

American Society for Nutrition Webinar Series

**National Nutrition Research Roadmap
2016–2021: Advancing Nutrition Research to
Improve and Sustain Health**

Webinar 1:

**The National Nutrition Research Roadmap:
Basic Science and Epidemiology of Nutrition**



A Few Reminders

CPE Credit

- ASN designates this educational activity for a maximum of 1 CPEUs. Dietitians and Dietetic Technicians, Registered should only claim credit commensurate with the extent of their participation in the activity.
- To claim credit, please take the post webinar evaluation to be emailed after the webinar.

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Please mute your phone and/or computer microphone.**

Questions & Answers

- Please use the “questions” box on your “Go To Meetings” screen to submit questions to our presenters.
- Please submit your questions at any time during today’s webinar.

Faculty

Speakers



- **Paul M. Coates, PhD**
Director, Office of Dietary Supplements
National Institutes of Health
Co-Executive Secretary to the Interagency
Committee on Human Nutrition Research



- **Patrick J. Stover, PhD**
Professor & Director
Division of Nutritional Sciences, Cornell
University



Moderator

- **Marian L. Neuhouser, PhD, RD**
Cancer Prevention Program, Fred Hutchinson
Cancer Research Center
President, American Society for Nutrition

Learning Objective

At the end of this program, attendees will be able to:

- Describe research gaps and opportunities, including the open funding opportunity announcements, training activities, and research resources related to the basic science and epidemiology of nutrition, as found in the National Nutrition Research Roadmap



National Institutes of Health
Office of Dietary Supplements



NIH Research Activities Addressing the National Nutrition Research Roadmap, 2016-2021

Paul M. Coates, Ph.D.

American Society for Nutrition Webinar Nov 2016



Disclosures for Paul Coates

AFFILIATION/FINANCIAL INTERESTS (within past 12 months)	CORPORATE ORGANIZATION
Grants/Research Support	None
Scientific Advisory Board/Consultant	Tufts Nutrition Council
Speakers Bureau	None
Stock Shareholder	None
Other	None



Agenda

- How does the NIH address nutrition research topics?
- Examples
- A plan
- Website for NNRR

<https://fnic.nal.usda.gov/surveys-reports-and-research/interagency-committee-human-nutrition-research>

National Nutrition Research Roadmap 2016–2021

**National Nutrition Research Roadmap
2016–2021:
Advancing Nutrition Research
to Improve and Sustain Health**

Interagency Committee on Human Nutrition Research

2016



https://www.google.ch/?gfe_rd=cr&ei=Og8SWOLrLcHCaNn8gOAN#q=national+nutrition+roadmal



Organizing Questions

- **Question 1: How can we better understand and define eating patterns to improve and sustain health?**
- **Question 2: What can be done to help people choose healthy eating patterns?**
- **Question 3: How can we engage innovative methods and systems to accelerate discoveries in human nutrition?**

	HHS Agency 			
	CDC	FDA	HRSA	NIH
1. How do we better understand and define eating patterns to improve and sustain health?				
Health Promotion and Disease Prevention and Treatment	X	X	X	X
Individual Differences including “Omics”		X	X	X
Population-level Monitoring	X	X	X	X
2. What can be done to help people choose healthy eating patterns?				
Influences on Eating Patterns	X	X	X	X
Interventions	X	X	X	X
Systems Science	X	X	X	X
Environmental Sustainability				
3. How can we develop and engage innovative methods and systems to accelerate discoveries in human nutrition?				
Assessing Dietary Exposures	X	X		X
Biobehavioral Science		X		X
Behavioral Economics	X	X	X	X
Big Data	X	X		X



NIH Human Nutrition Research

- **Many of the 27 NIH ICs and Offices support nutrition-relevant research; ~4-5% of the total NIH budget**
- **Initiatives, Funding Opportunity Announcements, supplements to existing grants**
- **Common Fund programs on microbiome and on metabolomics**
- **Intramural research programs, including the Clinical Center**
- **Training and career development**
- **Public health information emerging from NIH-supported research**



Let's use an example...

Question 1. How do we better understand and define eating patterns to improve and sustain health?

- **Topical Area 1. Health Promotion and Disease Prevention and Treatment**



Enhance optimal development and reduce the risk of chronic disease

- **What's the evidence? What's the gap?**
 - **Systematic reviews**
 - **Workshops**
- **Study designs**
- **Variability in individual responses**
- **Role of the microbiome**
- **Translational efforts**
- **Collaborative research**
- **Frame research around public health needs, e.g., Dietary Reference Intakes, NNRR areas of interest**
- **Big data**



There are plenty of others...

- **Establish the causal relationship between nutrition and disease pathophysiology**
 - e.g., FOAs related to the microbiome
- **Understand how nutritional status affects response to different types of physical activity across the lifespan**
 - e.g., nutrigenetics/nutrigenomics approaches; molecular transducers of physical activity
- **Examine the role of nutrition, physical activity and other health habits during pregnancy/gestation and early childhood to enhance health**
 - e.g., maternal nutrition and pre-pregnancy obesity: effects on mothers, infants, and children



But wait, there's more...

- **Workforce development (examples)**
 - Cancer Prevention Fellowship Program
 - Loan Repayment Programs
 - John A. Milner Fellowship Program
 - Mary Frances Picciano Dietary Supplement Research Practicum
 - T, F, K Awards at various stages of career development
 - Short-term experiences at NIH
- **Public-private partnerships (examples)**
 - Biomarkers of Nutrition for Development (BOND)
 - National Collaborative on Childhood Obesity Research (NCCOR)
 - Vitamin D Standardization Program (VDSP)
- **Big Data (examples)**
 - NIH Big Data to Knowledge (BD2K)
 - NIH Health Care Systems Research Collaboratory Program
 - Environmental Influences on Child Health Outcomes (ECHO)
 - Precision Medicine Initiative (PMI)



← → **Contact Program Director**

- **Contact the Program Office at early stages!**
- **Before submission**
 - **How? Pick up the phone and call!**
 - **E-mail a short precis (draft title, abstract, specific aims).**
 - **Follow up phone call or email.**
 - **Funding mechanisms (research, training, early- stage eligibility)**
 - **Review venues (study sections)**
 - **Responsiveness to IC general interests and solicitations**
 - **Relevance to the NNRR**
- **After submission**
 - **Tea and sympathy as a prelude to.....**
 - **Post-review guidance and strategies for resubmission**
 - **Appeals, restorations, other adjustments (sometimes)**

