Transdisciplinary Research in Energetics and Cancer: Lessons Learned from a NCI Program Perspective.

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TREC
Transdisciplinary Research on Energetics and Cancer Centers

http://trecscience.org

Overweight, Obesity and Increased Cancer Risk

- Postmenopausal obese women have 1.5 times the risk of **Breast Cancer** than women of a healthy weight
- Studies have consistently found a link between **Renal Cell Carcinoma** and obesity in women
- Obese women have two to four times greater risk of **Endometrial Cancer** than healthy weight women

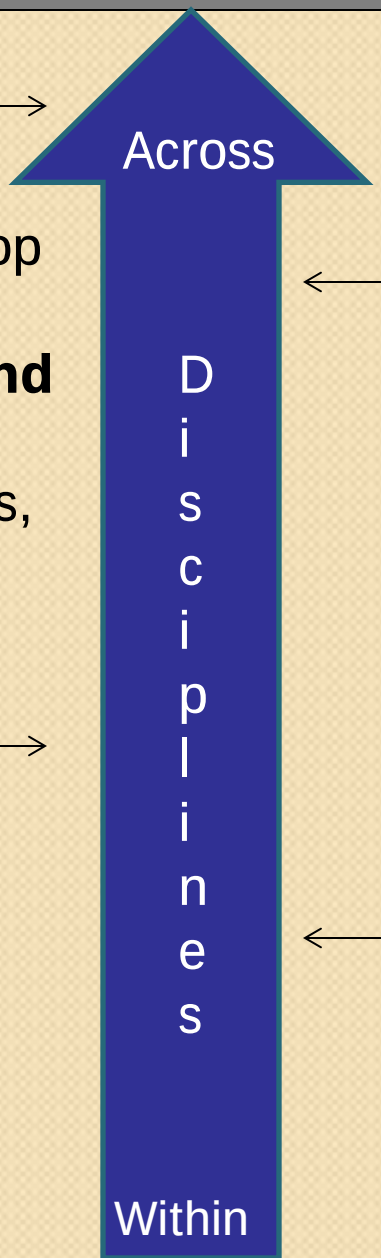
- Overweight and obese individuals are two times more likely than healthy weight people to develop **Esophageal Adenocarcinoma**; a smaller increase in risk has been found for **Gastric Cardia Cancer**
- An increased risk of **Colon Cancer** has been consistently reported for men with high BMIs
- An increased risk of **Gallbladder Cancer** is associated with obesity

Source: NCI: Obesity and Cancer (cancer.gov)

Why Transdisciplinary Approach?

A Continuum of Disciplinary Integration

Adapted from Rosenfield, 1992



Transdisciplinary

Researchers from *different disciplines work jointly* to develop and use a shared conceptual framework that **synthesizes and extends** discipline-specific theories, concepts, and methods, to create ***new approaches*** to address a common problem

Multidisciplinary

Researchers from *different disciplines work sequentially,* each from their own discipline-specific perspective, with a goal of eventually combining results to address a common problem

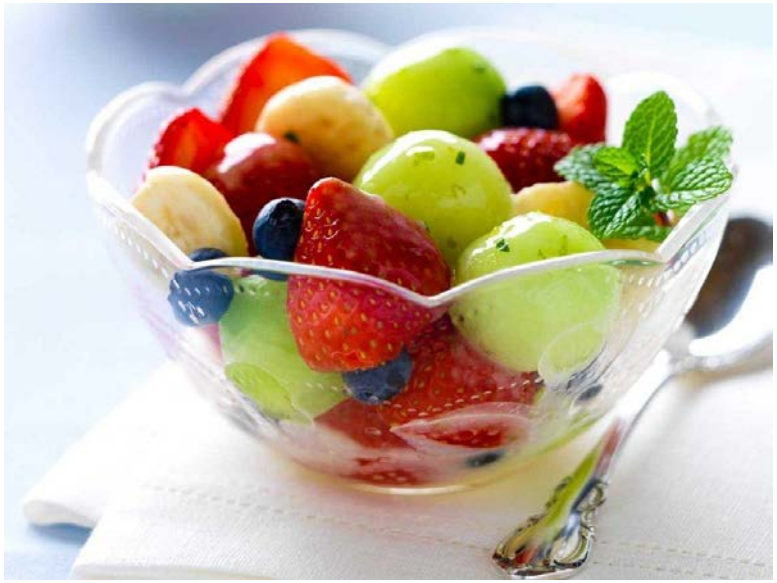
Interdisciplinary

Researchers from *different disciplines work jointly* to address a common problem. Some integration of perspectives occurs, but contributions remain anchored in their own disciplines.

