Inherited cancer gene testing: Should I test and should my family test?

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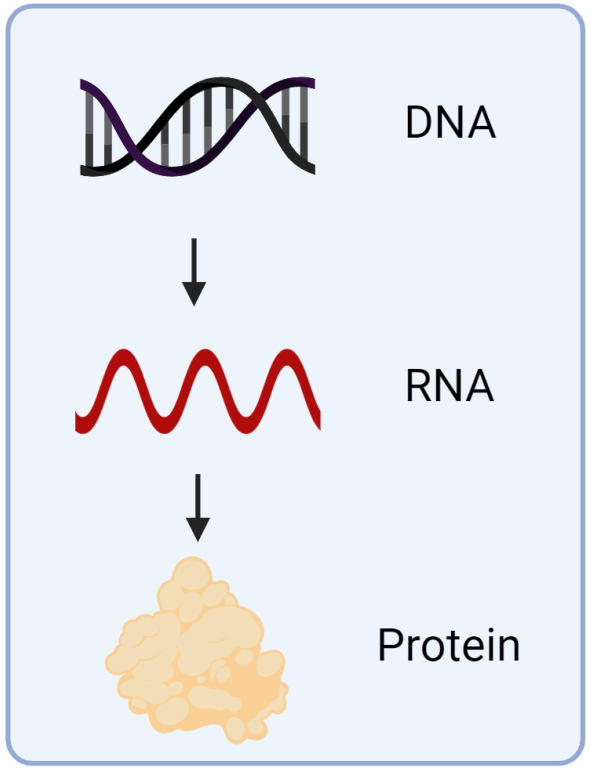
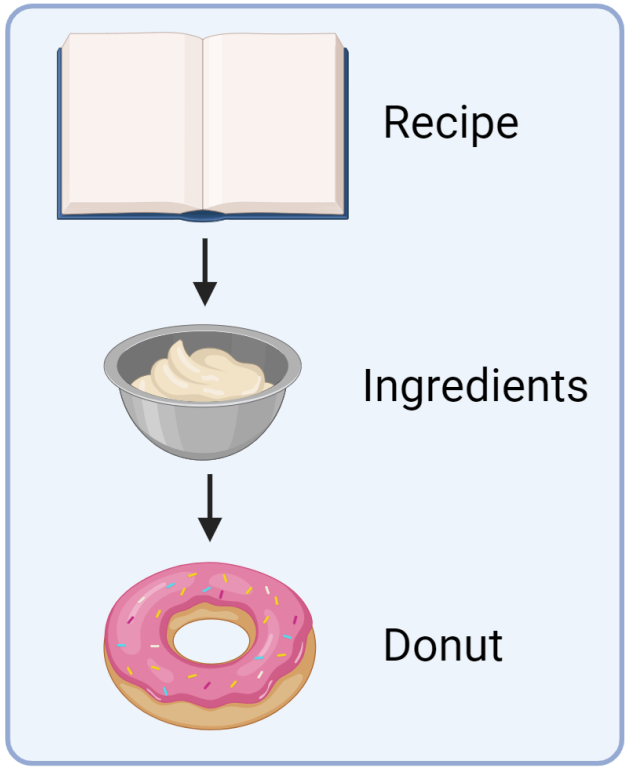
AGENDA

1. Cancer genetics 101
2. Why do we care about cancer genetics?
3. Germline genetics in prostate cancer
4. Should you be tested?
5. The PROMISE registry

