

1. Institution: CENTRO DE ESTUDIOS FARMACOLOGICOS Y BOTANICOS (Center for Pharmacological and Botanical Studies (National Research Council - University of Buenos Aires))

2. Principal investigator and contact person: ANA MARIA FRANCHI

3. Key personnel

NAME	EMAIL	RESEARCH AREA DETAILS
ANA MARIA FRANCHI	anafranchi2000@gmail.com	Physiopathology of Pregnancy and Labour
SILVINA PEREZ MARTINEZ	perezms@fmed.uba.ar	Regulation of sperm-oviduct interaction.
MARIA LAURA RIBEIRO	marialribeiro@yahoo.com.ar	Participation of lipid molecules in the process of embryo attachment to the endometrium and trophoblast invasion

4. Research profile

- Laboratory of Physiopathology of Pregnancy and Labour, Head: Dr. Ana M Franchi

Lab Members: Claudia A Vercelli, Julieta Aisemberg, Maximiliano Cella.

Preterm delivery is the leading cause of neonatal mortality and contributes to delayed physical and cognitive development in children. Although a significant number of preterm cases would benefit from delaying labour, there is considerable debate on the safety and efficacy of currently available medications for the maintenance of tocolysis. We developed a mouse model of infection-associated preterm labour (PTL), and we explore the mechanism involved in the triggering of labour. Also we study different tocolytic drugs to suppress PTL.

- Laboratory of Biology of Reproduction in Mammals, Head: Dr. Silvina Pérez Martínez

Lab Members: María Gracia Gervasi, Claudia Osycka Salut.

The mammalian oviduct acts as a functional sperm reservoir providing a suitable environment that allows the maintenance of sperm fertilization competence until ovulation takes place. After mating, mammalian spermatozoa are stored in the lower oviduct by adhesion to the epithelial cells. Spermatozoa attachment to and release from oviductal reservoirs play a role not only in the temporal coordination of fertilization but also in assuring that an adequate number of spermatozoa reach the site of fertilization in a controlled way. We are interested in studying different reproductive processes that occur in the mammalian oviduct, specifically the mechanisms by which sperm selection might operate within the oviduct. We are studying the participation of molecules, such as endocannabinoids, nitric oxide or fibronectin, and the signalling pathways that are activated in the regulation of sperm-oviduct interaction. We hypothesized that the subpopulation of spermatozoa that attach to the oviductal epithelial cells presents molecular markers on their surface (eg receptors to fibronectin, progesterone or endocannabinoids), while those spermatozoa that do not attach to the oviduct might lack some of them.

- Laboratory of Physiology and Pharmacology of Reproduction, Head: Dr. María Laura Ribeiro

Lab Members: Micaela S Sordelli, Jimena S Beltrame.

Implantation is a series of processes that are regulated by various kinds of signalling pathways between the embryo and the uterus during the initial period of gestation. Low implantation rates are common in women undergoing assisted reproduction, posing a challenge to both patients and doctors, so researchers are striving towards a deeper understanding of this process. In the past decade, several authors suggested the participation of different lipid molecules in the establishment of pregnancy. In fact, a localized depletion of neutral lipids from the luminal epithelium adjacent to the blastocyst has been reported and is interpreted as a mobilization of precursors for lipid synthesis involved in embryo invasion. Based on this evidence, our lab is interested in studying the role that some lipid molecules (anandamide, lysophosphatidic acid and prostaglandins) have at implantation and their participation in the process of embryo attachment to the endometrium and trophoblast invasion.

Our projects include studying maternal communication with the embryo, with the immune system and with gametes. The communication established between several types of cells at different points during gestation could be thought as interactions and signals that are exchanged between the mother, the embryo, the gametes and circulating cells as those from the immune system. Thus, to understand how these processes are being carried out inside the mother, it is necessary to improve our biological models, establishing better in vivo and in vitro systems. Also, we are interested in studying the triggering of intracellular signals in the endometrium and in the epithelial oviductal cells, which would enable the mother to sense an appropriate milieu to permit gestation to go on.

To study the principal aims of our laboratories, it would be really useful to conjugate the experience of European labs compromised with embryo-maternal interaction and our approach towards lipids and the immune system as putative integrators in the crosstalk between the gametes, the embryo and the maternal tissues. This proposal would require at least a few visits from researchers of the different groups, to accomplish the corresponding experiments.

5. Key technologies and tools:

Animal models of preterm labor, delay implantation, embryonic resorption and sperm-oviduct interaction

Western blot

Real time PCR

RIA of prostaglandins, steroid hormones.

Activity of PG enzymes, endocannabinoids enzymes.

Tissue culture

Immunohistochemistry

Nitric Oxide (NO) determination

Assessment of sperm capacitation and acrosome reaction in mammal spermatozoa

6. Selected publications (max. 5)

Role of nitric oxide in shiga toxin-2-induced premature delivery of dead fetuses in rats.

Burdet J, Zotta E, Cella M, Franchi AM, Ibarra C. PLoS One. 2010 5(12):e15127.

Dual effect of nitric oxide on uterine prostaglandin synthesis in a murine model of preterm labour. Cella M, Farina MG, Dominguez Rubio AP, Di Girolamo G, Ribeiro ML, Franchi AM.

Br J Pharmacol. 2010;161(4):844-55.

Anandamide capacitates bull spermatozoa through CB1 and TRPV1 activation.

Gervasi MG, Osycka-Salut C, Caballero J, Vazquez-Levin M, Pereyra E, Billi S, Franchi A, Perez-Martinez S. PLoS One. 2011; 6(2):e16993.

Nitric oxide mediates prostaglandins' deleterious effect on lipopolysaccharide-triggered murine fetal resorption. Aisemberg J, Vercelli C, Billi S, Ribeiro ML, Ogando D, Meiss R, McCann SM, Rettori V, Franchi AM. Proc Natl Acad Sci U S A. 2007; 104(18):7534-9.

The Effect of Anandamide on Uterine Nitric Oxide Synthase Activity Depends on the Presence of the Blastocyst. Micaela S Sordelli, Jimena S Beltrame, Juliana Burdet, Elsa Zotta, Romina Pardo, Maximiliano Cella, Ana M Franchi and Maria Laura Ribeiro. Plos One 2011 (in press).