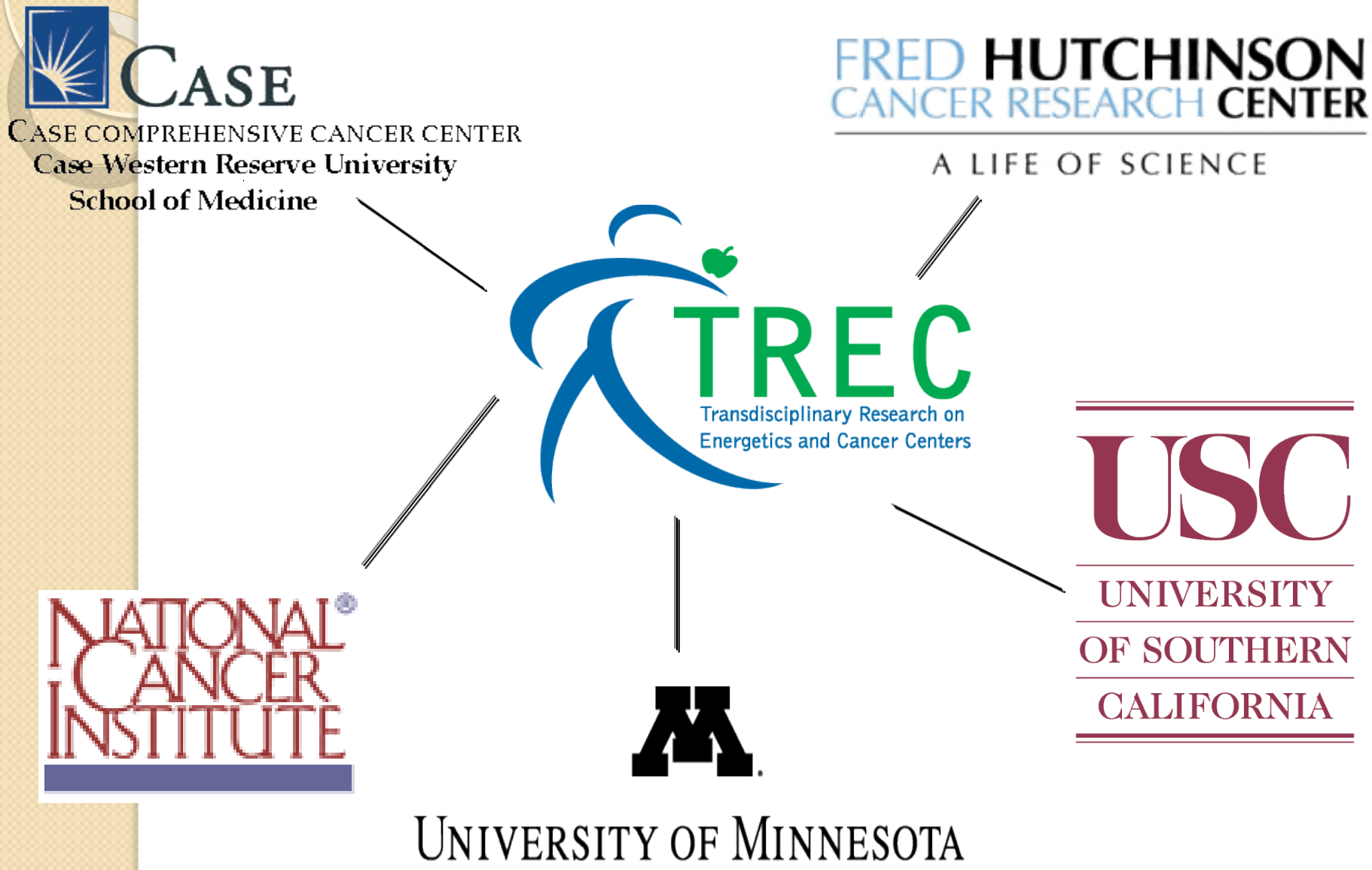
Unidisciplinary

Researchers from a *single discipline* work together to address a common problem

Salad or Smoothie?