CANCER GENETICS 101

Proteins are the functional unit of the cell and are encoded by DNA





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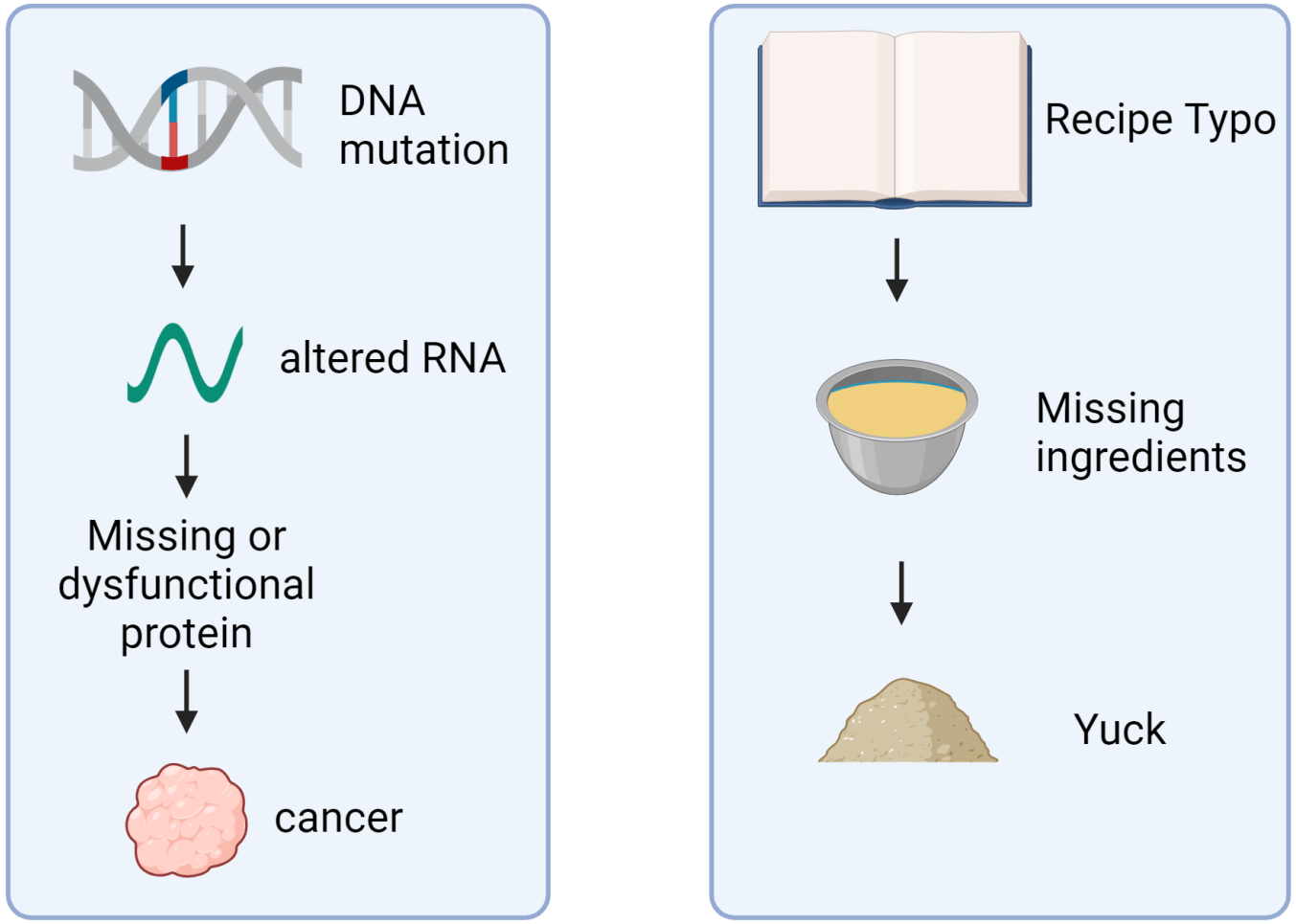
DNA mutation can lead to protein dysfunction and cancer



