# **The Metastatic Prostate Cancer Project:** Partnering directly with patients to accelerate our understanding of metastatic prostate cancer

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Dana-Farber/Harvard Medical School
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BROAD INSTITUTE

DANA-FARBER CANCER INSTITUTE

# Disclosures

- Consulting/Advisory
  - Tango Therapeutics
  - Genome Medical
  - Invitae
- Equity holder in Microsoft
  - Five shares for my bar-mitzvah in 1993
  - Thanks to the Gros family!

# Disclosures

STANFORD UNIVERSITY
SYMBOLIC SYSTEMS PROGRAM

‘03

Google™

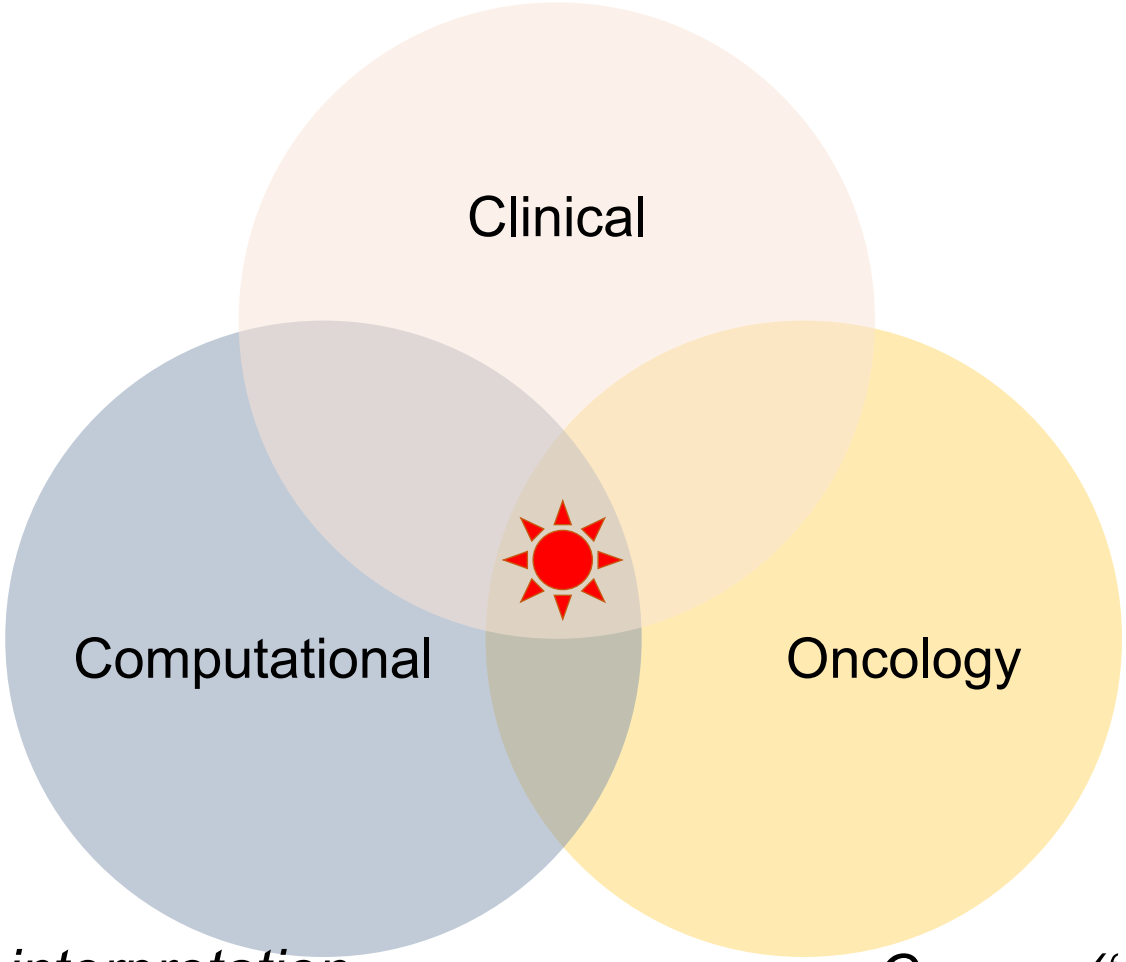
Camp Kesem

For children of patients who have/had cancer

…

# A “computational” oncologist

*Sampling patients directly*




*Analysis + interpretation algorithms*

*Cancer (‘omic) biology*

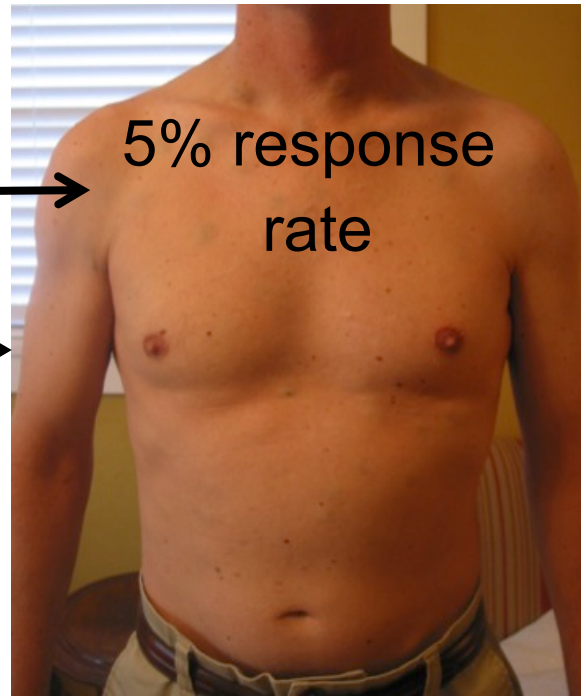
# Precision cancer medicine: A potential paradigm shift

Past
Dacarbazine

5% response rate

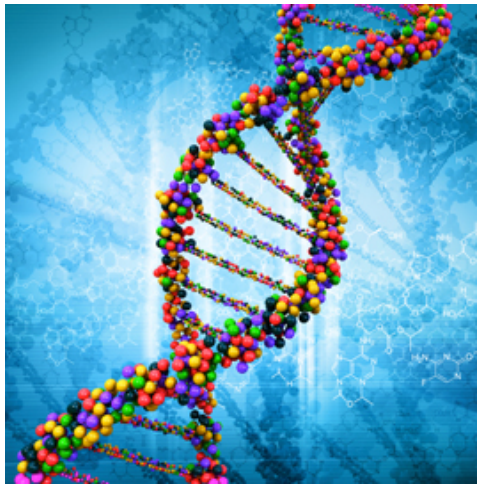
Present

*BRAF*$^{V600E}$
Vemurafenib



Wagle, Emery, et. al JCO 2011

# Metastatic prostate cancer



- Metastatic prostate cancer (MPC) is prostate cancer that has spread beyond the tissues of the prostate
- ~150,000 men are living MPC in the U.S.
- 30,000 men in the U.S. die of MPC each year
- Though treatments are improving, there is currently no cure for MPC – ***we seek to change that***

# Some questions we are trying to answer in metastatic prostate cancer

- What are all of the genetic changes that cause MPC?
- What explains why some MPC tumors never respond to treatments?
- Why can MPC happen at a young age?
- What are the differences in MPC for patients from different ethnic and ancestral backgrounds?

- ***How can we develop better treatments for men with MPC now and in the future?***

# Some questions we are trying to answer in metastatic prostate cancer

- What are all genetic changes cause MPC?
- Wh
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- Wh
- Wh
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***What will it take to answer these questions?***

***Detailed molecular and genomic characterization of thousands of tumor and germline samples from patients along with their medical information***

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- ***How can we develop better treatments for men with MPC now and in the future?***