The ICHNR National Nutrition Research Roadmap

Q1T1 – Health Promotion and Disease Prevention and Treatment

Selected NIH Funding Opportunities (1 of 3 slides)

- **Advancing Mechanistic Probiotic/Prebiotic and Human Microbiome (R01) – PA-15-135**
- **Ancillary Studies to Major Ongoing Clinical Research Studies to Advance Areas of Scientific Interest within the Mission of the NIDDK (R01) – PAR-16-034**
- **Behavioral Interventions to Address Multiple Chronic Health Conditions in Primary Care (R01) – PA-14-114**
- **Capturing Complexity in the Molecular and Cellular Mechanisms Involved in the Etiology of Alzheimer's Disease (R01) – PAR-15-358**
- **Diet and Physical Activity Assessment Methodology (R01) – PAR-15-170 and (R21) – PAR-15-171**



National Institutes of Health
Turning Discovery Into Health



The ICHNR National Nutrition Research Roadmap

Q1T1 – Health Promotion and Disease Prevention and Treatment Selected NIH Funding Opportunities (2 of 3 slides)

- **Food Specific Molecular Profiles and Biomarkers of Food and Nutrient Intake, and Dietary Exposure (R01) – PAR-15-024**
- **Maternal Nutrition and Pre-pregnancy Obesity: Effects on Mothers, Infants and Children (R01) – PA-15-100**
- **Obesity and Asthma: Awareness and Self-Management (R01) – PA-14-316**
- **Pilot and Feasibility Clinical and Translational Research Studies in Digestive Diseases and Nutrition (R21) – PA-15-317**
- **Pilot and Feasibility Clinical Trials in Diabetes, and Endocrine and Metabolic Diseases (R21) – PA-15-176**



National Institutes of Health
Turning Discovery Into Health



The ICHNR National Nutrition Research Roadmap

Q1T1 – Health Promotion and Disease Prevention and Treatment

Selected NIH Funding Opportunities (3 of 3 slides)

- **Revision Applications for Validation of Mobile/Wireless Health Tools for Measurement and Intervention (R01) – PA-16-043**
- **Secondary Analysis in Obesity, Diabetes and Digestive and Kidney Diseases (R21) – PA-15-169**
- **The National Institutes of Health Big Data to Knowledge (BD2K)**
- **The BRAIN Initiative**
- **Understanding Factors in Infancy and Early Childhood (Birth to 24 months) That Influence Obesity Development (R01) – PA-16-169**



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The ICHNR National Nutrition Research Roadmap

Q1T2 – Individual Differences Including Omics

Selected NIH Funding Opportunities

- **Advancing Mechanistic Probiotic/Prebiotic and Human Microbiome Research (R01) – PA-15-135**
- **Early-Stage Preclinical Validation of Therapeutic Leads for Diseases of Interest to the NIDDK (R01) – PAR-16-121**
- **Food Specific Molecular Profiles and Biomarkers of Food and Nutrient Intake, and Dietary Exposure (R01) – PAR-15-024**
- **High Impact, Interdisciplinary Science in NIDDK Research Areas (RC2) – PAR-16-126**
- **Pilot and Feasibility Clinical and Translational Research Studies in Digestive Diseases and Nutrition (R21) – PA-15-317**
- **Secondary Analyses in Obesity, Diabetes and Digestive and Kidney Diseases (R21) – PA-15-169**
- **Precision Medicine Initiative (PMI)**
- **Selected Common Fund Programs**
 - **Big Data to Knowledge (BD2K)**
 - **Epigenomics**
 - **Human Microbiome Project (HMP)**
 - **Metabolomics**



National Institutes of Health
Turning Discovery Into Health



The ICHNR National Nutrition Research Roadmap

Q1T3 – Population-Level Monitoring

Selected NIH Funding Opportunities

- **Diet and Physical Activity Assessment Methodology (R01) – PAR-15-170 and (R21) – PAR-15-171**
- **Obesity Policy Research Evaluation (R01) – PA-16-165**
- **Revision Applications for Validation of Mobile/Wireless Health Tools for Measurement and Intervention (R01) – PA-16-043**
- **The National Institutes of Health Big Data to Knowledge (BD2K)**
- **Time-Sensitive Obesity Policy and Program Evaluation (R01) – PAR-15-346**
- **Understanding Factors in Infancy and Early Childhood (Birth to 24 months) That Influence Obesity Development (R01) – PA-16-169**



National Institutes of Health
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The National Nutrition Research Roadmap: Basic Science and Epidemiology of Nutrition

**“Scientific Premise of Individual
Variances in Nutritional Status and
Response to Diet”**

**Patrick J. Stover, PhD
Professor & Director, Division of Nutritional
Sciences, Cornell University**

Disclosures for Patrick Stover

AFFILIATION/FINANCIAL INTERESTS (prior 12 months)	ORGANIZATION
Grants/Research Support:	NIH: T32-DK007158 R37DK58144 HD059120
Scientific Advisory Board/Consultant:	Raze Therapeutics; Chobani; NHSc-Pamlab; Biofortis, Marabou Foundation, ASN Board
Speakers Bureau:	None
Stock Shareholder:	TIAA
Other	None

Gerald Fink

Former Director

Whitehead Institute at the Massachusetts Institute of Technology



"I expect that in the year 2005 (when the entire human genome is scheduled to be mapped and sequenced), on the back of our foods, there are going to be a lot of things like that, because we are going to know a lot more about ourselves. And I think **the field of nutrition,** which, in my own opinion now, has not benefited from the advances in molecular genetics, **will be a completely different field. That will be the most revolutionized field in the year 2005.** And the reason is that we will know lots more, we will actually know something about nutrition so you won't pick up one day and say fat is good for you and the next day fat is bad for you. Because we will know that some people it is good for and some people it is bad for.

"We will be able to know what people can metabolize and what some people can't metabolize.We're going to have a new definition of what it means to be healthy."

The Human Genome Project: Part Two: Ushering in a new era of molecular medicine. Date of Publication: 1998



American Society for Nutrition Nutrition Research Priorities



Variability in Responses to Diet & Food

Achieving personalized nutrition with dietary recommendations tailored to each person's needs.



Medical Management

Slowing disease progression through nutrition with improved responses to therapy and survival rates.



Healthy Growth, Development and Reproduction

Understanding how nutrition during critical, early periods of development (including pregnancy) impacts future health.



