treatments.

Scientific coordinator: Xavier P. Burgos

Postdoctoral researcher: Elisenda Bonet-Carne

**Predoctoral student:** David Coronado **Technical support:** Sergio Navarro



# 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



SCIENTIFIC MANAGER:

**FINANCIAL MANAGEMENT:** 

**SCIENTIFIC WRITER:** 

**PROJECT MANAGER:** 

**ERASMUS MUNDUS COORDINATOR:** 

**SALES AND ADMINISTRATION:** 

**COMMUNICATION:** 

IT:

Elisenda Bonet-Carne
Ester Cardet
Maria Gómez and Iris Uribesalgo
Mireia Hoyos
Maite Aguilera
Marco Lescano, Anaïs Barba
Katherine González
Daniel Pérez

**BCNatal FMRC** has its own management department, it lends support to the 8 research lines in finances and project coordination. Indeed, the management department helps accelerating the professional development of our researchers organizing learning sessions, network activities, journal club, workshops and events in summer and Christmas.



# **JOURNAL CLUB**

Since 2005, we have invited researchers to participate in weekly meetings to share the latest findings and discuss ideas. In addition, external guests and experts in the field of Maternal and Fetal Medicine are invited to talk.





PE37 Project

# Research Projects and Grants

# **Ongoing in 2022**

Erasmus Mundus Joint Doctorate in Fetal and Perinatal Medicine. FetalMed-PhD. Eduard Gratacós European Comission. Erasmus + 01/08/2013-31/10/2022

Clasificación fenotípica para una nueva classificación clínica de la restricción de crecimiento fetal Eduard Gratacós Instituto de Salud Carlos III 01/01/2019-30/06/2023

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
01/01/2019-30/06/2023

FetalBrainCare: Tratamiento para la mejora del neurodesarrollo en el crecimiento intrauterino restringido Elisenda Eixarch Instituto de Salud Carlos III 01/01/2020-30/06/2024 Desarrollo y validación de una herramienta diagnóstica no-invasiva de infección intra-amniótica en flujo vaginal basada en la integración de matabolómica y microbioma
Teresa Cobo
Instituto de Salud Carlos III
01/01/2020-31/12/2023

ATHLETE: Advancing Tools for Human Early Lifecourse Exposome research and

Translation
Lola Gomez-Roig

European Comission. 01/01/2020-31/12/2024

Impacto del crecimiento intrauterino restringido sobre el desarrollo pulmonar Fatima Crispi Instituto de Salud Carlos III 01/01/2021-31/12/2023

Impacto de un programa de intervención prenatal estructurado, de disminución de consumo de alcohol en los resultados perinatales y de neurodesarrollo Lola Gomez-Roig Instituto de Salud Carlos III 01/01/2021-31/12/2023

Desarrollo del modelo multiparamétrico de predicción de diabetes gestacional en el primer trimestre del embarazo Francesc Figueras Instituto de Salud Carlos III 01/01/2021-31/12/2023

FET-SEAL: Sistema integrado de sellado de membranas fetales para cirugía fetal fetoscópica Elisenda Eixarch, Miriam Illa Instituto de Salud Carlos III 01/01/2021-31/12/2023

Preventing Prenatal Brain damage with tools for improving risk identification and therapy Eduard Gratacós Cerebra Foundation 01/01/2020-28/02/2024

Placenta Artificial:
Programa Interdisciplinar
para el Desarrollo de un
Prototipo Experimental de
Placenta Artificial y
Evaluación de Aplicación
Clínica
Eduard Gratacós
Fundació "la Caixa"
03/12/2020-31/07/2023

# Started in 2022

Estudio OPTIM-PTL: Optimización del tratamiento de gestantes con trabajo de parto prematuro y membranas íntegras aplicando modelos de predicción multivariable Montse Palacio Instituto de Salud Carlos III 01/01/2022-31/12/2024

Estudio multicéntrico del proceso de desarrollo cortical fetal anormal aplicando métodos estandarizados y protegidos de resonancia magnética fetal Elisenda Eixarch Instituto de Salud Carlos III 01/01/2022-31/12/2024

