

A theory for the evolution of the hemochorial placenta



**ASSIGN
BUSTER**

Introduction

Very few mammalian tissues vary as intensely in different species as the placenta. One of the problematic challenges for observing the placenta is this incredible variation. This fact is quite interesting considering the reproductive organs primary function in all mammalian species is uniform, exchanging resources both nutrients and waste between a mother and her unborn children. Through this important function, the placenta has a large hand in determining post-natal health and offspring's susceptibility to disease. The question this research review poses then, is simple. Why then, does the Eutherian placenta of other taxa differ from the primate and rodent hemochorial placenta? Why did the hemochorial placenta diverge? Current theories suggest that life history changes and/or parent-offspring conflicts over maternal resources promoted rapid evolution of the placenta (Haig, 1993). This research review aims argue that the hemochorial placenta evolved to increase permeability and allow maternal antibodies to penetrate the trophoblastic barrier. Newborn infant immune systems would not on their own be well equipped to survive in an environment with such high probability of exposure to pathogens. This adaptive function evolved to provide newborn infants with immune systems primed to survive in mothers' settings. The evidence that will be presented will review the hemochorial design for the placenta, that the specific invasiveness of this placenta allows for the exchange of antibodies between the maternal-fetal interface. We will also review the role of retroviral genome implantation and how it has served to shape the placental form. The role of the placenta is to provide sustenance throughout the whole of the pregnancy although defects within

this partnership create many complications as it appears. Still, evolutionary adaptation, development as a structure, and role for reproduction, the placenta remains one of most poorly understood organs within the mammalian taxa (Griffith, 2017).

Function and Variation of Primate Placenta

In order to understand the nature of our question it is first important to understand the function and differences between placental variation as several types exist within eutherian mammals. In large, the placenta is a reproductive adaptation that has allowed viviparity to become a successful strategy for developing offspring. Viviparity is a reproductive pattern in which females develop their offspring inside their reproductive tract before birthing fully developed young. This is contrary to oviparity in which females deposit their offspring in eggs that then later develop through incubation before hatching. The placenta is a defining feature of living mammals. But 200 million years ago, the first warm-blooded mammals still laid eggs, like the modern platypus. In the late 1990s, researchers discovered that the capacity to fuse embryonic and fetal tissues into a placenta was initially achieved by integrating genetic material from ancient retroviruses into the mammalian genome (Trans, 2013). The function of the placenta became even more important as evolution of this organ permitted primate offspring to become even more closely tied to the uterine wall lining while still allowing for selective permeability.

Placental structure widely varies in shape, size, cellular elements, and level of invasiveness within the female reproductive tract. The classification

<https://assignbuster.com/a-theory-for-the-evolution-of-the-hemochorial-placenta/>

system for categorizing this structure is constructed around which maternal layers are retained in the placenta. In humans this is also the layer that is in contact with the chorionic epithelium of the placenta. These classes are epitheliochorial, endotheliochorial, and hemochorial. Humans, nonhuman primates, rats and mice possess the hemochorial placenta. This variation of the structure can be characterized by a limited cell barrier and enlarged access to the maternal blood flow. Hemochorial placentation is the most maternally invasive and allows the fetal tissue structures to be in nearly direct contact with the maternal blood source. In horses, swine, and ruminants (cow and sheep) epitheliochorial placentas which are much less invasive, three layers of maternal tissue separate the fetus from the maternal blood stores (Hill, 1932). Examination of the placenta from different species will show impressive variation in their form and regions of contact between maternal and fetal tissues. In a Zonary placenta, typical to dogs and cats, the structure is a complete band of tissue that surrounds the fetus.

