

## CHAPTER 1

### **ROLE OF ENDOMETRIUM ON SPATIAL ORIENTATION AND NAVIGATION OF BLASTOCYST**

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#### **What is the definition of implantation and implantation zone?**

The embryo is the only mammalian cell with the ability to migrate and target in a dark environment. Like a lot of migrating animals blastocyst make a monthly migration from ampullary region to the endometrial implantation zone. After fertilization in ampulla, embryo begins to move when cell division proceeds. This journey can take a few days and cover over 6 cm. The uterine tube steers the embryo toward the cavity by cilia motion and tubal contractions. Approximately 3 to 4 days after fertilization embryo completes its journey and enters the endometrial cavity. Once reach in the endometrial cavity, embryo seek out the implantation zone that is specific and isolated endometrial area for attachment. The implantation zone can sometimes be superficial and sometimes deep. A superficial zone can be easily found by the embryo. In the presence of the deep zone, the embryo can not find the region to attach, even if it is of good quality.

Implantation of human blastocyst can be likened to polar foxes diving into the snow with their noses to catch rodent. Red foxes can hear low-frequency sounds beneath 3 feet of snow extremely well. Every failed dive can result in energy loss, hunger and death. Similarly, human blastocyst also shots to hold onto possible implantation site. The increase in the number of trial leads to attachment problems. Unlike moving and sounding rodent targets, the implantation zone is both motionless and silent. Moreover, the embryo has no hearing, no jumping, or diving ability. So that the embryo must send out a number of signals and be able to perceive the signals from the zone in order to find the implantation area. All of which require the presence of embryos that have the ability to sense and secrete healthy signals. However, although many naive or ICSI embryos that appear morphologically healthy they do not have ability to produce enough signal to find the implantation zone.

#### **What is the embryo navigation and spatial orientation?**

Blastocyst stage embryos have evolved a remarkable capacity to find small implantation site within the endometrium following trans-tubal migration. Fertilized

either narrow in on their arrival site or to pinpoint their final destination precisely. However, whether IB have this ability is debated. Unlike the NB, the IB is not a long-distance navigator. Although IB have lower implantation rates than in natural blastocyst, most IBs accurately locate their migratory destinations, and are likely to use a number of chemical and physical cues. Increased pregnancy rates after oocyte donation suggests that young IB, at least, may have a map sense and true navigation. However, evidence is lacking whether IBs have ability to use chemical and physical cues as in the NBs.

The navigation problems that both NB and IB need to solve as they migrate towards endometrium are very similar. The NB may solve these problems using the combination of several cues as a compass for finding its way. On the other hand, solving of navigation problems IB is more difficult. Finding of implantation zone by IB is hard due to embryo transfer technique. Both polyvinylpyrrolidone, and air inside transfer catheter as well as the pressure is applied on catheter by physician, all degrade the reliability of chemical cues for navigation of embryo throughout the endometrium cavity. Likewise, multiple egg development and deactivation of the tubes in the ART cycle adversely affect the signal communication between the embryo and endometrium.

### **Is it true to compare pregnancy rates in natural and IVF cycles?**

Exactly no. Because, in natural cycles fertilization of oocyte and early cleavage embryo development take place in ampulla of fallopian tubes and then blastocyst is transferred into the cavity where it is implanted into the endometrium. On the other hand, in the IVF cycles the early embryo development from zygote to blastocyst is realized in specific medium and conditions, where the development of blastocyst stage embryo is not possible for all embryos. Therefore comparing the results of pregnancy rates obtained in IVF and natural cycles is not logical.

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11. This section is mainly a summary of the published articles written by me and my colleagues in the following journals;
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