Grup de Medicina Maternofetal i Reproductiva mixte Hospital Clínic de Barcelona i Hospital Sant Joan de Déu Eduard Gratacós

Agencia de Gestió d'Ajuts Universitaris i de Recerca (AGAUR)

01/01/2022-31/12/2024

Papel de la disbiosis intestinal en gestantes con preeclampsia: impacto sobre el crecimiento. Fàtima Crispi Fundación Mutua Madrileña

desarrollo y microbiota fetal

19/07/2022-18/07/2024

Prevención cardiovascular desde la vida fetal: beneficios de la Dieta Mediterránea durante la gestación

Fàtima Crispi Fundació Jesús Serra 01/12/2022-01/12/2023

PE37: Ensayo clínico aleatorizado multicéntrico de cribado con sFlt1/PIGF e inducción selectiva del parto para la prevención de preeclampsia a término Eduard Gratacós Instituto de Salud Carlos III 01/01/2023-31/12/2025

Evaluación del efecto de diversos esquemas de nutrición y soporte hormonal sobre el desarrollo fetal en un modelo experimental de placenta artificial Elisenda Eixarch Instituto de Salud Carlos III 01/01/2023-31/12/2025

Validación externa de 4 modelos de predicción noinvasivos de infección intra-amniótica y parto en los siguientes 7 días en mujeres con amenaza de parto

Teresa Cobo Instituto de Salud Carlos III 01/01/2023-31/12/2025

Evaluación de los efectos de un sistema de placenta artificial en el neurodesarrollo un modelo animal de oveja a nivel multiescala Miriam Illa Instituto de Salud Carlos III 01/01/2023-31/12/2025

Impacto de una intervención de Dieta Mediterránea durante la gestación la sobre Microbiota Materno-Neonatal y su asociación con el Neurodesarrollo: un Clínico Ensayo Aleatorizado

Francesca Crovetto Instituto de Salud Carlos III 01/01/2023-31/12/2025

Sealing System Elisenda Eixarch II Premi Innovació Campus Clínic - Hospital Clinic 01/01/2023-31/12/2023

# **Scholarship and Personnel grants**

Intensificació de professionals de la Salut Elisenda Eixarch

Departament de Salut – Generalitat de Catalunya 01/06/2019-10/05/2022

Contratos de formación en investigación "Río Hortega" (Post Formación Sanitaria Especializada)

Leticia Benítez - Eduard Gratacós

Instituto de Salud Carlos III 31/01/2022 – 31/01/2024 Beatriu de Pinós: A
personalised medicine
approach for the
assessment and treatment
of pulmonary hypertension
in congenital heart disease
to reduce brain damage
and heart failure in
neonates

Patricia García – Fàtima Crispi

Agencia de Gestió d'Ajuts Universitaris i de Recerca (AGAUR) 01/01/2020-31/12/2022 Intensificación de profesionales de la Salud Fàtima Crispi Instituto de Salud Carlos III 01/01/2022 – 31/12/2023

Beca Inphinit Retaining Ayako Nakaki - Eduard Gratacós Fundació "la Caixa" 30/11/2019-29/11/2022

# Clinical transfer: clinical guides and protocols

Our mission is to translate our research into clinical practice, indeed, we aim to improve the current clinical practice in Maternal and Fetal Medicine.

As such, we elaborate clinical guidelines and protocols to Maternal, Fetal and Neonatal Units. Applying them promote preventive procedures, improve treatments and a better care to patients.







MILLION EUROS invested in research projects in Maternal and Fetal Medicine in the last 15 years

# CEREBRA Project

MOST OF NEURODEVELOPMENTAL DISORDERS ARE ORIGINATED DURING PREGNANCY. DIAGNOSING AND TREATING AT PRENATAL STAGE WOULD HELP TO MITIGATE BRAIN LESIONS

# WHAT IS THE OBJECTIVE?

Our objective is to palliate the prevalence and severity of brain lesions initiated at fetal stage. Hence, our research aims to diagnose neurodevelopmental disorders in fetuses and newborns and start a treatment at early stage to mitigate sequelae.

### **HOW WE DO IT?**

Our studies focus on understanding intrauterine growth restriction. The findings could be applied to other diseases that impact fetal programming.

