



Updates to Genetic Testing & Hereditary Prostate Cancer

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Nice to Meet
You

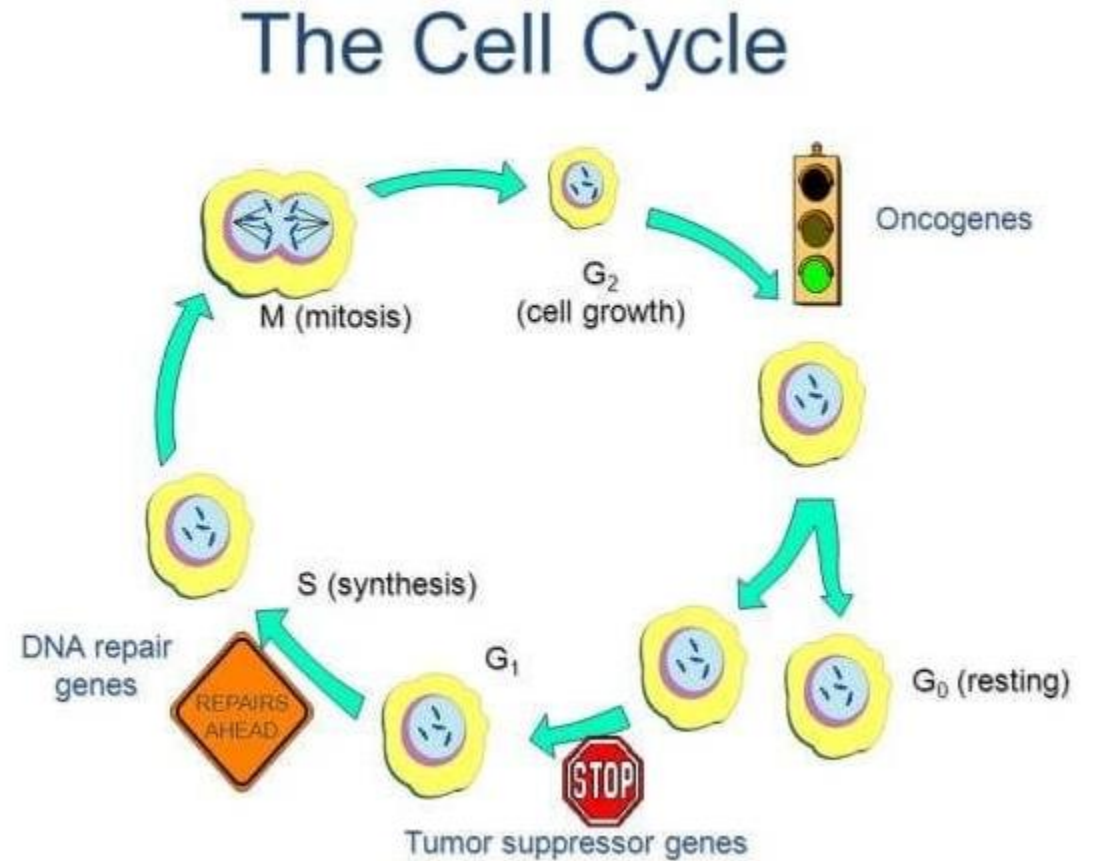
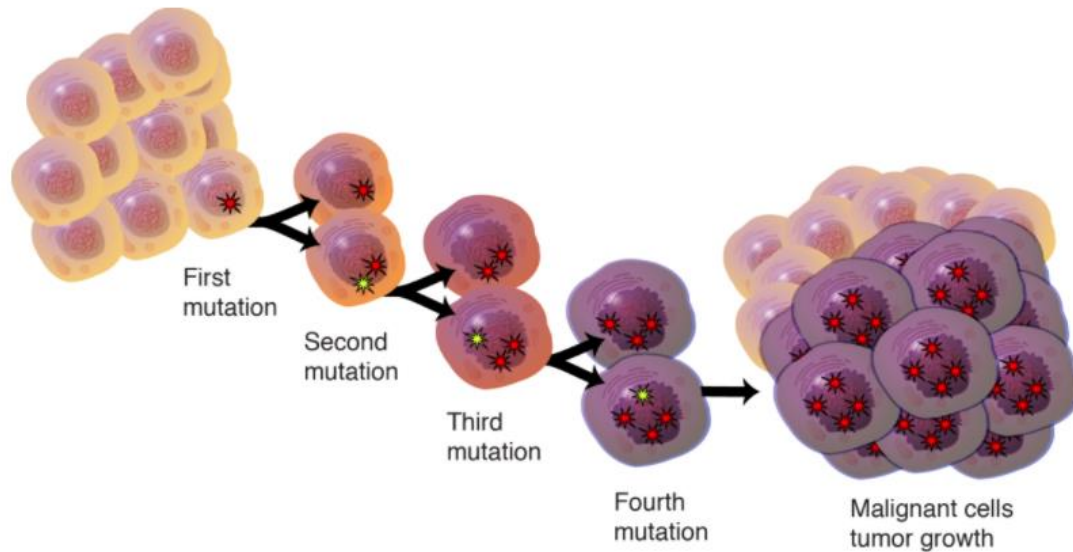


What is a Genetic Counselor?