TREC: 2005 - 2011



The Seattle Transdisciplinary Research on Energetics and Cancer Center

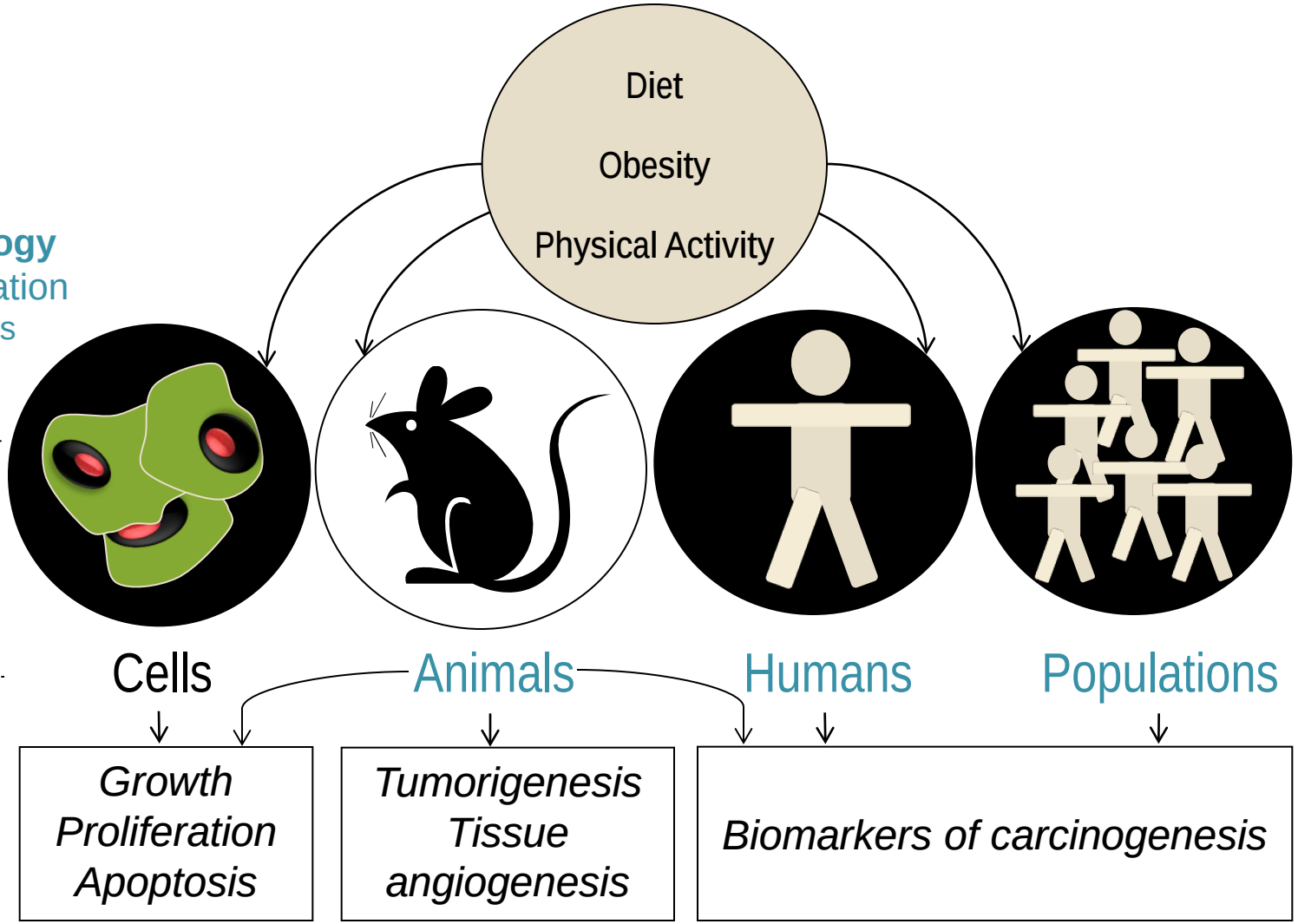
Exposures

Intermediate Biology

Glucose Inflammation
Insulin Adipokines
IGF

Models

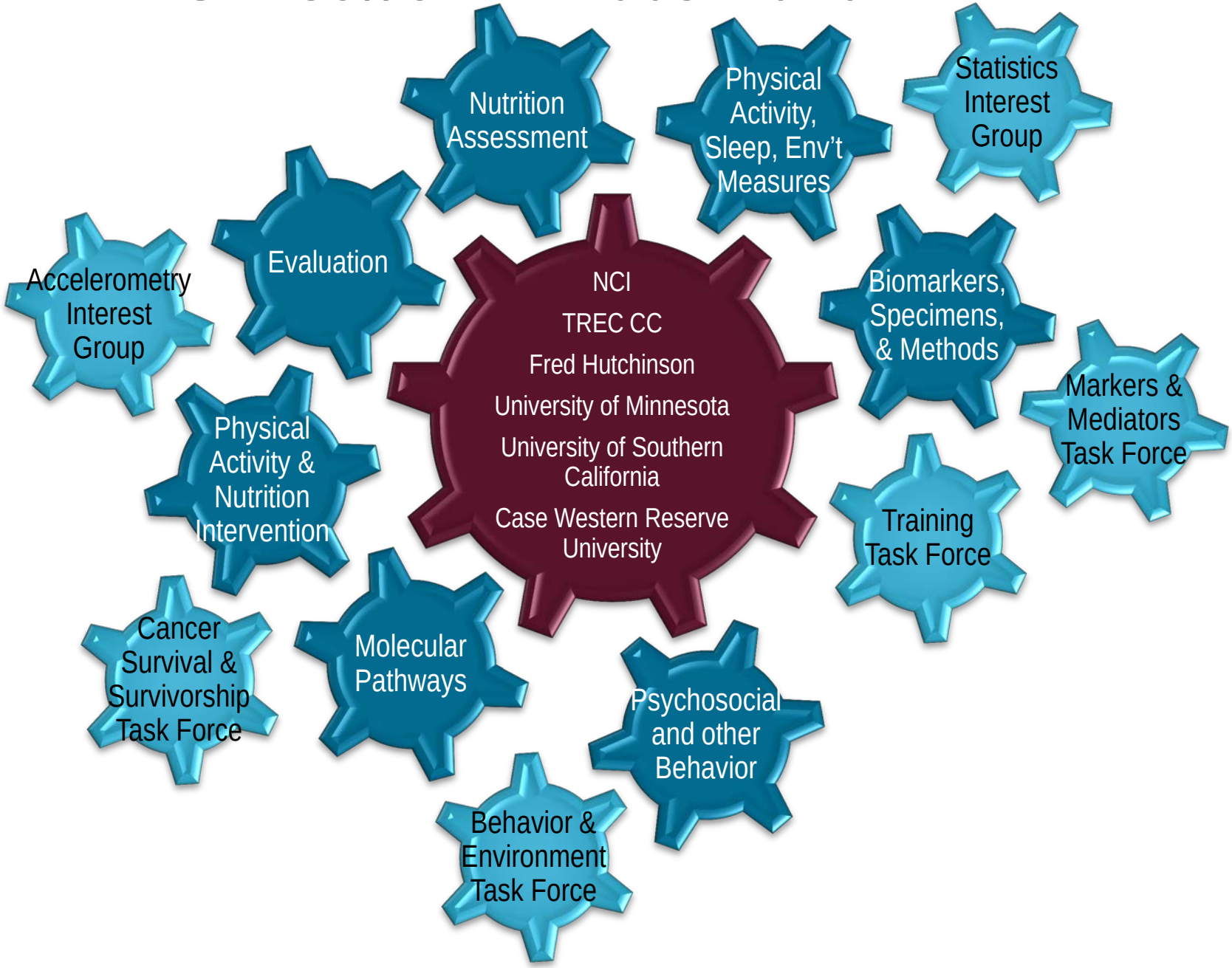
Outcomes



Common Elements in U54

- At each Center:
  - Center Director
  - 3-5 TD primary projects and Cores
- Opportunities for new TD research within/across centers
  - Meetings; developmental pilot projects
  - Cross-center working groups
  - Training opportunities

