International Journal of Cell Science & Molecular Biology
ISSN: 2572-1100

Juniper Publishers
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Mini Review
Volume 6 Issue 4 - November 2019
DOI: 10.19080/IJCSMB.2019.06.555693

Int J cell Sci & mol biol

Modulation of Human Placental Role: Revisited

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Submission: October 04, 2019; **Published:** November 01, 2019

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Keywords: Cells; Lactogen; Oestrogen; Progesterone; DNA; Blood group; Cell antigens; Carbon dioxide; Oxygen; Viruses; Heparin; Protamine; Insulin

Mini Review

The complex interplay of processes and cells involved in healthy pregnancy is still controversial and poorly understood. The correct receptive endometrial state, including the local immune environment, is crucial not only for fertility but also placenta formation since initiation of placentation highly depends on interaction with immune cells. Implantation failure, recurrent pregnancy loss, and other pathologies of endometrium and placenta, such as pre-eclampsia, represent an increasing societal burden. More robust studies are needed to investigate uterine colonization. Based on current data, future research needs to include the uterine microbiome as a relevant factor in order to understand the players needed for healthy pregnancy.

The placenta is an organ that develops in the uterus only during pregnancy. It remained a fascinating and puzzling organ and has undergone various phases of research; from waste material after delivery to a source of potential material for human welfare. It grows into the wall of the uterus and is joined to the fetus by the umbilical cord. The placenta has two parts, one of which is genetically and biologically part of the fetus, the other part of the mother. The placenta forms tiny hair like projections (villi) that extend into the wall of the uterus around 8 weeks of pregnancy. Prior to this the fertilized blastocyst embeds in the uterine wall, and development of the fetus and placenta begin [1,2]. The placenta produces a number of hormones that are needed during pregnancy, such as, lactogen, oestrogen and progesterone [3]. These hormones play an important role in both mother and child's physiological processes. The fetus is connected to the placenta by a tube called the umbilical cord. The placenta is derived from fetal cells, with a contribution from the lining of the mother's uterus. Therefore, the placenta has DNA from both the fetus and the mother. The cord contains two arteries and a vein. Substances pass back and forth between the mother's and fetus's blood through the placenta and cord [4,5].

The chemical pathologist Lo YMD, et al. [6] discovered a rich vein of fetal DNA in the mother's veins. About 10% of the DNA fragments floating in the mother's blood come from the fetus, from dying placental or fetal cells. Clinical tests capitalize on this DNA to discern the baby's sex and determine whether mother and child have incompatible Rh blood groups, which can lead to fatal complications. DNA sequencing of both the DNAs gives clues of genetic disorders in the embryo.

The placenta brings oxygen and nutrients to the fetus and removes harmful waste and nutrients away where it receives nutrients and oxygen from the mother's blood and passes out waste. The mother's blood does not mix with the blood of the fetus, but the placenta lets substances pass between the two blood supplies: oxygen and nutrients diffuse across the placenta from the mother to the fetus [4,5]. The placenta may be the only human organ (albeit a temporary one) that is almost wholly uninnervated, only the segment of the umbilical cord that is closest to the fetus containing nerve fibres [2].

Alcohol passes from the mother's blood into the baby's blood via the placenta. The placenta does not act as a barrier to alcohol and readily reaches the embryo in fairly high concentrations [7]. Other substances that pass through the placenta include red blood cell antigens, carbon dioxide, oxygen, some viruses, and nutrients. Drugs that have low molecular weight, lipid (fat) solubility, nonpolarity, and no protein binding properties will quickly and easily cross the placenta. Most drugs with MW < 500 Da cross the placenta, and most drugs with MW > 1000 Da do not cross the placenta (ex. heparin, protamine, insulin). The substances not likely to pass in significant amounts include bacteria, heparin, sIgA, and IgM [8].

Currently, the concept of the 'sterile womb', the paradigm that the fetus grows up in a sterile environment, is challenged [9]. Lessons learned from the gut microbiome suggest that the

microbiota of the uterus may potentially modulate immune cell subsets needed for implantation and have implications for tissue morphology. Microbiota can also be crucial in protection against uterine infections by defending their niche and competing with pathogens. Various recent reviews focused on correlations between commensal uterine colonization, fertility problems and pregnancy complications [10,11]. Culture-based approaches, rapidly growing, aerobic species dominate, leaving rare species that demand specific culture conditions undetected [12,13]. Molecular approaches allow detection of species that will not be revealed by culture-dependent techniques. Mitchell, et al. [14] examined uterine swabs and EF from hysterectomies by quantitative PCR (qPCR) for 12 bacterial species, including Atopobium vaginae, Prevotella spp., Lactobacillus crispatus, Lactobacillus iners, G vaginalis and bacterial vaginosis-associated bacterium 1 (BVAB1). All of the selected species could be detected in vaginal samples and to a varying extent in the endometrium. Clear differences could be found between vaginal and endometrial samples. While A. Vaginae was more commonly detected in vagina, L. iners and BVAB1 were more likely to be detected in endometrial samples. Of note, 95% of hysterectomy samples showed the presence of bacterial DNA.

Further, Younge et al. [15] studied the microbiota of human and mouse dyads to understand relationships between microbiota and developing fetus, localize bacteria in the fetus, and demonstrate bacterial viability. In human preterm and full-term mother-infant dyads at the time of Cesarean delivery, the oral cavity and meconium of newborn infants born as early as 24 weeks of gestation contained a microbiota that was predicted to originate from in utero sources including the placenta.

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DOI: 10.19080/IJCSMB.2019.06.555693

How to cite this article: Gupta PD. Modulation of Human Placental Role: Revisited. Int J Cell Sci & Mol Biol. 2019; 6(4): 555693.
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