Nutrition-Related Behaviors

Understanding how the human brain influences food choice and nutrition-related behaviors.



Health Maintenance

Improving health with noncommunicable disease prevention and weight maintenance.



Food Supply & Environment

Realizing the potential of the food environment to improve diet and lifestyle choices.

Responders vs. Non-responders



Ohlhorst et. al. (2013) *Am J Clin Nutr* doi: 10.3945/ajcn.113.067744.

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Interagency Committee on Human Nutrition Research

2016



https://www.google.ch/?gfe_rd=cr&ei=Og8SWOLrLcHCaNn8gOAN#q=national+nutrition+roadmal

National Nutrition Research Roadmap 2016–2021

Question 1: How can we better understand and define eating patterns to improve and sustain health?

Question 1 Topic 1 (Q1T1): How do we enhance our understanding of the role of nutrition in health promotion and disease prevention and treatment?

Question 1 Topic 2 (Q1T2): How do we enhance our understanding of individual differences in nutritional status and variability in response to diet?

Question 1 Topic 3 (Q1T3): How do we enhance population-level food- and nutrition-related health monitoring systems and their integration with other data systems to increase our ability to evaluate change in nutritional and health status, as well as in the food supply, composition, and consumption?

Question 2: What can be done to help people choose healthy eating patterns?

Question 2 Topic 1 (Q2T1): How can we more effectively characterize the interactions among the demographic, behavioral, lifestyle, social, cultural, economic, occupational, and environmental factors that influence eating choices?

Question 2 Topic 2 (Q2T2): How do we develop, enhance and evaluate interventions at multiple levels to improve and sustain healthy eating patterns?

Question 2 Topic 3 (Q2T3): How can simulation modeling that applies systems science in nutrition research be used to advance exploration of the impact of multiple interventions?

Question 2 Topic 4 (Q2T4): How can interdisciplinary research identify effective approaches to enhance the environmental sustainability of healthy eating patterns?

Question 3: How can we develop and engage innovative methods and systems to accelerate discoveries in human nutrition?

Question 3 Topic 1 (Q3T1): How can we enhance innovations in measuring dietary exposure, including use of biomarkers?

Question 3 Topic 2 (Q3T2): How can basic biobehavioral science be applied to better understand eating behaviors?

Question 3 Topic 3 (Q3T3): How can we use behavioral economics theories and other social science innovations to improve eating patterns?

Question 3 Topic 4 (Q3T4): How can we advance nutritional sciences through the use of research innovations involving Big Data?



National Nutrition Research Roadmap 2016–2021

Q1T2 Glossary

Epigenetics	Study of physiological traits caused by modifications of gene expression (but not DNA sequence)
Epigenomics	Study of the complete set of epigenetic modifications on the genome
Exposome	Measures of environmental exposures of an individual
Metabolomics	Study of small molecules and their interaction
Microbome	Ecological community of microorganisms that reside within the body
Nutrigenetics	Study of the effect of genetic variation on responses to diet
Nutrigenomics	Study of the effect of diet and nutrition on gene expression
Proteomics	Study of the structure, function, and interaction of proteins
Transcriptomics	Study of the complete set of RNA transcripts produced by the genome



Research and Resource Initiatives

Short-term Initiatives:

- Support collaborative, interdisciplinary research for understanding the effects of dietary and physical activity patterns and individual variability on biologic measures related to the epigenome, microbiome, metabolome, and proteome.
- Collate existing data in an effort to establish the relationship between eating patterns, individual variation, healthy development, and disease.
- Develop tissue-on-a-chip models including linked system models that incorporate human-like food metabolism to elucidate the effects of dietary components at a molecular and tissue level.



Research and Resource Initiatives

Short-term Initiatives (Continued):

- Support research in humans to understand the effects of diet-induced changes in the microbiome, and other omics (e.g., epigenome, metabolome) on subsequent changes in biologic processes and health.
- Support research to understand the potential health effects of consuming nutrients (i.e., pre- or probiotics) that alter the gut or oral microbiome.
- Characterize the absorbable nutrient contributions of the gut microbiome under various conditions and with diverse populations.

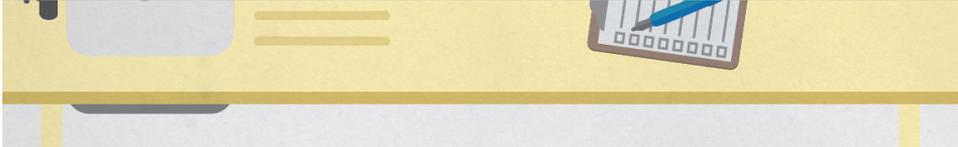


Research and Resource Initiatives

Long-term Initiatives

- Characterize individual differences in “omics” using randomized controlled trials and other research designs as appropriate.
- Utilize adaptive and other controlled trial designs to test the potential for individualized nutrition and lifestyle interventions (i.e., physical activity) based on “omic” signatures to affect specific health outcomes.
- Support research to identify genetic characteristics related to differences in nutritional requirements and metabolism.

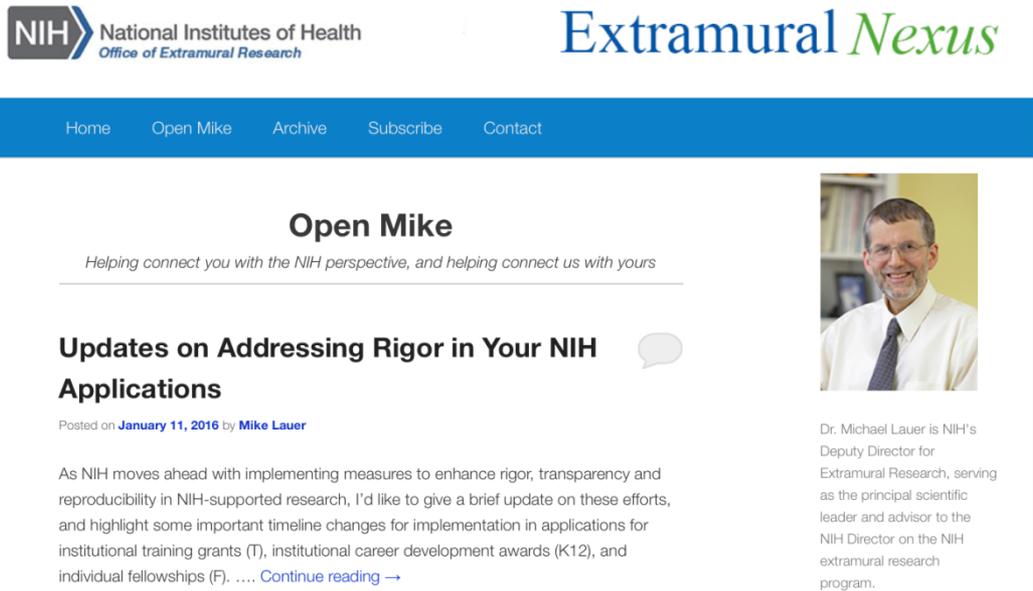




NIH plans to enhance reproducibility

Francis S. Collins and **Lawrence A. Tabak** discuss initiatives that the US National Institutes of Health is exploring to restore the self-correcting nature of preclinical research.

