The Immune System Within A Pregnancy

The immune system within a pregnancy is very complex. Being susceptible to certain infectious diseases puts a pregnant woman within a special population group with an ‘immunological’ condition that is caused by pregnancy. Although, it may bring up some challenges in making decisions in regard to treating and preventing these infectious diseases and how to approach them. For years the complexity of pregnancy and its immunology has been the center focus of complication in developing new standards with clinical implications that can answer the most relevant questions. Pushing scientists and clinicians to better understand how the mother and fetus benefit from the immunology of pregnancy in different situations. In order to control pregnancy, the immune system has to be at the forefront of maintaining the viruses and bacteria’s that enter the body. Making this an interesting aspect of how maternal and fetal cells stay in tune with each other to create a healthy pregnancy.

It has always been said that the immune system plays a key role in protecting its host from pathogens. Other than organizing cell migration for observation, the immune system must also play a role in identifying and responding to microorganisms that invade the body. During a normal pregnancy, the human decidua contains a large number of natural killer cells (70%), regulatory T cells (3 to 10%), and macrophages (20 to 25%) (Mor & Cardenas; 2010). Dendritic cells by the decidua, NK cells, and macrophages all infiltrate and accumulate in the first trimester of the pregnancy causing a significant invasion of trophoblast cells. Studies have shown that the endometrial vascularity lacks a good amount of trophoblast cells without the presence of NK cells which eventually leads to the termination of the pregnancy; making uNK cells critical for the uterus during trophoblast invasion. In order to allow the interaction of the fetal-maternal immune to be more complex, functional, active, and carefully controlled, this event needs to avoid blastocyst implantation and decidual formation with the depletion of dendritic cells (Mor & Cardenas; 2010).

It was observed that T-cell (Treg) recruitment, differentiation, and bacterial or viral infections have been induced by the mechanisms of trophoblast cells (Ramhorst, Fraccaroli, Aldo, Alvero, Cardenas, Leirós, & Mor; 2011). This study correlates with the recognition of the three trimesters of pregnancy and the three immunological phases. In the first trimester, the linking of a pro-inflammatory environment is correlated with successful implantation; the second trimester involves the symbiosis of the placenta and fetus with the induction of an anti-inflammatory; and in the final trimester, parturition (an inflammatory process) is started, beginning the process of contraction in the uterus, delivery of the baby and removal of the placenta (Ramhorst, Fraccaroli, Aldo, Alvero, Cardenas, Leirós, & Mor; 2011). The relationship between first-trimester trophoblast cells and Treg cells was a key focus in this study; exhibiting the role of trophoblast cells and their capability to produce iTreg differentiation from peripheral blood of maternal naïve T cells along with the potential to recruit Tregs. Control fertile women who had two or more previous normal pregnancies without any miscarriages participated in this study.

The peripheral blood mononuclear cells of these fertile women were used to differentiate naïve CD45RA+ CCR7+ cells in a cultured IL-2 and TGFB in the span of 5 days. The first two-trimester trophoblast cell lines Swan-71 and HTR8 were able to obtain the induction of Tregs (CD4+ Foxp3+ cells) using a low serum conditioned media (LSCM) (Ramhorst, Fraccaroli, Aldo,

Alvero, Cardenas, Leirós, & Mor; 2011). PGN, LPS, or Poly [I: C] was involved in a migration assay co-cultured experiment that determined the presence or absence of trophoblast cells. Multiplex analysis was also used to measure the production of cytokines. TGFB was considered to be a key cytokine with the contribution that trophoblast cells played in the differentiation of maternal naïve T cells. However, it was also determined that trophoblast cells played a key role in the recruitment of Tregs with the presence of microbial factors. After 48-hour culture, FAC analysis was able to reveal a sizeable increase in the number of Foxp3+ cells with the absence or presence PGN, LPS, and Poly[I:C]. This all demonstrates trophoblast cells contributing to the differentiation and recruitment of iTregs, maintaining an intensified presence of bacterial or viral products in which plays a role in the regulation of the immune placental-maternal interface (Ramhorst, Fraccaroli, Aldo, Alvero, Cardenas, Leirós, & Mor; 2011).

There is also the consideration of maternal influences on fetal microbial colonization and immune development. The early development of a functional immune system is determined by the human fetus being exposed to various microbial antigens. For example, toward the end of the first trimester of pregnancy, CD4+ and CD8+ T cells can already be detected. It was recently discovered that the abundant and functional pool of FOXP3+ T regulatory (Treg) cells is required to manage fetal T cells that are highly responsive to a stimulus (Romano-Keeler & Weitkamp; 2014). Intriguingly, antigen-specific tolerance has been induced due to fetal Treg cells and their significant number of maternal cells crossing into the placenta. During pregnancy, there is a higher frequency of genetic material or whole bacteria being carried by maternal mononuclear blood cells; representing a few of these bacterial signatures in the feces of infants (Romano-Keeler & Weitkamp; 2014). One can now take into consideration how the development of the microbiome postpartum can enable the in utero transfer of maternal microbial antigens during fetal development once the immune response of the newborn is balanced. There is still much to learn about the gathering evidence towards microbial programming beginning in utero and its role in developing a balanced mucosal immune system in a newborn.

To maintain and establish a pregnancy, the hormone is known as progesterone (P4) plays a key role; it also causes the onset of labor as it starts to withdrawal (Shah, Imami, & Johnson; 2018, May 23). A study was performed on 42 healthy pregnant patients to compare the effects of P4 supplementation longitudinally, with treatment using P4 antagonist mifepristone (RU486) in mid-trimester pregnancies (Shah, Imami, & Johnson; 2018, May 23). Giving the opportunity to demonstrate in the data collected that the immune-modulatory functions of P4 along with its reduction of pro-inflammatory and cytotoxic T cell responses in pregnancy were caused by P4. Which in turn had its effect reversed with the use of RU486. In a normal pregnancy, it was previously demonstrated that the elevation of recalled antigens in IFN-? and IL-10 responses happens in the third trimester. The destruction of antigen-specific T cell responses came from the possibility of IL-10 restricting the activation of the immune system; only if CD4 TEM shows an increase during the second trimester (Shah, Imami, & Johnson; 2018, May 23). The responses of IL-10, exhibited an increase in pregnancy across gestation even though a steady decline of IL-10 antigen-induced immune tolerance was indicated by a leukocyte phenotype.

An ongoing decline of immune-modulation indicated a more common IL-4 SFCs in pregnancy alongside an enhanced increased granzyme B cytotoxic T cell activity, and IFN-? and IL-10 responses to CD8 epitopes at delivery with humoral and cytotoxic responses (Shah, Imami, & Johnson; 2018, May 23). Granzyme B is fundamentally delivered by initiated CTLs and NKs cells, making it a valuable indicator for the useful movement of CTLs. As mentioned before, pro-

inflammatory and cytotoxic T cell responses are reduced by P4 in pregnancy. It has the ability to achieve this because the impact that cell-mediated interactions have, allows the sensitivity of memory T cell antigen and the regulation of leukocyte migration to be altered; with RU486 reversing these effects. In the end, results have distinguished which characteristics of the maternal immune response regulates P4. Therapeutic targets have a chance in helping these pathways modulate the maternal immune response to pregnancy. That is why the future of in vivo human work plays such an important part in the establishment of cellular interactions and their role during human pregnancy.

edubirdie.com