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IFPA meeting 2014 workshop report: Animal models to study pregnancy pathologies; new approaches to study human placental exposure to xenobiotics; biomarkers of pregnancy pathologies; placental genetics and epigenetics; the placenta and stillbirth and fetal growth restriction

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ABSTRACT

Workshops are an important part of the IFPA annual meeting as they allow for discussion of specialized topics. At IFPA meeting 2014 there were six themed workshops, five of which are summarized in this report. These workshops related to various aspects of placental biology but collectively covered areas of animal models, xenobiotics, pathological biomarkers, genetics and epigenetics, and stillbirth and fetal growth restriction.

1. Animal models to study pregnancy pathologies

Organizers: Ted Golos, Anne Tarrade.

Speakers: Phelipe Favaron, Ted Golos, Antonio Gonzalez-Bulnes, Thomas Jansson, Anne Tarrade, Pauline Peugnet, Christiane Pfarrer, Jacqueline Wallace.

Outline: Human placental models offer the advantage of direct observation of human trophoblast biology, and mouse models offer the ability to genetically modify specific loci for direct mechanistic study. However other models offer advantages of size, accessibility of fetal physiology, or comparative insights for providing a broad understanding of placental function and fetal growth and development. The goal of this workshop was to make placentologists aware of opportunities for research with other systems beside human or mouse models. In this workshop placental researchers presented the advantages and disadvantages of their models of choice.

1.1. Summary

Anne Tarrade discussed the advantages of rabbit models to study feto-placental development. Rabbit placentation is haemochorial, it has a short intergenerational period and several tools are available in this species such as dedicated transcriptomic and soon to come methylome microarrays, as well as fetoplacental imaging. Taking advantage of this species' lipid metabolism which is close to that of humans, the effects of maternal high fat diet on placental function of the first and second generation were investigated. Moreover, the duplex uterus has a definitive advantage for the evaluation of the impact of periconceptional maternal hyperglycemia on the feto-placental phenotype. These examples demonstrate that the rabbit has a legitimate place among the standard models to study placental development.

Phelipe Favaron discussed new world species models of placental biology. Despite human placentation differing in several aspects from other mammals; some of its characteristics are shared with rodents. Considering the importance of establishing new animal models, his group has studied placentation in cricetid rodents, which generally present a discoidal, labyrinthine and haemotrichorial placenta. Peculiarities in relation to the trophoblast giant cells, implantation, and yolk sac placentation were previously described. Special attention, have been given to the *Necromys lasiurus*, that provided data on the possibility of obtaining multipotent mesenchymal stem cells from the yolk sac membrane.

Jacqueline Wallace discussed fetal growth and lessons learned from sheep paradigms. Sheep have long been used as experimental models for perinatal research. The dam is similar in size and adiposity to the human mother and pregnancies can be limited to a single fetus, which accumulates fat prenatally and is of equivalent weight/maturity at birth. Furthermore, sheep have a relatively long gestation, similar ontogeny for all major organ systems and when required the uteroplacental/fetal circulation can be catheterized to directly measure nutrient uptakes/metabolism *in utero*. The adolescent sheep model of placental growth-restriction mimics key features of compromised human pregnancies and has been used to evaluate therapeutic approaches to promote fetal growth.

Christiane Pfarrer discussed the pros and cons of the experimental value of the bovine placenta. Despite some similarities (9 months gestation, one fetus, fetal villous trees arranged in cotyledons), the bovine species does not make an ideal model for human pregnancy because it is a large animal with a synepitheliochorial placenta. However, the occurrence of pathologies compromising the fertility of cows has major influence on economic issues of dairy and beef farming. Therefore studies dealing with early pregnancy loss, placenta retention and postpartum metritis are needed. Due to the complexity of the feto-maternal interface, functional *in vitro* systems have been developed by several groups. For example, the P-glycoprotein expressing bovine caruncular epithelial cell line 1 (BCEC-1) can be used for transportation studies with xenobiotics (organ- and species-specific). In addition, three-dimensional spheroid cultures were established for bovine placental trophoblast and caruncular epithelium. Co-cultures of these may be suitable for studying bovine trophoblast invasion and function *in vitro*.

Antonio Gonzalez-Bulnes discussed porcine models of nutritional challenges during pregnancy. The pig is an outstanding model for translational research and, specifically, for the study of nutrition-related pregnancy pathologies. The pig model has the advantage of body size, facilitating application of imaging techniques and sampling of large amounts of blood and tissues, and has numerous and essential similarities to humans: omnivorous habits, propensity to sedentary behavior and obesity, and similar metabolic, inflammatory, gastrointestinal and cardiovascular features. Moreover, the pig genome sequence is currently complete and indicates extensive conserved homology with the human genome, which reinforces the usefulness and reliability of swine for understanding complex traits in human health.

Pauline Peugnet discussed the placenta in an equine model of fetal programming. The concept that there are developmental origins of health and disease is applicable to the horse in which early developmental events impact post-natal growth, insulin sensitivity and predisposition to osteochondrosis in foals. Using embryo transfers between equine breeds of different sizes (ponies, saddlebreds and draft horses), the placenta has been