- Advanced training in Medical Genetics and Counseling
- Help you **understand the risk for a genetic condition**
- Provide guidance around **genetic testing**
- **Explain test result** and what it means for you & family
- Work with Medical Team to **personalize care plan**

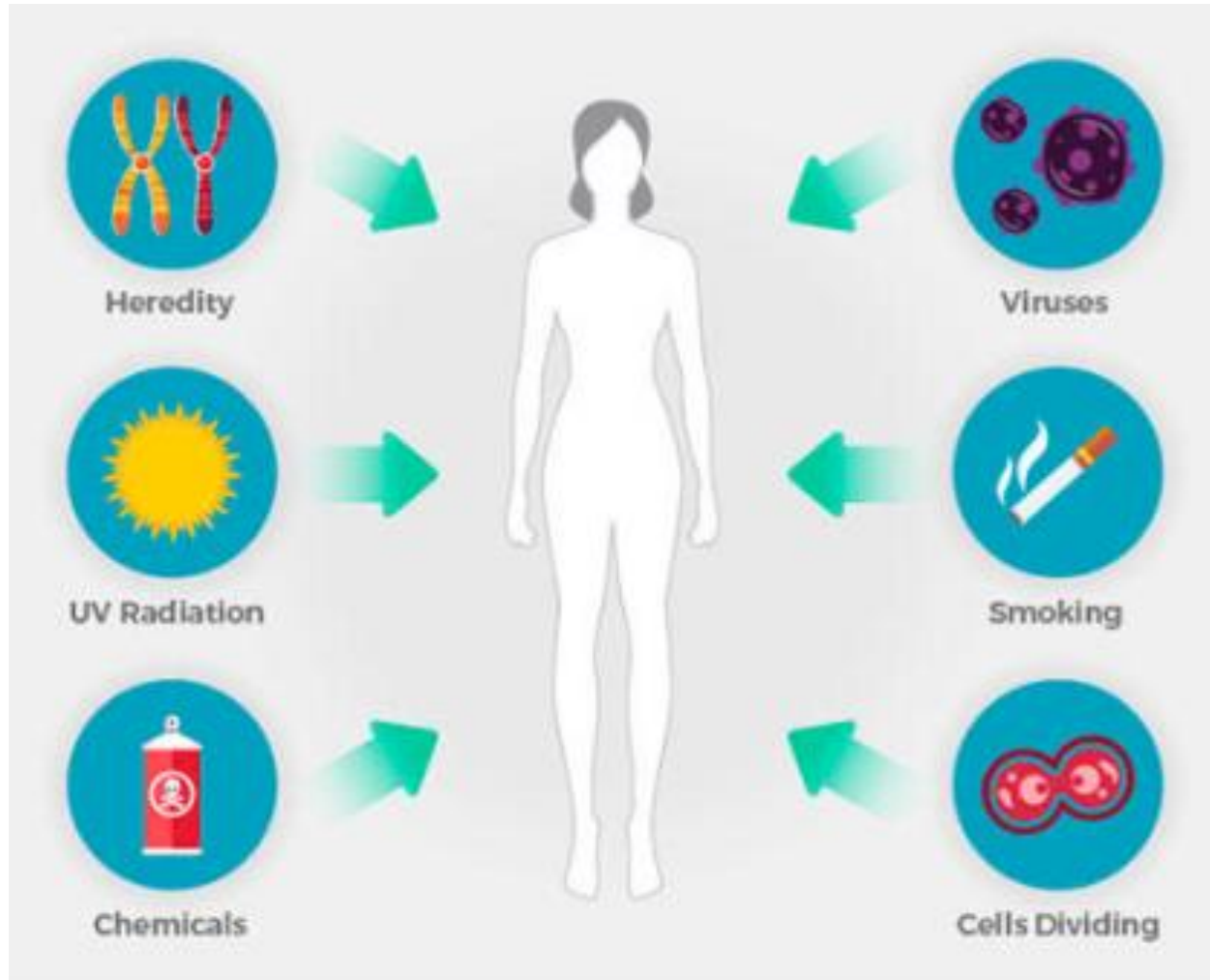


Cancer is a disease of many mutations

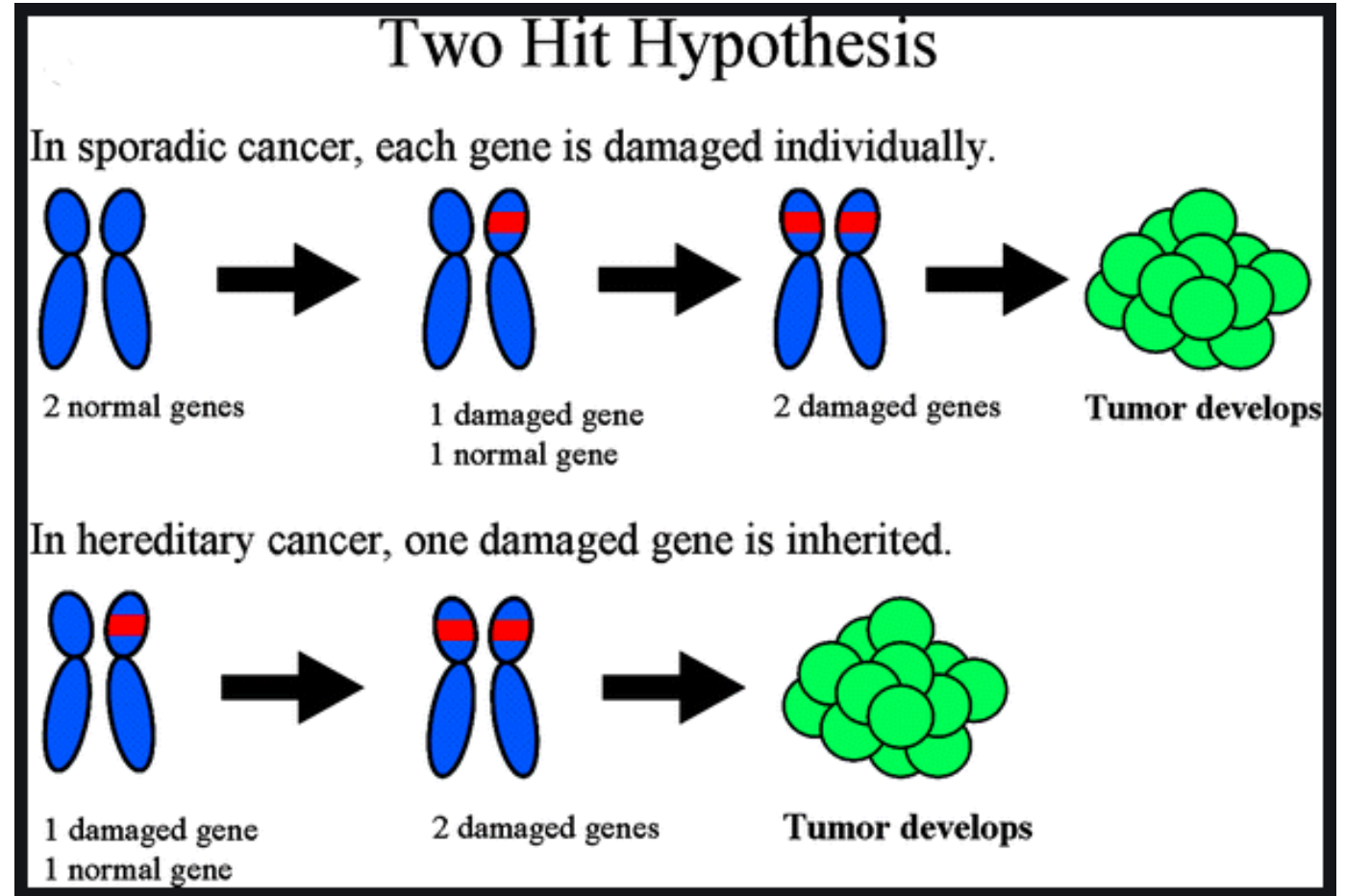
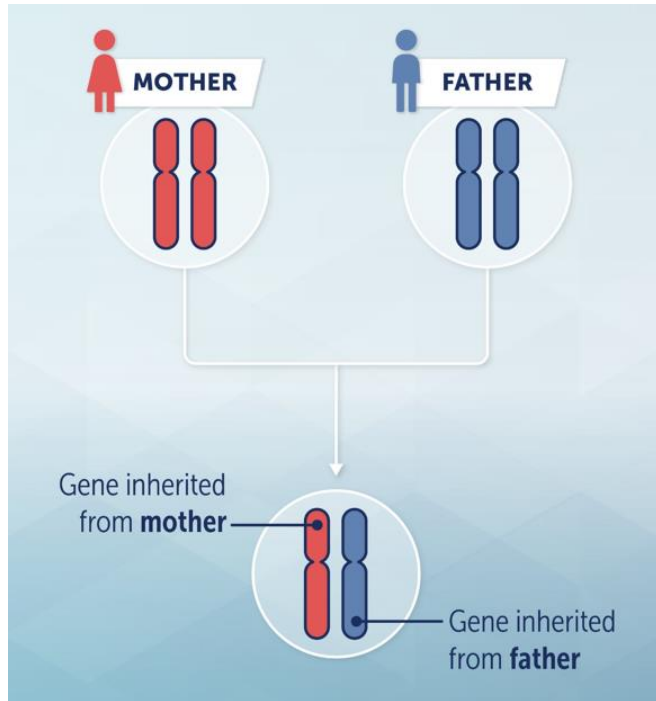


