Role of Prevention Research in DCEG

National Cancer Advisory Board

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Prevention Research Continuum

**Etiology**
- Tobacco
- Physical inactivity, diet, and obesity
- Infectious agents
- Radiation
- Occupational carcinogens
- Hormones
- Genetics

**Prevention**
- HPV vaccine trial
- Melanoma screening
- Genetic risk prediction
- Radiation
- Nicotine addiction
- Occupational exposure dose response and threshold levels

**Implementation**
- HPV screening recommendations and management guidelines
- Lung cancer screening guidelines
- Radiation protection guidelines
DCEG Examples that Span the Prevention Continuum

- HPV
- Tobacco
- Obesity
- Radiation
HPV Etiologic Studies

• HPV natural history

• Established HPV as necessary cause of cancer of the cervix

• Risk of cancers of the oral cavity, anus, and other sites

HPV Prevention Research

• HPV vaccine trial
• One dose vs. two doses vs. three doses
• Protection against anal and oral HPV infections
• Long-term follow-up

Kreimer AR, et al. JNCI 2011
HPV Implementation Research

- Screening guidelines
- Clinical management guidelines

Gage JC, et al. *JNCI* 2014
Tobacco

• NIH-AARP cohort
• Smoking & second cancer risk
• Smokeless tobacco
• New & emerging tobacco products
• Screening guidelines

Freedman ND, et al. *JAMA* 2011
Shiels MS, et al. *JCO* 2014
Carter BD, et al. *NEJM* in press
Radiation Exposure

• Medical radiation exposures
  • Diagnostic and screening procedures (low dose)
  • Radiotherapy treatments (high dose)
  • Occupational (repeated low dose)

• Environmental (nuclear testing, nuclear power plant accidents)

• Etiology of radiosensitive malignancies

Zablotska LB, et al. *Env Health Persp* 2013
Role of DCEG in Prevention Research

• Focus on foundational, etiologic research

• Randomized prevention trials as outgrowth of etiologic work
  • HPV
  • Chinese Nutritional Intervention Trial

• Observational studies can be critical when trials not feasible/ethical
  • Radiation
  • Chemical carcinogens
Mission

To accelerate progress in human health by helping to establish a common framework of harmonized approaches to enable effective and responsible sharing of genomic and clinical data, and by catalyzing data sharing projects that drive and demonstrate the value of data sharing.
Goals of the BRCA Challenge

1. Synchronize BRCA data in federated public database
   • Existing and future data
2. Review existing variants
   • Curate reference list
3. Create an API for display of annotated variants
4. Create a template for other genes
Coordinated Activities

1. Data Collection
   - Evidence Group
   - Variant Classification Group

2. Interpretation of Variants

3. Community Engagement and Regulation
BRCA 1/2 Variants in Public Databases

NCBI ClinVar database:
6431 variants

LOVD Databases:
3262 variants

French Universal Mutation Database: 3913 variants

GOAL:
Expand to include ENIGMA, CIMBA, & other data sets from around the world
2 ‘Views’ of Variant Classification

Scientific
- Pathogenic
- Likely pathogenic
- Variant of Uncertain Significance
- Unlikely pathogenic
- Non-pathogenic

Clinical
- Manage as pathogenic
- Manage as not pathogenic
- Custom management
These data stores may be country or project or lab specific.
Deliverables

1. Display population-based allele frequencies using available sequencing resources
   - Prototypes being tested

2. Federated collection of Pathogenic Variants for BRCA1/BRCA2
   - In development

3. Improve penetrance estimates
   - Long-term goal
BRCA Challenge Steering Committee

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