

The Effects of Genes and Environment on Our Health

Our 46 and Our Environment

John Edgar (Jef) French, Ph.D. February 12, 2018



FOCUS OF THE NUTRITION RESEARCH INSTITUTE

Why do metabolism and nutrition *differ* between people?

Identify *how* our genes and environment change our responses to nutrition.

Precision Nutrition: the next frontier





Currently, 17 faculty scientists and their research teams are exploring how nutrition impacts some of today's most pressing health issues

Birth defects

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- Brain development
- **Obesity & Cancer** (HURSTING)
- Eye disease
- Fetal Alcohol Spectrum . **Disorders (SMITH)**

- Gout
- Heart disease (MEYER)
- Liver disease •
- Memory loss ٠
- Muscle function
 - Obesity







- Genome
- Epigenome
- Exposome
- Microbiome







Helix (Illumina spinoff)

- Maternal mitochondria markers
- Paternal Y-chromosome markers
- Whole genome exon sequencing
- Your DNA is proprietary
- Your DNA sequence can be shared with other specialists







Your Results

Helix Geno 2.0: John Edgar French











ADH1B; rs1229984; A/G, Protective for esophageal cancer.

Hunter Version

CYP1A2; rs762551; A/A, High metabolism; less stimulating variant.







Weight Gain from Saturated Fat



Weight Gain from Carbohydrates





Weight Gain from Dietary Fat











Using the mouse to model human disease: increasing validity and reproducibility

Monica J. Justice^{1,*} and Paraminder Dhillon² Disease Models & Mechanisms 9:101-103, 2016



From mouse to humans: a community effort

The Genes, Environment, and Health Initiative (GEI) 2006

Genetic Susceptibility - Linking Exposure to Disease



Human populations



1000 Genomes Project 88 million variants (SNP & SV)

Auton et al. Nature 526, 68-74 (2015) doi:10.1038/nature15393



Classical strain Diversity





Using the mouse to model human disease: increasing validity and reproducibility

Monica J. Justice^{1,*} and Paraminder Dhillon²



From mouse to humans: a community effort

Mouse Models for Drug Discovery. Can New Tools and Technology Improve Translational Power?

Aamir Zuberi and Cathleen Lutz ILAR Journal, 2016, Vol. 57, No. 2, 178–185



Collaborative Cross (CC) & Diversity Outbred (J:DO) Models





High-Resolution Genetic Mapping in the Diversity Outbred Mouse Population Identifies Apobec1 as a Candidate Gene for Atherosclerosis

Tangi L. Smallwood,* Daniel M. Gatti,[†] Pamela Quizon,[‡] George M. Weinstock,[§] Kuo-Chen Jung,* Liyang Zhao,** Kunjie Hua,* Daniel Pomp,*** and Brian J. Bennett^{*,‡,**,1}

Smallwood et al. G3 4:2353, 2014

| | Baseline (AIN-76A) | | High Protein | | High-Fat, Cholic Acid | |
|----------------------|--------------------|--------------|--------------|---------------|-----------------------|------------------|
| | n | Mean | n | Mean | n | Mean |
| Cholesterol, mg/dL | 277 | 91.7 ± 25.1 | 128 | 97.6 ± 31.5** | 136 | 199.9 ± 68.6*,** |
| Triglycerides, mg/dL | 262 | 59.5 ± 26.5 | 128 | 57.7 ± 30.8** | 136 | 32.3 ± 12.1*,** |
| Glucose, mg/dL | 257 | 155.2 ± 43.8 | 130 | 190.5 ± 49.9 | 137 | 177.9 ± 45.1 |
| Insulin, ng/mL | 235 | 0.8 ± 0.4 | 129 | 1.7 ± 1.1* | 133 | 1.4 ± 0.7* |

Table 1 Effects of high-protein, high-fat, cholic acid diets on cardiovascular risk factors in the DO mice



Obesity & Mammary Gland Cancer and Resistance to Chemotherapy



Steven Hursting, PhD, MPH



Melissa VerHague, PhD









The Obesity-Cancer Link: Lessons Learned from a Fatless Mouse

Stephen D. Hursting,^{1,2} Nomeli P. Nunez,¹ Lyuba Varticovski,³ and Charles Vinson⁴

www.aacrjournals.org

Michael Coleman, PhD

Alcohol Toxicity and Fetal Alcohol Syndrome Disorder



Susan M. Smith, PhD





George Flentke, PhD



Eneda Pjetri, MD, PhD

frontiers in Genetics



Obesity and Cardiovascular Disease



Microbiota-Dependent Metabolite Trimethylamine N-Oxide and Coronary Artery Calcium in the Coronary Artery Risk Development in Young Adults Study (CARDIA)

Katie A. Meyer, ScD, MPH; Thomas Z. Benton, BA; Brian J. Bennett, PhD; David R. Jacobs, Jr, PhD; Donald M. Lloyd-Jones, MD, SM; Myron D. Gross, PhD; J. Jeffrey Carr, MD, MSc; Penny Gordon-Larsen, PhD; Steven H. Zeisel, MD, PhD

Katie Meyer, ScD



John Shea



Salvadore Fabela, PhD



(J Am Heart Assoc. 2016;5:e003970 doi: 10.1161/JAHA.116.003970)



MDS1



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