Our CEREBRA's project accelerates research that will reduce the prevalence and severity of diseases of the neurodevelopment originated prenatally



# Fields of Action



### **DETECTION OF FETUSES AT RISK**

We aim to integrate new criteria of diagnosis to substantially improve detection of intrauterine growth restriction.



### **NEW BIOMARKERS**

New biomarkers are developed to identify cases with neurodevelopmental disorders. We use advanced techniques such as evaluation of cortical development using echographies, evaluation of microstructures by spectroscopy and diffusion, and analyses of brain connections using magnetic resonance.



# **NEW THERAPIES**

We are continuously developing new therapies targeted at fetal stage and after birth to mitigate brain lesions.

# CaixaResearch ARTIFICIAL PLACENTA Project

ARTIFICIAL PLACENTA IS A DISRUPTIVE SOLUTION THAT WILL REDUCE SUBSTANTIALLY COMPLICATIONS ASSOCIATED WITH EXTREME PREMATURITY AND OTHER FETAL CONDITIONS DECREASING MORBIDITY AND IMPROVING SURVIVAL RATE

# WHAT IS THE OBJECTIVE?

This project aims to develop and artificial placenta to create an environment mimicking the maternal uterus and, ultimately, improving viability of extreme premature babies and reduce their possible associated sequelae. Dr. Eduard Gratacós explained in the presentation of the project "Artificial placenta is a unique project in Europe, represents a medical and technological challenge to find a transformative solution that will offer an opportunity to the 25,000 babies born at 6-month or less of gestational age in Europe. The organism at birth is not prepare to breath or eat as it is in full term babies. Artificial placenta offers what resembles the natural environment in the maternal uterus".

### **HOW WE DO IT?**



This is an ambitious project funded by la Fundació "La Caixa". In addition, we collaborate with other technology centres to develop the project and generate knowledge, we foresee a transference of the Artificial Placenta system into the clinical practice.

We are committed to generate new knowledge needed to develop the Artificial Placenta

# Fields of Action



### **DEVELOPMENT OF AN ARTIFICIAL PLACENTA SYSTEM**

Development, integration of components and monitorization of an Artificial Placenta system to artificially create environmental conditions, access to nutrients and oxygen mimicking the maternal uterus.



# FETAL DEVELOPMENT AND PROGRAMMING

Study the impact of fetal development in Artificial Placenta and evaluate brain functions, cardiorespiratory, endocrine, digestive and metabolic system.



# PRE-CLINICAL AND CLINICAL STUDY

Activities will be designed at pre-clinical stage to promote participation in the project and spread the word. At clinical stage, we will develop protocols and clinical procedures to conduct a pilot study with the Artificial Placenta in the clinic.

# PE37 Project

PE37 IS A PROSPECTIVE CLINICAL TRIAL AIMING TO DEVELOP A METHOD TO IDENTIFY THE RISK OF LATE PREECLAMPSIA TO INDUCE BIRTH BEFORE MANIFESTING COMPLICATIONS

## WHAT IS THE OBJECTIVE?

Late preeclampsia is characterized by high blood pressure and it may affect organs such as liver and kidney, as a consequence, it may threaten maternal and fetal health. Preeclampsia may be difficult to detect as it can be presented in pregnancies without risk factors. PE37 study evaluates with biomarkers in a blood test that are associated with high risk of developing preeclampsia.

### **HOW WE DO IT?**

PE37 is a prospective and randomized clinical study conducted in parallel groups. Blood test will be taken in 5,500 to 6,000 women at 35-37 week of gestational age to evaluate levels of placental function biomarkers, sFlt1 and FIGF. This study analyses whether a proportion between these biomarkers is able to predict high risk of developing preeclampsia at the end of pregnancy.

Identify biomarkers that detect high risk of late preeclampsia would benefit maternal and newborn health

# Fields of Action



## PROSPECTIVE CLINICAL TRIAL

Between 5,500 and 6,000 women participate in this study. The inclusion criteria seek for pregnant women above 18 years old, at 35-27 gestational age, first pregnancy and without previous complications. A blood test will be taken to detect biomarkers of placental function, sFlt1 and FIGF.