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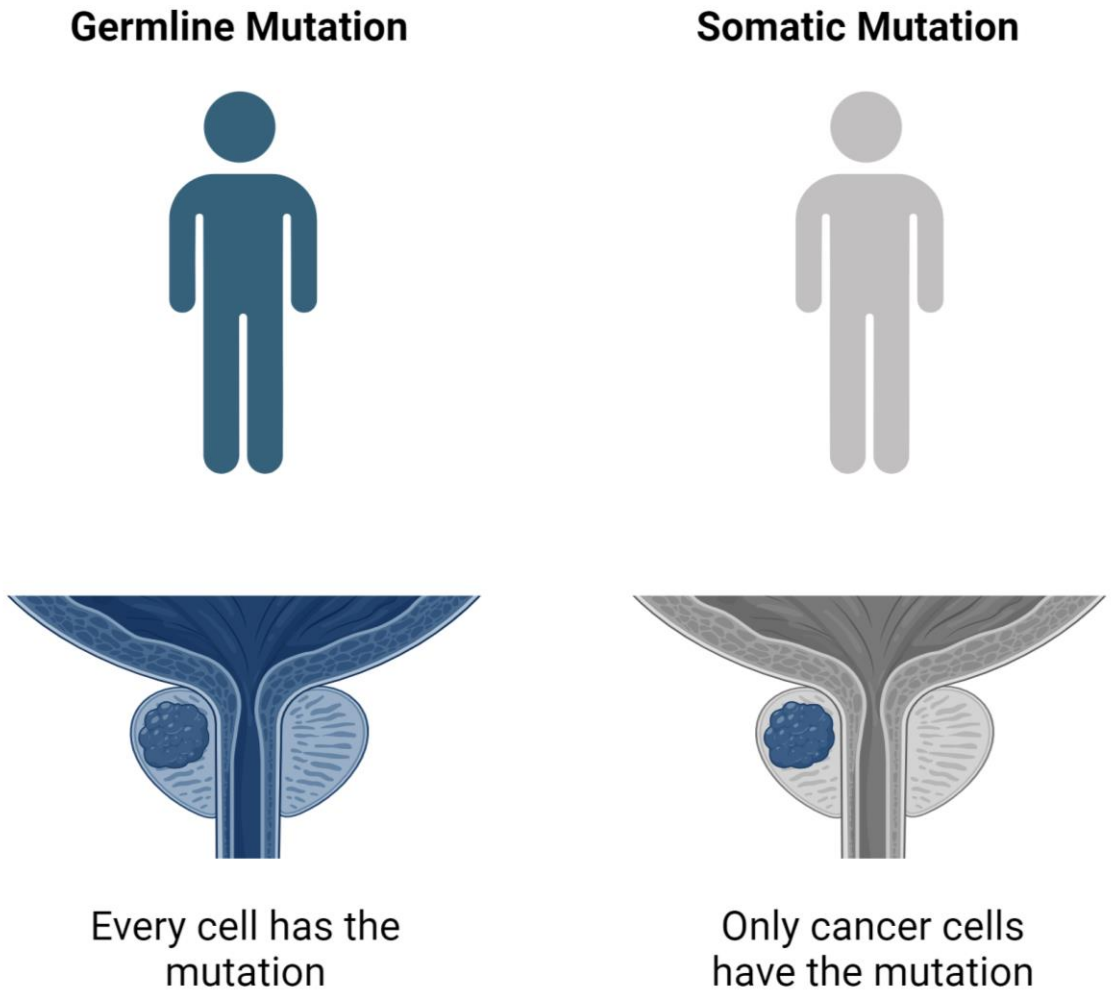
DNA mutations can be inherited (germline) or sporadic (somatic)



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Germline mutations can result in Hereditary Cancer Syndromes, which include different types of cancer

Syndrome	Clinical Manifestations	Gene
Hereditary Breast-Ovarian Cancer Syndrome	Breast cancer Ovarian cancer Pancreatic cancer Prostate cancer	BRCA1 BRCA2
Hereditary Non-Polyposis Colon Cancer (HNPCC) Also Known as Lynch Syndrome	Colon cancer Endometrial cancer Stomach cancer Ovarian cancer Prostate cancer Other forms of cancer	MLH1 MLH2 MSH6 PMS2
Familial Adenomatous Polyposis (FAP)/Attenuated FAP	Numerous adenomatous colonic polyps Colon cancer Desmoid tumors	APC
Hereditary Melanoma	Melanoma Pancreatic cancer	CDKN2A
Multiple Endocrine Neoplasia (MEN) 2a and 2b; Familial Medullary Thyroid Cancer	Medullary thyroid cancer Parathyroid hyperplasia Pheochromocytoma	RET

WHY DO WE CARE ABOUT CANCER GENETICS?

