

The Actions of Orphan Nuclear Receptor RORgamma on Hepatic Cholesterol Metabolism in Piglets

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Time-restricted feeding (TRF) is a dieting strategy based on nutrients availability and diurnal rhythm, shown to improve lipid metabolism efficiency. Previous study reveals that retinoic acid-related (RAR) orphan receptor (ROR) γ is closely linked to animal lipid metabolism. However, the functional role of ROR γ in liver physiology of pigs in response to TRF has not been determined, largely due to the lack of functional models and molecular tools. We established porcine liver organoids and subjected them to restricted nutrients supply for 10-h during the light portion of the day. Our results showed that TRF regimen did not alter hepatocyte physiology but downregulated the hepatic CHO biosynthesis program along with the reduced cellular CHO content in porcine liver organoids. Using unbiased bioinformatic analysis of a previous ChIP-seq data and ChIP-qPCR validation, we revealed ROR γ as the predominant transcription factor that responded to TRF. This was likely through ROR γ direct binding to the MVK gene (encoding mevalonate kinase) and recruiting the enrichment of co-factor p300, histone marks H3K27ac and H3K4me1/2, as well as RNA Polymerase II (Pol-II) at the locus of MVK. Our findings demonstrate that TRF triggers the ROR γ -mediated chromatin remodeling at the locus of CHO biosynthesis genes in porcine liver organoids and further improves lipid metabolism.



Research Biography

Demin Cai received his PhD degree on animal physiology and biochemistry from Nanjing Agricultural University, College of Veterinary Medicine in 2015. He belonged to Department of Biochemistry and Molecular Medicine of University of California at Davis from 2014-2015 as a Joint-PhD student, from 2016-2019 as a post-doc fellow and from 2019-2020 as a faculty of assistant research scientist. Since 2020, he has served Yangzhou University College of Animal Science and Technology as a professor. His research interest is to study the actions of circadian rhythm, epigenetics, and orphan-nuclear-receptor-controlled molecular metabolism for improving pig growth and health.