National Cancer Institute

Biospecimen Resources for Population Scientists for Cancer Research

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Overview of Presentation

- Why Biospecimens?
- What Resources Are Available?
  - Help to Design Your Study
  - Biospecimen Sources
- How Can These Resources Help You?

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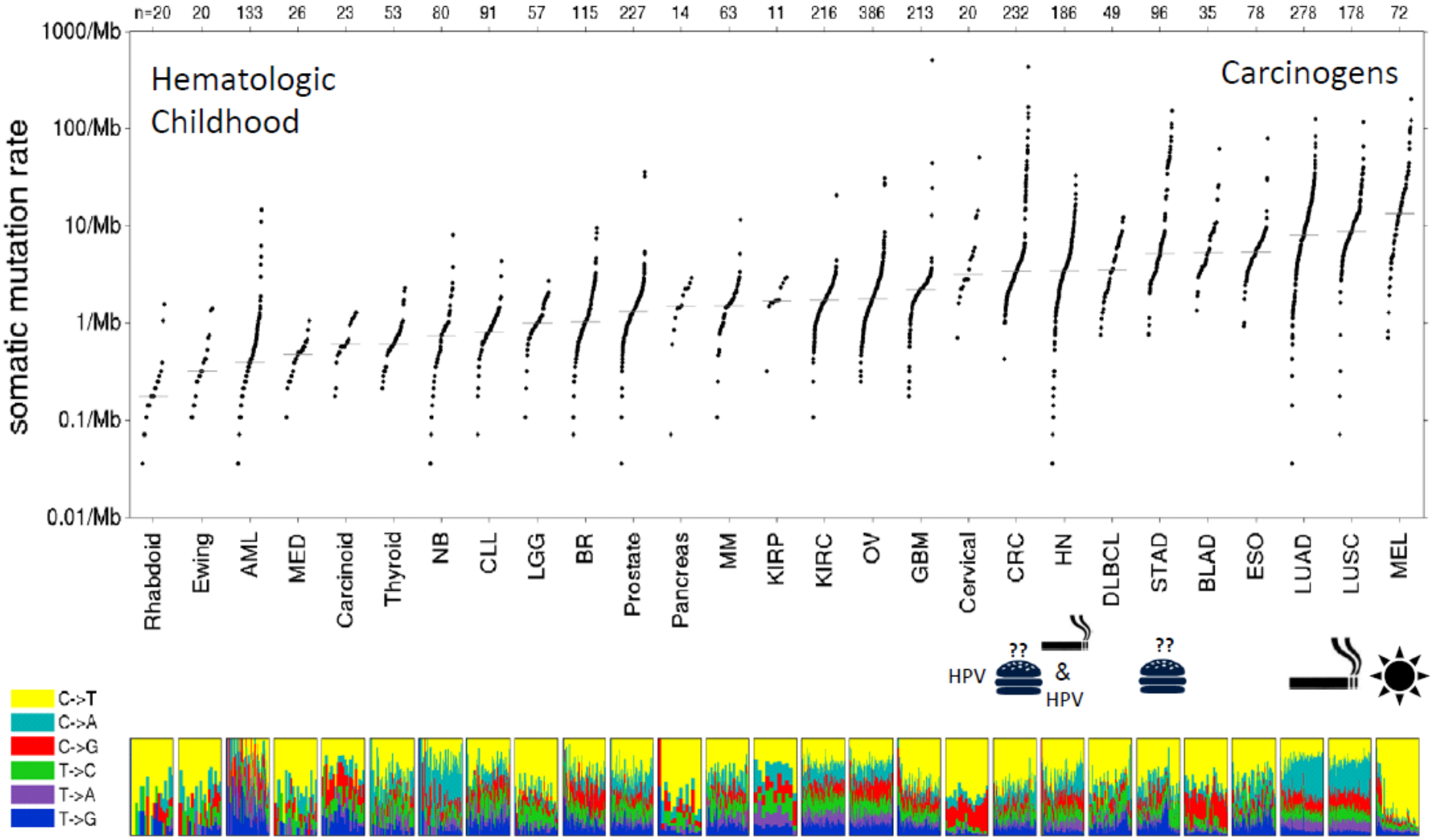
Why Biospecimens?

- Understand disease etiology
- Identify susceptible subgroups
- Select most appropriate treatments
- Develop effective screening methodologies

Somatic Mutation Rates Across Cancer Types

The Cancer Genome Atlas

(http://cancergenome.nih.gov/)



