FN590: Nutrition and Genetics

2 credits

Facilitator: James C. Fleet, Ph.D. (fleet@purdue.edu)

Wednesdays 3:30-5:20 pm, UNIV 217

Purpose: The risk for many chronic diseases is increased by both inherited factors and environmental variables like diet. With the completion of the Human Genomic Project, there is considerable hope that genetic profiles defining disease risk will be possible for optimal prevention and treatment of diseases. Nutrition science and nutritionists have developed dietary recommendations for healthy living that are applied to the general population. This ignores both the potential limits on diet-based disease prevention due to genetic predisposition AND the potential benefits of diet-based disease prevention for people with specific genetic profiles. The goal of this course is to give you an overview of the principles of genetics, to identify approaches to study genetic contributors to a phenotype, and to discuss existing situations where it is clear that diet/lifestyle factors and genetic profiles interact to influence a physiologic response or disease risk.

Format: This will be a discussion based course. There will be no formal lectures. As such, you will need to read all assignments prior to attending class and you will need to come equipped with questions re: concepts, implications, methodology, and interpretation. You must also be prepared to state your opinion on the subject being discussed. If you do not understand the issue to be discussed due to lack of background in physiology, biochemistry, nutrition, I expect that you will conduct additional research and reading in the area.

Assignments and Grading:

1) You will write two short papers in the format of a Brief Critical Review (BCR) for the journal Nutrition Reviews.

BCR 1 is due: Mar 3
- This BCR must be on one of the following topics: (1) a rare genetic disease influencing nutrient metabolism (e.g. hemochromatosis), (2) something that demonstrates a nutritional phenotype is heritable

BCR 2 is due April 28
- This BCR can be on any subject that links nutrition to genetic variation, i.e. GWAS studies, gene x diet interactions, etc.

A Brief Critical Review is written for an informed audience of nutrition professionals; it discusses a current research paper (or two) in a relevant area of nutrition research and
explains the findings within the context of the larger body of research on that topic. *Your job is to clearly explain why the journal article(s) is important and what it adds to our understanding of the topic.* Instructions for the completion of the Brief Critical Reviews are below. I’ve attached an example of a BCR. *Failure to follow these instructions will compromise your grade.*

**Instructions for Brief Critical Reviews:**

a) Select a high-quality, recent or seminal primary research article on some aspect of nutrition and genetics. (You may want to ask Dr. Fleet if the manuscript is acceptable)

b) The length of the review is approximately 1500 words (excluding title, summary, and references)

c) The following elements must be present. These are not headings!
   a) *Title* - The title of 200 characters or less should clearly indicate the important point of the paper. It need not be the same as the title of the paper being reviewed.
   b) *Summary* - a brief summary of the papers subject matter, its findings, and the implications of the findings (25-50 words). This should not be a condensation of the papers original abstract but *your interpretation of what is important from the journal article.*
   c) *Introduction* - one to two paragraphs introducing the subject matter and summarizing the question to be answered by the paper. Remember that the BCR is being written for an audience that has not yet read the paper under review so the paper itself must be introduced and cited.
   d) *Study description* - Explain the type of study conducted (e.g. cell, animal, human), describe the study conditions, explain what was measured (briefly stating how and why). Do not give a detailed description of the assay methods. Instead make it clear why each assay was conducted and what important information each assay should reveal.
   e) *Description of the important results and the authors interpretation of the results* - This is a summary of the results and discussion from the journal article.
   f) *Additional interpretation by you* - Make sure to clearly differentiate your thoughts from the authors.
   g) *Questions raised by the paper suggesting future areas for research*

*note: no more than 10 references can be used. However, it should be clear that you have read these articles and not just pulled them from the text of the paper you are reviewing.*

**Paper formatting:**
- double spaced
- 12 pt type
- 1 inch margins
- number each page and include your name at the top of each page
2) Be prepared to provide a verbal overview of your BCR on the due date. This will not be a detailed discussion but rather you will need to explain:

* Why did you choose the paper?
* What were the major findings of the paper and why were they interesting?

