An integrated approach to development of food products that deliver nutrition from “farm to cell”

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The Challenge

- Health care cost for the U.S. continue to increase
- Population 75 years and over is projected to increase to 12% by 2050
- ~36% of US Adults and 17% of children/adolescents are Obese
- Chronic Disease burden continues to increase
- Key players include:
  - Lifestyle
  - Diet

(CDC, 2013)
Food is composed of both nutritive and nonnutritive components that combine to impact health.

Nutritive Components:
- Macronutrients: Protein, Lipids, Carbohydrate
- Micronutrients: Vitamins, Minerals
- Fiber
- Flavor
- “Other”
- Bioactives: Phytochemicals

Non-nutritive Components:
Food is the central player in health

Food

Nutrients

Negative Health Impact

Non-Nutrients

Positive Health Impact

Nutrients

Non-Nutrients
Commercial Food Supply: Continuum from Farm to Fork

Basic Producers (Farmers)
- livestock
- grains
- fruits
- vegetables
- sugar
- seafood

Commodity Producers

Value Added Food Processors
- Packaged foods

Food Ingredient Manufacturer
- Ingredients and additives

Distributors (Market)

Consumer

Adapted from Rizvi (2011)
Integrating disciplines to deliver food with improved impact on health and wellness

- Consumer Science – Defining “What People Want and Why”
- Agriculture – Creation of Raw Food Materials “Building blocks”
  - Investigates aspects of production agriculture and post harvest processes to deliver nutrient dense agricultural materials
  - From “Farm to Factory”
- Food Science – Defining “What Food Is”
  - Impact of food composition, processing and consumption on nutrient and phytonutrient stability and functionality in foods
  - “From Factory to Fork”
- Nutrition Science – Defining “What Food Does”
  - Investigates delivery and impact of food and food components on metabolic and physiological response of the body
  - “From Fork to Cell”
Translation of cutting edge nutrition research to product application requires multiple disciplines and planning

- Defining composition and bioactive properties of product and compounds
- Establishing nutritional needs of the target consumer
- Identification/Development of ingredient technology
- Product Evaluation
  - Safety
  - Bioavailability
  - Functionality
  - Efficacy
- Health Outcomes
- Product Optimization
- Product scale up
- Industrialization
- Cost in use
- Regulatory

Innovative new product

Consumer science

Agriculture
Vegetables, fruit, and cancer prevention: A review

Steinmetz KA, Potter JD

Journal of the American Dietetic Association 96: (10) 1027-1039, 1996

“In this review of the scientific literature on the relationship between vegetable and fruit consumption and risk of cancer, results from 206 human epidemiologic studies and 22 animal studies are summarized. The evidence for a protective effect of greater vegetable and fruit consumption is consistent for cancers of the stomach, esophagus, lung, oral cavity and pharynx, endometrium, pancreas, and colon. The types of vegetables or fruit that most often appear to be protective against cancer are raw vegetables, followed by allium vegetables, carrots, green vegetables, cruciferous vegetables, and tomatoes. Substances present in vegetables and fruit that may help protect against cancer, and their mechanisms, are also briefly reviewed; these include dithiolthiones, isothiocyanates, indole-3-carbinol, allium compounds, isoflavones, protease inhibitors, saponins, phytosterols, inositol hexaphosphate, vitamin C, D-Limonene, lutein, folic acid, beta carotene, lycopene, selenium, vitamin E, flavonoids, and dietary fiber.”
Both nutrients and non-nutrients play prominently in food and health products

Bioactive food components

“Expanding knowledge of the role of physiologically active food components, from both plant (phytochemicals) and animal (zoochemicals) sources, has notably changed the role of diet in health”


Phytochemicals

Non-nutritive plant chemicals expressed as secondary metabolites which may have protective or disease-preventing properties in humans and animals.