Our genes help stop cancer growth by regulating how cells grow and divide

What causes genetic changes?

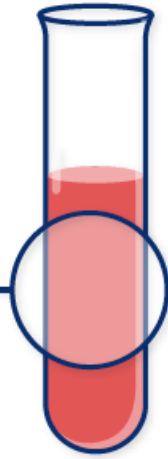


Can cancer be passed down in families?



Inheriting a genetic change can cause a predisposition to develop certain cancers over a lifetime

Germline testing can help determine if a mutation was inherited and help guide treatment and risk management options



BLOOD TEST
SALIVA TEST

Germline mutations are in **EVERY** cell of the body, including tumor cells.

Tumor testing can help guide treatment options (e.g., chemotherapy)

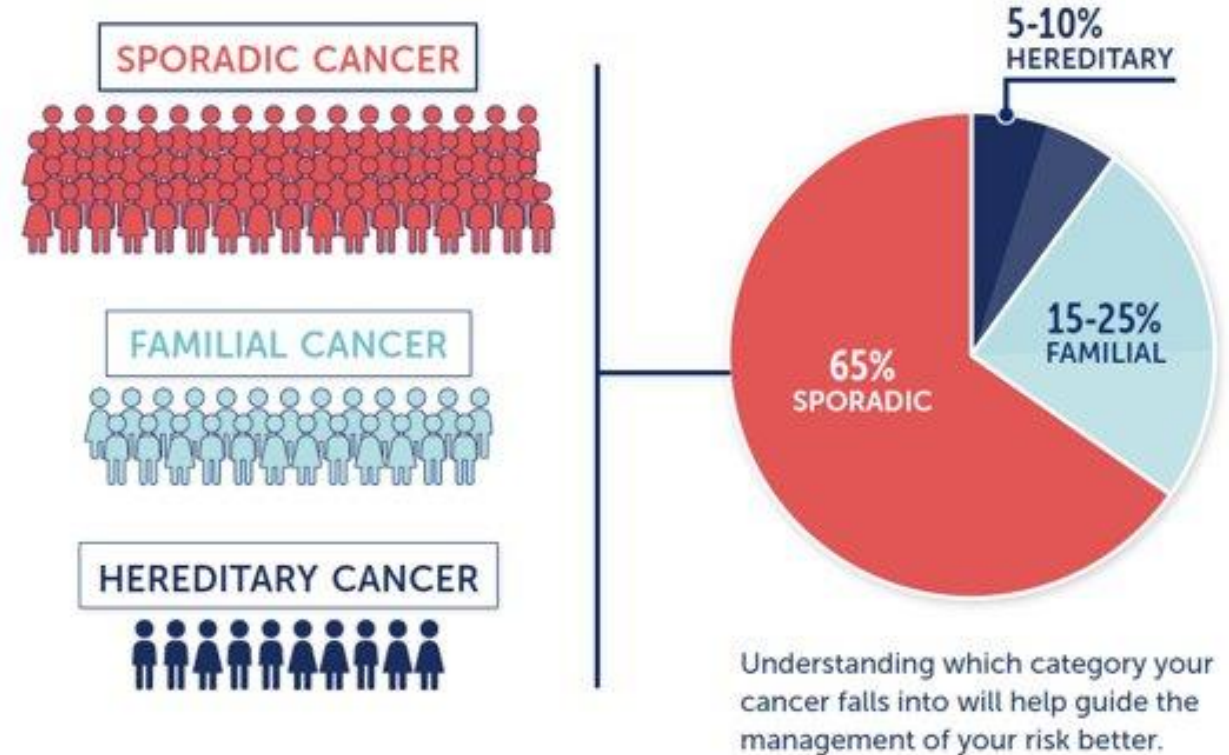


TUMOR BIOPSY

No two tumors are exactly alike, but common mutations can guide therapy choice.