TREC Network – 2005-2010




Energy Balance and Cancer
Nathan A. Berger
Editor
Cancer and Energy Balance, Epidemiology and Overview
Human Molecular Genetics
Human Molecular Genetics Advance Access originally published online on May 19, 2009
Human Molecular Genetics 2009 18(16):2975-2988; doi:10.1093/hmg/ddp236
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Diet-induced hepatocellular carcinoma in genetically predisposed mice
Annie E. Hill-Baskin[1,†], Maciej M. Markie
Haifeng Shao[1,†], David DeS
Nathan A. Ber
Joseph H. Nade
THE INTERNATIONAL JOURNAL OF NUTRITION AND PHYSICAL ACTIVITY
The validation of a home food inventory
Jayne A Fulkerson[1], Melissa C Nelson[2], Leslie Lytle[2], Stacey Moe[2]
Keryn E Pasch[2]
1 School of Nursing, University of Minnesota, Minnesota, USA
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author email corresponding author email
International Journal of Behavioral Nutrition and Physical Activity 2008, 5:55
The electronic version of this article is the complete one and can be found onl
http://www.ijbnpa.org/content/5/1/55
Background
Home food inventories provide an efficient method for assessing h
validated. The present study's aim was to develop and validate a
completed by research participants in their homes and includes
less healthful foods that are associated with obesity.
nature REVIEWS CANCER
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Podcasts
Posters
Journal information
Guide to Nature Reviews Cancer
Review
Nature Reviews Cancer 8, 205-211 (March 2008) | doi:10.1038/nrc2325
Mechanisms linking physical activity with cancer
Anne McTiernan[1] About the author
top
About 25% of cancer cases globally are due to excess weight and a sedentary lifestyle. Physical activity may decrease risk for various cancers by several mechanisms, including decreasing sex hormones, metabolic hormones and inflammation, and improving immune function. The level of physical activity might also be associated with prognosis among individuals with cancer. Randomized clinical trials have shown that physical activity interventions can change biomarkers of cancer risk. Observational studies can also provide useful information on mechanisms that might link physical activity to cancer.

Research Objectives

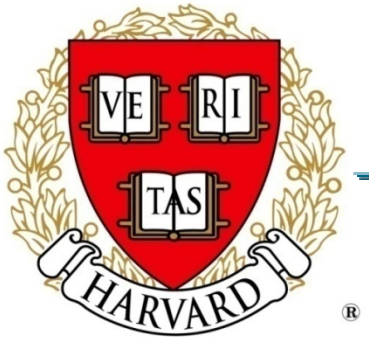
Elucidate underlying biological mechanisms of obesity as a risk factor for cancer

Integrate individual and social-environmental approaches to explaining and modifying energy balance-related health behaviors

Strengthen development, use and integration of validated measures and theoretical constructs

In 2011 - Expanded translational research focus with an emphasis on cancer survivors

TREC II: 2011 - 2016



Capacity for Cross-site Collaboration

Research Themes	Penn	Harvard	UCSD	WU-St.L
Assess multiple links btwn Obesity and CA (Breast, Prostate, Colon)				
- Genetics, genomics	X	X	X	X
- Behaviors: sleep, diet, PA	X	X	X	X
-Biological markers (insulin, IGF pathways, adipokines)	X	X	X	X
- Env't determinants, geospacial analysis	X	X	X	X
Application				
Biomarkers inform behavior research	X	X	X	X
Biological basis – Obesity and Cancer	X	X	X	X
Approach				
Develop theory-based interventions	X	X	X	X
Special Populations/Survivors	X	X	X	X

Penn TREC Survivor Center

Kathryn Schmitz, PhD, MPH, FACSM
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Dept of Biostatistics & Epidemiology
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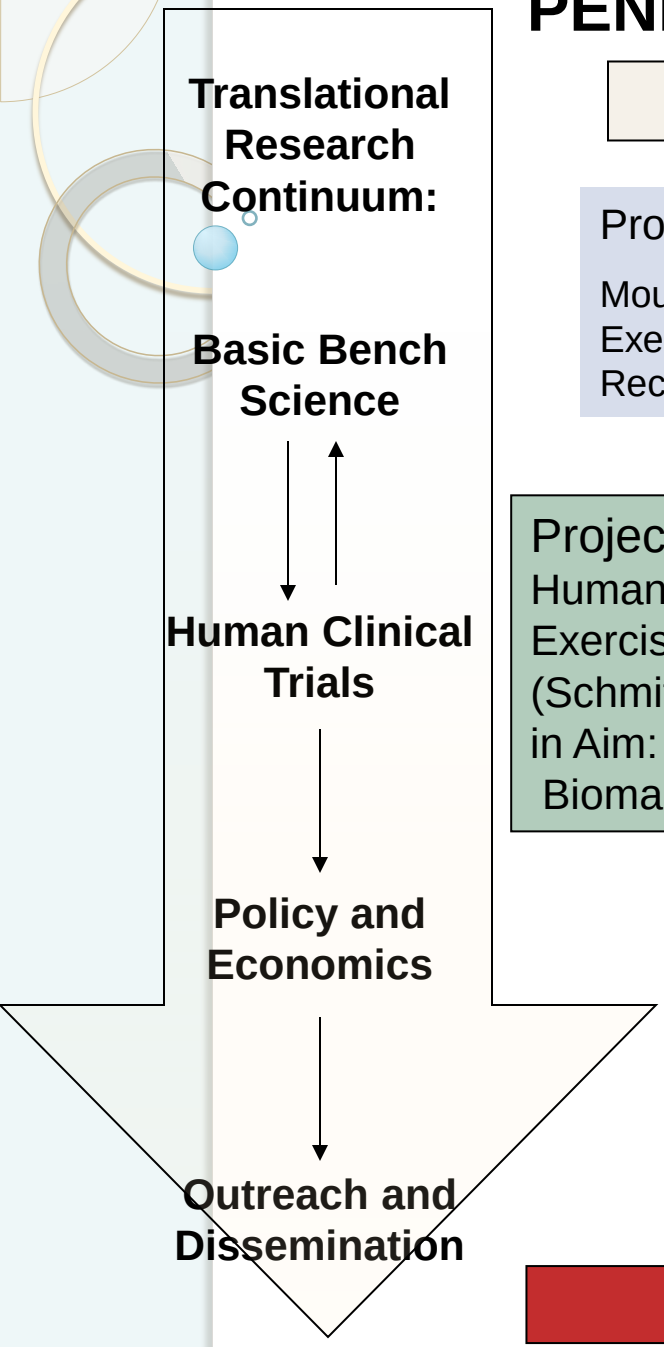
PENN TREC Challenges in Cancer Survivors