Nature 2014;505:612-13



NIH National Institutes of Health
Office of Extramural Research

Extramural *Nexus*

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Helping connect you with the NIH perspective, and helping connect us with yours

Updates on Addressing Rigor in Your NIH Applications

Posted on **January 11, 2016** by **Mike Lauer**

As NIH moves ahead with implementing measures to enhance rigor, transparency and reproducibility in NIH-supported research, I'd like to give a brief update on these efforts, and highlight some important timeline changes for implementation in applications for institutional training grants (T), institutional career development awards (K12), and individual fellowships (F). [Continue reading](#) →

Dr. Michael Lauer is NIH's Deputy Director for Extramural Research, serving as the principal scientific leader and advisor to the NIH Director on the NIH extramural research program.

<http://nexus.od.nih.gov/all/category/open-mike/>

Scientific Premise is an Important Aspect of Rigor and Reproducibility

What does "scientific premise" mean for a grant application?

- ❖ The scientific premise will be reviewed as part of the *Significance* criterion for research grant applications.
- ❖ Concerns the *quality and strength* of the research base used to form the basis for a proposed research question.
- ❖ Consideration of general strengths and weaknesses to include attention to the *rigor* of the previous experimental designs, as well as **relevant biological variables** and authentication of key resources.



FASEB: Enhancing Research Reproducibility



“Today, as we learn more about the complexity of living organisms, ***both successful and failed attempts to replicate a given study can provide valuable insights into biological processes.***”

FASEB: Enhancing Research Reproducibility

*“It is important to recognize that variations in experimental results may signal unexpected phenomena leading to new scientific understanding. **Lack of reproducibility, generalizability, and translatability are distinct from and do not imply error or scientific misconduct.**”*

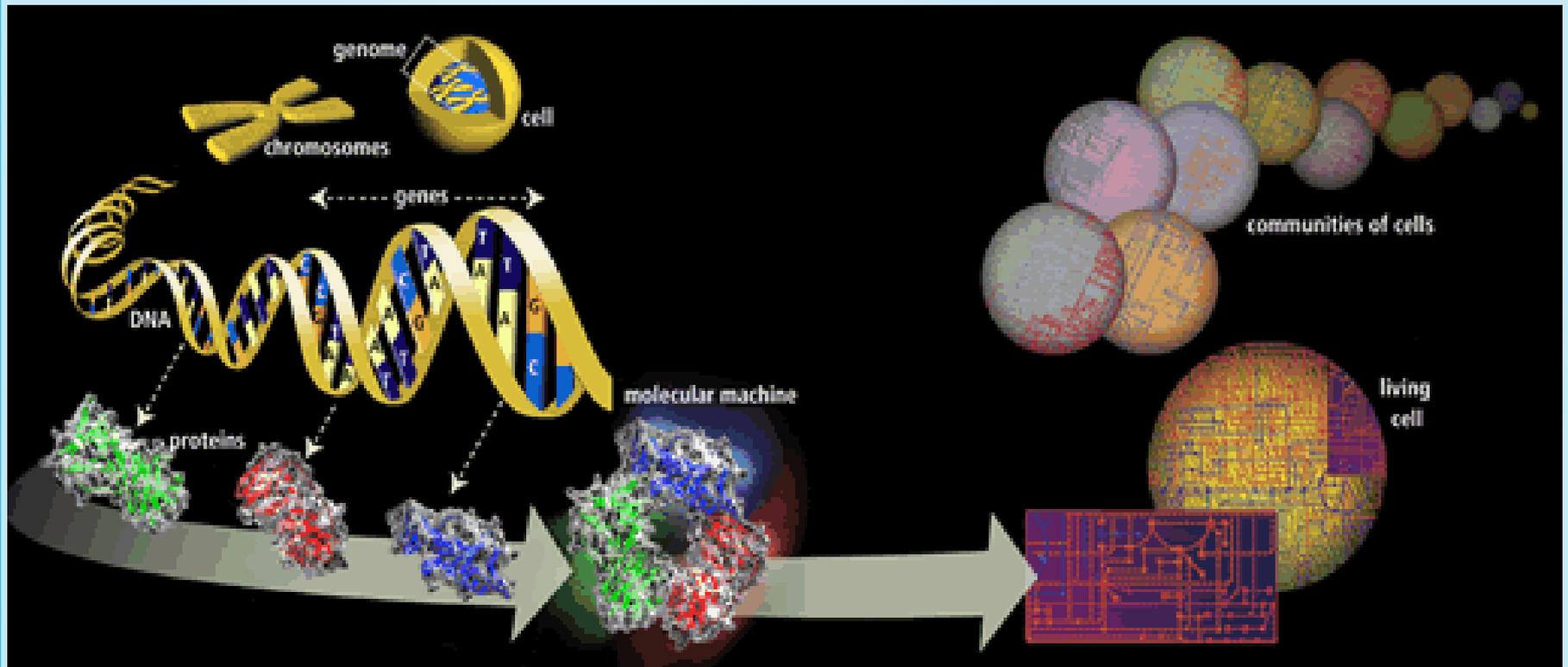
Researchers should articulate the rationale for the choice of an animal model as well as its value and limitations in recapitulating human disease and its treatment.