### **DEVELOP NEW BIOMARKERS**

Study of the proportion of placental biomarkers, sFlt1 and FIGG, to evaluate whether these biomarkers are enough to predict high risk of hypertensive complications in pregnancies at early stage. In addition, PE37 evaluates whether it is possible to predict late preeclampsia.



### IMPACT AND INNOVATION

The results could change the patient handling in pregnancies, improving the quality of life of mothers and newborns worldwide.

# SCIENTIFIC RESULTS

National and International Congresses

and courses

# National and International Congresses and courses

# FACE-TO-FACE

Discovering fetal brain from diagnosis to counselling. 10 June Milano, Italy.

XIII Congreso Internacional sobre Dieta Mediterránea. 6-7 April Barcelona, Spain

Good and bad news on ultrasound, fetal therapy and obstetrics-International symposium in honour of Prof. Roland Zimmermann. **10-11 June** Zurich, Switzerland.

Congreso Association for European Pediatric Cardiology (AEPC). **25-28 May** Geneva, Switzerland.

XXXI Congreso Nacional de la Sección de Ecografía (SESEGO). 26-27 May Barcelona, Spain

Symposium Internacional Medicina Fetal. **3 March** Gijón, Spain.

XV Reunión Anual CIBERER. 26-27 April Barcelona, Spain

19th World Congress in Fetal Medicine. **26-30 June** Crete, Greece.

32nd World Congress of the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG). **16-18 September** London, United Kingdom.

CIBER XV Annual Meeting. 26-27 May Madrid, Spain



# **ONLINE**

Congreso Regional de Ginecología y Obstetricia de la FIGO. **3-5 November.** 

8

INVITED TALKS AND ORAL COMMUNICATIONS

111

CONFERENCES AND COURSES (FACE-TO-FACE AND ONLINE)

13

POSTERS AT CONGRESSES

NATIONAL AND
INTERNATIONAL

# **Posters and Oral Posters**

# ISUOG 2022

Investigator	Title		
Francesca Crovetto	Effects of a Mindfulness Based Stress Reduction intervention during pregnancy for the prevention of severe Preterm Birth. The IMPACT BCN trial.		
Francesca Crovetto	Effects of a Mediterranean diet intervention or a Stress Reduction program during pregnancy on maternal gut microbiota. The IMPACT BCN trial.		
Ayako Nakaki	Effects of Mediterranean diet or Mindfulness-Based Stress Reduction during pregnancy on newborns' neuro behavior. The IMPACT BCN trial		
Yvan Gómez	The effect of the maternal well-being status on fetal cortical development. Sub-analysis from the IMPACT BCN trial.		
Lina Youssef	The Effect of Mediterranean diet or Mindfulness-Based Stress Reduction on Fetal Cardiac Remodeling in Small for Gestational Age. The IMPACT BCN trial.		
Lina Youssef	The Effect of Mediterranean diet or Mindfulness-Based Stress Reduction during pregnancy on fetal growth. The IMPACT BCN trial		
Lina Youssef	Sex Differences in the effect of Mediterranean diet or Mindfulness-Based Stress Reduction on Prevention of Small for Gestational Age Newborns. The IMPACT BCN trial.		
Irene Casas	Effects of Mediterranean diet intervention on maternal stress, well-being and sleep quality throughout gestation. The IMPACT BCN trial.		
Irene Casas	Anxiety, stress, and well-being throughout gestation in a cohort of pregnant women in Barcelona city		
Irene Casas	Sleep quality throughout gestation in a cohort of pregnant women in Barcelona city.		
Helena Castillo	Descriptive study of vitamin D deficiency in a non-supplemented Mediterranean cohort of pregnant women. The IMPACT BCN trial.		
Marta Larroya	Adherence to Mediterranean diet in a cohort of pregnant women in Barcelona city.		
Marta Larroya	Does Mediterranean diet provide most of the necessary nutrients in adequate proportion during pregnancy? Data from a cohort in Barcelona city.		

