Developmental vitamin D deficiency leads to altered adult liver energy metabolism

Aastha Dubal

Suboptimal intrauterine environments, such as altered levels of micronutrients, have been linked to adverse postnatal health outcomes. In humans, developmental vitamin D deficiency (DVD) is associated with increased adiposity. We previously published a mouse model of DVD on the CC001 and CC011 (Collaborative Cross) strain backgrounds that recapitulated DVD-induced adult adiposity into adulthood. In this study, we took a multi-omics approach to investigate whether DVD-induced changes in liver energy metabolism could explain the observed DVD-induced adult adiposity.

CC001 x CC011 F1 offspring were exposed to either a vitamin D sufficient (VDS; 1000 IU/kg) or vitamin D deficient (DVD; 0 IU/kg) diet during gestation and lactation. At weaning, male offspring were placed on standard chow through adulthood (PND56). We used global transcriptomics, metabolomics, and methylomics to define the role of DVD in programming of adult liver cellular energy metabolism.

Offspring exposed to DVD displayed a significant increase in liver weight to body weight ratios (CON; 0.028±0.0007g, VDD; 0.031±0.0007g). Global attenuation of the cholesterol biosynthesis pathway was observed in the livers of DVD-treated offspring, specifically for key catalytic enzymes in the mevalonate pathway such as Mvk and Hmgcr (Fig. 1). Consistent with this finding, DVD-treated mice exhibited altered liver DNA methylation at cholesterol signaling-related genes such as Atg101. Lastly, we detected changes in liver metabolites related to cholesterol biosynthesis such as 7-hydroxycholesterol and 7-Hoca. Taken together, we found that DVD led to altered liver energy metabolism in adult offspring, providing additional evidence in support of the role of suboptimal intrauterine environments in the origins of disease.