NIH-NCI
Phytochemicals in Fruit and Vegetables

Phytochemicals (Plant metabolites)

Carotenoids
- Xanthophylls
- Carotenes

Phenolics
- Phenolic Acids
- Flavonoids
- Stilbenes
- Ellagic Acids
- Anthocyanins
- Flavan-3-ols
- Flavonols
- Flavones
- Flavanones
- Proanthocyanins
Bioactive food components as part of food matrix

<table>
<thead>
<tr>
<th>Macro Nutrients:</th>
<th>Micronutrients:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates, Lipids, Protein, (Fiber)</td>
<td>Vitamins, Minerals</td>
</tr>
<tr>
<td><em>Catechins</em></td>
<td><em>Chlorophyll</em></td>
</tr>
<tr>
<td><em>Polyphenols</em></td>
<td><em>Omega-3 FA</em></td>
</tr>
<tr>
<td><em>Anthocyanins</em></td>
<td><em>Flaxseed</em></td>
</tr>
<tr>
<td><em>CLA</em></td>
<td><em>Phenolics</em></td>
</tr>
<tr>
<td><em>ACE peptides</em></td>
<td><em>Carotenoids</em></td>
</tr>
<tr>
<td><em>Lecithin</em></td>
<td><em>Flavonones</em></td>
</tr>
<tr>
<td><em>Carotenoids</em></td>
<td><em>Flavonoids</em></td>
</tr>
<tr>
<td><em>Phytosterols</em></td>
<td><em>Carotenoids</em></td>
</tr>
<tr>
<td><em>Phenolic Acids</em></td>
<td><em>Sulfides &amp; Thiol Compounds</em></td>
</tr>
</tbody>
</table>

**Aroma**
- Catechins
- Polyphenols
- Anthocyanins
- CLA
- ACE peptides
- Lecithin
- Carotenoids

**Taste**
- Phenolics
- Phytosterols
- Phenolic Acids
- Chlorophyll
- Omega-3 FA
- ACE Peptides
- Flaxseed
- Carotenoids
- Flavonoids
- Phenolic Acids
- Phytoestrogens

**Texture**
- Anthocyanins
- Phenolic Acids
- Carotenoids
Innovation at the interface of food and nutrition science has given rise to...

- **Functional Foods**
  
  Food or dietary component that may provide a health benefit beyond basic nutritional value
Food as an Opportunity

Define, develop and market commercially viable food products that positively impact health and wellbeing

AND

people actually want...
Nonlinear approach integrates farm to cell concept

- **Consumer Science/Communication**: Defining and communicating to consumers
- **Basic Nutrition Science**: Defining Innovative Nutrition Targets
- **Food Science**: Translation to Consumer Products
- **Clinical Nutrition Science**: Measuring Impact
- **Agriculture**: Evolving and refining food composition
Clear and not so clear communication...

Welch's 100% Grape Juice is delicious and healthy because it's prepared from whole Concord grapes—skin, seeds and all. Relatively rare polyphenol antioxidants included per serving, help maintain healthy blood cell quality, helping prevent cell damage caused by free radicals. So drink Welch's Concord Grape Juice, it helps support a healthy heart, mind and immune system. To learn more, visit: welch.com.

Health’s Angel.
Only POM Wonderful is backed by $31 million in clinical research.

“...Natural Fruit Product with Health Promoting Characteristics.” – FTC Judge
Consumer messages can create challenges in communication of food attributes.

~46% of Americans feel nutrition and health messages are confusing.

(IFIC Food and Health Survey, 2010)
Impacting health requires physiological delivery from “fork to cell”

**Consumer/Marketing Perspective**

**Technical Perspective**

Agriculture & Food Science

Nutrition Science

"Physiological Delivery" Bioavailability
Carotenoid Pigments:
Nutritive and Nonnutritive Bioactives

Lycopene

HO
OH

α− & β-carotene

Lutein and zeaxanthin

Novel Sources

http://www.usda.gov

http://www.picture-newsletter.com/vegetables/

http://www.oardc.ohio-state.edu
**Provitamin A activity of carotenoids**

- **β-carotene**
  - Converted to **Retinal** by CMO1
  - Edited by **Retinal reductase** to form **Retinol**
  - Converted by **LRT** to **Retinyl Esters**
  - Converted to **Retinoic Acid**
Carotenoids: Eye and brain health

Inflammation and Diabetes
(pro-inflammatory molecules
  e.g. IL-6, Angiotensin II)