Signs of Hereditary Cancer

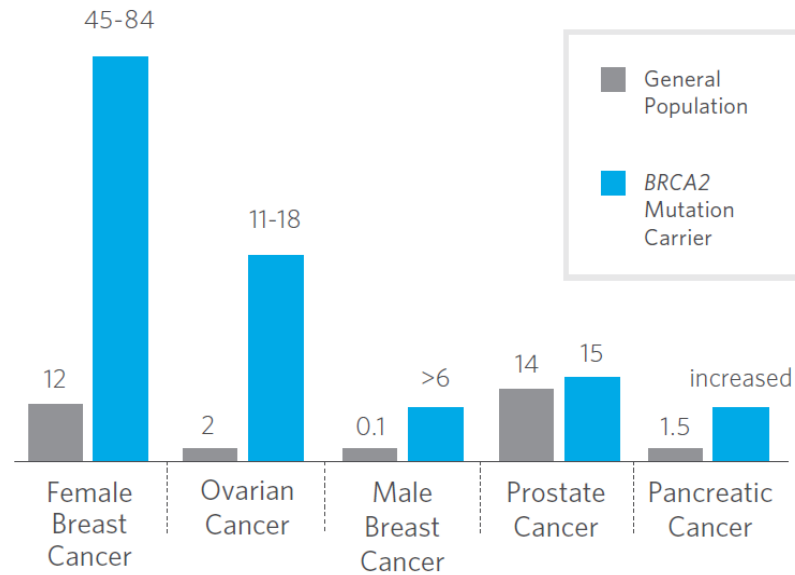
- Young ages of diagnosis (<50y.o)
- Multiple cancers in close family members
- Rare types of cancers
 - Ovarian, pancreatic, male breast, aggressive/metastatic prostate cancer
- Ancestry origins
 - Ashkenazi Jewish, Icelandic, etc.



How does a Mutation Impact Cancer Risk?

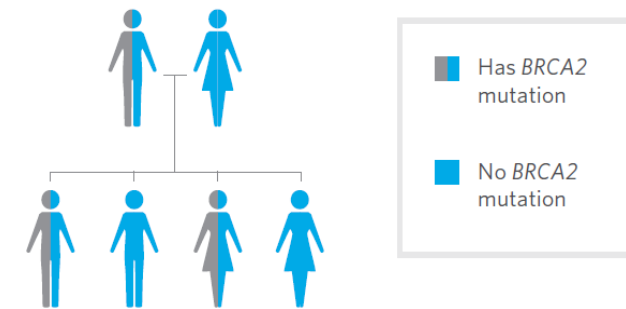


BRCA2 Mutation Lifetime Cancer Risks (%)*



BRCA2 Mutations in the Family

There is a 50/50 random chance to pass on a *BRCA2* mutation to your sons and daughters. The image below shows that both men and women can carry and pass on these mutations.



Major Genes Associated with Increased Risk for Prostate Cancer

most common	Gene	Syndrome	Prostate Cancer Risk	Other Associated cancers*
	BRCA1/2	Hereditary Breast and Ovarian Cancer Syndrome	Up to 2-5x ¹	Breast, Ovary, Pancreas, Melanoma
	ATM		elevated	Breast, Pancreas
	CHEK2		elevated	Breast, Colorectal
	PALB2		elevated	Breast, Pancreas
	HOXB13		Up to 2-6x ²	
	MSH2 [†]	Lynch Syndrome	elevated	Colorectal, Uterine, Upper GI, Ovary, Urinary Tract, Brain, Sebaceous Neoplasms


*most commonly associated cancers

† possibly other Lynch syndrome genes as well

¹ <https://doi.org/10.1016/j.eururo.2019.08.025>

² PMID: [22841674](#), [23457453](#), [25595936](#), [26517352](#), [24026887](#)

Updates in genetic testing guidelines



Evidence-based criteria to identify who is more likely to test positive

- In the past, EXPENSIVE and single-gene testing
- Meets criteria often = insurance billable/covered test
- Historically BRCA-focused

SHIFT TO OFFER TESTING MORE OFTEN

More inclusive criteria (thank you, panel tests!)

Lower cost and better payer coverage (thank you, lab competition!)