Recurrence risk

Persistent Adverse Tx Effects

Project 1:

Mouse Model Study of Exercise, Weight Loss, and Recurrence (Chodosh)

EDUCATION & TRAINING

DEVELOPMENTAL

Project 2:
Human Clinical Trial of Exercise & Weight Loss (Schmitz)
in Aim: Improve Recurrence Biomarkers

Aim: Improve Clinical Lymphedema Outcomes Breast Cancer Survivors

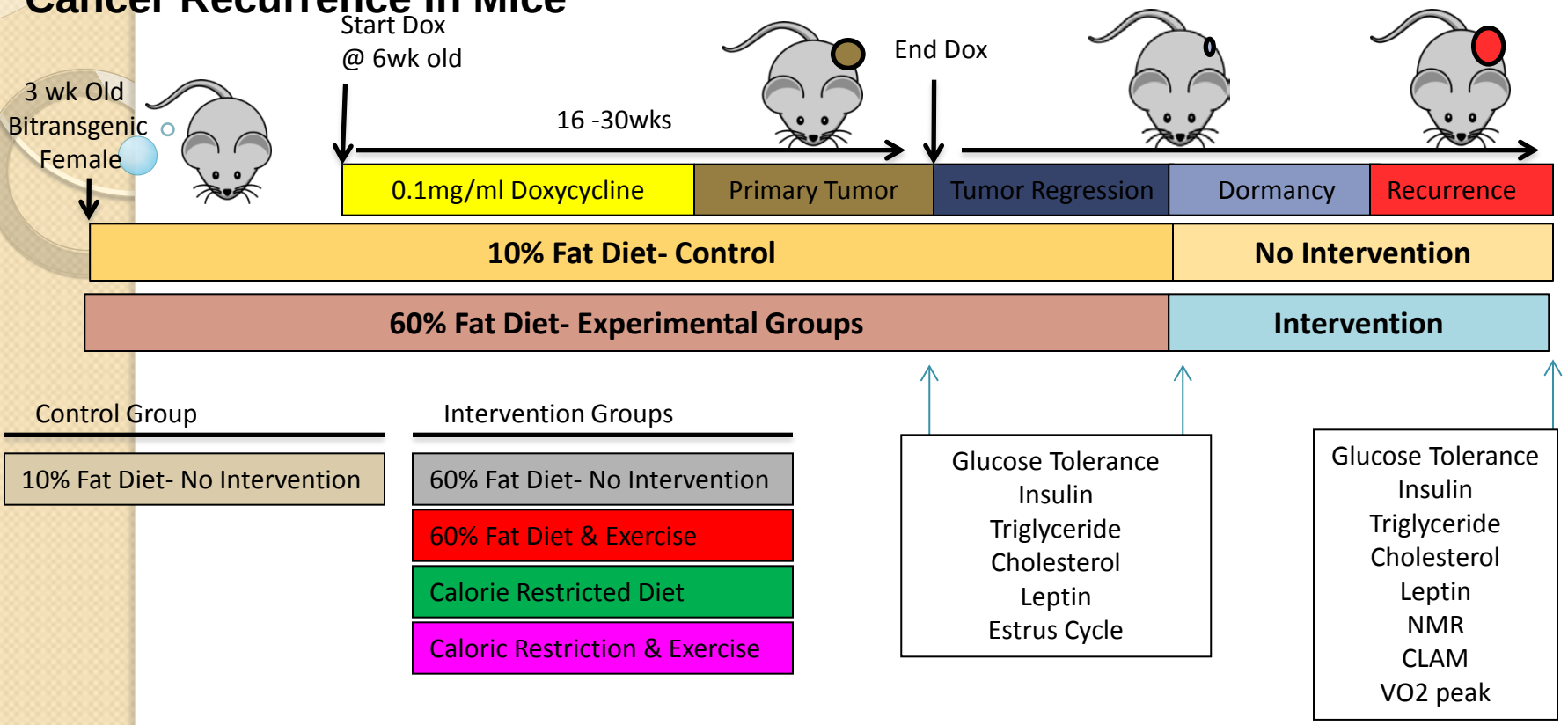
Project 3:

Cost Effectiveness Analysis of Exercise and Weight loss for Breast Cancer Survivors with Lymphedema (Schwartz)

Pilot

Outreach & Dissemination Activities

TREC Project 1: Impact of Exercise and Caloric Restriction on Breast Cancer Recurrence In Mice



Circulating Biomarkers

Insulin-IGF1 axis (Insulin, GTT)
Adipokines (leptin, adiponectin, HGF)
Sex steroids (E, T, SHBG)
Inflammation (IL-6, CRP, corticosterone)
Angiogenesis (platelet TSP-1)

Tumor/Tissue Biomarkers (Mammary gland, Tumor, MRD)

Proliferation, apoptosis
Vascular density
PI3K-Akt-mTOR
Adipokines (leptin, adiponectin, HGF/MET)

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Project 2: WISER Survivor

To assess the effects of one year of exercise, weight loss, or the combined intervention on:

- Aim 1
  - Clinical lymphedema outcomes
- *Aim 2*
  - *Circulating biomarkers for mechanistic pathways hypothesized to link energy balance with recurrence risk*
    - *Based on project 1*
- Aim 3
  - Quality of life outcomes

