Nutrigenomics - a tool to meet the future demands for animal-derived foods

Mark Gaffney, Ph.D.
Alltech Bioscience Center, Ireland
23rd June 2011
The World needs to double the meat production in the next 50 years.
What are the challenges?

- Changes in the world economy
- Changes in the environment
- Decreased availability of land and water
- Impact of the transportation of foods
- Food security: Food chain safety and traceability
- Food sufficiency: Efficiency of food production
- Demand for functional foods
- EU ban on AGPs
- Effective nutrient utilization
The future and the deficit: A CRISIS in the making

- Continued increases in production at past rates will result in a deficit in overall food production.
Small changes in food production efficiencies will not be sufficient

• It is time to make quantum leaps
  – Time to identify new resources
  – Time to develop new production technology
    • New tools and more efficient systems
    • Time for dramatic changes in management styles
  – Time to redefine nutritional strategies
The new tool: Nutrigenomics

What can molecular tools tell us about nutritional programming strategies?
Nutrigenomics opens the gateway to a new paradigm


- Seeks to provide a molecular understanding for how common dietary chemicals affect health by altering gene expression.
Bioactive food components can influence gene expression and ultimately cellular function.
How can we best assess the effect of nutrition?
Traditional trial approach
Nutrigenomics approach

Gene expression and metabolism

Diet

Health

Fertility

Performance
Ultimately, genes control biological function.

Altered Gene Expression = Altered Biological Function
Potential issues

- Incomplete annotated genome sequences
- Gene transcription is only one step in the regulatory pathway
- Not always possible to correlate changes in mRNA levels with phenotypic or protein changes
- Transcriptomics still represents a major tool to elucidate key processes in metabolic regulation
Looking at practical examples – What can you learn?

- Different tissues respond differently to the same nutrient
- Different forms of the same nutrient differently alter gene expression patterns
- Biomarkers relating gene expression to nutrition induced changes in physiology
Gene expression in intestinal tissue

- 1,304 transcripts were significantly affected by at least one selenium treatment in intestine (P ≤ 0.05)
- Sel-Plex supplementation strategy altered 68%
- Sodium selenite group altered 24%
- Only (8%) were altered in the same way by both selenium supplementation strategies
Gene expression in uterine tissue

- 5,105 transcripts were significantly affected by at least one selenium treatment in oviduct ($P \leq 0.01$)
- 57% were influenced by sodium selenite supplementation
- 19% influenced by Sel-Plex supplementation (19%)
- Both sodium selenite and Sel-Plex had similar effects on 24% of these genes.
Observations

Nutrient type dictated which genes were altered

Different tissues were altered in different ways with the same supplementation strategy
Looking at practical examples – What can you learn?

• Different tissues respond differently to the same nutrient

• Different forms of the same nutrient differently alter gene expression patterns

• Biomarkers relating gene expression to nutrition induced changes in physiology
Cross-tissue analysis: GADD45β

- GADD45β expression significantly decreased across all tissues tested by Sel-Plex® only
- Indicates lower endogenous oxidative stress and DNA damage throughout the entire animal
**GADD45β: From youth to old age**

**Fold change data: Brain cortex**

<table>
<thead>
<tr>
<th></th>
<th>Young</th>
<th>Middle-aged</th>
<th>Old</th>
</tr>
</thead>
<tbody>
<tr>
<td>SM</td>
<td>-1.22</td>
<td>-1.10</td>
<td>-1.18</td>
</tr>
<tr>
<td>SS</td>
<td>1.01</td>
<td>-1.44</td>
<td>-1.10</td>
</tr>
<tr>
<td>SP</td>
<td>-1.48</td>
<td>-1.53</td>
<td>-1.42</td>
</tr>
</tbody>
</table>

Mouse age: 3 months
Human equivalent: <10 years

Mouse age: 15 months
Human equivalent: 45 years

Mouse age: 25 months
Human equivalent: 75 years

- **GADD45β expression significantly decreased across all age groups by Sel-Plex® only**
Physical measurement of GADD45 and DNA damage
(Barger et al., 2009)
Effect of selenium supplementation on the number of differentially-expressed genes in four tissues of mice

(Barger et al., 2009)

Selenomethionine can only elicit a fraction of the selenium-associated gene responses

Forms of selenium
Free L-selenomethionine induces the p53 tumor suppressor gene in intestine. Genotoxicity?

(Barger et al., 2009)

- Not all selenium sources are the same
- Care must be taken in selecting the form of specific nutrients

Forms of selenium
Antioxidant Systems

“The cooperative interaction between antioxidants in the cell is vital for maximum protection from the deleterious effects of free radicals”

(Surai, 2001)
The challenge: measuring antioxidant effects

- Antioxidants are required for optimal growth, immunity, and reproduction
- Historically added vitamin E at 5 to 10 times NRC requirements to meet a perceived need to maintain product quality
- Alternative approaches have been proposed, but have been difficult to evaluate
- Gene expression to evaluate alternative strategies
Hierarchy clustering of regulated intestinal genes in diets containing two levels of vitamin E and EconomasE

Genes included were significantly changed by EcoE and E100 (134 transcripts in total).

