Transdisciplinary Research on Energetics and Cancer

Concept Renewal Presentation

Division of Cancer Control and Population Sciences
Outline

- What we know.
- What has TREC accomplished.
- Where does TREC II go next?
- Questions
Macro-Level

Community and Organizational

Home/ Family

Individual

Agriculture and economic policies, food subsidies
Local public health programs, policies
Individualized health care interventions
Local health care services/coverage
Gov’t food assistance programs
National healthcare policy

Societal and cultural norms
Access to healthy and unhealthy foods in schools
Media and public education campaigns
Access to healthy foods in communities (grocery stores, fast food, farmers markets)
Food advertising and marketing

Psychosocial
- food norms, preferences
- knowledge
- attitudes
- skills, supports
- role models

Biological
- age
- gender
- genes
- physiology

Household environment and feeding practices, incl. portion size

Parent/child care provider training and education

Point-of-purchase information, promotions in restaurants, convenience/grocery stores

Federal policies (dietary guidelines, food labeling)

Food Industry action (product, packaging, pricing)
Proposed Mechanisms that Link Energy Balance and Carcinogenesis

(Gunter MJ et al. 2006)
Metabolic Syndrome & Obesity: Influence on Cancer Cell Metabolism and Growth

Growth Signal

Glucose -> ATP ↓ → Transcription → ATP ↑ → Translation → Pyruvate ↓ → Glucose – P → CO₂ + H₂O

Fuel Signal

Glucose -> ATP ↓ → Transcription → ATP ↑ → Translation → Pyruvate ↓ → Glucose – P → Lactate → CO₂ + H₂O

Source: C. Thompson (Penn) NCI Executive Committee Retreat, 2009
Percentage of U.S. Adults Meeting Physical Activity Recommendations

<table>
<thead>
<tr>
<th>% Meeting Recommendation</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRFSS Self-Report*</td>
<td>49.9</td>
<td>46.4</td>
</tr>
<tr>
<td>NHANES Self-Report**</td>
<td>57.8</td>
<td>42.5</td>
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<tr>
<td>Accelerometer***</td>
<td>3.8</td>
<td>3.2</td>
</tr>
</tbody>
</table>

* BRFSS 2005 (30 min x 5d mod or 20 min x 3 d vig)
** NHANES 2003-2004 (150 min/week)
*** NHANES 2003-2004, 20-59 y (Troiano et al., 2008) 30 min x 5d mod or greater
What Has TREC Accomplished?
March 2009

Transdisciplinary Research on Energetics and Cancer

39th Regular Meeting of the Board of Scientific Advisors

Division of Cancer Control and Population Sciences
Diet-induced obesity: Gene - diet interactions

B6 is obese only with a HFHS diet
A/J is lean regardless of diet

Hill-Baskin et al., 2009
<table>
<thead>
<tr>
<th>Metabolic Syndrome, NASH, HCC</th>
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</table>

<table>
<thead>
<tr>
<th>On High Fat, High Sucrose Diet:</th>
<th>B6</th>
<th>A/J</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Hypertension</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Insulin Resistance</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Cardiovascular Disease Risk</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Non-alcoholic steatohepatitis</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>✓</td>
<td>X</td>
</tr>
</tbody>
</table>

**Genetics of disease** | **Genetics of health**

The FHCRC Transdisciplinary Research on Energetics and Cancer Center

Exposures

Intermediate Biology
Glucose
Insulin
IGF
Inflammation
Adipokines

Models
Cells
Animals
Humans
Populations

Outcomes
Growth
Proliferation
Apoptosis
Tumorigenesis
Tissue
Angiogenesis
Biomarkers of
carcinogenesis
Glycemic Load (GL) Effects of Diet on Cancer Incidence

- High GL
- Low GL

Incidence of Palpable Mammary AC (%)

Days Post Carcinogen

20 25 30 35 40 45 50 55 60
Sleep Disturbance and Metabolic Effects

- Increased cortisol, insulin resistance
- Inflammatory cytokines
- Sympathetic nervous system over activity
  - Vascular effects (hypertension)
- Abnormalities in appetite regulatory hormones
  - Decrease Leptin; Increase Ghrelin

Redline, 2009
TREC Midcourse Accomplishments

- Rate of Progress
- Collaboration Ethos
- Career Development (73 New Investigators)
- Developmental Projects (n=96)
- New NIH Grants (n=13)
- Outreach
  - Publications, Presentations, Workshops


Translational


Behavioral


Trans-NIH Initiatives Related to Multilevel Obesity Research

NIH Active Initiatives

- OBSSR Systems Methods Initiatives
- NICHD/NIDDK School, Site-Specific, & Primary Care Interventions
- NHLBI Trans-Behavior Obesity RFA

NIH Upcoming Initiatives

- NICHD/NIDDK Multilevel Obesity Methods RFA; Policy PA
- NICHD Training Dev. Country (PA)
- NCI Geocentricity & Obesity (PA)
- NHLBI Behav Intervention Ctr RFA
- NHLBI Childhood Obesity Prev & Treat RFA
- NICHD Global Multilevel Centers RFA

NCI TREC
- Translational research (adults / children); obesity and cancer outcomes; training

NCI Economics & Obesity; Built Environment

TREC 2 RFA
- 2009
- 2010
- 2011
Where Does TREC Go Next?

TREC II
Recommendations – TREC II

- Elucidate underlying biological mechanisms of obesity and cancer, explore new biomarkers
- Explore potential for genetics/genomics to advance individualized treatment
- Expand translational research focus, particular emphasis on cancer survivors
- Strengthen use and integration of theoretical constructs
Recommendations – TREC II

- Establish Expert Consultants Committee
- Establish virtual and technical cores
- Expand career development
- Continue developmental projects
- Broaden network outside of TREC
- Actively synthesize and disseminate findings

TREC Expert Report, March 2009
Evaluation Plan

- Success establishing transdisciplinary collaborative research
- Success/impact of training
- Quantity/quality of publications and impact
- Level of utilization of shared resources
- Success obtaining new funding
- Long-term impact on policy and health
TREC II Renewal

- U54/U01 – Competitive Renewal
- $1.5 M/yr direct cost for 6 sites
  - Two new sites added
- Coordination Center - $1 M/yr direct cost for one award
  - External expert committee added
Acknowledgements

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