Kansas Nutrition Project

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Funding

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Collaborators

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M. Zloutro           University of Kansas, USA
M. Crawford        University of Kansas, USA

Acknowledgements

R. Duggirala       Southwest Foundation in Biomedical Research
                    San Antonio, Texas
Purpose of Study

To profile the dietary habits of Kansas farming communities

To examine the relationship of these dietary habits with prevalence of chronic disease

*To identify genes and dietary habits that affect the prevalence of dyslipidemia in this population
Primary focus of research

High Density Lipoprotein

- HDL is a complex trait, influenced by both genetic and environmental factors.
- Low levels of HDL are associated with increased risk of cardiovascular disease.
- Sexual dimorphism is widely reported across populations for levels of HDL and CVD.
- New multipoint linkage scans in animal and human studies suggest sex-specific QTLs (quantitative trait loci) affecting HDL variation.
Over the past twenty years Kansas Mennonite population reports increase of individuals with HDL levels in the high risk category:

- Males: 55% < 40 mg/dl (1.03 mmol/L)
- Females: 28% < 45 mg/dl (1.16 mmol/L)

Heritability of HDL in Kansas Mennonite population:
- Additive genetic effect for HDL = 70
- Environmental factors = 30

(MLE Heritability (h²) from variance component analysis)

\[ V_p = V_g + V_e \]

Duggirala, 2002
Khoury’s Model for Genetic Epidemiology

Population Dynamics

Mutation → Genotype → Phenotype

Environment
Study Design

Religious Semi-Isolate
(reduced heterogeneity)

RFLP → Genotype → Plasma Lipids

Environment
(Nutrition and Anthropometrics)

Measured Genotype

\[ Y = MG + PG + E \]
Study Question

Is sexual dimorphism a factor in genetic or macronutrient effects on plasma HDL variation in Kansas Mennonite?
Data Collection

- Genealogies: to examine the genetic components
- Anthropometrics: skinfolds, height, weight
- Serum lipids, fasting insulin, leptin, adiponectin
- Genotyping: APOE, B, A-1, C-3 and LPL (RFLPs)
- Medical histories
- Nutritional profiles:
  - 3 - 24hour intake diaries
  - food frequency -- 11 categories, 90 foods
  - Activity pattern: 3-24 hour non consecutive records
Kansas Study Population
General Conference Mennonites

Located in Goessel and Meridian in central Kansas
Well defined religious semi-isolate group
  1) unique immigrant history
  2) extensive written genealogy
  3) complex, extended families providing numerous family relationships to study heritability and linkage
  4) genetic, environmentally, and culturally homogenous population thought to decrease background “noise” when studying genetic effects
Cultural Factors

1) Active rural and agricultural lifestyle
2) Close social support system
3) No smoking
4) No drinking
5) Above Average life expectancy
   82 for males
   85 for females
6) Cardiovascular diseases leading cause of mortality
Population History

- Descendents of 191 families from 16C/17C Anabaptist movement who migrated to US in 1874
- Originate from Dutch, Northern German & Swiss
- Population fission along familial lines after arrival in US
- Gene flow from surrounding Mennonite subdivisions
- Currently a series of populations resembling Western Europe with substantial levels of heterozygosity
Migration path

- Dutch and N. German Mennonites to Danzig area around 1565
- S. German and Swiss Mennonites to America, beginning 1683-1714
- To S. Russia 1768-1835
- To America 1874
- Molotschna Colony
- Chortitsa Colony
Mennonite Land
## Descriptive Statistics

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<tr>
<th></th>
<th>Males</th>
<th>Females</th>
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<tr>
<td>Age -years</td>
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<td>58</td>
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<tr>
<td>Ht –inches</td>
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<td>65</td>
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<tr>
<td>Wt-pounds</td>
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<tr>
<td>BMI</td>
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<td>25</td>
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<tr>
<td>TC mg/dl</td>
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<td>193</td>
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<td>HDLmg/dl</td>
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<td>LDLmg/dl</td>
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<td>113</td>
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<tr>
<td>TG mg/dl</td>
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<td>120</td>
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<table>
<thead>
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<tbody>
<tr>
<td>Males</td>
<td>74</td>
<td>17</td>
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<tr>
<td>Females</td>
<td>80</td>
<td>16</td>
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Mennonite Lipid Profiles

$P=0.01$

$P=0.001$
## Nutritional Profiles in 2003

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<th>Males</th>
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<td>35</td>
<td>5.7</td>
<td>% Fat</td>
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<tr>
<td>14</td>
<td>8</td>
<td>% Prot</td>
</tr>
<tr>
<td>321</td>
<td>125</td>
<td>mg chol</td>
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<tr>
<td>13/1</td>
<td>8</td>
<td>Omega 6/3</td>
</tr>
</tbody>
</table>

**Current Recommendations**

- 55% Carb – 30% Fats – 15% Prot
- <300mg chol
- 6-3 Ratio 4/1
Nutritional focus for research
Glycemic Index

- Ranks carbohydrates according to their immediate impact on blood glucose measures
- Ranks foods against reference value of oral glucose effect on blood glucose
- High glycemic index >70
- High glycemic foods in FFQ
  - breads, rolls, white rice, white potatoes
Variation of response in blood sugar levels

Rapid absorption, higher postprandial glucose and insulin responses
HDL and High Glycemic Intake

**HDL, adjusted for central fat indices and standardized**
**APOE and Triglyceride/HDL Ratio**

- **Males**
  - $P=0.041$

- **Females**
  - $P=0.152$

- **Between sexes**
  - $P=0.001$

- **Groups**
  - APOE2/3
  - APOE3/3
  - APOE3/4
Summary

- Lower intake of high glycemic food associated with higher HDL in males
- Triglyceride/HDL ratios associated with APOE genotypes, with differences within males and between males and females
- Sex specific genetic and environmental effects in HDL related traits were identified
Is the sex specific variation in plasma lipids and response to diet due to genetic factors?

- Studies have shown APOE to have sex-specific effects associated with lipid profiles.
- Association studies of APOE in two Siberian populations are inconsistent with these findings, suggesting environmental effects.
- Carbohydrate intake and APOE significant in effects on low density lipoprotein in females of Siberian Buryat only.
Limitations

- Over 100 genes influence lipid metabolism
  Few studied in terms of sex-effect
- Artifact or bias due to small sample sizes
  Small sample sizes may be hypothesis driving
- Validity of self reporting nutritional intake
Suggestions for future research

- Suggest multipoint linkage analysis of lipid phenotypes, contingent on measured genotypes, to include nutrient intake and age categories to further identify factors affecting HDL variation