http://www.genome.gov/multimedia/slides/tcga1/tcga1_lawrence.pdf

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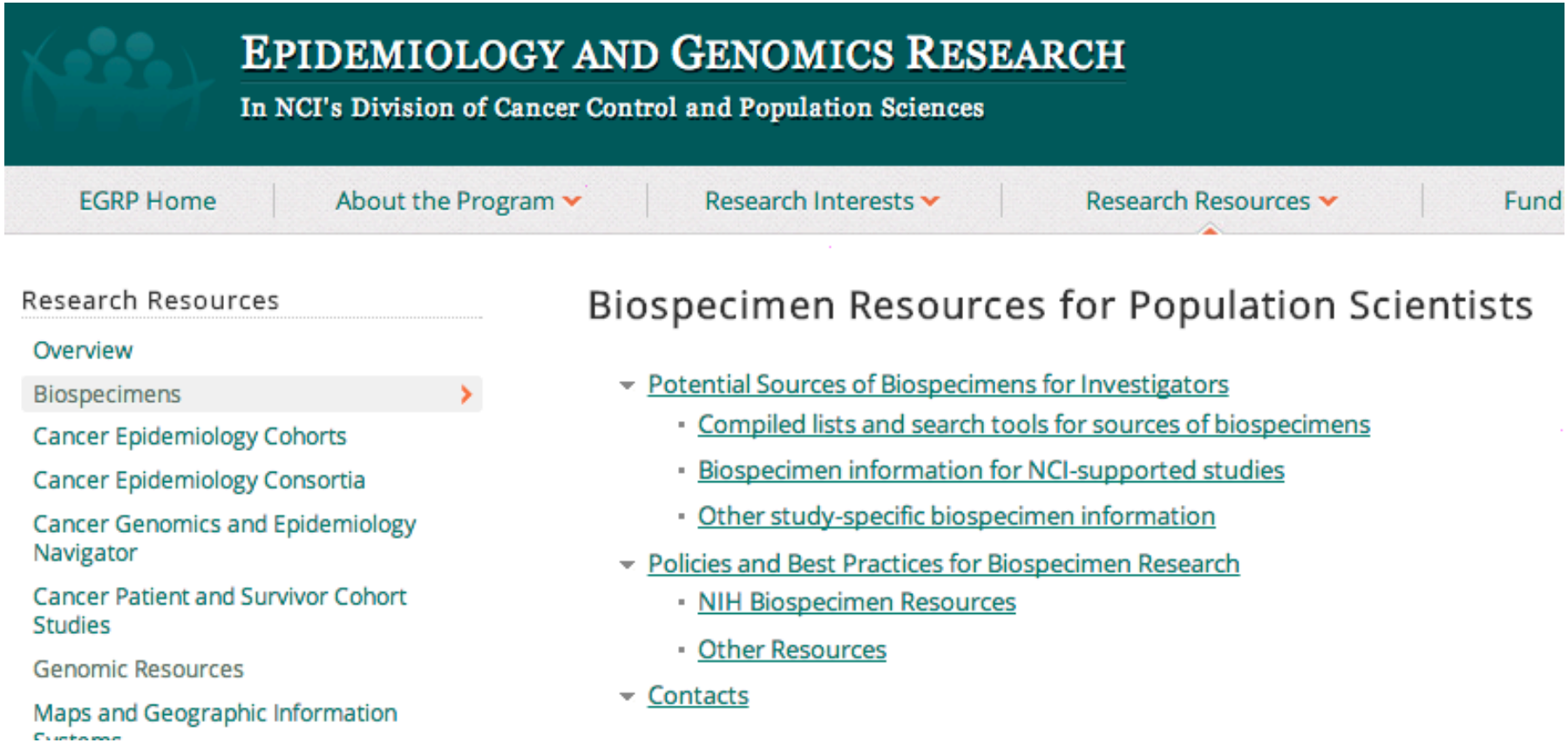
Biospecimen Resources for Population Scientists

http://epi.grants.cancer.gov/biospecimens.html



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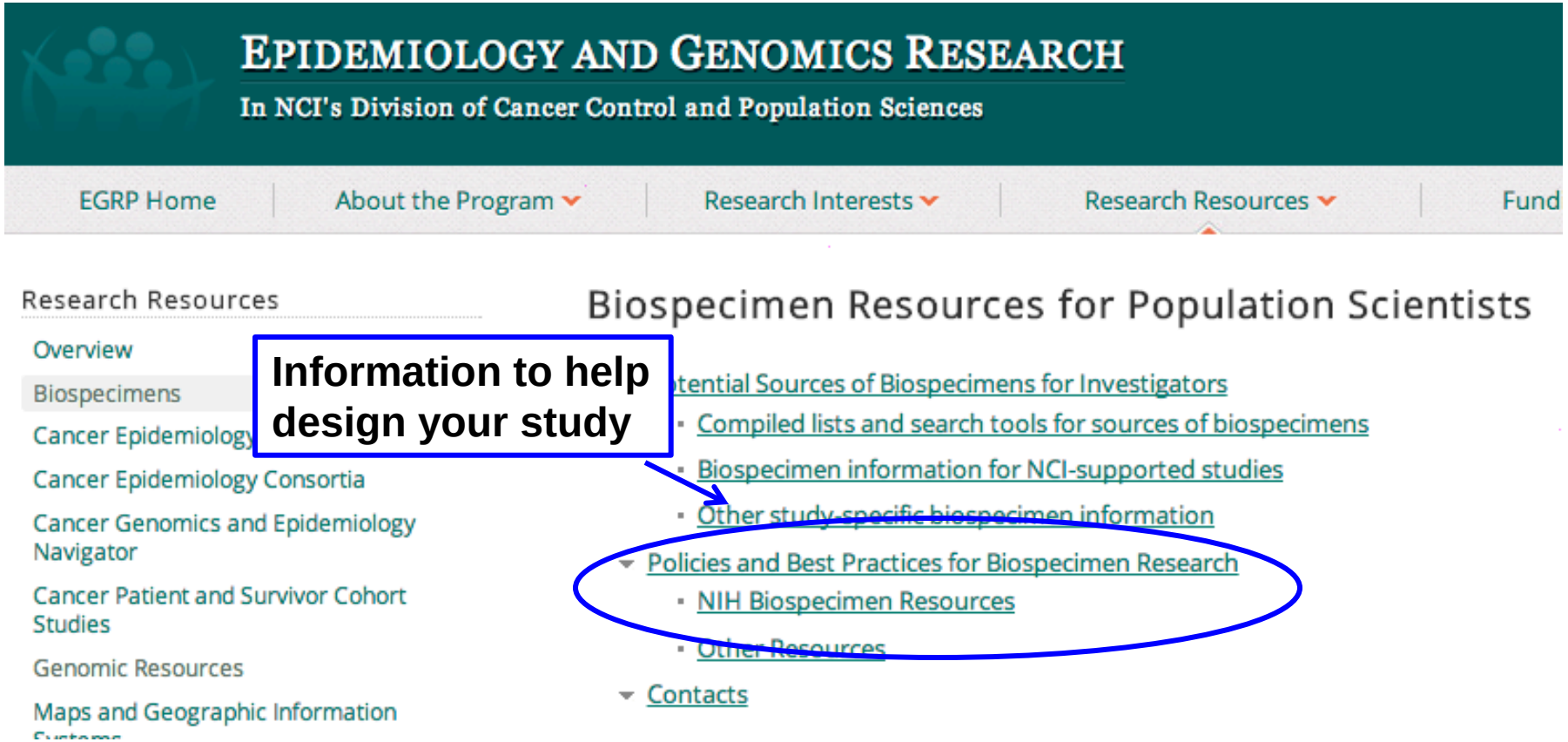