1. They may help us to predict the behavior of the cancer.

2. They may open up new options for therapy.

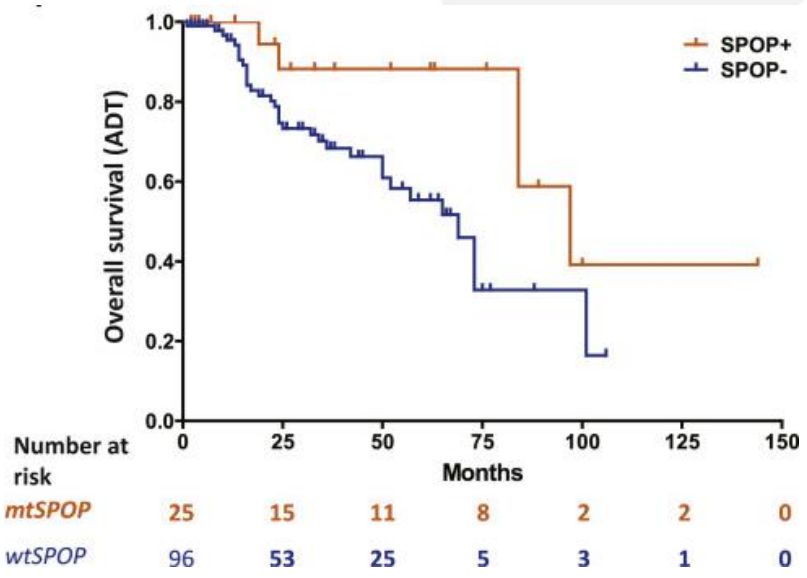
3. Germline mutations may partially explain why prostate cancer developed, and may increase risk of cancer in family members.

Cancer genetics can help us predict cancer behavior

Disney.fandom.com/wiki/Carl_Fredricksen

82 year-old man with newly diagnosed widely metastatic prostate cancer and heart failure.

Tumor genetic analysis revealed an **SPOP mutation**.

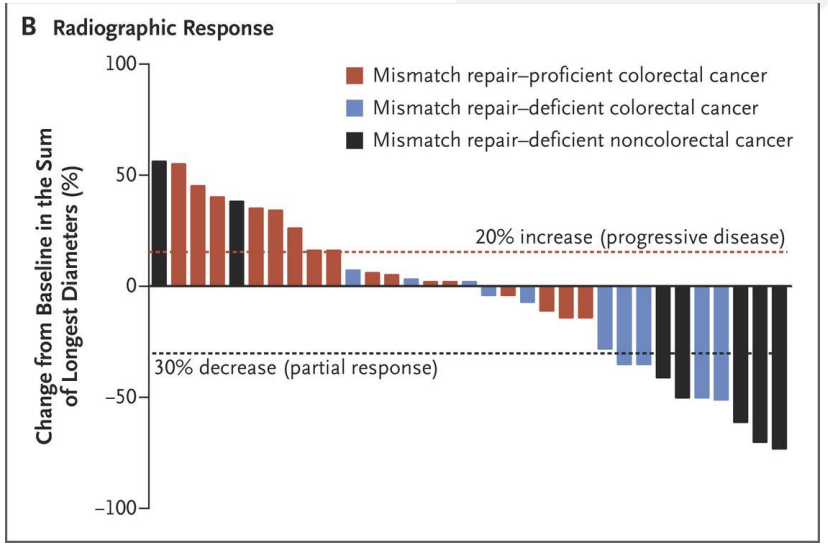


Swami U, Isaacsson Velho P, Nussenzveig R, et al. Association of SPOP Mutations with Outcomes in Men with De Novo Metastatic Castration-sensitive Prostate Cancer. Eur Urol. 2020;78(5):652-656.

Cancer genetics can open new therapy options

Disney.fandom.com/wiki/Joe_Gardner

58 year-old man with rising PSA after radical prostatectomy. Germline genetic analysis revealed an **MSH6 mutation** (i.e., Lynch Syndrome).



Le DT, Uram JN, Wang H, et al. PD-1 Blockade in Tumors with Mismatch-Repair Deficiency. *N Engl J Med*. 2015;372(26):2509-2520.

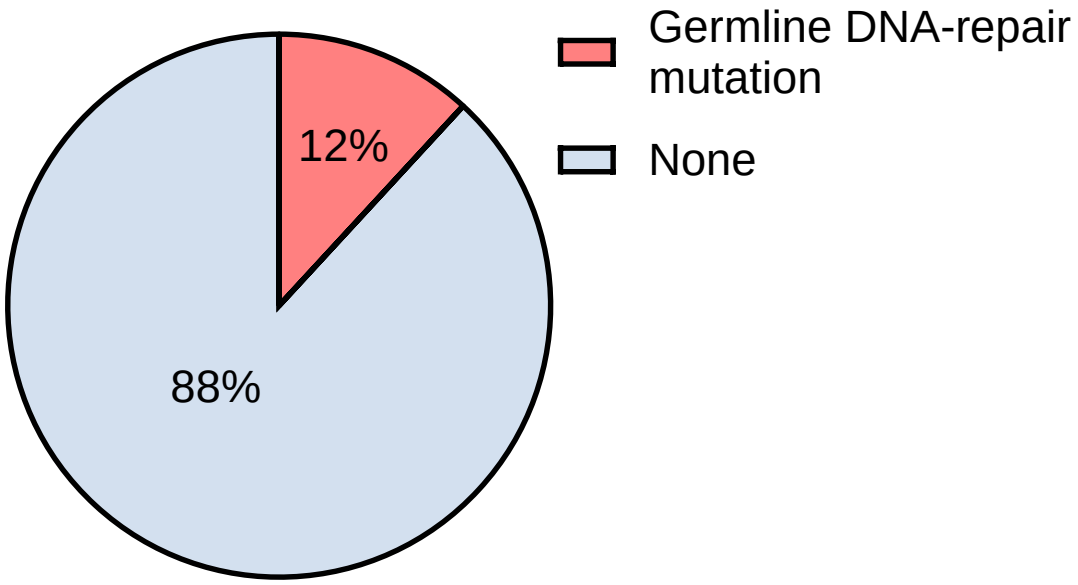
Cancer genetics can help family members get earlier cancer screening and prevention