Testing Recommendations

Prostate cancer diagnosis:

- Aggressive or advanced stage
- Additional family history of cancer
 - Prostate, Breast, Ovarian or Pancreatic*
 - Diagnosis <50y.o
- Negative BRCA1/2 testing in past
- Ashkenazi Jewish ancestry
- Positive genetic result in the family
- Tumor testing mutation that could be inherited
 - To aid in therapy decision making

*Other cancer types include: colorectal, endometrial, gastric, bile ducts, kidney, melanoma, small bowel, urothelial)


Updates in Mutation Detection Rates

- **Metastatic Prostate:** 11.8% positive¹
- **Any Prostate and Referred for Testing:** 9.3-17.2% positive ^{2,3,4}
 - Did not see differences by Gleason score³ or cancer stage⁴
 - Many tested did NOT meet criteria

Positive Mutation %

- Gleason≤6: 15.1%
- Gleason≥6: 16.3%

Results: Variant rates overall and among patients with discernible* risk level (staging) information

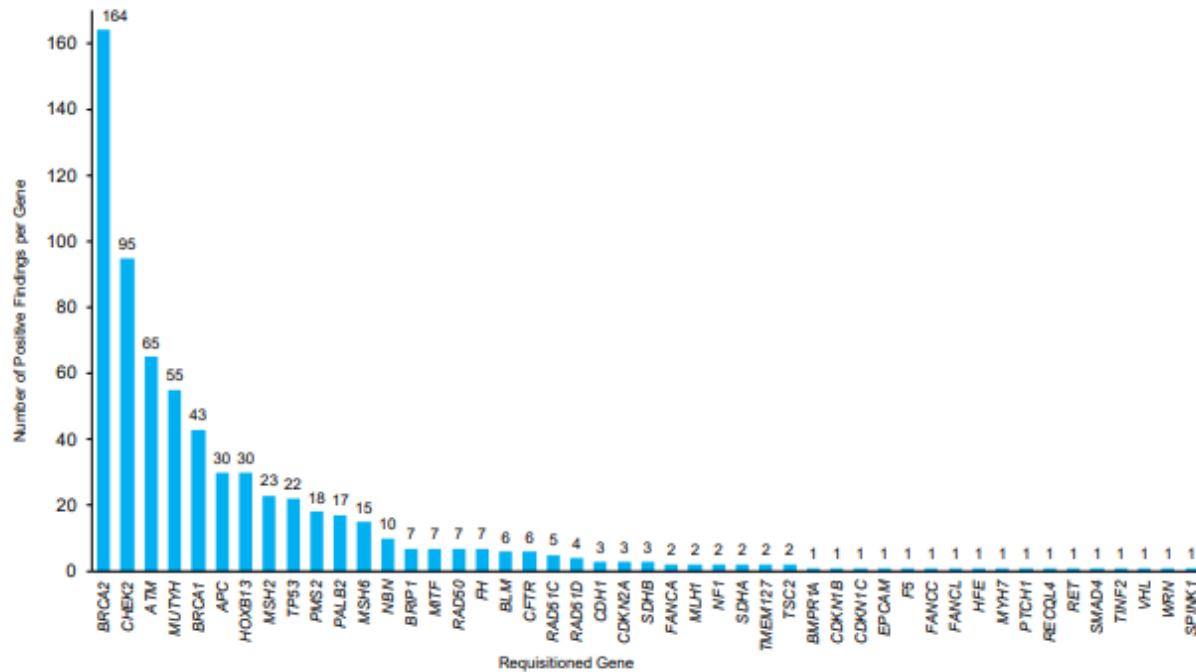


	Total	P/LP**	IRA	Over-lap	P/LP + IRA = Pos	% Pos
All patients (regardless of discernable risk/staging info)	4,420	388	54	8	434	9.8
Metastatic (stage IV)	1,049	88	12	2	98	9.3^
High/very high (stage III)	349	35	3	0	38	10.9^
Intermed/low (stage II)	719	60	12	0	72	10.0^