NCI Best Practices for Biospecimen Resources

(http://biospecimens.cancer.gov/bestpractices/)

ALERT: After an extensive process and the inclusion of feedback from the public comment period, the National Cancer Institute (NCI) is pleased to release the 2011 Best Practices for Biospecimen resources Learn more.

One of the most widely recognized and significant roadblocks to progress is cancer research is the lack of standardized, high-quality biospecimens. The National Cancer Institute (NCI) developed the NCI Best Practices for Biospecimen Resources (NCI Best Practices) based on extensive research and expert input into the state of NCI-funded biospecimen resources and the quality of biospecimens used in cancer research. The NCI Best Practices outline the operational, technical, ethical, legal and policy best practices for NCI-supported biospecimen resources.

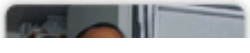
Scope, Applicability, Implementation

The NCI Best Practices incorporate key principles that:

- define state-of-the-science biospecimen resource practices
- promote biospecimen and data quality
- support adherence to ethical and legal requirements

The NCI Best Practices define principles to guide procedures developed by biospecimen resources. They are intended to be adapted based on the mission and scientific needs of biospecimen resources. While adoption of the NCI Best Practices is voluntary, the NCI believes that these principles optimize biospecimens for cancer research. Learn more

Technical and Operational Best Practices



Although the specific mission of a biospecimen resource will define its

Standard Operating Procedures

(http://biospecimens.cancer.gov/resources/sops/)