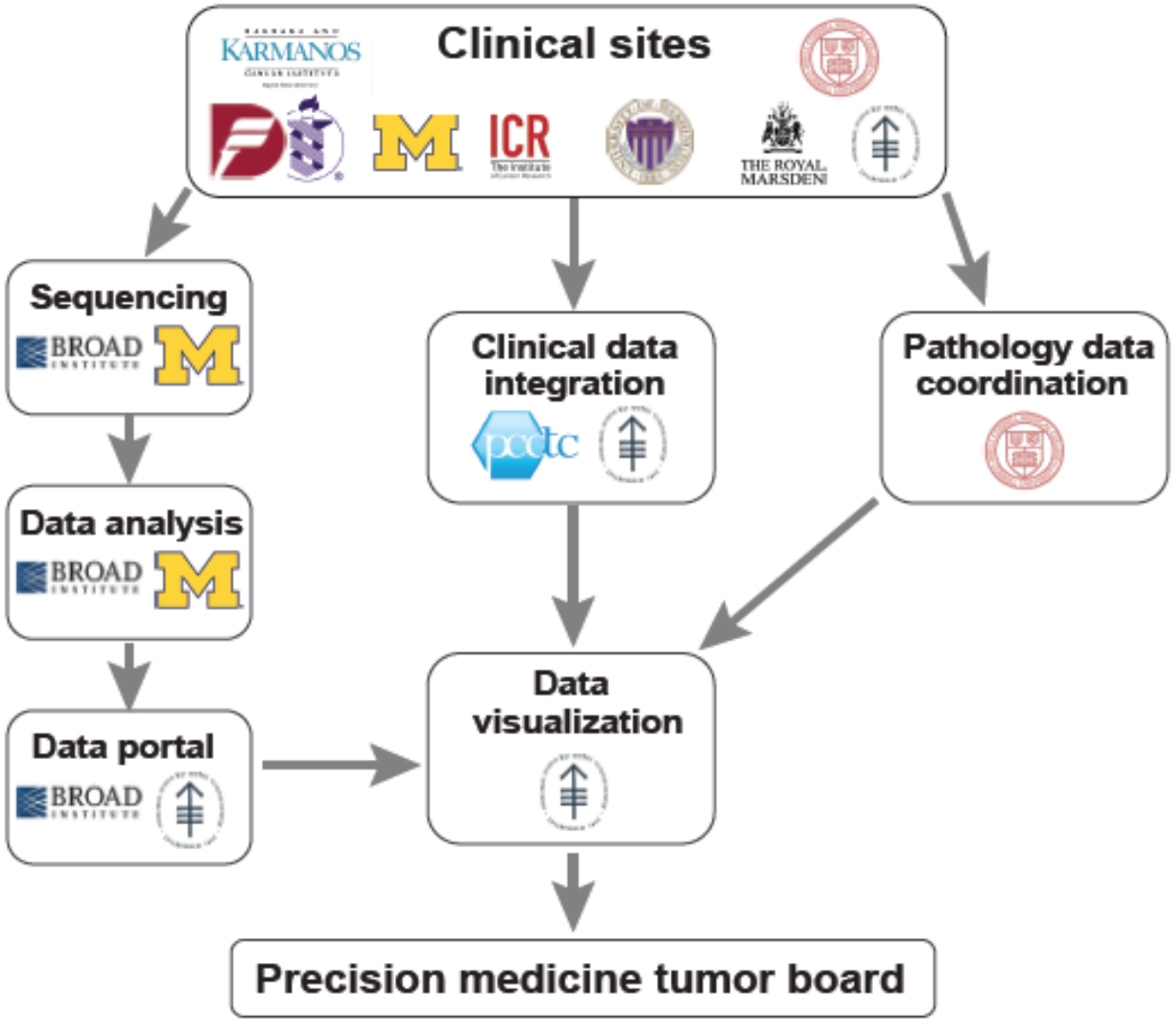
# What do we already know about the genetics of prostate cancer?

- Genetics of primary prostate cancer is complex
- Numerous genetic events contribute to the development of prostate cancer
- Which genetic events are relevant for indolent vs. aggressive prostate cancer are still not known

- Genetics of metastatic prostate cancer is ***vastly more complicated***
- Numerous potentially actionable targets

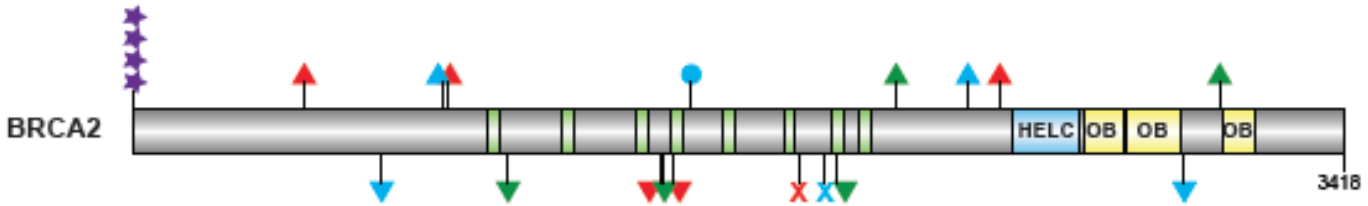
TCGA *Cell* 2015
Robinson, Van Allen et al *Cell* 2015
Armenia et al *Nature Genetics* 2018

# Team science for advanced prostate cancer



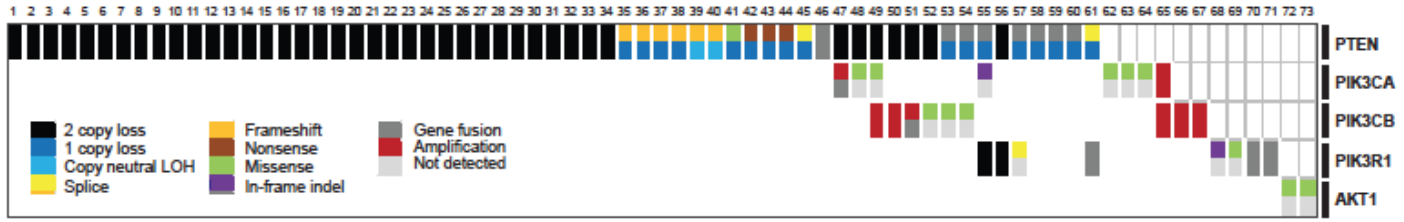

TCGA *Cell* 2015
Robinson, Van Allen et al *Cell* 2015
Armenia et al *Nature Genetics* 2018