Disney.fandom.com/wiki/Joy

36 year-old woman found to have a germline **BRCA2 mutation** after being referred for testing because her father with prostate cancer was found to have the same mutation.

GERMLINE GENETICS IN PROSTATE CANCER

Patients with metastatic prostate cancer



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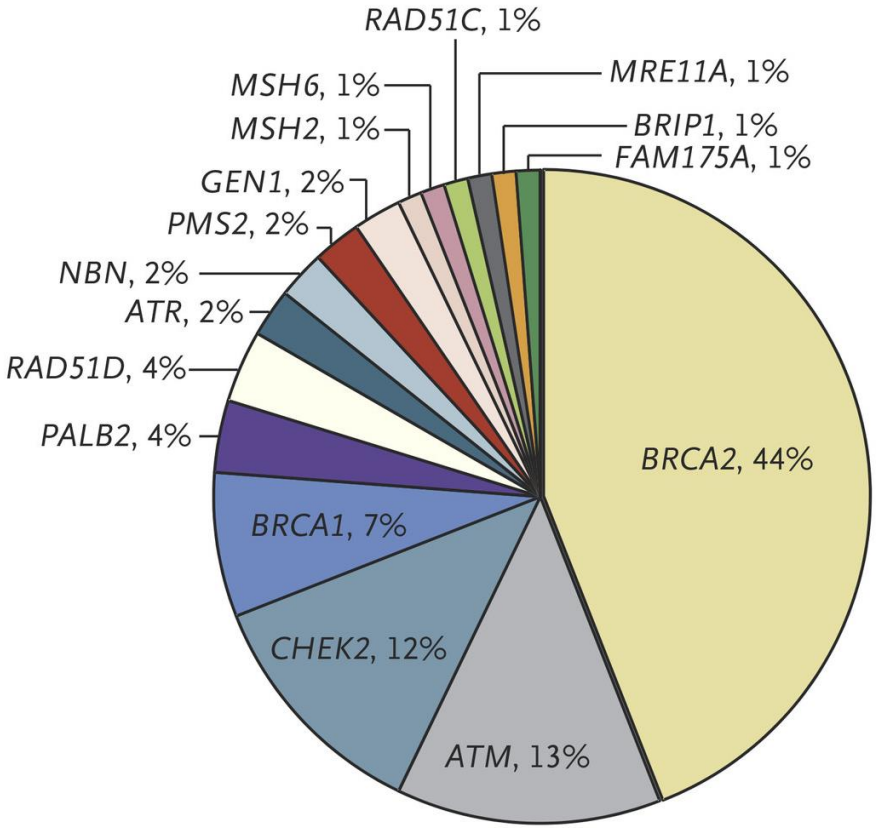
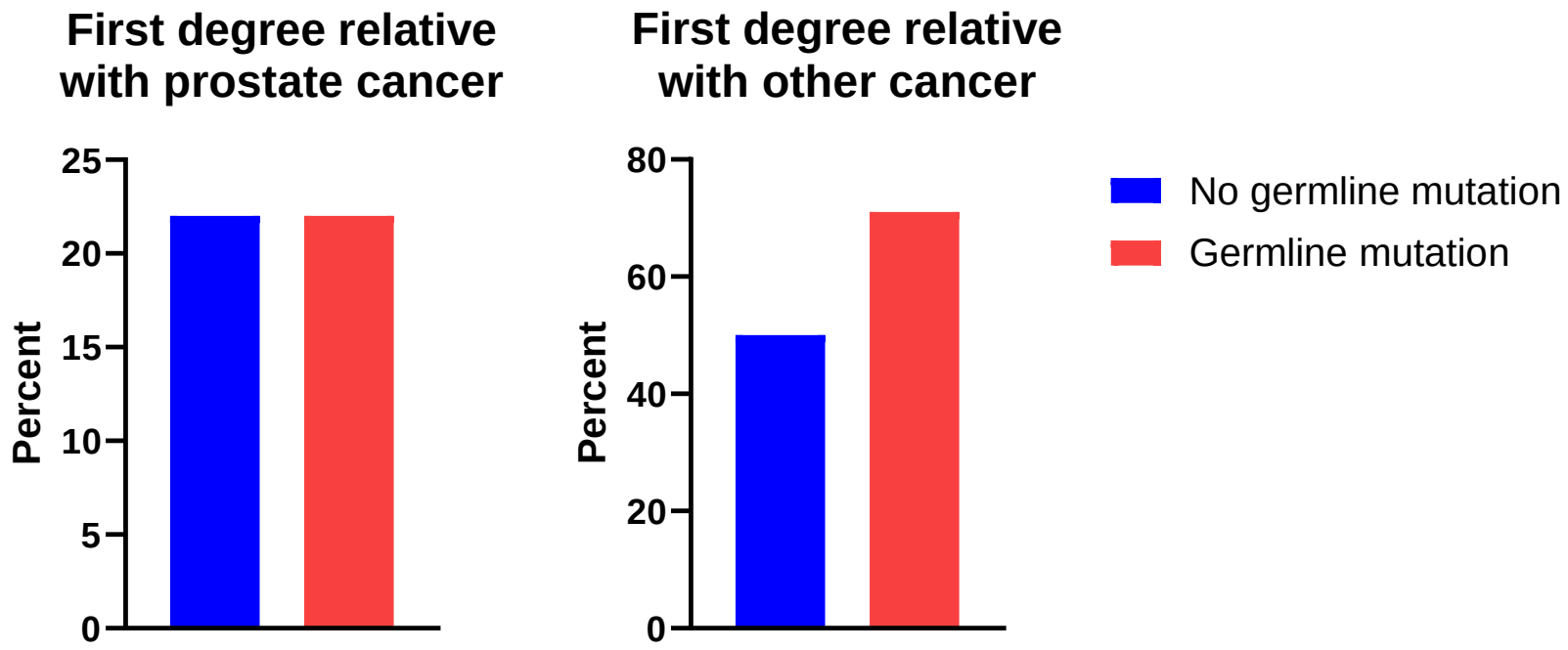