Biospecimen Resources for Population Scientists

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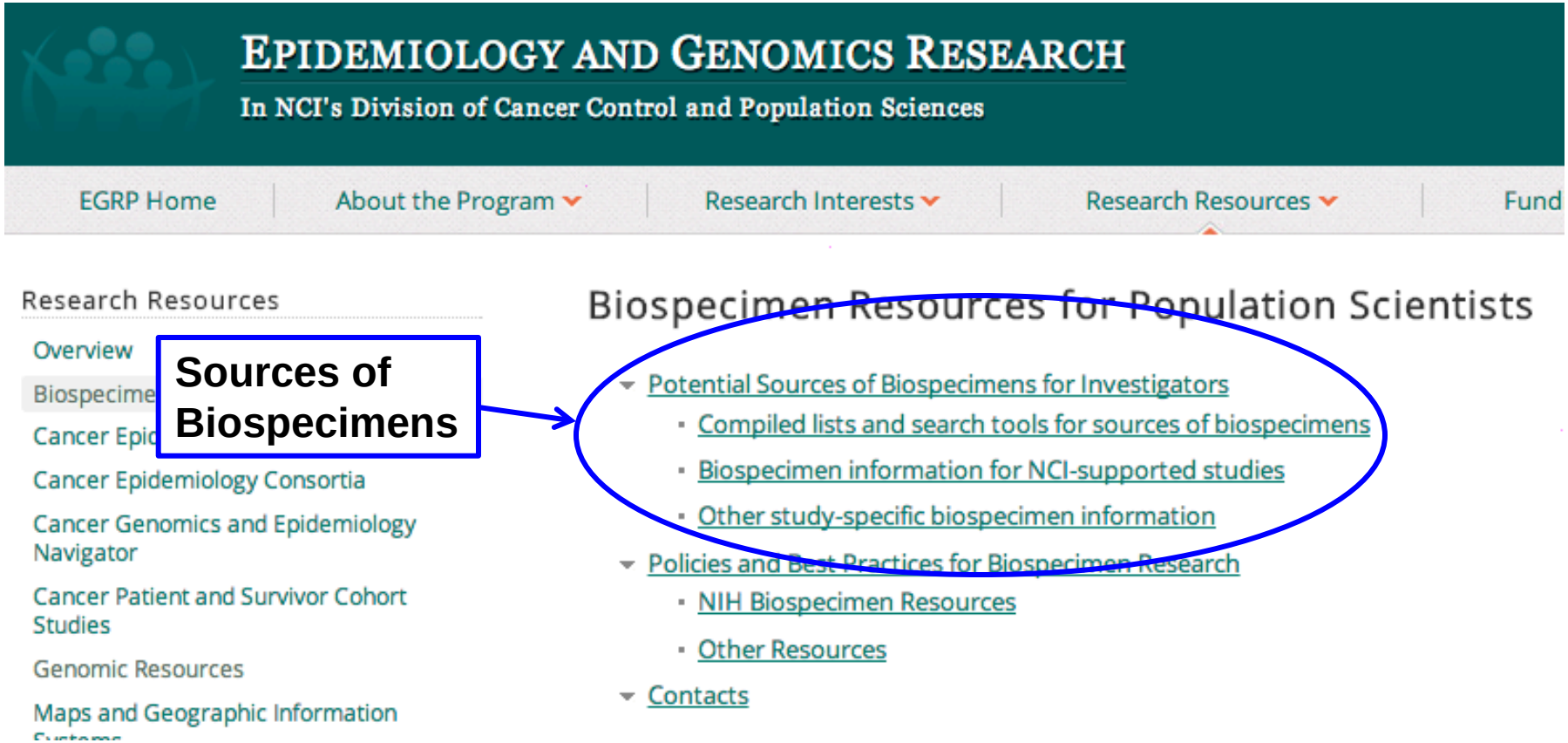
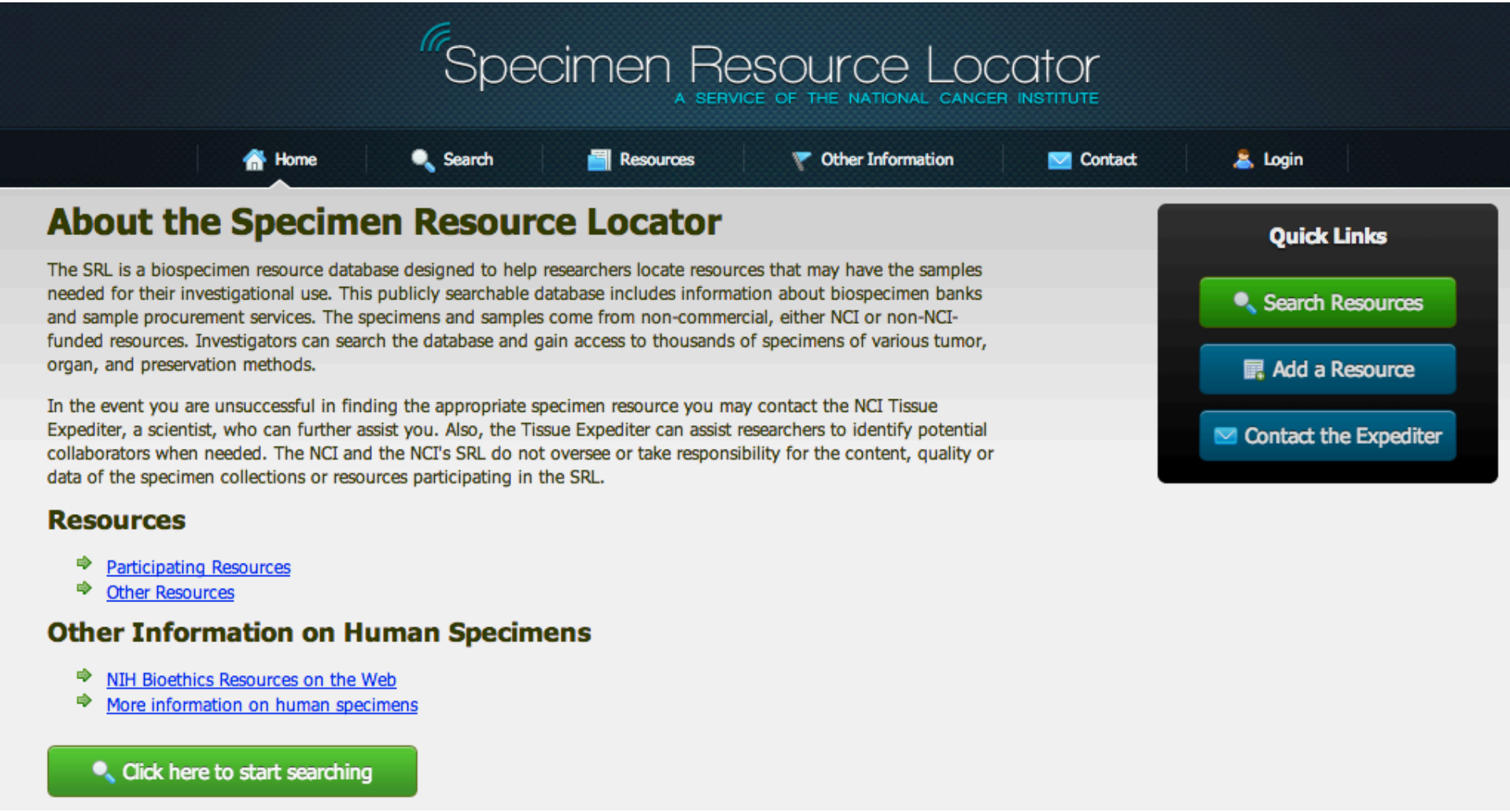


Specimen Resource Locator
(https://specimens.cancer.gov/)