Placental Anatomy

During formation of the placenta six layers of tissue separate the maternal blood from the blood of the fetus. In all mammals, there are three layers of the membranes of the fetus that are retained to form the fully developed placenta and are maintained throughout the pregnancy. The layers of these structures are the endothelium lining allantoic capillaries, chorionallantoic mesoderm (this is the connective tissue), and the chorionic epithelium (the most outer fetal membrane layer that is formed by the trophoblasts). In conjunction with these three layers, three more layers exist within the maternal aspects of the structure. However, the extent that these parts are

<https://assignbuster.com/a-theory-for-the-evolution-of-the-hemochorial-placenta/>

kept and not absorbed or destroyed during implantation varies greatly between eutherian mammals. These layers are the endothelium lining endometrial blood vessels, endometrial epithelial cells, and connective tissue of the endometrium.

The hemochorial placenta is comprised of special epithelial cells which are much more commonly referred to as trophoblast cells. In all placental variants, these cells are situated against mesenchymal cells at the maternal-fetal " interface" and are always the most superficial layer of fetal cells that cover the inner layers of fetal capillaries and mesenchyme. Trophoblast cell structures are incredibly capable of directional manipulation of the flow of nutrients and wastes at this interface. This process supports fetal development by facilitating the delivery of maternal resources and protecting the fetus from adverse exposures provisioned by the mother. The most invasive form is seen when trophoblast cells infiltrate through the maternal vessels to come into direct contact with maternal blood in hemochorial placentation. In this hemochorial form, trophoblast cells disrupt the endothelial cells and, in some cases, the muscle coat of the uterine arteries as well (Moffett, 2006). Because these trophoblast structures penetrate the uterus so deeply, the fetus has a much more productive availability to maternal resources and nutrients. As described by Brosens, Robertson and Dixon (1967) for the human being, the peripheral portions of the uteroplacental arteries, i. e. the spiral and radial arteries show peripheral dilation. Whereas in most other organs including the epitheliochorial placentae the diameter of the arteries becomes smaller and smaller as they approach the target cells, the spiral arteries of hemochorial placentae dilate

progressively as they reach the trophoblastic sinuses. Although these arteries give greater access of nutrients to the fetus this is not a completely open system.

Sub Anatomy of the Placenta and STB Structure

Syncytiotrophoblasts (STB) are specifically responsible for the nutrient and primary gas exchange between the maternal-fetal interface. This cell type is the outer layer of the trophoblasts and actively penetrates the uterine wall. In doing so, the STB rupture the maternal capillaries and establishes the crossing point between maternal blood and embryonic extracellular fluid. This syncytial property which creates a multinucleated continuous cell is especially important as maternal blood includes immunoglobulins that would otherwise be able to migrate through tissue by squeezing through cellular gaps. If these antibodies were allowed to penetrate to the fetal fluid of the placenta, many foreign proteins could be recognized thus triggering a strong immune reaction in the fetus. This syncytium however acts as a giant cell wall in which there are no gaps for immune cells to migrate without permission.

The protein syncytin, which is essential for the development and formation of the placenta originally came to our ancestral genome through retroviral infection. The genetic material of retroviruses is ribonucleic acid (RNA), but during infection it is transcribed into DNA and stored within the chromosome of the infected cell. This is a very important step in the retrovirus maturation and known as retro-transposition. When in some cases, the infected cell is a germ cell, the viral DNA becomes a permanent part of the animal and its

offspring. One of these retroviral genes are known as ERV (endogenous retrovirus). Genome-sequencing projects of many species have revealed that ERVs have a ubiquitous presence in vertebrate genomes, constituting over 8% of the human genome (Landers, 2001). In the case for eutherian placenta ERV has been repurposed by mammals to code for the syncytin genes. As well, traces of syncytin-like retroviral proteins have been centrifuged from almost all mammalian placenta. Still, different variations of the syncytin protein can be traced back to unconnected retroviruses in at least 10 unrelated infectious diseases. These findings have led to speculation that the co-option of unrelated ERVs in different species was a driving force underlying the evolutionary diversification of the placenta (Imakawa, 2015). This retroviral adaptation gives the syncytiotrophoblasts their structure. This is an important evolutionary key in understanding how the hemochorial placenta evolved as without this STB capability, permeability of the maternal-fetal complex would have a much different profile today.