# Oral communications

# ISUOG 2022

Investigator	Title	
Leticia Benitez	Effect of an intervention based on Mediterranean diet during pregnancy on vitamin D deficiency. The IMPACT BCN trial.	
Leticia Benitez	Maternal anti-inflammatory diet profile at 20 weeks is associated with a lower risk of Small for Gestational Age newborns in a Mediterranean area.	
Elisenda Eixarch	Setting up of an artificial placenta experimental system in fetal sheep: critical issues for successful transition and short-term survival.	
Ayako Nakaki	Effects of a Mediterranean diet intervention during pregnancy on fetal brain cortical development. The IMPACT BCN trial.	
Francesca Crovetto	Mediterranean diet or Stress reduction program during pregnancy for the prevention of SGA newborns according to pre-pregnancy BMI. The IMPACT BCN trial.	
Francesca Crovetto	Effects of a Mediterranean diet or a Stress Reduction intervention during pregnancy on the incidence of early-late preeclampsia. The IMPACT BCN trial.	
Lina Youssef	The Effect of Mediterranean diet or Mindfulness-Based Stress Reductionon Placental histopathological lesions. The IMPACT BCN trial.	
Irene Casas	Reduction of Maternal Anxiety and improvement of Well-being after aStress Reduction intervention during pregnancy. The IMPACT BCN trial	

Sharing our findings in national and international congresses make possible to spread new knowledge in the scientific community

# 5 EDUCATION

**Training in Maternal and Fetal Medicine** 

# Training in Maternal and Fetal Medicine

AT BCNATAL FMRC, WE STRIVE TO PROVIDE TOP-NOTCH EDUCATION; OUR DEDICATED MULTIDISCIPLINARY TEAM IS COMMITTED TO TRAINING THE NEXT GENERATION OF MEDICAL DOCTORS SPECIALIZED IN MATERNAL AND FETAL MEDICINE. AS A RESULT OF OUR EFFORTS, SEVERAL DOCTORAL STUDENTS GRADUATE EACH YEAR IN OUR GROUP

Student	Thesis Title	Directors	University
Ximena Torres	Evaluation of cardiac morphometry and function by advanced echocardiography in monochorionic twin pregnancies	Josep M <sup>a</sup> Martínez Mar Bennasar	UB
Marta Rial	Clinical impact of cerebroplacental ratio evaluation at third trimester of pregnancy in the general population	Francesc Figueras Stefan Hansson	UB
Britta Kuhne	Safety and efficacy investigations for new prenatal neuroprotective therapies. Applications in a model of intrauterine growth restriction (IUGR)	Miriam Illa Marta Barenys	UB
Ameth Hawkins	Assessment of prenatal imaging, fetal blood parameters, and new pharmacological interventions, in congenital cytomegalovirus infection	Anna Goncé	UB

# Research Fellowships

Investigator	University/Country
Mandakh Yumjirmaa	Lund University, Sweden

# Ongoing doctoral thesis

Student	Thesis Title	Directors	University
Iris Soverla Rodríguez de Silva Dias	Evaluation of left-sided congenital heart defects by advanced fetal echocardiographyand cold blood biomarkers	Olga Gómez Fátima Crispi	UB
Laura Pla	Diagnosis and perinatal therapies in animal model of intrauterine growth restriction	Míriam Illa Elisenda Eixarch	UB
Laura Almeida	Mouse model of fetal alcohol syndrome mice according to two patterns of human consumption and the role of epigallocatechin in its prevention. Study of bioavailability of epigallocatechin gallate in humans	Lola Gómez-Roig	UB
Irene Ribera	Study of predisposing factors of neurodevelopmental neurodevelopment in congenital caridiopathies.	Elena Carreras Elisenda Eixarch Elisa Llurba	UAB
Rosalia Pascal	Impact of stress on pregnancy mental health	Francesca Crovetto Lola Gómez-Roig	UB
Ayako Nakaki	Impact of maternal life-style on fetal brain	Francesca Crovetto Eduard Gratacós	UB
David Coronado	Deep Learning applied tomedical image analysis	Elisenda Bonet Xavier Burgo	UB
Marta Larroya	Role of the gut disbiosis in pregnancies with preeclampsia: the effect on fetal growth, neurodevelopment and microbiota.	Francesca Crovetto Fàtima Crispi	UB
Britta Ana Kühne	Safety and efficacy investigations for newprenatal neuroprotective therapies. Applications in a model of FGR	Míriam Illa Marta Barenys	UB