- More Population Based Resources Coming Soon to SRL

Example NCI Supported Studies

- Agricultural Health Study (AHS)
- AIDS and Cancer Specimen Resource (ACSR)
- Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC)
- Atherosclerosis Risk in Communities Study (ARIC) Cancer
- Breast and Colon Cancer Family Registries (CFRs)
- Carotene and Retinol Efficacy Trial (CARET)
- Cooperative Breast Cancer Tissue Resource (CBCTR)
- Cooperative Human Tissue Network (CHTN)
- Health Professionals Follow-Up Study (HPFS)
- The Nurses' Health Study (NHS)
- Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial
- Southern Community Cohort Study (SCCS)
- Southwest Oncology Group (SWOG) – Prostate Cancer Prevention
- SEER Residual Tissue Repository (RTR) Program

http://epi.grants.cancer.gov/biospecimens.html

Colon Cancer Family Registries (CFR)

- Resource for conducting studies on the genetics and molecular epidemiology of colon cancer
  - >41,000 men and women from 14,500 families
  - DNA, tissue sections, lymphocytes, lymphocyte cell lines, plasma
- Contact Principal Investigators to initiate collaborations

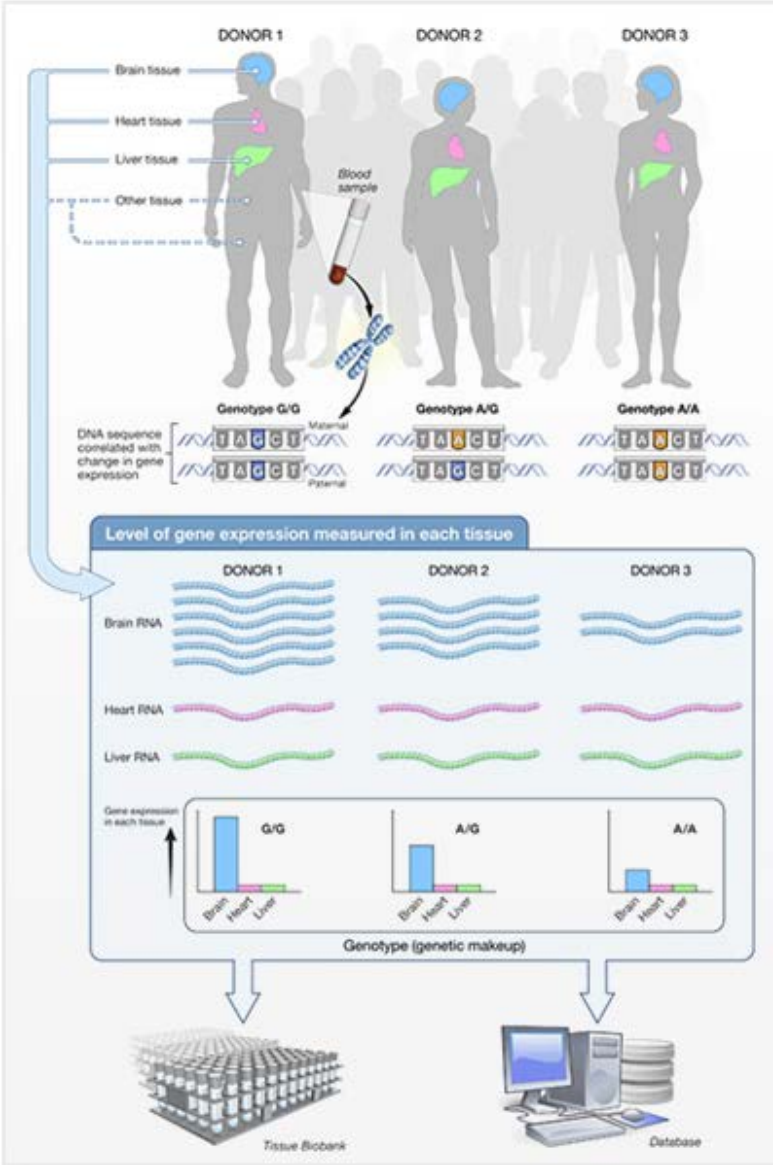
For more information about the Colon CFR:
http://epi.grants.cancer.gov/CFR/about_colon.html

Cancer Research Network (CRN)
(http://crn.cancer.gov/)

- Goal to facilitate cancer research in non-profit health care delivery setting
  - Supports data and research infrastructure for 9 CRN sites (9 million members)
- CRN Encourages Collaboration
  - Scientific Working Groups
  - CRN Scholars Program
  - Pilot and Developmental Projects Program
  - Data Inquiry and Proposals
- NCI Contact: Paul Doria-Rose (doriarop@mail.nih.gov)

CRN CANCER RESEARCH NETWORK

Genotype-Tissue Expression Project (GTEx) (http://www.broadinstitute.org/gtex/)



- Data resource for study of genetic variation and regulation of gene expression in multiple reference human tissues
- Biospecimen resource including tissues, nucleic acids, and cell lines
- > 185 donors and ~9-30 tissues collected per donor

DCCPS GTEx Contact:
Danielle Carrick (carrick@mail.nih.gov)

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Leveraging Existing Resources Is More Efficient

DCCPS Biospecimen Portfolio (Active Grants July 2012)

Estimated cost per/participant (based on target enrollment)

Grant Mechanism	Using Existing Biospecimens	Using Existing and Collecting New	Collecting New Biospecimens	P-value
All mechanisms	$362	$699	$1508	P<0.0001
R01	$262	$647	$926	P<0.0001