Immunological Role of Immunoglobulin G

Alongside nutrients that pass through this STB barrier are one important immunoglobulin protein molecule. Placental transfer of Immunoglobulin G (IgG) antibodies to the fetus is an important adaptation that aids by protecting the child while humeral responses are for the most part, insufficient. Of the 5 significant immunoglobins found in the maternal system, IgG is the single immunoglobulin class that extensively crosses this interface into the fetal system. It is suggested by Marodi that this process is facilitated by Neonatal Fc Receptor (FcRn) expressed on the

syncytiotrophoblast cells (Marodi, 2006). The maternal-fetal transfer of <https://assignbuster.com/a-theory-for-the-evolution-of-the-hemochorial-placenta/>

immunoglobulins appears to be an adaptive mechanism that allows for the minimization of insufficiencies in antibodies of the fetus and allows for short-term resistance as development occurs. However, even the transport selectivity of IgG depends on its subclass (A. Hart, 1999). A process that would have been first derived from and not possible without retroviral encoding and expression.

This phenomenon is not completely clear as to why some antibodies exhibit different transferability properties in different studies. As Ferrante suggests, these antibodies affinities to cross the syncytium may do so based on responses to different antigens and their affinities to the IgG transporting FcRn receptors. Transfer of antibodies that protect against viral proteins and antitoxins occur more readily as IgG1 and IgG3. Transfer of antibodies more apt to fighting encapsulated bacteria such as Haemophilus influenzae, marked IgG2, are much less effectively and transferred less efficiently to the fetus (Ferrante, 1990).

The IgG receptor has three distinct functions that aid in the process of immunological resistance: activation of cells, inhibition of cells, and transport/recycling of waste products. It is the most abundant type of antibody found in all body fluids (accounting for about 10-20% of plasma protein) (Schur, 1988) and protects against viral and bacterial infections. As we discussed there are several types of IgG receptors in humans as well as mice, rats, and primate species. One variant of this inhibitory receptors acts as a positive feedback loop to prevent the development of new antibody responses to antigens that have already previously been produced by the host. The FcRn is involved in transporting the IgG across tissue barriers <https://assignbuster.com/a-theory-for-the-evolution-of-the-hemochorial-placenta/>

found in the gut, lungs, and placenta. The way that the antigen is contracted within the body, and the composition of the antigen has a direct impact on the type of immune response that is solicited, this directs the type of IgG antibody that utilized.

Although IgG transference is an important facet of fetal development that also aides in the newborn's overall survivability, it is apparent that the hemochorial placenta cannot come without some cost. Throughout pregnancy, the placenta must serve a barrier function, maintaining the fetal compartment free of viruses and bacteria. If this barrier for some reason fails and sterility is compromised, or placental tissues become infected, such as in the case of chorioamnionitis, the pregnancy may be lost (Cardenas, 2010). Science is no stranger to the fact that immunoglobulin transportation during pregnancy is widely affected by a host of issues and circumstances. Placental abnormalities, the gestation term of the fetus, IgG concentrations that exist within maternal plasma and parental pathologies can hinder sufficient immunological transfer. Common chronic conditions like hypertension, gestational diabetes, and preeclampsia may also play some role in this transmission but is less clear in study (Beebe, 1996). Although this research review has exclusively focused on the encouraging aspects of antibody transference, this adaptation also carries with it the possibility for harmful, negative consequences as well. In the case of Rhesus incompatibility, a mother who is Rhesus negative may begin to build immunoglobulin in response to the RBC's of the fetus if those cells express Rh antigen (a protein acquired in the case that paternal blood was Rh-positive). Then when the antibody is transferred from maternal blood line to the fetus

it can cause the destruction of red blood cells, organ damage, and even death of the fetus. While studying the placental transfer of antibodies in primate species, researchers found a link between the crossing of some immunoglobulin types and offspring born with neurological conditions. Some mothers who bear children with autism may then produce antibodies that eventually affect and block proteins that are important for neural development and brain function. When this antibody was purified and administered to pregnant rhesus monkeys, it crossed the placenta and affected the neural and behavioral development of their offspring (Bauman, 2013).

