

Debate

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## Trophoblast biology: Forum introduction

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### Abstract

In mammals, a carefully orchestrated dialogue between the mother and conceptus (embryo/fetus and associate extraembryonic membranes) is initiated during the peri-implantation period of pregnancy as the trophoblast develops, functions to signal pregnancy recognition, and initiates implantation. The purpose of this Forum is to highlight comparative aspects of trophoblast morphogenesis and function in mammals.

In mammals, a carefully orchestrated dialogue between the mother and conceptus (embryo/fetus and associate extraembryonic membranes) is initiated during the peri-implantation period of pregnancy as the trophoblast develops, functions to signal pregnancy recognition, and initiates implantation. As implantation proceeds, the trophoblast of most species continues to develop and differentiate to form a variety of specialized cell types that are involved in placentation and secretion of unique hormones that directly regulate maternal adaptations to pregnancy. Trophoblast morphogenesis and function during implantation and placentation are critical for reproductive success in mammals. Many causes of infertility and embryonic/fetal losses in pregnancies of humans and domestic animals are due to failure or abnormalities in implantation and placentation related to inadequate or insufficient interactions between the trophoblast and uterus. In addition to clinical infertility, several of these problems lead to fetal growth retardation and life threatening complications such as pre-eclampsia.

The purpose of this Forum is to highlight comparative aspects of trophoblast morphogenesis and function in mammals. The first paper of our Forum by A.M. Carter and A.C. Enders [1] provides an excellent summary of pla-

centration in eutherian mammals. The second paper by R.M. Roberts, T. Ezashi and P. Das [2] focuses largely on the transcription factors that regulate specification and development of the early trophoblast. Much of the genetic and developmental information is from studies of mice given the abundance of knowledge in this model system, but comparative aspects of trophoblast development are presented. The third paper [3] by J.D. Aplin and S.J. Kimber summarizes the cellular and molecular aspects of trophoblast-uterine interactions during implantation in mammals.

In domestic animals, primates and humans, the peri-implantation period of pregnancy is marked by production of a hormonal signal from the trophoblast for pregnancy recognition and maintenance of the corpus luteum. The fourth paper by T.E. Spencer and F.W. Bazer [4] reviews mechanisms whereby the conceptus signals for establishment and maintenance of pregnancy. This paper is comparative in nature and focuses on pregnancy recognition signaling in domestic animals (sheep and pig). The fifth paper by P. Cameo, S. Srisuparp, Z. Strakova and A.T. Fazleabas [5] highlights the multifaceted effects of chorionic gonadotropin in uterine dialogue in the primate. An emerging theme from these two papers is the concept that

pregnancy recognition signals (interferon tau, estrogen and chorionic gonadotropin) not only prolong lifespan of the corpus luteum in order to ensure production of progesterone, but also act in a paracrine manner on the endometrium to influence expression of genes that enhance epithelial secretions and uterine receptivity to the conceptus. The sixth paper by M.J. Soares [6] reviews the roles of prolactin and growth hormone families of genes that are expressed in different types of trophoblasts of mammals including humans, laboratory and domestic animals. An overriding theme characteristic of the prolactin and growth hormone families is their association with pregnancy and regulatory mechanisms controlling viviparity.

The successful maintenance of the semi-allogeneic mammalian fetus during pregnancy provides an apparent immunological paradox. One mechanism whereby the conceptus avoids immunological rejection is the absence of expression of major histocompatibility complex (MHC) molecules on the trophoblast. Therefore, the seventh paper in the forum by S.P. Murphy, J.C. Choi and R. Holtz [7] focuses on the novel mechanisms underlying the silencing of MHC class II molecule expression on trophoblast cells. The final paper in our Forum by S.J. Fisher [8] links abnormal cytotrophoblast differentiation to preeclampsia in the mother. This pregnancy complication is the leading cause of maternal mortality in the Western world and is a major cause of perinatal mortality and intrauterine growth retardation. A better understanding of the basic biology of trophoblast morphogenesis and function is necessary to develop therapies to diagnose and treat various types of infertility and to improve reproductive success, as well as maternal and fetal health.

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