Limited to grants with serum/plasma (N=183)

Average number of publications/year

Grant Mechanism	Using Existing Biospecimens	Using Existing and Collecting New	Collecting New Biospecimens	P-value
All mechanisms	2.1	2.9	1.5	P=0.0005

All biospecimen grants (N=455)

Carrick et al., under review

Example of Leveraging Existing Resource
Association of Circulating Cytokines with Lung Cancer

Cytokine Level		NCI-MD Case-Control Study OR (95% CI)	PLCO Nested Case-Control OR (95% CI)
IL-6			
	1st quartile	1.0	1.0
	2nd	0.98 (0.51-1.86)	1.14 (0.79-1.65)
	3rd	2.28 (1.29-4.06)	1.25 (0.88-1.78)
	4th	3.29 (1.88-5.77)	1.48 (1.04-2.10)
IL-8			
	1st quartile	1.0	1.0
	2nd	1.48 (0.84-2.63)	1.03 (0.72-1.48)
	3rd	2.62 (1.52-4.51)	1.41 (0.99-2.01)
	4th	2.44 (1.46-4.08)	1.57 (1.10-2.24)

Adjusted ORs and CIs are reported.

Pine et al. J Natl Cancer Inst (2011) 103 (14): 1112-1122.

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Contact Information

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Thank you

Extra Slides

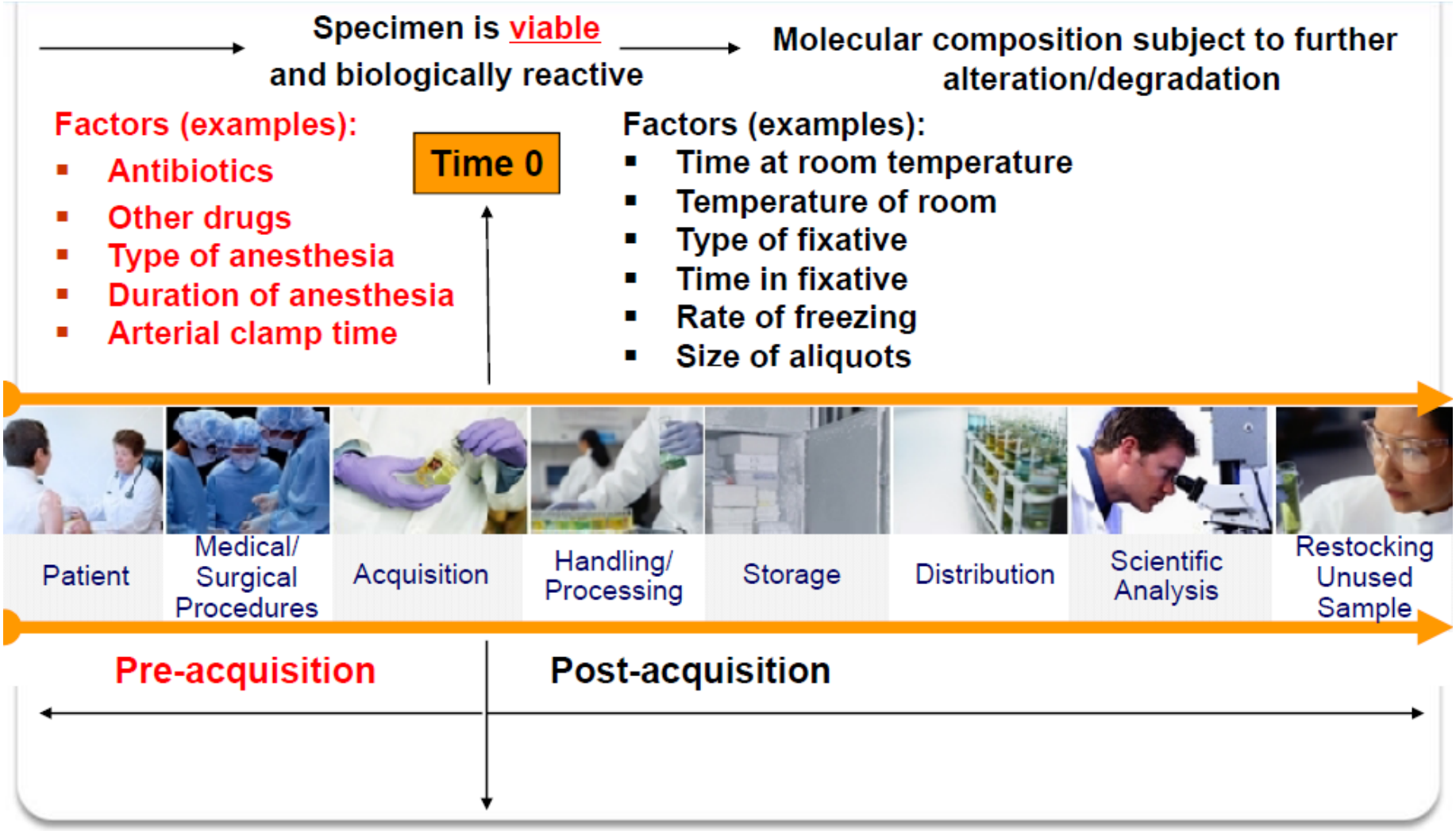
DCCPS Breast and Colon Cancer Family Registries

http://epi.grants.cancer.gov/CFR/about_breast.html
http://epi.grants.cancer.gov/CFR/about_colon.html