Student	Thesis Title	Directors	University
Raigam Martínez	Developing an effective model for the prediction of gestational diabetes in the first trimester of pregnancy(GDIsT).	Francesc Figueras	UB
Anna Peguero	Third-Trimester biochemical markers for the prediciton and prognosis of preeclampsia.	Francesc Figueras	UB
Yolanda Giménez	Postpartum depression, maternal bonding and maternal lactation in pregnant women with preeclampsia.	Francesc Figueras	UB
Clara Murillo	Impact of the threat of preterm labor and preterm rupture of membranes on neurodevelopment and the fetal and neonatal cardiovascular system.	Montse Palacio Tere Cobo	UB
Júlia Ponce	Characterization of preterm delivery in multiple gestation and development of a predictive model for spontaneous preterm delivery.	Montse Palacio Mar Bennasar	UB



# Erasmus Mundus FetalMed-Phd Joint Doctorate

BCNatal FMRC has coordinated the interdisciplinary doctoral programm Erasmus Mundus Joint Doctorate in Fetal and Perinatal Medicine (EMJD Fetlamed- PhD) in collaboration with three top tier universities and research centers in Europe: BCNatal FMRC (University of Barcelona, Spain), Leuven University (Belgium) and Lund University (Sweden).

Student	Thesis Title	Directors	University
Maria Laura Boutet	Fetal programming in assisted reproductive technologies	Gemma Casals Stephen Hansson	UB, Lund
Ana Lisbeth Moreno	Prediction of neonatal respiratory morbidity assessed by quantitative ultrasound lung texture analysis in specific populations of high-risk pregnancies	Montse Palacio	UB, Lund
Lucas Trigo	Structural and Function Brain Effects of prenatal Spina bifida	Elisenda Eixarch Eduard Gratacós Jan Deprest	UB, Leuven
Paz Ahumada	Effectiveness of repeated motivational intervention sessions during pregnancy tostop ethanol use	Lola Gómez-Roig Elisenda Eixarch	UB, Lund

The forth and last edition ended in 2021 with more than 40 doctors graduated. Some of the students had to postpone their research and finalized their studies in 2022 due to global pandemic

