BDR SEMINAR in Kobe

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16:00-17:00, 7F Seminar Room, DB Building A

Maternal bile acid critically regulates organ and tissue development

Summary

During tissue and organ development, immature cells rapidly proliferate and efficiently differentiate towards more specialized cell types within a limited time. Often mechanisms enabling such a dramatic change are unique during the pregnancy, uncovering of which is also imperative for developing future regenerative therapies. We have recently discovered that bile acids (BA) play a crucial role in regulating expansion of murine hematopoietic stem cells (HSCs) in the fetal liver through suppression of unfolded protein response (UPR) (Miharada et al., *Cell Rep.*, 2014; Sigurdsson et al., *Cell Stem Cell*, 2016). BA have been known for their function in the digestive system, facilitating intestinal nutrient absorption and dietary lipid digestion, but they are also recognized as chemical chaperones and signaling molecules. Importantly, depletion of a key BA synthetic enzyme, Cyp27a1, in the maternal body critically reduced BA content and the number of HSCs in the fetuses, while depletion of the enzyme in the fetus showed a minimum impact as long as the mothers were wildtype or heterozygote. Furthermore, newborn mice grown in the *Cyp27a1* knockout mothers died right after the delivery due to acute respiratory distress syndrome resulted from lack of alveolar structures. In addition, these newborn mice also showed abnormalities in the brain and liver (Suzuki et al., in preparation). Thus, our findings strongly suggest that BA, particularly maternal supply, are critical developmental factors regulating multiple organ/tissue development.

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