Sample Type	B-CFR # of Individuals	C-CFR # of Individuals
Genomic DNA	22,952	31,413
Tissue sections on slides	5,318	8,722
Slow-frozen lymphocyte cells	11,704	22,928
Plasma	16,119	24,694
LCL (lymphoblast cell line)	8,556	4,718

Sheri D. Schully, Ph.D (schullys@mail.nih.gov)

Pre-analytical Factors Can Affect Biomarkers



Tissue types

(#s are as of Sept. 2012)

- Blood (PAXgene RNA) (n=149)
- Skin for fibroblast cell line (~90% success)
- Blood (ACD) for lymphoblastoid cell line (~60% success)

PAXgene* Preserved Tissues

- Adipose - SubQ and Visceral (n= 144;17)
- Adrenal Gland (n=107)
- Artery – Aorta (n=133)
- Artery – Coronary (n=97)
- Artery – Tibial (n=142)
- Bladder (n=121)
- Breast - Mammary Tissue (n=87)
- Cervix – Ecto- & Endocervix (n=32;34)
- Colon – Transverse & Sigmoid (n=144;15)
- Esophagus - Gastroesoph Junction, Mucosa, & Muscularis (n=16;139;140)
- Fallopian Tube (n=32)
- Heart – Atrium & Left Ventricle (n=12;116)
- Kidney – Cortex & Medulla (n=73;41)
- Liver (n=81)
- Lung (n=129)
- Muscle – Skeletal (n=146)
- Nerve – Tibial (n=139)
- Ovary (n=45)
- Pancreas (n=130)
- Pituitary (n=33)
- Prostate (n=83)
- Skin – Lower leg and Suprapubic (n=147;17)
- Spleen (n=137)
- Stomach (n=144)
- Terminal Ileum (Peyer's patch) (n=15)
- Testis (n=92)
- Thyroid (n=126)
- Uterus (n=41)
- Vagina (n=48)
- Brain – Cerebellum (n=36)
- Brain – Frontal Cortex (n=35)

Overnight Shipped Brain Regions

- Brain – Cerebellum (n=35)
- Brain – Frontal Cortex (BA9) (n=35)
- Hippocampus (n=34)
- Substantia nigra (n=33)
- Anterior cingulate cortex (BA24) (n=35)
- Amygdala (n=34)
- Caudate (basal ganglia) (n=35)
- Nucleus accumbens (basal ganglia) (n=35)
- Putamen (basal ganglia) (n=33)
- Hypothalamus (n=34)
- Spinal cord (cervical c-1) (n=24)

Highlighted brain tissues are used to compare immediate PAXgene & Frozen

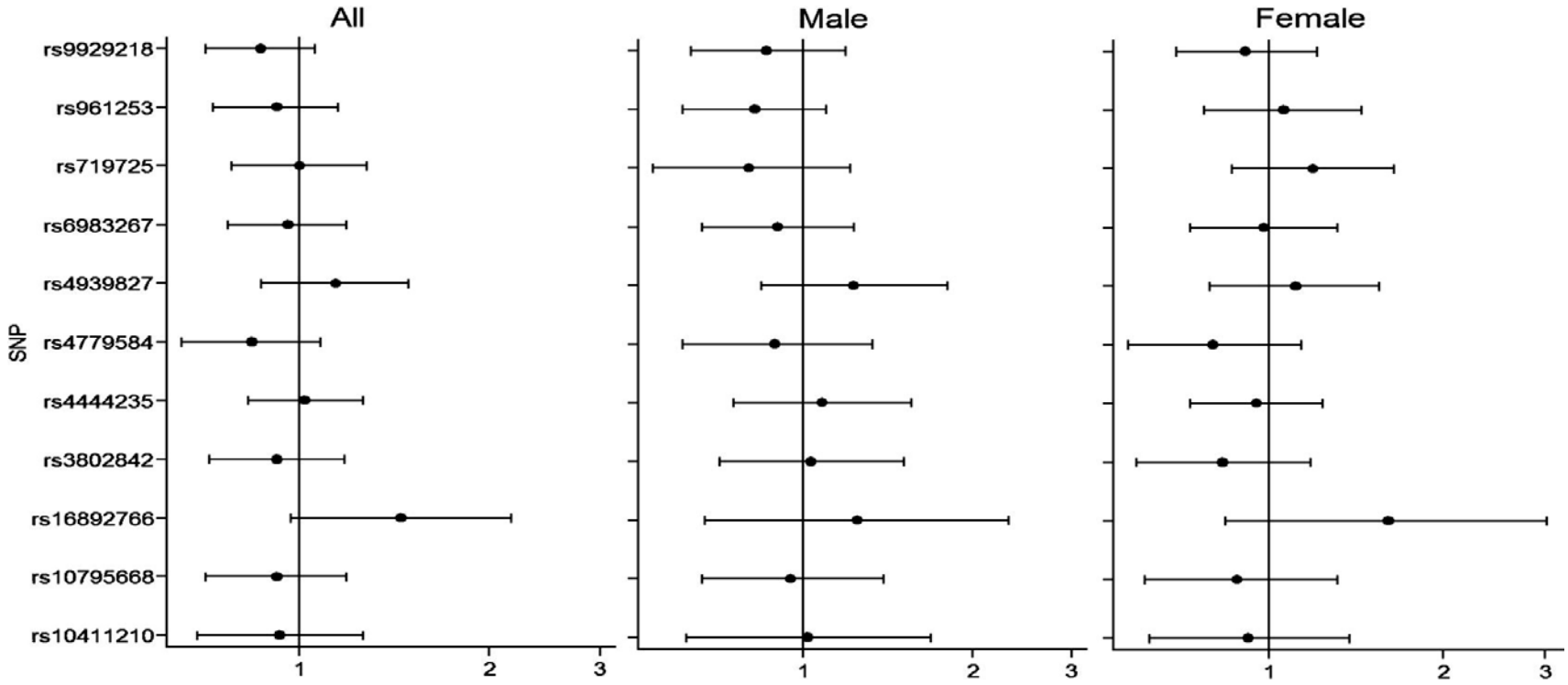
(n= Number of times sampled in the first 150 donors)