Two Examples

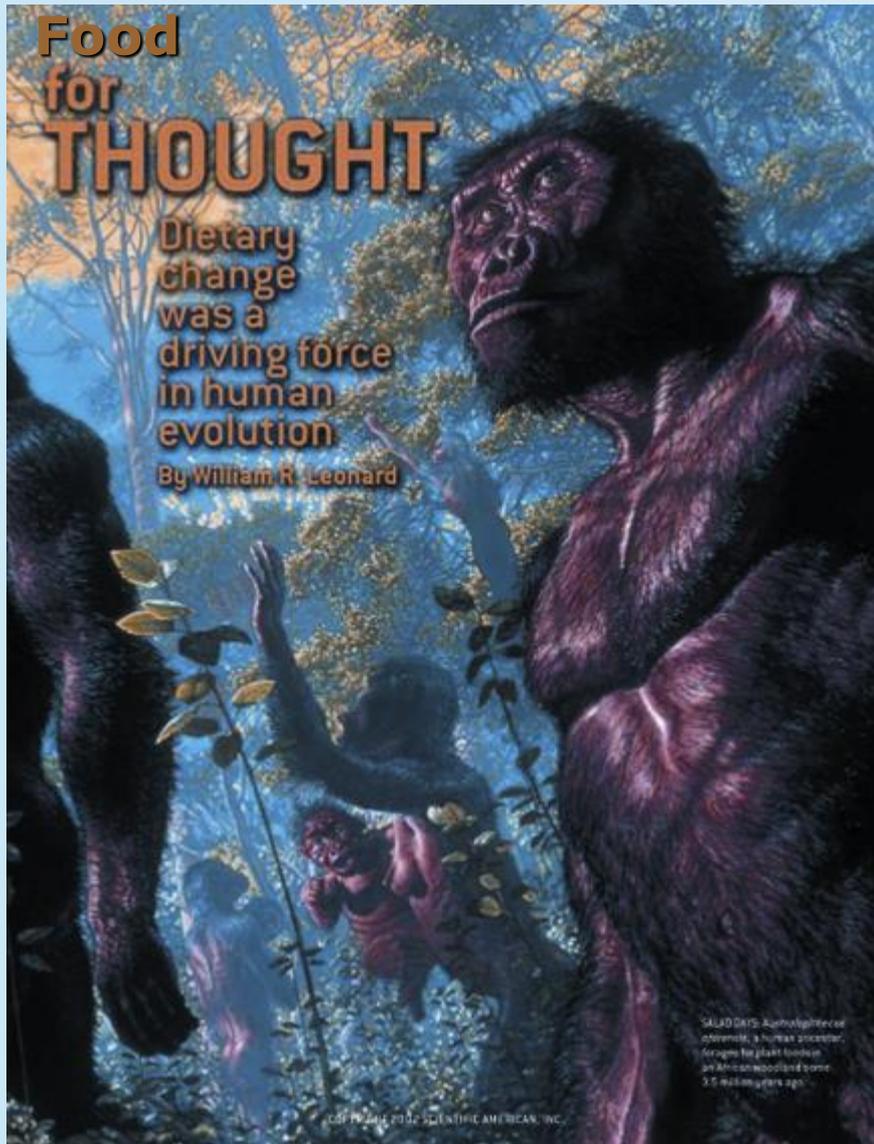
Origins of Individual Variation in Response to Diet

Human Genome Project (1990-2003)

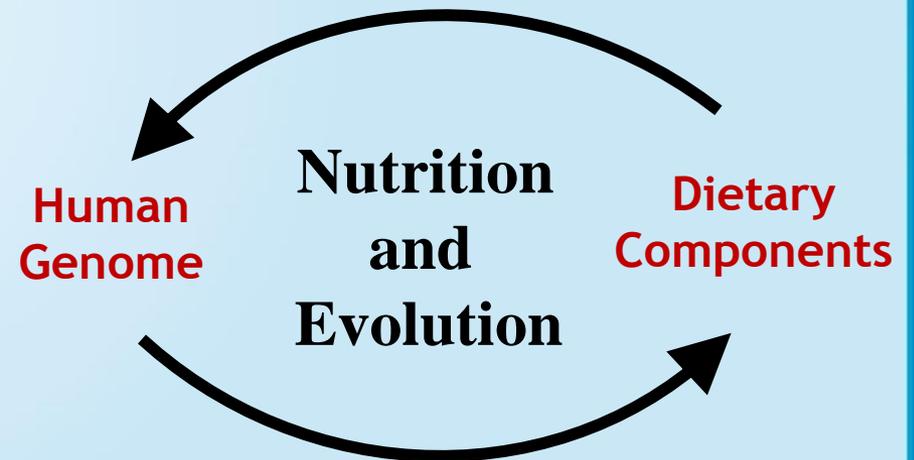


http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml

- Assemble & understand cellular networks
- Manipulate cellular networks for benefit
 - Pharmaceuticals & Nutrients

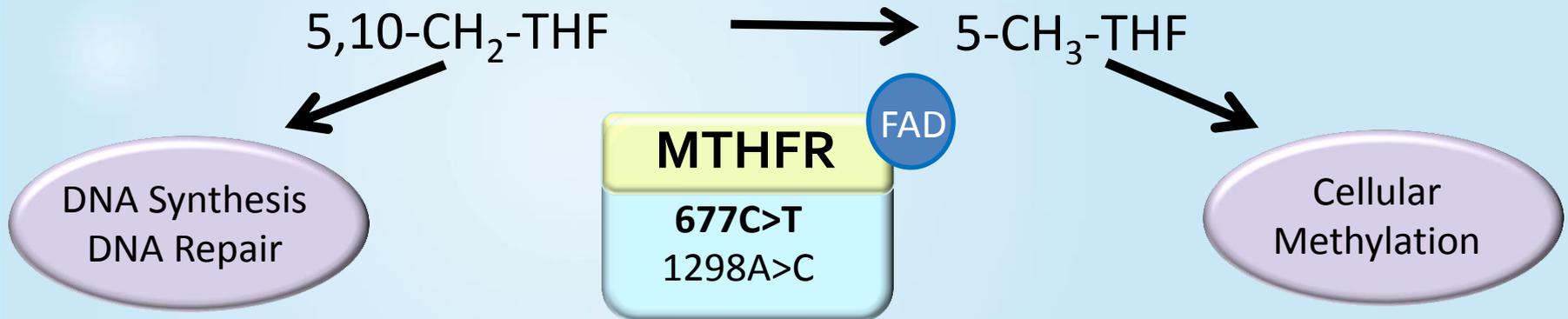


Genome Primary Sequence
- *in utero* viability
- mutation rate
- selection
Genome Programming
Gene Expression



Food Intolerances
Dietary Requirements
Susceptibility to Metabolic Disease

MTHFR 677C>T SNP modifies folate metabolism



- Diminished folate status
- Moderate hyperhomocysteinemia
- Altered risk of folate related diseases
- ~ 12% of US population with 677TT genotype



Allelic Frequency of the MTHFR 677 C->T Polymorphism



(TT) Frequency

Mexicans	30%
Tuscanian (Italy)	30%
Africans	0%
African Amer	2%
Yemenite Jews	2%
Muslim Arab Israelis	16%
Asians	19%
Caucasians	9%

Connections Between Birth Defects and Cancer

Benefit and Risks of MTHFR Polymorphism

COMMON Allele	
Gene sequence	..GCG GGA G C C GAT ...
Protein Sequence	.. Ala Gly Ala ASP...
677 C -> T Allele	
Gene Sequence	..GCG GGA G T C GAT...
Protein Sequence	...Ala Gly Val Asp ...