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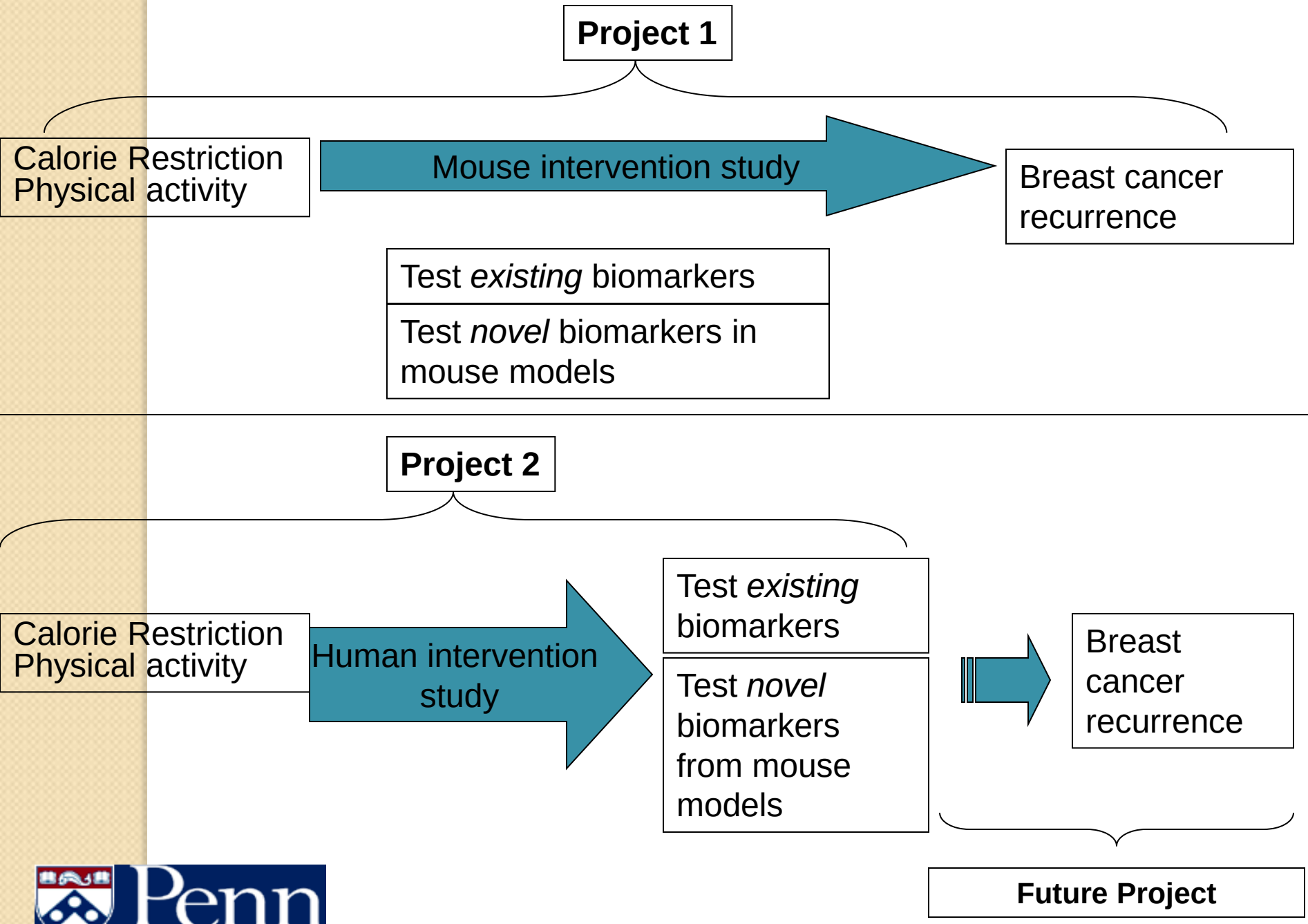
wiser Survivor
women in steady exercise research



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Project 3: Translation to Practice

- For exercise, weight control, or combined interventions to be applied broadly within the population of cancer survivors will require:
  - Knowledge of costs
  - Effective interventions
  - Cost effectiveness analysis
  - Infrastructural understanding

