Current and Future Perspectives on Cancer Prevention Research

National Cancer Advisory Board
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Phases of the Cancer Prevention Research Continuum

1. Hypothesis Development
2. Methods Development
3. Controlled Intervention Trials
4. Defined Population Studies
5. Implementation Projects

Research Training
Public and Professional Education

NCI Division of Cancer Prevention 2012
Example of the Cancer Prevention Continuum

Preclinical Program

Preclinical Efficacy
Biologic Rationale
Molecular Targets

Early Detection
Research Network

Phase I/II Trials
Safety
Preliminary Efficacy

Early Phase Trial
Consortia

Phase III Trials

CCOP Network

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Major Accomplishments

• Breast Cancer Prevention
  o Breast Cancer Prevention Trial (tamoxifen) (BCPT)
  o Study of Tamoxifen and Raloxifene (STAR)

• Prostate Cancer Prevention
  o Prostate Cancer Prevention Trial (finasteride) (PCPT)
  o Selenium and Vitamin E Cancer Prevention Trial (SELECT)

• Cancer Screening Trials
  o Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO)
  o National Lung Screening Trial (NLST)

All have biorepositories in use for hypothesis testing.
Future Scientific Directions

• Agent Development and Decision Making
• Overdiagnosis and Precancerous Lesions
• Cancer Immunoprevention
• Role of Microbiota
• New Approaches to Clinical Prevention Studies
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Agent Development and Decision-Making (1)

• Development of Promising Agents Based on Clinical Need

• Transparent Agent Review & Prioritization Process
  PREVENT Cancer Program, modeled after DCTD’s NExT Program
  - External Steering Panel (Leaders from Academia and Pharma)
  - External Special Emphasis Panel (Review)
  - Management & Administration Committee (DCP & DCTD experts)

• Preclinical Drug Development
  - Predetermined Decision Gates (Go/No-Go)
  - Hand-off to Early Phase Clinical Development

- **Determine Which Preclinical Models Predict Clinical Outcome** (Positive & Negative Predictive Values)
  - Evaluate Efficacy of Cancer Preventive Agent Development in Preclinical Models in Relation to Clinical Data

- **Back Validate Successful Clinical Trials in Collaboration with DCB’s Mouse Models for Human Cancers Consortium (MMHCC)**
  - DCP participates in MMHCC Prevention Subcommittee (DCB)
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Overdiagnosis and Precancerous Lesions (1):
Early Detection Research Network

- Biomarkers developed & tested for pancreatic, lung, prostate, ovary & liver cancers (>300)
- 8 Validation studies in progress; 4 FDA-approved markers
- Standard Reference Samples (serum & plasma) to test emerging biomarkers
- Collaborations
- Biomarker Database
- Biomarker plus Imaging Studies (DCTD)

Network Consulting Team
Biomarker Development Laboratories
Biomarker Reference Laboratories
Clinical Validation Centers
Steering Committee
Data Management & Coordinating Center

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Molecular Characterization of Overdiagnosis & True Interval Cancers from Existing Screening Programs

Overdiagnosis & Interval Cancers Think Tank

Barrett’s Esophagus Translational Research Network (BETRNet) (DCB)

Proposed: The Genome Atlas for preCancers (TGAC) (DCB)
  - Risk Stratification
  - Driver Mutations
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Cancer Immunoprevention

• Infectious Causes of Cancer
  ○ Human Papilloma Virus, Hepatitis C Virus, etc.
    (NCI Center for Global Health, DCB, DCEG and NIAID)

• Non-Infectious Tumor Antigens
  ○ Carcinoembryonic Antigen (CEA), Mucin 1 (Muc1), Human Epidermal Growth Factor Receptor 2 (Her2/neu) etc.
    (CCR, DCB)
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Role of Microbiota

- Study prevention interventions (agents, vaccines, diet) as modifiers of the balance of microorganisms in the body
  - Energy Exchange
  - Inflammation & Immunity
  - Dietary Choices
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New Approaches to Clinical Prevention Studies

- Repurposing Commonly Used Drugs For Cancer Prevention
  - NSAIDs (including aspirin), statins

- Using Non-cancer Disease Trials To Detect Cancer Prevention Signals
  - Metformin studies at NIDDK
  - Lutein/omega-3 fatty acid study at NEI

- Reciprocal Control Trials With Other Institutes/Centers
  - NHLBI
New Approaches to Clinical Prevention Studies

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- National Clinical Trials Network and CCOP Network Continue as Effector Arm for Implementing Large Trials
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DCP Controlled Funding FY 2011

- CCOPs & R&D Support ($94.7 M)
- Salaries & Other Objects ($17.3 M)
- PREVENT Cancer Program & R&D Support ($16.5 M)
- Nutrition Science ($1 M)
- Early Phase Consortium ($6.8 M)
- PLCO & NLST ($6.7 M)
- BETRNet RFA ($2.2 M)
- EDRN IAAs ($2 M)
- Other R&D (SAIC, Westat, PIO, Biometry, etc) ($10.2 M)

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