In utero Risk

“T” allele

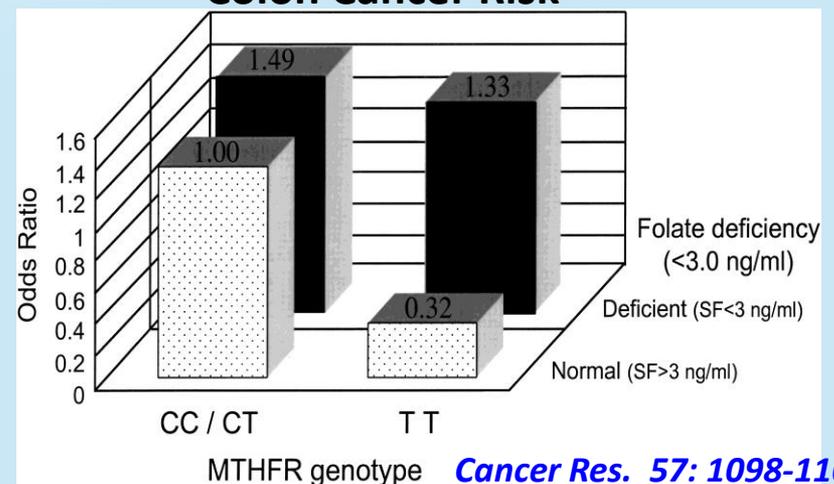
- Low folate status
- Higher folate requirement
- Birth defects
- Miscarriage



Adult Benefit

“T” allele

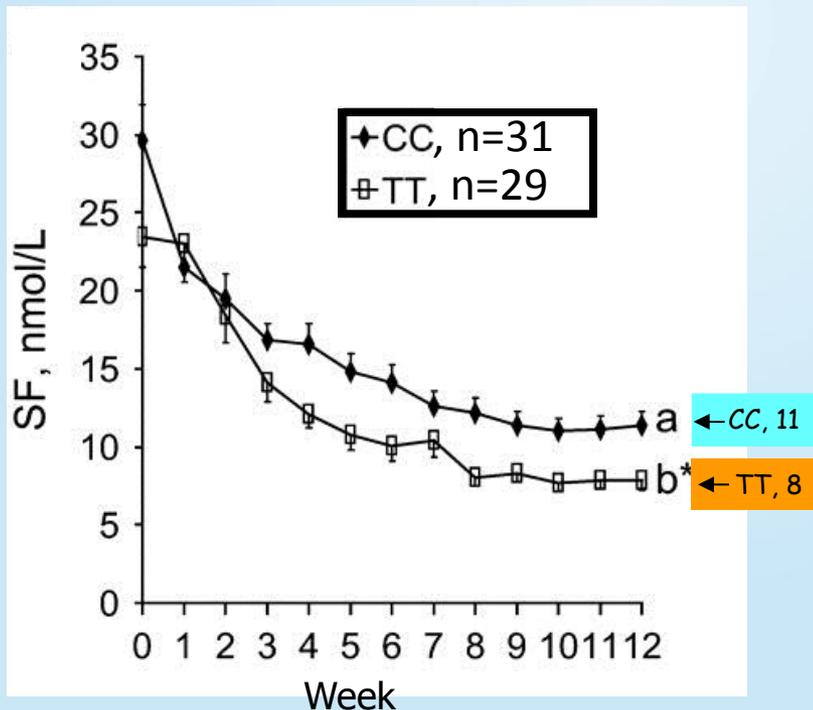
- Physician's Health Study –
Colon Cancer Risk



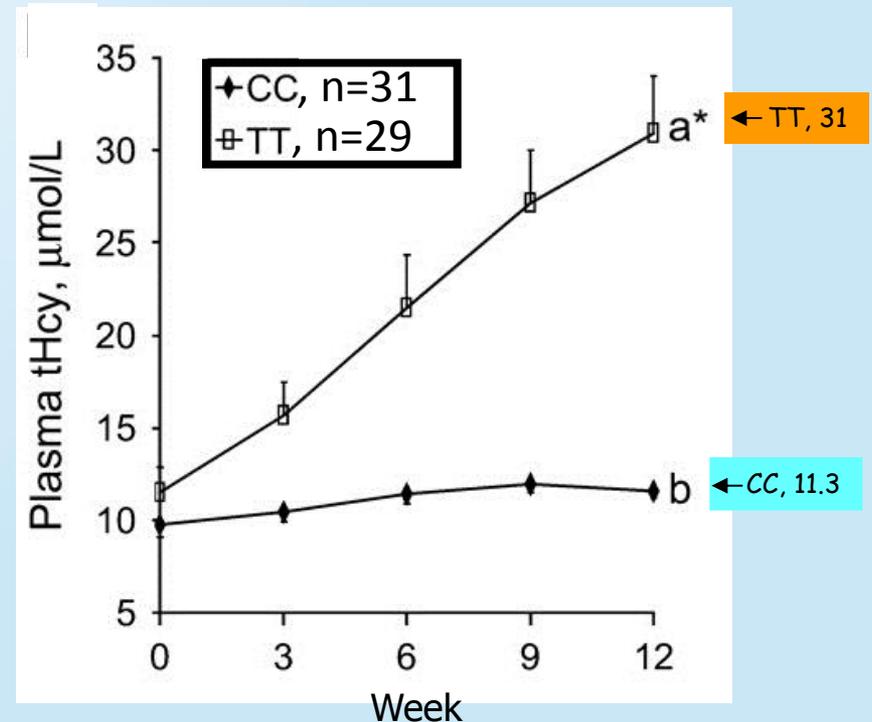
MTHFR 677TT genotype markedly affects biomarkers of folate status in men consuming the folate RDA