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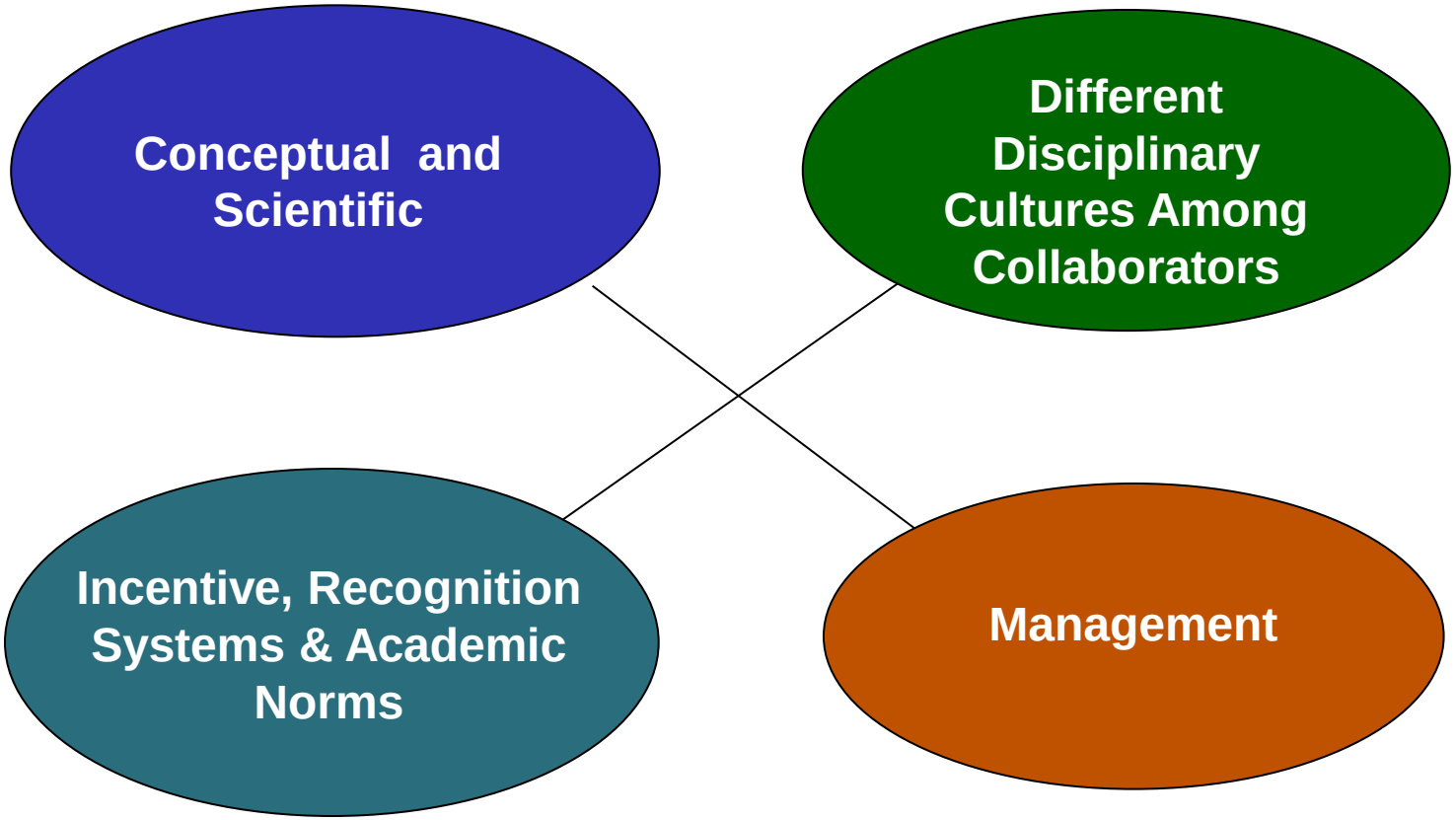
Reported Challenges in Transdisciplinary Collaboration



Challenges

- **Conceptual and scientific**
  - Forced to work outside of "comfort zone"
  - Lack of clarity about what TD is and how to get there
  - TD research is more complex – more variables, assays, larger sample sizes and complex endpoints
- **Need to learn a new "culture"**
  - Methods; terminology and work styles

Vogel A, et al, 2012

Challenges

- **Management challenges**
  - More scientific complexity but research is more time consuming and expensive
  - Large teams can be innovative but more complex to manage
  - Complex data harmonization

