Developmental vitamin D deficiency leads to altered adult liver energy metabolism

Aastha Dubal1,2, Megan Knuth2,3, Jing Xue2,4, Yi Li2, Jeremy Simon2,5,6, Cory Brouwer7,8, Raad Gharaibeh7,8,9, and Folami Y. Iderraabdullah1,2,3,4

1Department of Nutrition, Gillings School of Global Public Health, UNC-Chapel Hill, Chapel Hill, NC 27599, USA; 2Department of Genetics, UNC-Chapel Hill School of Medicine, Chapel Hill, NC 27599, USA; 3Lineberger Comprehensive Cancer Center, UNC-Chapel Hill, Chapel Hill, NC 27599, USA; 4Nutrition Research Institute, 500 Laureate Way, UNC-Chapel Hill, Kannapolis, NC 28083, USA; 5Neuroscience Center Bioinformatics Core, UNC-Chapel Hill, Chapel Hill, NC 27599, USA; 6School of Medicine Bioinformatics and Analytics Research Collaborative, UNC-Chapel Hill, Chapel Hill, NC 27599, USA; 7Department of Bioinformatics and Genomics, UNC-Charlotte, Charlotte, NC, USA; 8UNC-Charlotte Bioinformatics Service Division, North Carolina Research Campus, Kannapolis, NC, USA; 9Department of Medicine, Division of Gastroenterology, University of Florida, Gainesville, FL, USA.

Background
- 80% of human offspring are born under conditions of vitamin D deficiency1.
- Developmental vitamin D deficiency (DVD) is associated with:
  - obesity1
  - insulin resistance1
  - altered cholesterol biosynthesis2
- Obesity, insulin resistance, and cholesterol pathogenesis are known instigators of fatty liver disease.
- No study has investigated the role of DVD in programming of liver cellular energy metabolism as a risk factor for adult liver disease.

Hypothesis
DVD perturbs adult liver cholesterol biosynthesis.

Methods

Treatment Timeline
- Gestation (3 weeks)
- Lactation (3 weeks)

Experimental Endpoints (PND56)

Results

Figure 2. Changes in Bodyweight and Body Composition at PND56.

Figure 3. Attenuation of Cholesterol Biosynthesis Pathway at PND56.

Current Work
Repeated our study to see if we could reproduce adult phenotypes to further investigate the mechanisms by which DVD perturbs adult liver cholesterol biosynthesis.

Additional measurements:
- Change in bodyweight over time
- Change in body composition over time
- Liver & adipose histopathology

Extended study to PND84
Targeted gene expression
Liver and adipose weights
Total HDL & LDL

Conclusions
Developmental vitamin D deficiency impairs adult liver energy metabolism via disruption of cholesterol biosynthesis.

References

Funding
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Table 1. Changes in liver metabolites related to cholesterol biosynthesis at PND56.

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Fold change</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Lipid</td>
<td></td>
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<tr>
<td>Cholesterol biosynthesis</td>
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<td>HDL</td>
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<td>LDL</td>
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Table 2. Changes in liver DNA methylation at PND56.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Methylation Change</th>
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<tr>
<td>Adult DVD offspring</td>
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Figure 4. HYPOTHESIZED MODEL OF CHOLESTEROL BIOSYNTHESIS IN LIVER AT PND56.

Figure 5. Extended study to PND84.