Conclusion

The hemochorial placenta is on its own an incredibly intricate mammalian organ. It is difficult to derive one specific evolutionary event that caused it to diverge from other eutherian species. Evidence for the retroviral coding for ERV's and subsequent syncytin protein and STB structures that make up the outer layers of the placenta provide strong argument that the placenta may have diverged because of immunological response. This adaptation eventually allowed for immunoglobulin G to permeate the maternal-fetal interface providing offspring an immunological crutch until humeral immunity could develop outside the womb. Although this adaptation has allowed our species to overcome pathological attacks while permitting slow development of the unborn fetus, pathological conditions were also increased in risk. This research review argues that in the case for evolutionary adaptation, the cost for immunological buffering is not outweighed by pathological risk. Without this chain of events stemming from <https://assignbuster.com/a-theory-for-the-evolution-of-the-hemochorial-placenta/>

viral infection in our early ancestors, we would not have the fighting chance to survive in a world filled with microscopic invaders.

Reference and Citation

A. Ferrante, L. J. Beard, and R. G. Feldman, “ IgG subclass distribution of antibodies to bacterial and viral antigens,” *Pediatric Infectious Disease Journal*, vol. 9, supplement 8, pp. S16–S24, 1990.

Bauman MD, Iosif AM, Ashwood P, Braunschweig D, Lee A, Schumann CM, Van de Water J, Amaral DG

Maternal antibodies from mothers of children with autism alter brain growth and social behavior development in the rhesus monkey. *Translation Psychiatry*. 2013 Jul 9; 3(): e278.

Braunschweig D, Ashwood P, Krakowiak P, Hertz-Picciotto I, Hansen R, Croen LA, Pessah IN, Van de Water J. Autism: maternally derived antibodies specific for fetal brain proteins. *Neurotoxicology*. 2008 Mar; 29(2): 226-31

Cardenas I, Means RE, Aldo P, Koga K, Lang SM, Booth CJ, Manzur A, Oyarzun E, Romero R, Mor G

J Viral infection of the placenta leads to fetal inflammation and sensitization to bacterial products predisposing to preterm labor. *Immunol*. 2010 Jul 15; 185(2): 1248-57.

Griffith OW, Wagner GP. The placenta as a model for understanding the origin and evolution of vertebrate organs. *Nat Ecol Evol.* 2017; 1: 72. pmid: 28812655

Haig D. Genetic conflicts in human pregnancy. *Q Rev Biol.* 1993; 68: 495–532. pmid: 8115596

Hill JP. Croonian lecture: The developmental history of the primates. *Philos Trans R Soc Lond B.* 1932; 221: 45–46.

H. L. Wesumperuma, A. J. Perera, P. O. Pharoah, and C. A. Hart, “ The influence of prematurity and low birthweight on transplacental antibody transfer in Sri Lanka,” *Annals of Tropical Medicine and Parasitology*, vol. 93, no. 2, pp. 169– 177, 1999.

Imakawa K, Nakagawa S, Miyazawa T. Baton pass hypothesis: successive incorporation of unconserved endogenous retroviral genes for placentation during mammalian evolution. *Genes Cells.* 2015; 20: 771–788. pmid: 26442811

L. A. Beebe, L. D. Cowan, and G. Altshuler, “ The epidemiology of placental features: associations with gestational age and neonatal outcome,” *Obstetrics and Gynecology*, vol. 87, no. 5, part 1, pp. 771–778, 1996.

Lander ES, Linton LM, Birren B, Nusbaum C, Zody MC, Baldwin J, et al. Initial sequencing and analysis of the human genome. *Nature.* 2001; 409: 860–921. pmid: 11237011

L. Marodi, "Innate cellular immune responses in newborns," *Clinical Immunology*, vol. 118, no. 2-3, pp. 137-144, 2006.

Moffett, A., Loke, Y. W. & McLaren, A. *The Biology and Pathology of Trophoblast* (Cambridge University Press, Cambridge, 2006).

Schur PH. IgG subclasses. A historical perspective. *Monogr Allergy* (1988)23: 1-11.