NO.7

NOTCH SIGNALING REGULATES PULMONARY SURFACTANT PROTEINS EXPRESSIONIN FETAL MOUSE LUNGS

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Objective

Notch signaling is required for proper development of proximal epithelial structures in the lung. Disruption of Notch signaling dramatically expands the population of distal progenitors in the early lung. Developmental changes in lung Hes1 and Hey1 mRNAs, two Notch target genes, in two mouse strains with different length of gestation suggesting a potential repressive role for Notch signaling in perinatal lung maturation. In addition, Notch signaling inhibited expression of several maturation-associated lung mRNAs in vitro. Thus, we hypothesize that inhibition of Notch signaling in late gestation may improve fetal lung maturation. The aim of this study is To evaluate the role of Notch signaling on production of surfactant proteins (SP) in fetal mouse lungs and possible mechanism.

Methods

The embryonic day 15 (E15) lung explants were cultured with or without gamma-secretase inhibitor (DAPT; Notch inhibitor) for 48 or 72 hours. Real time PCR and immunohistochemistry staining were used to analyze pulmonary surfactant proteins, regulating factors, VEGF and Notch components.

Results

Blocking Notch signaling in E15 lung explants not only induced the expressions of SP-A, SP-B, SP-C and SP-D with time-depend manner, but also slightly increased endothelial markers including vascular endothelial growth factor receptor-2 (vegfr2) and PECAM-1 expression. DAPT treatment did not change the expression of transcription factors in the respiratory epithelium, including thyroid transcription factor-1 (Ttf-1), forkhead homolog a2 (Foxa2), and CCAT enhancer binding protein a (C/EBPa), regulate groups of genes that are required for the differentiation and maturation of the lung. Indeed, inhibition of Notch signaling enhanced expression of genes known to be associated with surfactant lipid synthesis and transportation, including Lpcat1, Napsa and Abca3.

Conclusions

Brief blocking Notch signaling may have the potential therapeutic effect on preventing premature mice from neonatal respiratory distress syndrome.

NO.8

EARLY ORAL PROBIOTICS AND LACTOFERRIN RREDUCE REDUCE NECROTIZING ENTEROCOLITIS OR AND LATE-ONSET SEPSIS FOR PRETERM VERY LOW BIRTH WEIGHT INFANTS

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Objective

We aimed to investigate whether early oral probiotics and Bovine lactoferrin (BLF) would reduce necrotizing enterocolitis (NEC) and late-onset sepsis (LOS) in preterm very low birth weight (PVLBW) infants below 32 weeks gestational age (GA).

Methods

From July 1, 2012 to Jan 31, 2014, a prospective, randomized, double blind controlled trial was conducted in five NICUs at Taiwan. Preterm infants below 32 weeks GA and birth weight below 1500 gm and survive to NICUs were eligible for the trial. They were assigned randomly to the study or control group after informed parental consents were obtained. Enrolled infants receive either group A: BLF with probiotics or group B: probiotics alone, group C: control group received 1 mL of a 5% glucose solution. Each group of A.B and C were prepared by milk team who did not know the grouping. Administration of BLF or probiotics or glucose begins within 48 hours of life with 1-5 consecutive doses; the frequency of dosage depends on the GA. The study protocol was approved by the institutional review board of each hospital. Primary outcome was NEC and late-onset sepsis.

Results

One hundred twenty-five infants were enrolled, 61 in the study group and 64 in the control group. The demographic characteristics was not different between groups. The incidence of death or necrotizing enterocolitis (stage 2) and LOS was lower in the study group (7 of 61 infants vs 13 of 64 infants but not statistic significantly. No adverse effect, such as probioticssepsis, flatulence, or diarrhea, was noted.

Conclusions

Oral Probiotics and Lactoferrin fed enterally to PVLBW infants till GA 34 weeks might reduce the incidence of NEC and LOS with adequate sample size.