Expression level represented as higher (Red) or lower (Blue) than normalized median value of the corresponding genes.

Results indicate that majority of genes are similarly changed by E100 and EcoE.
Genes changed unidirectionally by EconomasE and Vitamin E

* Genes included are those changed by both EcoE and E100
Effects of Vitamin E and EconomasE on expression of sterol carrier protein 2: Controlling tissue peroxidative stress and meat quality

Intracellular Dissemination of Peroxidative Stress

INTERNALIZATION, TRANSPORT, AND LETHAL TARGETING OF A CHOLESTEROL HYDROPEROXIDE SPECIES BY STEROL CARRIER PROTEIN-2-OVEREXpressING HEPATOMA CELLS*

Received for publication, January 25, 2006; published JBC Papers in Press, June 12, 2006; DOI 10.1074/jbc.M500744200

Tamas Kriska1, Vladislav V. Levchenko2, Witold Korytowski1, Barbara P. Atshaves1, Friedhelm Schroeder1, and Albert W. Girotti1

From the 1Department of Biochemistry, Medical College of Wisconsin, Milwaukee, Wisconsin 53226, 2Institute of Molecular Biology, Jagiellonian University, 31-120 Krakow, Poland, and 5Department of Physiology and Pharmacology, Texas A&M University, College Station, Texas 77843

* p≤0.01
Effects of EconomasE on gene expression of proteins associated with meat color

**Peroxiredoxin 3**

**Potential of Peroxynitrite To Alter the Color of Myoglobin in Muscle Foods**


**JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY**

BRIAN J. CONNOLLY, ROBERT G. BRANNAN, AND ERIC A. DECKER®

Department of Food Science, University of Massachusetts, Amherst, Massachusetts 01003
EconomaseE and Vitamin E® affect gene expression

- Influence of EconomaseE® and vitamin E on gene expression is at the transcriptomic level

- Vitamin E and EconomaseE® exert similar influences on gene expression

Adapted from Brennan et al., 2010; Xiao et al., 2010
Individual compounds will give a unique gene expression fingerprint
The revolution:
Lessons learned from Nutrigenomics work with minerals and antioxidants

Simple changes in nutritional and supplementation strategies can have dramatic effects on biological functions.
Strategic nutritional programming to improve the quality of beef

- Meat at the butcher
  - Lower pH
  - Lighter Color
  - Improved mineral status
  - Greater moisture content
Programming for improving performance of feedlot beef

Bonus:
- Average daily gain improved
- Time to market weight decreased by 30 days
Where can the nutritional programming approach leading us?

- Strategic use of nutrients
- Developing programs to take advantage of our new understanding of physiological regulation

*We have never had the tools to evaluate these approaches in the past*
The Key Points:

- Rapid and effective evaluation of nutritional strategies is becoming a reality through molecular based technologies.
- Thousands of data observations generated per experiment.
- Provides a valuable and novel approach for improving the efficiency of animal production.
- Programming strategies can be used to enhance performance, health and product quality.
- It is the strategy that will drive advances in nutritional efficiency and not individual ingredients or supplements.
Nutrigenomics

Provides a molecular understanding for how common dietary chemicals (i.e., nutrition) affect health and performance by altering the gene expression patterns.

It will be used to Redefine Nutrition.
Nestlé partners with King's College London on food and gene research

June 10, 2011

The Nestlé Research Center in Switzerland will collaborate with King's College London on a joint research project into the relationship between food and genes.

Due to begin later this year, the six-month project will examine the interactions between genes and food ingredients, and how they can affect human health.

It will look at how our genes and their encoded proteins determine important bodily functions, including how efficiently we metabolise food, respond to the environment and detoxify our bodies from potentially harmful agents.

UNILEVER STUDYING NUTRIGENOMICS

Interestingly, Unilever announced on Oct 5 that they too have begun to collaborate and explore the link between diet and health. Such research has become a priority for them, with Unilever's aim to reduce the risk of diabetes, heart disease and the two killers of all of death worldwide. A wide range of experts in medicine and nutrition will help prevent these disorders at an early stage. Emerging scientific evidence that diet can influence risk of disease is an important area of research. In particular, the study of nutrigenomics, a field that is increasingly important in this process. Evidently, the field for new research. From the clinical insights, laboratories which express the very important role of the gene.

Molecular nutrition (also known as nutrigenomics)

The science, which studies the link between nutrition and health at the molecular level, is called nutrigenomics. It integrates biochemistry, genetics and nutrition. The gene is the basic unit of heredity, and it determines how an organism develops and functions. Each gene consists of a specific sequence of DNA, which provides the instructions for making specific proteins. These proteins are the building blocks of the body, and they are responsible for all of the body's functions.

Nutrigenomics is the intersection of diet and health as gene expression is directly influenced by nutrition. Alltech has invested in this exciting domain, culminating in the creation of a dedicated Centre for Animal Nutrigenomics and Applied Animal Nutrition at its corporate headquarters in Kentucky.
Thank You