Pritchard CC, Mateo J, Walsh MF, et al. Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer. *N Engl J Med*. 2016;375(5):443-453. doi:10.1056/NEJMoa1603144

Family history is insufficient to screen for germline mutations – we need to test!



Pritchard CC, Mateo J, Walsh MF, et al. Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer. *N Engl J Med*. 2016;375(5):443-453. doi:10.1056/NEJMoa1603144

SHOULD YOU BE TESTED?

National Comprehensive Cancer Network guidelines are based on pre-test risk

1. **Patients with prostate cancer is metastatic or high risk for metastasis (Quick check: have you been referred to a medical oncologist for your prostate cancer?)**
2. People with at least 1 close blood relative with history of breast (age<50 or triple negative), ovarian, pancreatic, or metastatic prostate cancer, or >3 family members on the same side with breast or prostate cancer with unknown germline testing
3. People with a close blood relative with known germline mutation

Risks of germline testing

1. May cause anxiety and/or guilt
2. Potential for uncertain results:
    A. Variants of uncertain significance (VUS)
    B. Positive result but no management guidelines currently available
3. Concern for genetic discrimination
4. Cost
5. Insufficient access to genetic counseling

Many eligible patients do not obtain germline testing

Genetic registries can increase access to testing and help research

The PROMISE Team

Principal Investigators

Channing Paller, MD

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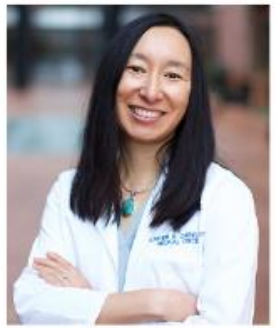


Heather Cheng, MD, PhD

Fred Hutch Cancer Center

PROMISE REGISTRY

A **P**rostate Cancer **R**egistry of **O**utcomes and Germline **M**utations
for **I**mproved **S**urvival and Treatment **E**ffectiveness

How It Works

Get Registered

Learn if PROMISE is right for you and register online.