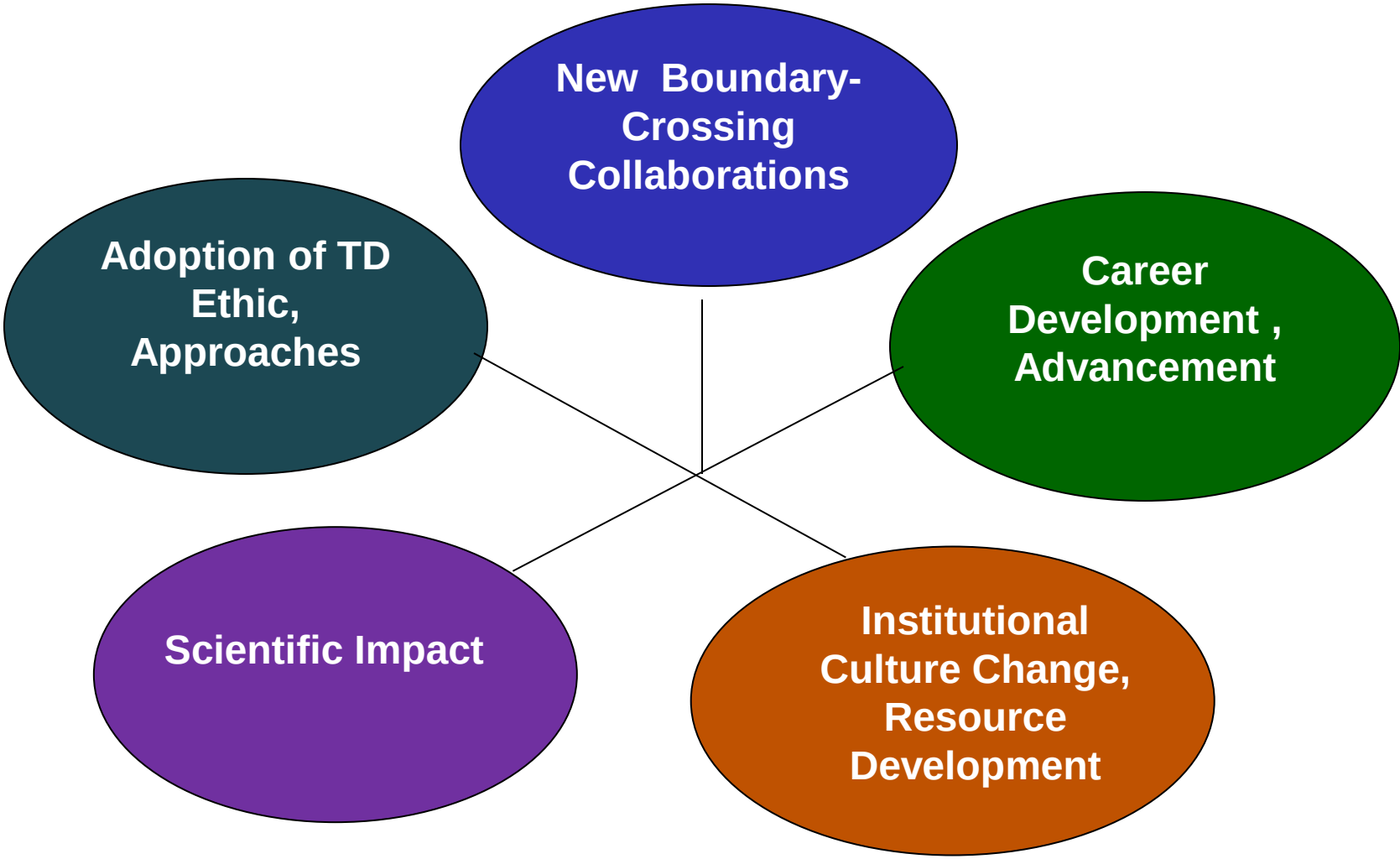
Vogel A, et al, 2012

Challenges

- **Academic incentive and recognition systems slow to evolve**
  - Lack of systems for cross-departmental, cross school collaborations.
  - P & T review may not adequately credit TS
  - Unclear where to publish TS, challenges with funding
  - Challenges with TD research influence across areas of career advancement &review.

Vogel A, et al, 2012

Impact of Participating in Transdisciplinary Research



Factors for Success

- **Create a TD Ethic**
  - Build awareness of strengths and weaknesses of disciplines
  - Recognize the scientific value added
  - Openness to exploring other areas of science
- **Team Processes**
  - Identify shared goals
  - Build trust
  - Develop mutual understanding and partnerships

Vogel A, et al, 2012

Impact from Participating

Reinforced TD ethic and approach, decrease in specialization

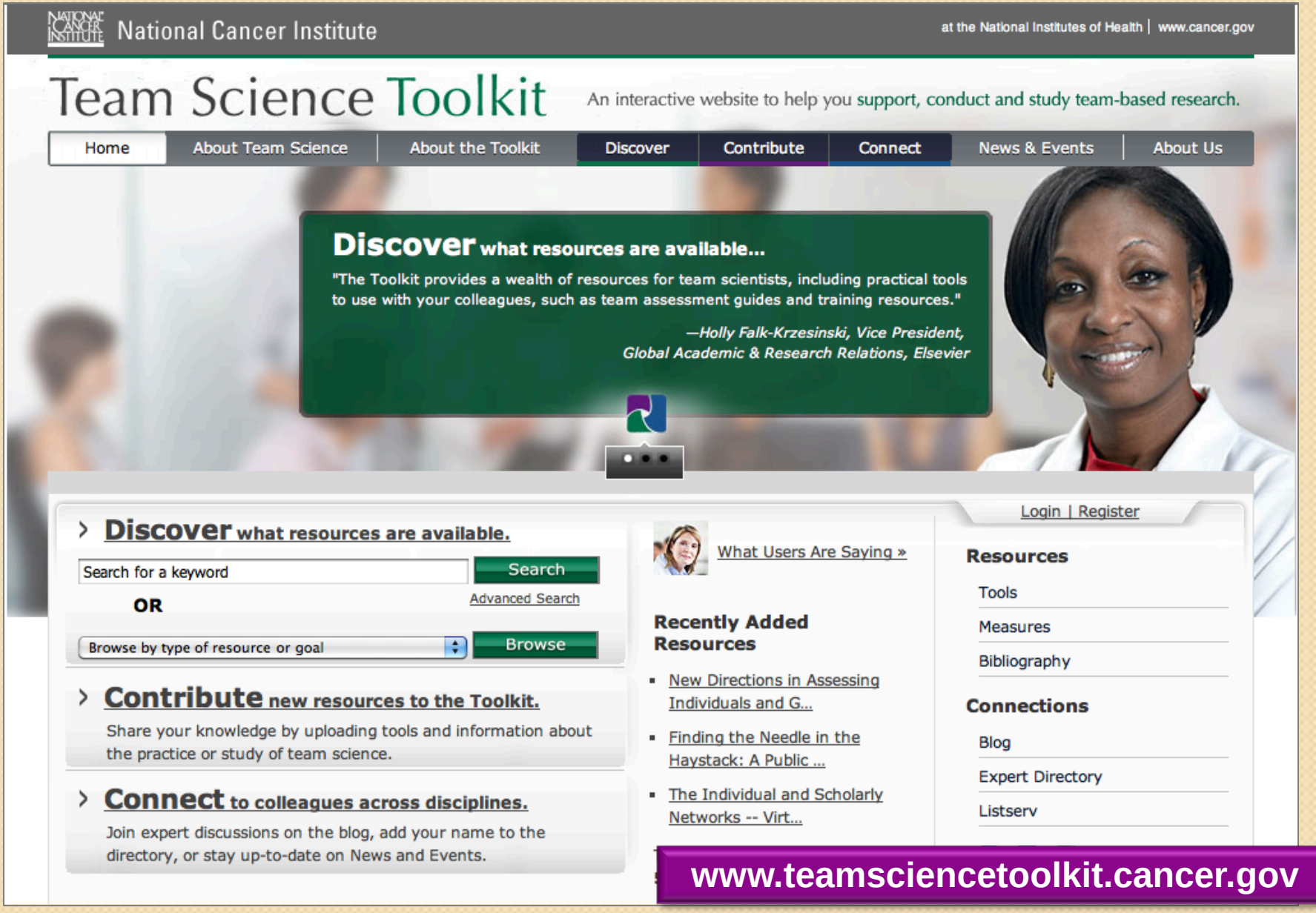
- Willingness to continue learning in other areas of science and apply concepts, theories and methods from other disciplines
- *"Transformed" their attitudes about TD research, their research approach*
- Plans to use TD approach in future research

Established new boundary-crossing collaborations

Career development and advancement

Greater support for TD research at institution: culture and resources

- Cross-disciplinary hiring, new courses in energetics and cancer
- New infrastructure for teamwork
- Inspired TD research elsewhere at institution, especially at the cancer center



The Team Science Toolkit is an interactive website that provides resources to help users support, engage in, and study team-based research.