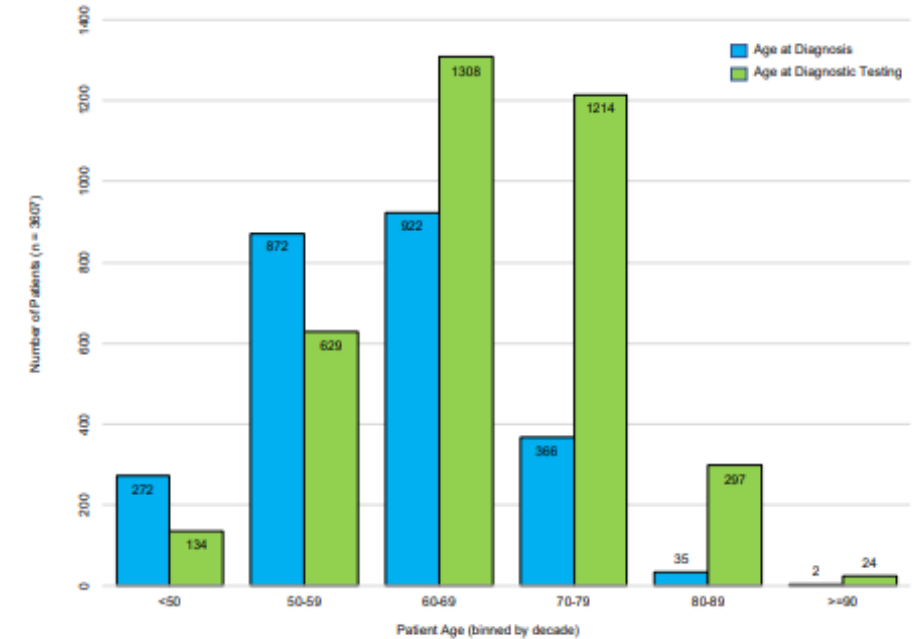
* 2117 men had discernable risk level or staging information available
**Excludes low-indeterminate risk genes and recessive alleles
^ The differences in positive rates among stages is not statistically significant ($p > 0.05$)

What Genes & When?

eFigure 2. Distribution of Genes in Which Pathogenic, Likely Pathogenic, and Increased Risk Allele Variants Were Detected in This Study. The number of positive findings detected in each gene is listed above the histogram. A small number of genes had several positive findings, whereas there was a long tail of genes in which only one positive finding was detected.