Light Exposure

Oxidative Stress

Degradation of Functional Proteins

DNA damage

Neuronal Dysfunction
(e.g. Rhodopsin<photo-transduction,
  Synaptophysin<neuronal activity &
  neurotrophic factors)

Neuronal Death

Ozawa et al. (2012)

Alves-Rodrigez et al. (2004)

Snider 2008
Biofortified Grains:
Enhancing provitamin A carotenoid content through breading and transgenic

Pyruvate + glyceraldehyde-3-phosphate $\rightarrow$ DXS

Geranylgeranyl diphosphate $\rightarrow$ PSY phytoene $\rightarrow$ CRT-I lycopene

β-LCY, ε-LCY $\rightarrow$ β-LCY, β-LCY

α-carotene $\rightarrow$ β-carotene $\rightarrow$ β-carotene $\rightarrow$ CRT-RB α-cryptoxanthin $\rightarrow$ β-cryptoxanthin $\rightarrow$ CRT-RB lutein $\rightarrow$ CRT-RB zeaxanthin $\rightarrow$ CRT-RB

Yellow Endosperm Sorghum

Biofortified Sorghum
Development of high carotenoid staple foods

Traditionally bred high provitamin A Maize

Variety 1
Variety 2
Variety 3
Variety 4
Variety 5
Variety 6

Traditionally bred high provitamin A Cassava

Transgenic Golden Rice

http://www.goldenrice.org
Several unit operations are required for even a simple food process and product.

- Washing
- Sorting
- Peeling
- Juicing
- Hot/Cold Break
- Formulating
- Homogenization
- Filling
- Heat Sterilization
- CIRIO Rustica
- CIRIO Verdure Grigliata
Processed to preserve nutrient/phytonutrients

Golden Whole Kernel (GWK)  White Shoepeg (WS)


Table 1
Carotenoid concentrations in WS and GWK corn (µg/100 g fresh weight)

<table>
<thead>
<tr>
<th></th>
<th>Lutein</th>
<th>Zeaxanthin</th>
<th>α-cryptoxanthin</th>
<th>β-cryptoxanthin</th>
<th>α-carotene</th>
<th>β-carotene</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresh</td>
<td>5.5±1.2</td>
<td>28.5±5.2</td>
<td>0.3±0.1</td>
<td>0.4±0.1</td>
<td>0.04±0.0</td>
<td>0.82±0.08</td>
<td>35.5±6.3</td>
</tr>
<tr>
<td>Canned</td>
<td>6.6±0.5</td>
<td>30.5±3.4</td>
<td>0.3±0.1</td>
<td>0.5±0.2</td>
<td>0.05±0.1</td>
<td>0.68±0.17</td>
<td>38.7±6.4</td>
</tr>
<tr>
<td>Frozen</td>
<td>6.3±1.1</td>
<td>47.7±10.2</td>
<td>0.5±0.1</td>
<td>0.9±0.2</td>
<td>0.23±0.1</td>
<td>2.37±0.42</td>
<td>57.9±10.0</td>
</tr>
<tr>
<td><strong>GWK</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresh</td>
<td>330.3±19.8</td>
<td>209.0±12.0</td>
<td>104.0±8.4</td>
<td>31.6±15.5</td>
<td>11.7±1.8</td>
<td>15.69±0.60</td>
<td>702.2±46.6</td>
</tr>
<tr>
<td>Canned</td>
<td>336.4±67.5</td>
<td>215.9±42.2</td>
<td>97.4±26.0</td>
<td>42.8±10.0</td>
<td>4.4±0.6</td>
<td>11.66±2.47</td>
<td>715.8±192.9</td>
</tr>
<tr>
<td>Frozen</td>
<td>361.6±34.2</td>
<td>212.3±36.0</td>
<td>109.1±13.9</td>
<td>33.1±3.9</td>
<td>6.8±1.5</td>
<td>16.68±1.83</td>
<td>739.6±59.9</td>
</tr>
</tbody>
</table>

Values are presented as means ± SEM.
Corn and brine were analyzed in all canned samples with brine content factored out of final calculations.
Many “food” factors impact bioavailability, metabolism and activity of bioactives

Can be impacted by:

- Food Matrix
- Type and extent of food processing
- Presence of other macronutrients

Bioactive
In Food Matrix

Oral consumption

Digestive release
In GI tract

Solubilization & Intestinal uptake

Uptake by intestinal epithelia

Intestinal transport

Secretion to Blood

Transport/Deposition To Target Tissue

Excretion

Bioaccessibility

Bioavailability
Can food processing improve the bioavailability of nutrients and bioactives?