Solis et al. JN 2008

Folate Treatment with 400 μg DFE/d

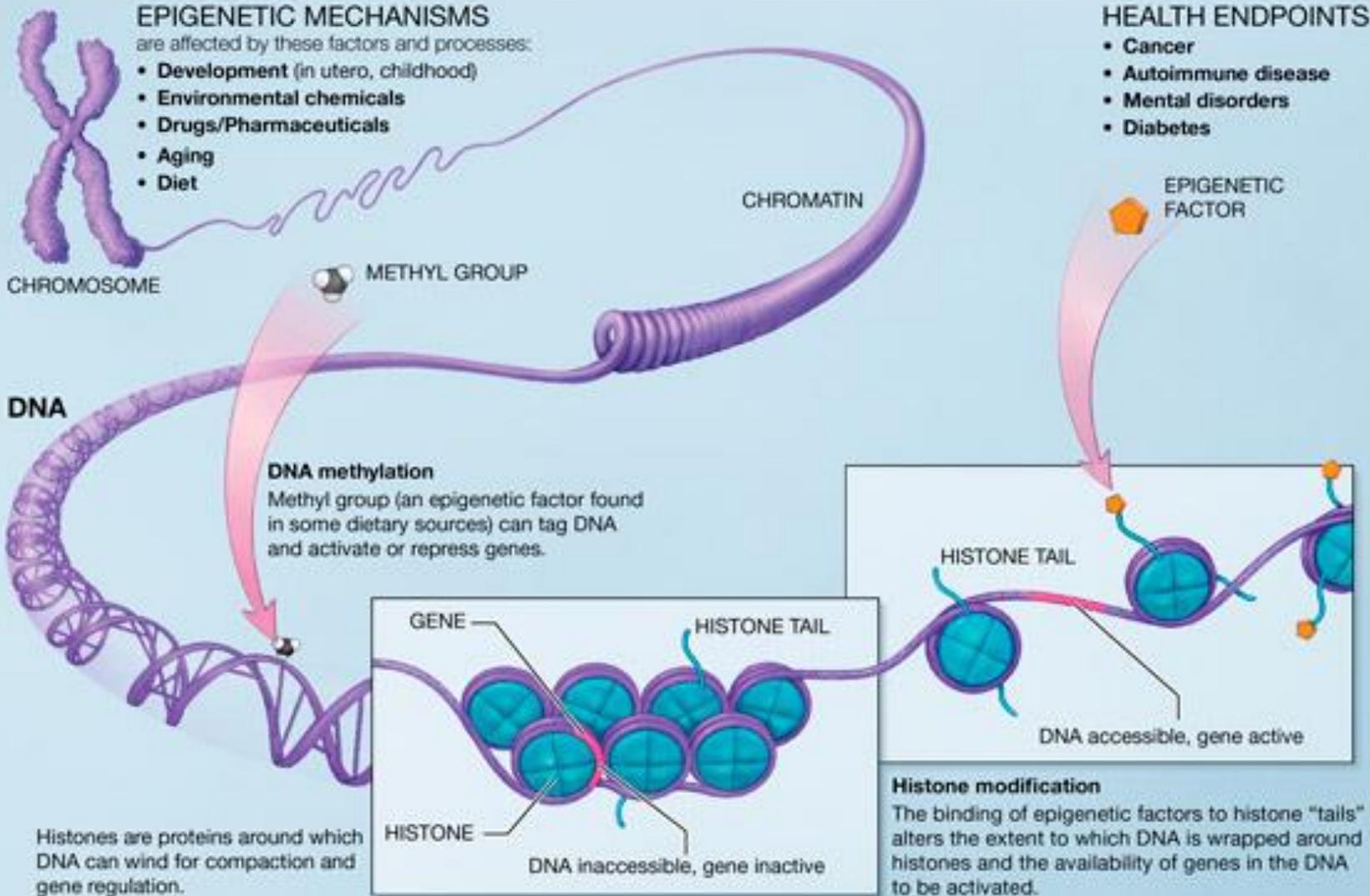


Deficient (<6.8 nmol/L)
 34% TT (10 of 29)
 16% CC (5 of 31)