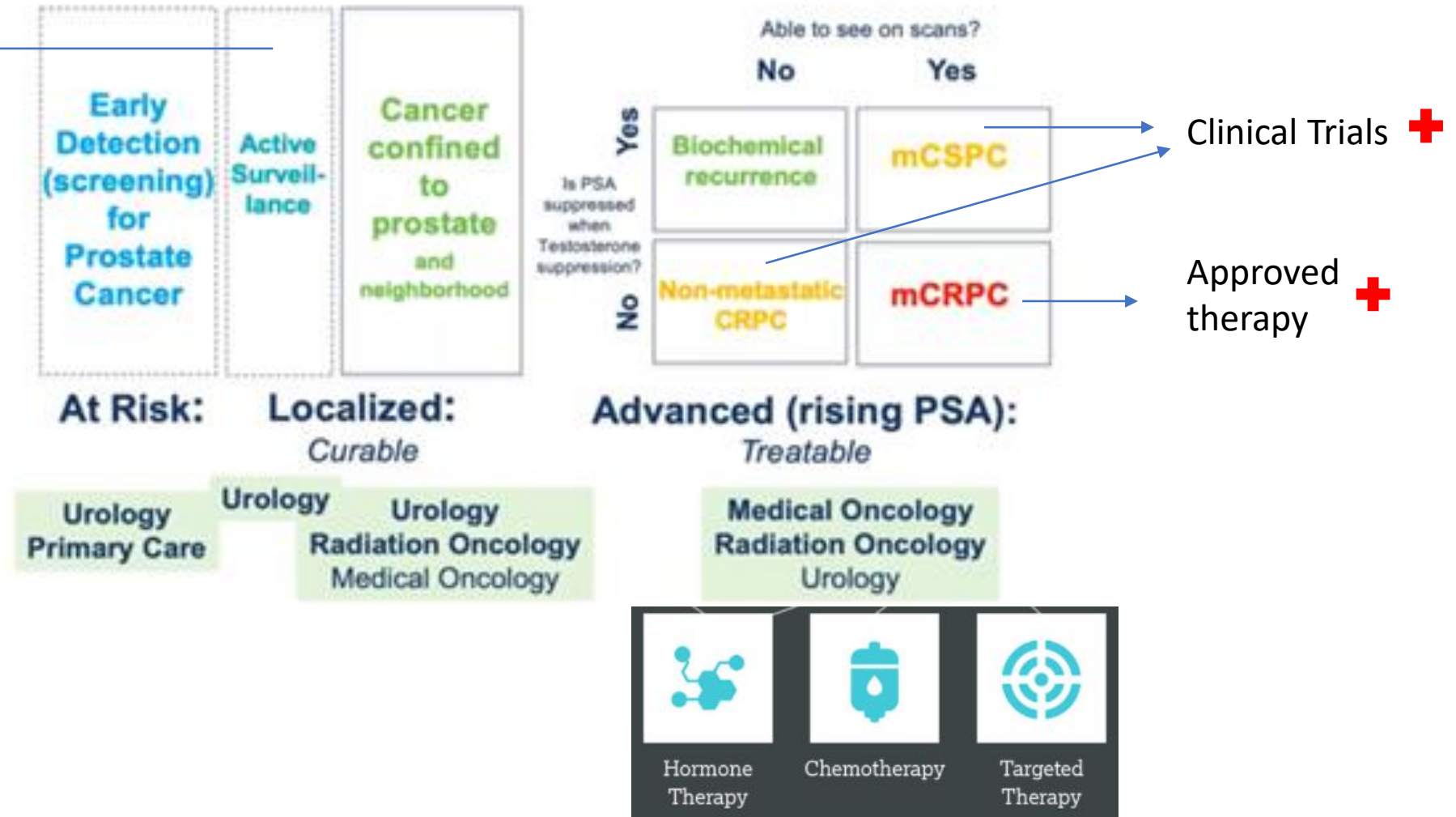


eFigure 1. Age at Diagnosis Compared With Age at Testing in Men with a Personal History of Prostate Cancer. A distinctive rightward shift was identified and indicated a lag between the initial diagnosis of prostate cancer and referral for germline genetic testing.



Can Genetic Testing be Helpful for Treatment and Screening in the Family?

+ Early screening,
Clinical Trials





DDR Gene Mutations and Targeted Therapy:

DNA Damage Response Genes

- Includes BRCA1/2, ATM, and others
- Germline or somatic DDR mutations (up to 1 in 4 patients with metastatic prostate cancer eligible)

Approval of PARP inhibitor Treatments

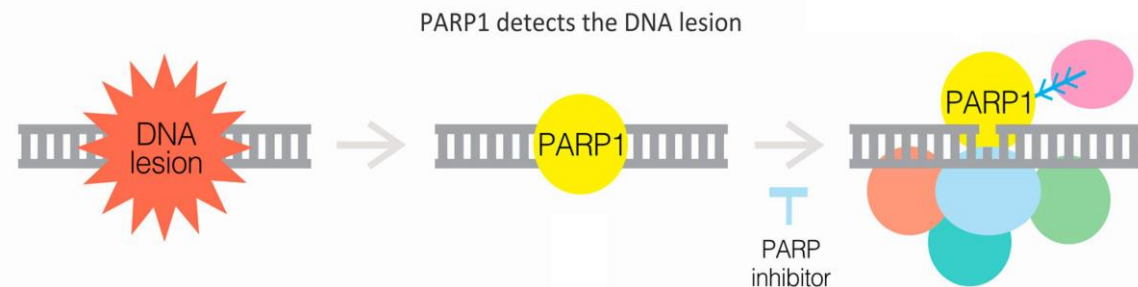
- May 2020 - FDA approval of olaparib & rucaparib
- Showed better response in shrinking tumor and keeping from progressing

Also:

- BRCA1/2 + - may consider platinum chemotherapy
- MMRd tumors- may consider anti-PDL1 therapy (immunotherapy)

Who?

- Adult patients with certain mutations
- Metastatic disease resistant to other treatments



I Would Like Testing...Now What?

- Meeting with a genetic counselor or consulting your medical providers may help determine if you &/or your family meet NCCN/Insurance criteria for genetic testing. Tumor testing is often ordered by a Medical Oncologist.



www.nsgc.org



Find a
Genetic Counselor

Find a Genetic Counselor

The Find a Genetic Counselor directory offers access to over 3,300 genetic counselors (US and Canada).

To start your search, tell us **how you would prefer to meet with a genetic counselor.**

- Searches of the "In Person" directory will show genetic counselors who meet patients in a designated location and in person. Searches can be limited to a given location.
- Searches of the "Via Telehealth" directory will show genetic counselors who meet with patients via phone, video conferencing and other virtual methods.



I Would Like Testing...Now What?

I Meet Criteria:

- Several "billing friendly" labs
 - The average patient pays \$0-100 OOP for germline testing
 - Many labs offer financial assistance based on medical and income eligibility



I Don't Meet Criteria, but Still Want Testing:

- Several labs offer \$250 self-pay option for germline testing
- Some labs offer sponsored/no-cost testing that has more inclusive criteria



INVITAE



- ☐ Stage IIa, age at diagnosis 55 or under
 - ☐ Stage IIb or IIc at any age
 - ☐ Stage III at any age
 - ☐ Stage IV at any age
-
- ☐ Gleason 6, age at diagnosis 55 or under
 - ☐ Gleason 7 or greater at any age
 - ☐ Metastatic disease at any age
 - ☐ Gleason undetermined, suspected low risk (stage IIa) or above at any age

Thank you!