Get The DNA Kit

We'll send you a DNA test kit. A saliva sample is all we need.

Get Results

You'll get information, tailored to your DNA, to better understand potential treatment options and genetic risk.

ProstateCancerPromise.org

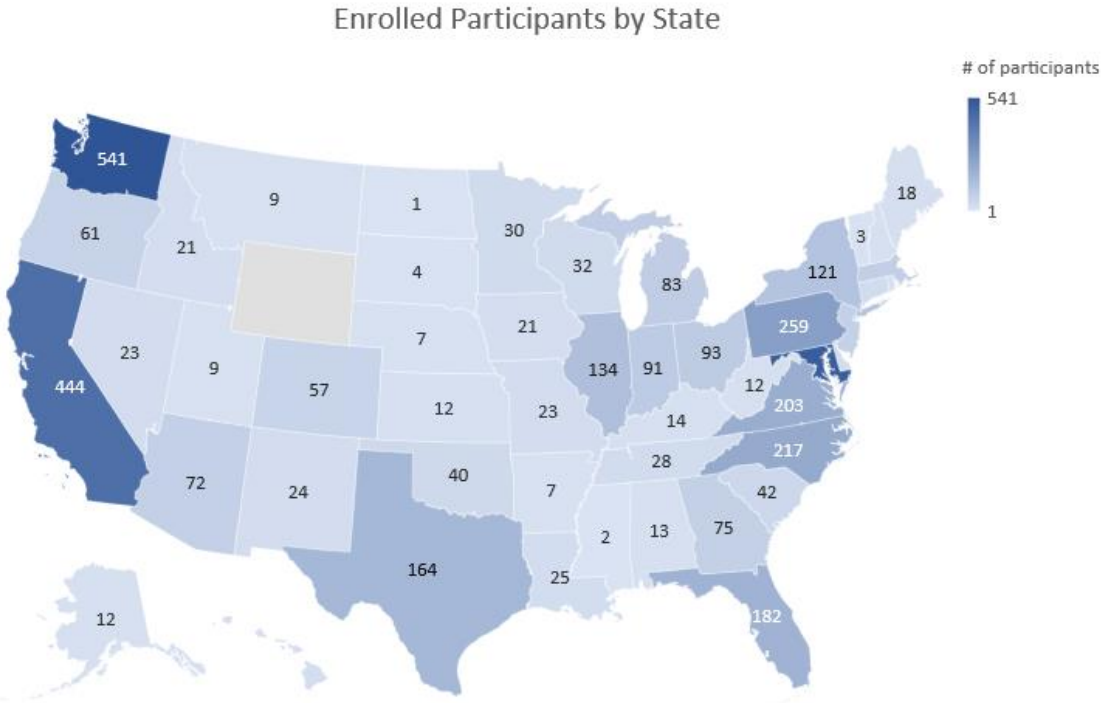
PROMISE has screened 1,785 people to date

1,785 consented participants

(goal: 5,000)

177 participants eligible for long-term follow-up

(goal: 500)



- Allegheny Health Network
- University Hospitals Seidman Cancer Center
- Cleveland Clinic
- Dana-Farber Cancer Institute
- Duke Cancer Institute
- Florida Urology Partners
- Fred Hutchinson Cancer Center
- Hendrick Health
- Indiana University Health Arnett Cancer Center
- INOVA Genetic Counselors
- Johns Hopkins Medicine
- Karmanos Cancer Center
- Lenox Hill Hospital (Northwell Health)
- Lakeland Regional Health
- Northwestern Medicine Regional Medical Group
- Oregon Health & Science University Knight Cancer Institute
- Rutgers Cancer Institute of New Jersey
- Tennessee Valley Urology Center
- Tulane Medical Center
- University at Buffalo Medical Center
- University of California San Diego Medical Center
- University of Chicago Medical Center
- University of Pittsburgh Hillman Cancer Center
- University of Virginia Comprehensive Cancer Center
- Virginia Oncology Associates
- WellSpan Health

PROMISE Explained: A genetic registry study for patients with prostate cancer

THANK YOU