

THE EFFECT OF NOTCH ON EMBRYO IMPLANTATION

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Purpose: Implantation is essential for survival of all mammalian species. As so, of the pregnancies that are lost, 50–75% represents a failure of implantation. To improve the implantation rate is an important issue in the assisted reproductive technology. Notch, a protein was shown to promote neural fate in *Drosophila*, it has been found in many other organisms, from worms to humans to regulate cell proliferation and cell death. In this proposal we investigate the evolution of the mouse as a model for understanding uterine implantation in Notch signaling pathway, including new advances.

Material and methods: For the collection of embryo we raised female ICR mice aged 4 to 5 weeks and male ICR mice aged 3 to 12 months for use in these experiments. Ovulation are induced in female mice by an intraperitoneal injection of 10 IU pregnant mare serum gonadotropin followed by 10 IU human chorionic gonadotropin 48 hours later. The following morning the females exhibiting vaginal copulatory plugs are separated for the proposed experiments. The day of appearance of a vaginal plug are set as D0.5 and 8 cells were collected on D2.5. The embryos are cultured in HTF-BSA (4mg/ml). By matrigel assay we observed the growth competency and implantation ability with supplemented different concentration of Notch and its inhibitor (γ -secretase inhibitor, DAPT).

Result: Notch1 inhibitor, DAPT, supplementation reduced the attachment rate of blastocysts on the matrigel. In vitro mouse embryo model showed the 10nM DAPT treated group had lower implantation rate than the control group (66.7% vs. 87.2%, $p < 0.05$), and 30nM DAPT treated group had much lower implantation rate than the control group (53.3% vs. 87.2%, $p < 0.05$).

Conclusion: Based on recent data we have, the inhibition of Notch-1 seemed reduce the implantation rate. Also we can see there's a dose dependent effect which eliminate the possibility of completely block of blastocyst survival when add the Notch-1 inhibitor. Further and ongoing study are focused on: 1) Explores the detailed mechanism underlying the effect of Notch1 on embryo implantation during the window of uterine receptivity. 2) To explores the regulation between Notch and chorionic gonadotropin (CG), progesterone, as well as Notch inhibitor during the window of uterine receptivity, 3) Effect of Notch in developmental potential of blastocyst implant in vivo, and 4) The mechanism of Notch1 to improve the implantation such as the well-organized stress fiber distributed in embryos. We hope that the forthcoming information will generate some new ideas and concepts for the process of implantation that is essential for maintaining procreation and solving major reproductive problem in human infertility, which is the critical problem of the IVF clinics around the world.