RIKEN SEMINAR

〈 12th Epigenetics Seminar Series 2017 〉

Title

Role of DNA methylation in early life and its impact in later life

Nutritional environment in the fetal and neonatal periods might affect the susceptibility to adult-onset metabolic diseases such as obesity and type 2 diabetes, which may be referred to as the "Developmental Origins of Health and Disease (DOHaD)" hypothesis. However, its detailed molecular mechanism has been ill-defined.

The liver is a major organ of lipid metabolism, which is markedly changed in response to physiological nutritional demand. We provided evidence that ligand-activated PPARα-dependent DNA demethylation regulates the fatty acid β-oxidation genes in the postnatal liver (Diabetes 64: 775-784, 2015). Given that PPARα is known to be activated in the liver in response to milk-derived lipid ligands during the suckling period, it is likely that milk lipids serve as a nutrient signal during the neonatal period, so that they can be oxidized efficiently as an energy source.

Fibroblast growth factor 21 (FGF21; *Ffg21*) is a major PPARα target gene that occurs in the liver. We have found that DNA demethylation of *Fgf21* can be modulated and/or enhanced by pharmacologic activation of PPARα during the suckling period. Importantly, DNA methylation status of *Fgf21*, once established in early life, is relatively stable and remains into adulthood as an epigenetic memory. With increased DNA demethylation, hepatic induction of *Fgf21* has been exaggerated upon PPARα activation, which may account in part for the attenuation of diet-induced obesity in adulthood. This study represents the first demonstration that DNA methylation status of a particular gene, once established in early life, contributes to the phenotypes in later life.

Selected Publications

1. T. Ehara et al. Ligand-activated PPARα-dependent DNA demethylation regulates the fatty acid β-oxidation genes in the postnatal liver. Diabetes 64: 775-784, 2015.
2. T. Ehara et al. Role of DNA methylation in the regulation of lipogenic gene expression in the neonatal mouse liver. Diabetes 61: 2442-2450, 2012.

Speaker

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Language : English

Date/Time : Tuesday, Dec. 19, 2017 / 16:00-17:00

Location : Moriwaki Hall, Tsukuba

- Live telecast fromTsukuba Main

<Wako: 408 Seminar Room, Chemical Biology Bldg.>
<Yokohama: C210/C212, Central Research Bldg.>
<Kobe: N701-703 Seminar Room, CDB Bldg. A>

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