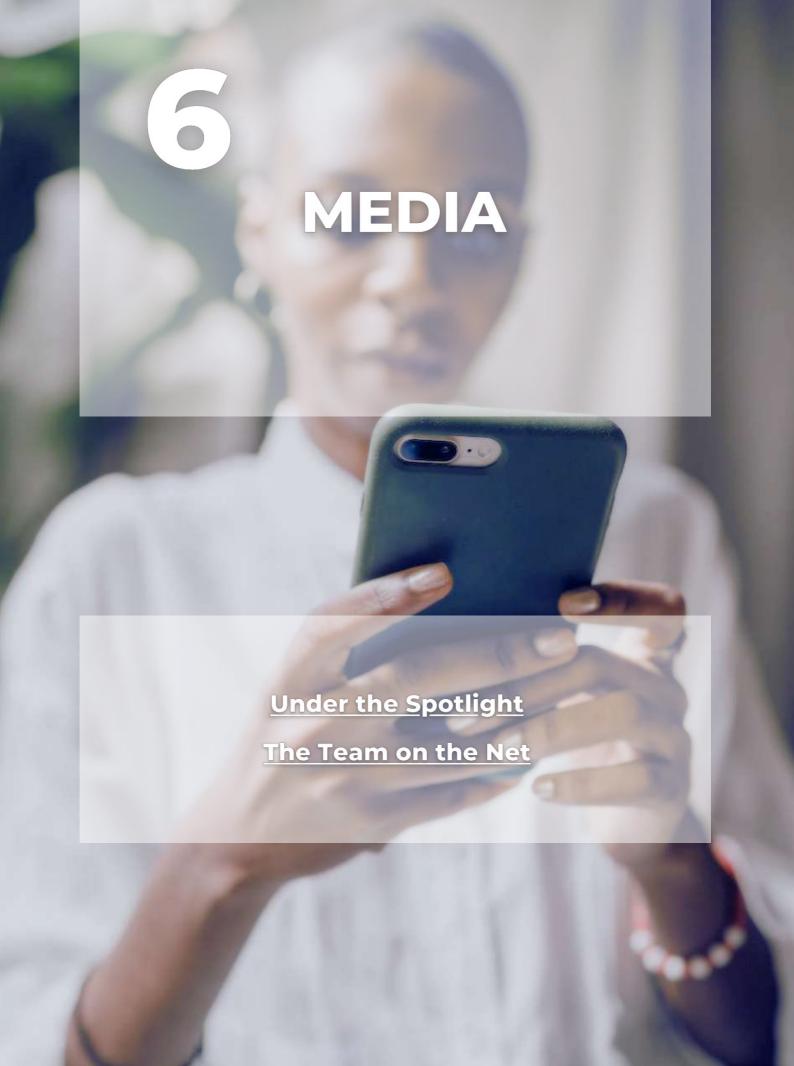












# UNDER THE SPOTLIGHT

IN 2022, BCNATAL FMRC HAS COME UP IN MULTIPLE MEDIA CHANNELS. WE ARE STEADILY APPEARING IN NATIONAL AND INTERNATIONAL NEWS AS CENTER OF REFERENCE IN MATERNAL AND FETAL MEDICINE RESEARCH, THERAPY AND SURGERY.



WE SHOW HOW OBESITY INCREASES CARDIOVASCULAR DISEASES IN LOW BIRTH WEIGHT

Our study showed that low birth weight has a higher risk of cardiovascular diseases in obesity. "Hearts of babies with low birth weight are different in structure and function. These differences are seen in fetal life and sustain until adolescence", Dr. Eduard Gratacós explains that exist an atypical response in these babies, seen even in adulthood. We observed in a sample group of young adults that their heart cannot increase muscle mass affecting the blood pumping.

Media channel: La Sexta, La Vanguardia, COPE, Sinc





WE FIND OUT THE WAY TO DISTINGUISH SEVERE COVID-19 AND PREECLAMPISA IN PREGNANT WOMEN



Due to similar symptomatology between both diseases, it has been critical the identification of biomarkers able to distinguish both diseases. This problem has led to medical errors and has slowed down recovery from the disease. Thank to biological differences of both diseases, we have been able to distinguish completely preeclampsia and severe COVID-19; we have improved the medical procedures and well-being of pregnant patients.

Media channel: Levante, Sinc, Infosalus

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# INTERVIEW TO FÀTIMA CRISPI REGARDING HER RESEARCH STUDY AWARDED BY JESÚS SERRA FOUNDATION

After being awarded for leading the IMPACT project, we were honoured to interview Dr. Fàtima Crispi to know the details of her research. She explains how diet and stress levels during pregnancy have an effect in low birth weight. Fàtima explains how suboptimal diet can affect placental function limiting some developmental functions that will lead to low birth weight. Indeed, having a low birth weight baby carries short-term risks such as complications during delivery and long-term risks such as cardiovascular diseases. susceptibility endocrine and We strongly recommend Mediterranean diet to maintain healthy dietary habits during pregnancy and mindfulness to reduce stress, both factors affecting fetal development. Media channel: El País, Infosalus, El Correo





# THE TEAM ON THE NET

THE TEAM AT BCNATAL FMRC IS AWARE OF THE RELEVANCE OF COMMUNICATING RESULTS TO THE SOCIETY

We are committed to share our findings in Maternal and Fetal Medicine to the population through multiple channels: press release, press conferences and share our progress online. We constantly post in our website (www.bcnatalresearch.org), in traditional media channels and in our social network. We aim to increase awareness of the importance of maintaining Maternal and Fetal health.

In Ibero-America we are well recognised in Maternal and Fetal Medicine and we have appeared in multiple media channels such as press, radio, television and online

We share the outcomes of our 8 lines of research currently active, as well as, personnel in a directory and a record of scientific publications in our web at <u>bcnatalresearch.org</u>



2.915

Followers at

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2.541

Followers at

**FETAL MEDICINE RESEARCH** 



1.905

Followers at BCNATAL FETAL MEDICINE RESEARCH



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