- **Example: Canned Vegetable Products**

- **Processing Operations:**
  - Cutting (Size reduction)
  - Juicing (Size reduction)
  - Blanching (Heat Transfer)
  - Mechanical homogenization (Size reduction)
  - Thermal Processing (Heat transfer)
  - Concentration (Mass transfer)

Can formulation and/or ingredient interactions impact “nutritional” quality?

Co-consumed lipid is required for optimal absorption of fat soluble nutrients

Adapted from Brown et al. (2004)
Leveraging nutrition research for consumer communication
### Bioaccessibility (%) of β-carotene from Transgenic Sorghum based Porridge (ABS-188)

<table>
<thead>
<tr>
<th>Sample</th>
<th>5% lipid (Da, et al 1982)</th>
<th>10% lipid (Kean, et al 2011)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homo188-A</td>
<td>4.9 ± 0.5&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>8.1 ± 2.9&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td>Homo188-B</td>
<td>2.9 ± 0.4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6.1 ± 0.8&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Homo188-C</td>
<td>3.6 ± 0.5&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>9.0 ± 5.0&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td>Homo188-D</td>
<td>1.9 ± 0.1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>21.6 ± 6.2&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

### Extending findings back to grains:

**Carotenoid bioaccessibility in sorghum porridge is higher with more lipid**

- For children 4-8 Yr EAR = 275 ug RAE
- 200g of porridge from Homo 188-A: 500ug BC eq 30– 48% of the vitamin A EAR

* Assumes bioconversion rate between 6:1 and 3.8:1 by weight

*Lipkie et al. J Agric Food Chem. 2013*
Emerging example: Improvement in infant formula requires coordination of agriculture, nutrition and food science
Challenge: Bioavailability of carotenoids from infant formula is different than from human milk

• Lutein bioavailability was ~4x lower from formula than human milk

Why?

Does source of lutein matter?

Human milk v/s Bovine Milk?

Human Milk and Formula differ not in digestibility and release but in intestinal uptake of lutein

Starting content of Lutein in Formula or Milk

% Lutein made Bioaccessible through GI digestion

% of Bioaccessible Fraction absorbed by Intestine

Some Final Thoughts on a Farm to Cell Consideration for delivery of healthy foods...

- Agriculture and food science matter in design, development and delivery of healthy foods

- Food materials, processing and matrix matter...

- Physiological delivery of nutrients and bioactives is a critical component to delivery of beneficial attributes

- As a “Discipline” we are moving toward characterizing “what food does” and “how it does it” rather than specifically “what food is”

- A challenge remains how we communicate advances and knowledge to consumers and professionals in a manner consistent with promotion of public health and wellbeing
Acknowledgments

Purdue Faculty
Wayne Campbell, Ph.D.
Bruce Hamaker, Ph.D.
Gebisa Ejeta, Ph.D.
Torbert Rochford, Ph.D.
Connie Weaver, Ph.D.

The Ohio State University
Earl Harrison, Ph.D.
Mark Failla, Ph.D.

Harvest Plus
Fabiana F. De Moura

Post Doctoral Researchers
Nicolas Bordenave, Ph.D.

Graduate Students
George Kean, Ph.D.
Shellen Goltz, Ph.D.
Tristan Lipkie, Ph.D.
Milena Leon Garcia, M.S.
Darwin Ortiz

Pioneer Hybrids
Zuo-Yu Zhao, Ph.D.
Marc C. Albertsen, Ph.D.

Funding
NIH/NCCAM Botanicals Center- P50-AT00477
USDA-NRI
USDA- National Needs Fellows Program
North American Millers Association
Bill Melinda Gates Foundation
Mead Johnson Nutritionals
Pioneer Hybrids