LABORATORY OF CELL SOCIOLOGY

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Mammalian eggs implant onto the maternal uterine wall after hatching at the blastula stage, due to a lack of enough nutrients to support development until birth. In order to transfer nutrients and oxygen into the fetus, and metabolic wastes into the mother, the placenta has evolved to establish close connections between the maternal and fetal vasculature. There is amazing diversity from one animal to another in the features, such as gross structures, microscopic arrangements and developmental processes, but the function of this organ is invariable.

Primates and rodents have the ancestral type of placenta, classified as heomochorial, in which maternal blood is not contained within endothelial cell lined vessels but rather is in direct contact with epithelial cells of the fetal placenta that are derived from the trophoblast cell lineage. In mice, maternal blood coming out from the spiral arteries invaded by trophoblast cells that replace the endothelium passes across the fetal layers of the placenta and then enters into the labyrinth where fetal blood vessels form and feto-maternal exchange occurs. Maternal and fetal vascular circuits in the established mouse placenta are shown schematically in Figure 1.

Notch2 null mutation induces lethality around embryonic day 11 because of impaired maternal vasculature formation. However, both cellular and molecular events in the process of vasculature formation are little known, especially as to how the maternal blood bed expands among the tightly packed trophoblast mass. Our histological studies showed that a stream of maternal blood along the interface between the labyrinthine trophoblast and spongiotrophoblast was slightly opened in the mutant placenta. Expression of the Notch2 gene is observed in spongiotrophoblast and Giant cells, but in neither the labyrinthine trophoblast nor in the multi-nuclear Syncytiotrophoblast that is derived by cell fusion of the mono-nuclear labyrinthine trophoblast (Figure 2). Thus, we conclude that cellular and molecular events to form the maternal blood bed occur in the spongiotrophoblast and Giant cell layers.

We have assumed that the cellular event that expands the maternal blood bed is the deletion of spongiotrophoblast cells in a significant number from the developing placenta. Thus, we are trying to detect trophoblast cell death or detachment with various methods.
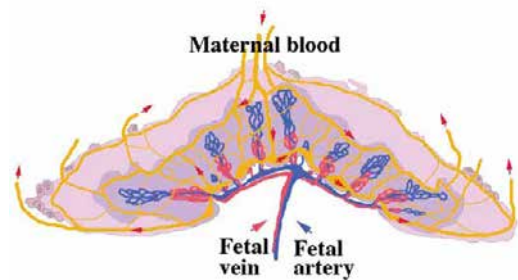

Figure 1. Schematic maternal and fetal vascular circuits in mouse placenta. Maternal blood flows in streams drawn in yellow in the direction shown by small red arrows. Fetal blood flowing in the artery (blue line) reaches the border of the spongio- and labyrinth layers and returns to the fetal vein (red line).
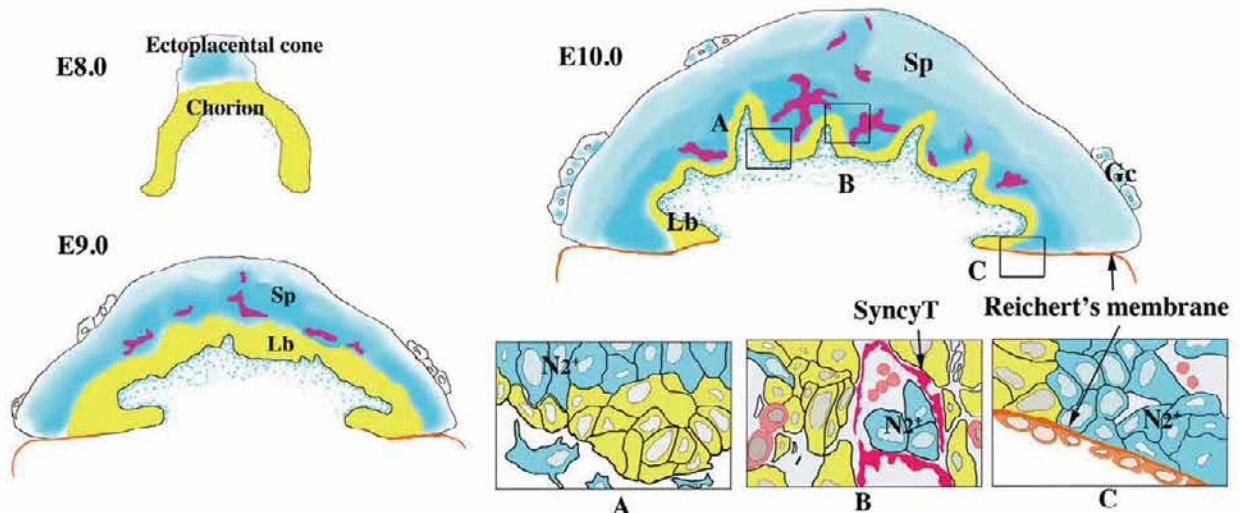

Figure 2. Expression of Notch2 gene in developing mouse placenta. The Notch2 gene is expressed in the ectoplacental cone at E8.0, but not in the chorion. At E9.0, the ectoplacental cone and chorion differentiate into spongiotrophoblast (Sp) and labyrinthine trophoblast (Lb), respectively. The expression is detected in Sp. At E10.0, differentiation of syncytiotrophoblast (SynT) and vasculogenesis of fetal blood are obvious in the placenta. Notch2 expression occurs in Sp, Giant cell layer (Gc), and mesenchymal cells derived from allantois. However, it is not detected in SynT and Lb far away from maternal blood or separated by SynT.