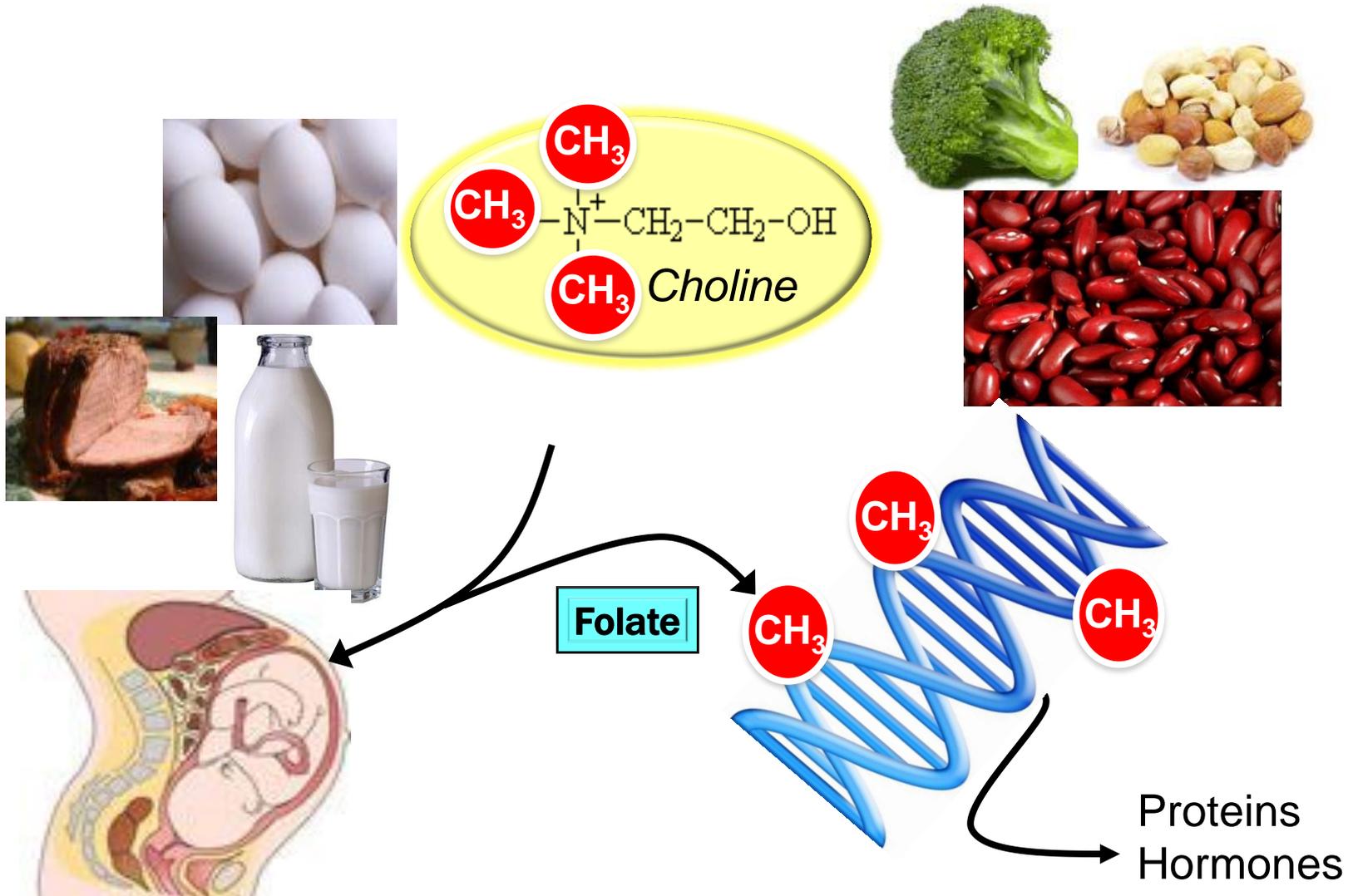


Deficient (>14 $\mu\text{mol/L}$)
 79% TT (23 of 29 men)
 7% CC (2 of 31 men)





Choline is an essential nutrient that plays a key role in fetal development

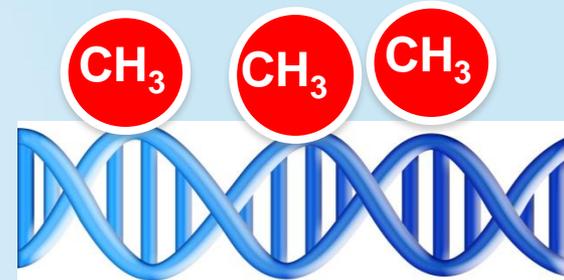


Supplementing the maternal diet with extra choline may ease baby's stress by changing production of the stress hormone, cortisol



Supplementing the diet with extra choline

=

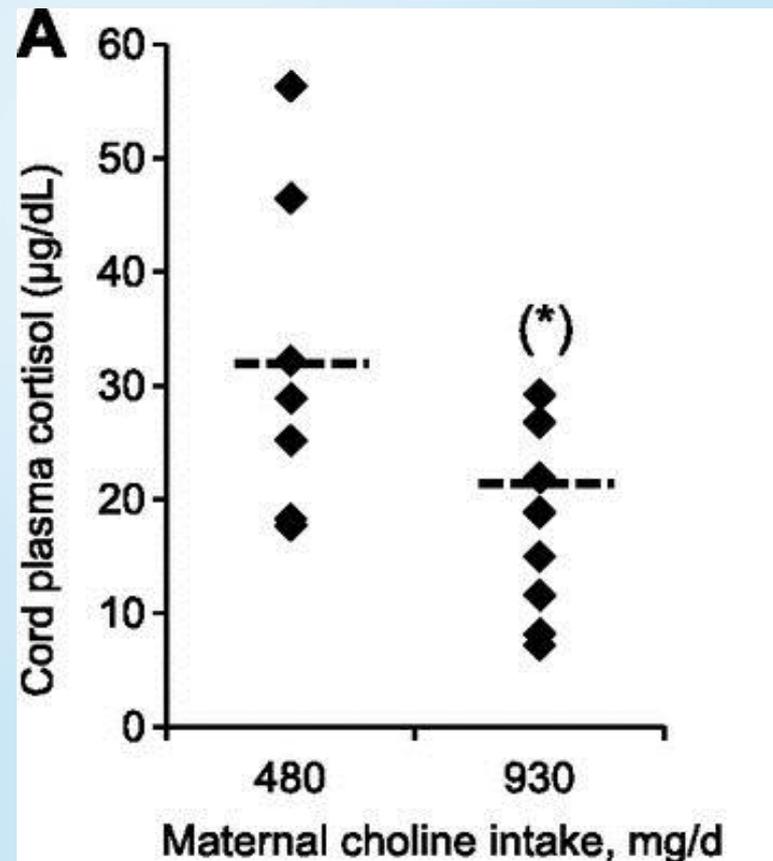


Cortisol

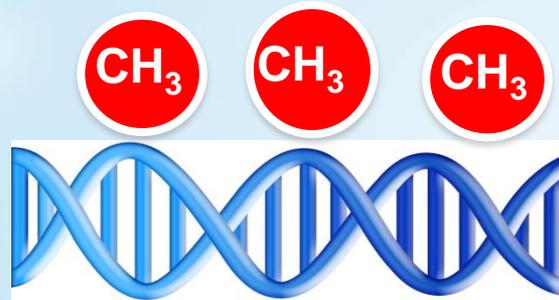


“Choline” Baby

Effect of maternal choline intake (930 vs. 480 mg/d) on maternal and fetal cortisol.



This lower production of cortisol in “choline” babies may reduce risk of stress-related diseases



Cortisol



“Choline” Baby



- Hypertension
- Obesity
- Diabetes
- Depression



- Memory
- Learning
- Attention

National Nutrition Research Roadmap 2016–2021

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Epigenomics	Study of the complete set of epigenetic modifications on the genome
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Proteomics	Study of the structure, function, and interaction of proteins
Transcriptomics	Study of the complete set of RNA transcripts produced by the genome



Questions & Answers

Please submit your questions to
via the “questions box” on your
screen.

Thank you for joining us!

Make plans to participate in our next webinar:

**The National Nutrition Research Roadmap:
Measuring and Monitoring Individual Dietary
Intake and the Food Environment**

Wednesday, January 18, 2017

3:00 pm - 4:00 pm (ET)

Visit www.nutrition.org for details.

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