DO NOT PREPARE OVERHEADS OR POWERPOINT PRESENTATIONS
PROVIDE THE CLASS WITH THE ABSTRACT OF YOUR SELECTED PAPER

3) Participation:

Each student will be required to participate in discussions of class material and research articles. While voluntary participation will be appreciated, I will call upon students for their answers/insights/opinions. Failure to actively participate will negatively influence your grade. The following guidelines will help you understand the level of participation that is required for each grade level:

- no participation = no points
- participation only when called upon
  - response demonstrating a lack of understanding of the material = 260 pts.
  - response provides only the minimum (correct) information = 300 pts
  - response provides insightful or thoughtful information = 340 pts
- voluntary participation
  - response demonstrating a lack of understanding of the material = 260 pts.
  - response provides minimum (correct) information = 340 pts
  - response provided insightful or thoughtful information = 400 pts

Grading

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Class Schedule and Readings:

**Text books:** These are available in my office. You may borrow them only to copy.
- Strachan and Read, Human Molecular Genetics, Wiley-Liss, 1996.
- Lynch and Walsh, Genetics and Analysis of Quantitative Traits, 1998

**Jan 13:** General discussion and class business


**Jan 20:** Key Genetic Concepts I

- Chapter 3 Strachan, Genes in pedigrees
- Selected passages from other readings on:
  - Hardy-Weinberg principle
  - Linkage Disequilibrium

**Jan 27:** Nutrition and Genetics I: rare single gene defects

- Familial Hypercholesterolemia

- Hemochromatosis
  - Allen et al., 2008, Iron-overload-related disease in HFE hereditary hemochromatosis NEJM 358:221

**Feb 3:** Key Concepts II: Heritability

- Chapter 18, Strachan Complex Diseases pages 479-486
Feb 10:  **Key Concepts III: Gene Mapping/Linkage Studies**

Chapter 12 in Strachan, Genetic mapping
Chapter 14 in Strachan, Identifying human disease genes

Feb 17:  **Key Concepts IV: Complex Traits/candidate genes/genetic epidemiology**

Chapter 18, Strachan Complex Diseases pp 486-504

Feb 24  **Candidate genes 1**

**VDR polymorphisms**
Abrams et al., 2005, Vitamin D receptor FokI polymorphisms affect calcium absorption, kinetics, and bone mineralization rates during puberty. J. Bone Min. Res. 20:945.
Morrison et al., 2007, Vitamin D receptor genotypes influence the success of calcitriol therapy for recurrent vertebral fracture in osteoporosis. Pharmacogenetics and Genomics 15:127.

**Lactase persistence genotype**
Emattaj et al., 2004, Genetic variant of lactase-persistent C/T-13910 is associated with bone fractures in very old age. J. Am Geriatr Soc. 53:79.

Mar 3:  **Discussion of BRC1**

Mar 10:  **Candidate genes 2**

Rankinen et al., 2006, The human obesity gene map: The 2005 update. Obesity 14:529. (Just peruse this – you don’t have to read carefully).
Mar 17: NO CLASS - SPRING BREAK

Mar 24: Key Concepts V: Mouse Genetic models for complex traits


We will also look at mouse genetic resources like Web QTL and the Jackson Labs Mouse Phenome Project during this and the next lecture.

Mar 31: Mouse QTL

Wang et al., 2007, Genetic variation in Mon1a affects protein trafficking and modifies macrophage iron loading in mice. Nature Genetics 39:1025-1032


We will also look at genetic resources that list human SNPs and that identify orthologous genes across species.

April 7: Key Concepts VI: Genome wide association studies


April 14: Genome wide association studies: examples

Liu et al., Powerful bivariate genome-wide association analysis suggest the SOX6 gene influencing both obesity and osteoporosis phenotypes in males. PLOS One 4:e6827.

Bauer et al., 2009, Obesity genes identified in GWAS are associated with adiposity measured and potentially with nutrient-specific food preferences. AJCN 90:951-959.
April 21: Key concepts VII: Epigenetics


April 28 NO CLASS EB 2010