* Tissues fixed in an alcohol-acetic acid based fixative (PAXgene Tissue, Qiagen)

Are the common genetic variants associated with colorectal cancer risk for DNA mismatch repair gene mutation carriers?

For All 11 SNPs

HR per risk allele 0.97 (95% CI: 0.88-1.07)



Aung Ko Win et al. (2013). European Journal of Cancer, in press

Breast Cancer Family Registries (CFR)

- Resource for conducting studies on the genetics and molecular epidemiology of breast cancer
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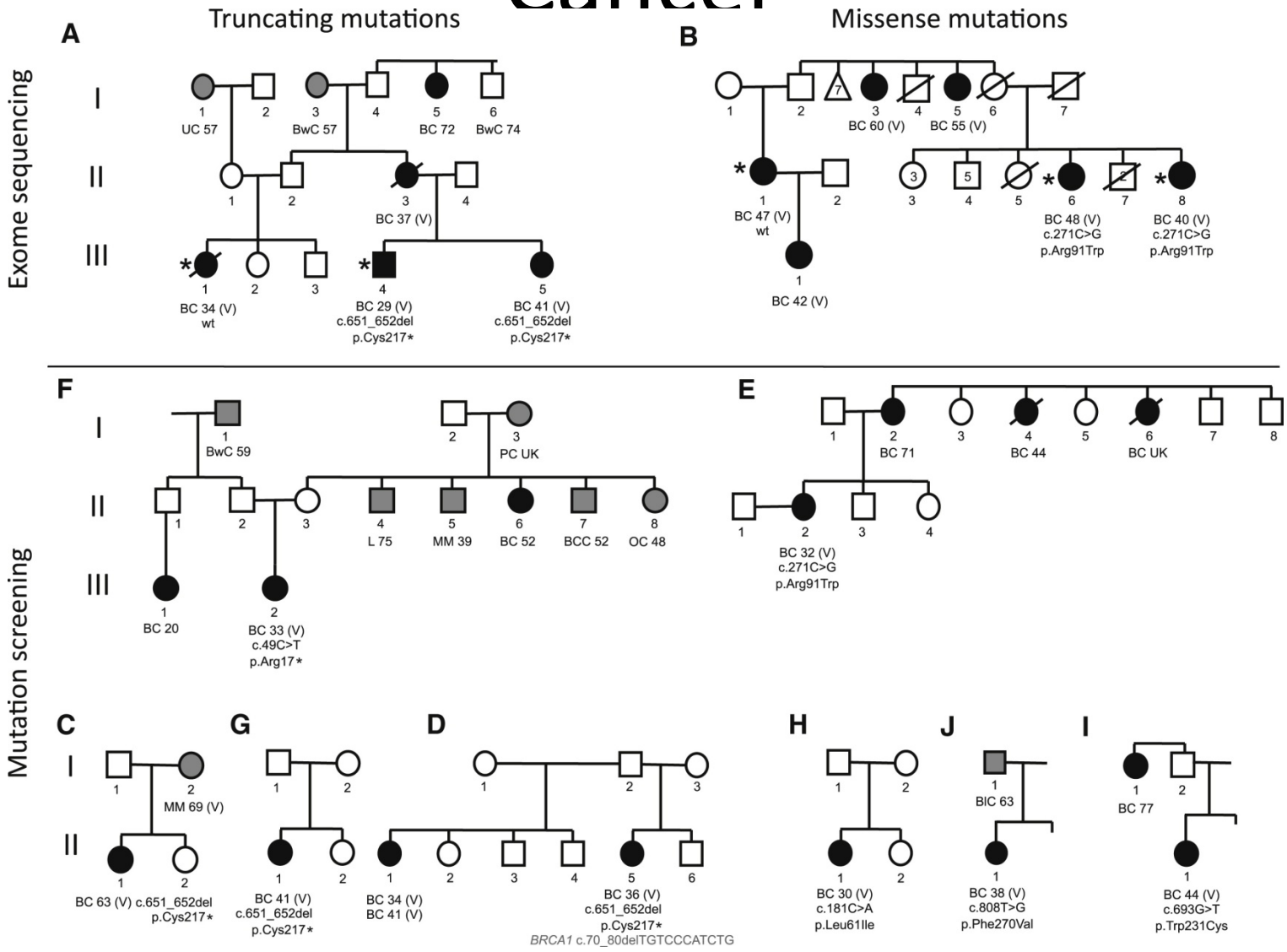
Rare Mutations in *XRCC2* and Breast Cancer



Park et al. (2012). AJHG. 90(4): 734-739