# Immediate clinical impact

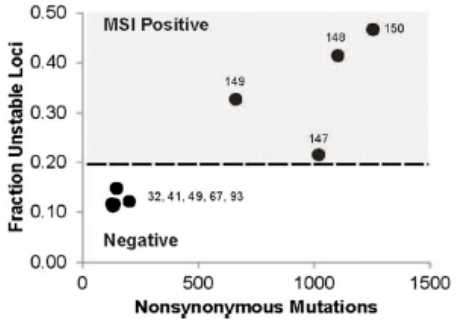



PARP inhibitor clinical trials
Platinum chemotherapy

Universal genetic testing




PI3K inhibitor clinical trials




Immune checkpoint blockade clinical trials

TCGA *Cell* 2015
Robinson, Van Allen et al *Cell* 2015
Armenia et al *Nature Genetics* 2018

# Drugs in development for advanced prostate cancer

| | Gene Rx Target | Drug in Clinical Trials (+/-) | Drug in Pipeline (+/-) | PCF Biopharma Partners (+/-) | Rx Target in Other Cancers |
|---|---|---|---|---|---|
| 1 | Anti AR Pathway | + | + | + | TN Breast Cancer |
| 2 | Anti ETS Fusions | - | - | - | Sarcomas in Children |
| 3 | Anti P53 Mutation | + | + | + | Pancreatic, Lung, Colon, Breast + 19 Others |
| 4 | Anti PTEN Phosphatase Loss | - | - | - | Brain, Breast Cancers |
| 5 | Anti FGFR Mutations | - | + | - | Bladder Cancer, Multiple Myeloma |
| 6 | Anti PIK3C Mutation | - | + | + | Breast Cancer |
| 7 | Anti AKT-1 Mutation | - | + | - | Ovarian, Breast Cancers |
| 8 | Anti RAF | - | + | + | Melanoma |
| 9 | Anti WNT | - | + | - | Colon Cancer, Uterine, Ovarian |
| 10 | Anti BRCAness-DNA Damage Repair (DDR) | - | ++ | + | Ovarian, Breast Cancers |
| 11 | Anti Cell Cycle Kinase | - | + | + | Breast Cancer |
| 12 | Anti SPOP-Anti DEK | - | - | - | Prostate Cancer |
| 13 | Anti CHD1 Mutation | - | - | - | Prostate, Lung, Gastric |
| 14 | Precision Immunotherapy – DDR/HRD Truncal NeoAntigens | + | + | + | Lung, Bladder, Kidney Cancers – All Solid Tumors |
| 15 | Anti GR | - | + | + | Breast Cancer |
| 16 | Anti N-Myc | - | - | - | Pediatric Neuroblastoma |
| 17 | Anti IDH1 | - | + | + | Adult Leukemia, Glioblastoma |
| 18 | Anti Trop2 | + | + | + | Prostate Cancer, Breast Cancer |
| 19 | Anti PSMA Surface Targeted Radiopharmaceutical | + | + | + | Prostate Cancer |
| 20 | Anti SOX2 | - | - | - | Prostate Cancer, Lung Cancer, Breast Cancer |
| 21 | Anti Rb | - | - | - | Prostate Cancer, Glioblastoma, Esophageal |

Source: Prostate Cancer Foundation

# How far have we actually come?

| | |
|---|---|
| Estimated New Cases in 2016 | 180,890 |
| % of All New Cancer Cases | 10.7% |
| **Estimated Deaths in 2016** | 26,120 |
| **% of All Cancer Deaths** | 4.4% |

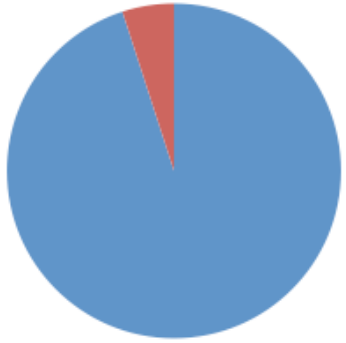
Accrual of ~400 patients over 6 years for study

Lacking clinical “context”

So much to learn…

Can ***patients*** drive the field forward?

# Challenges of Studying Patient Tumor Samples



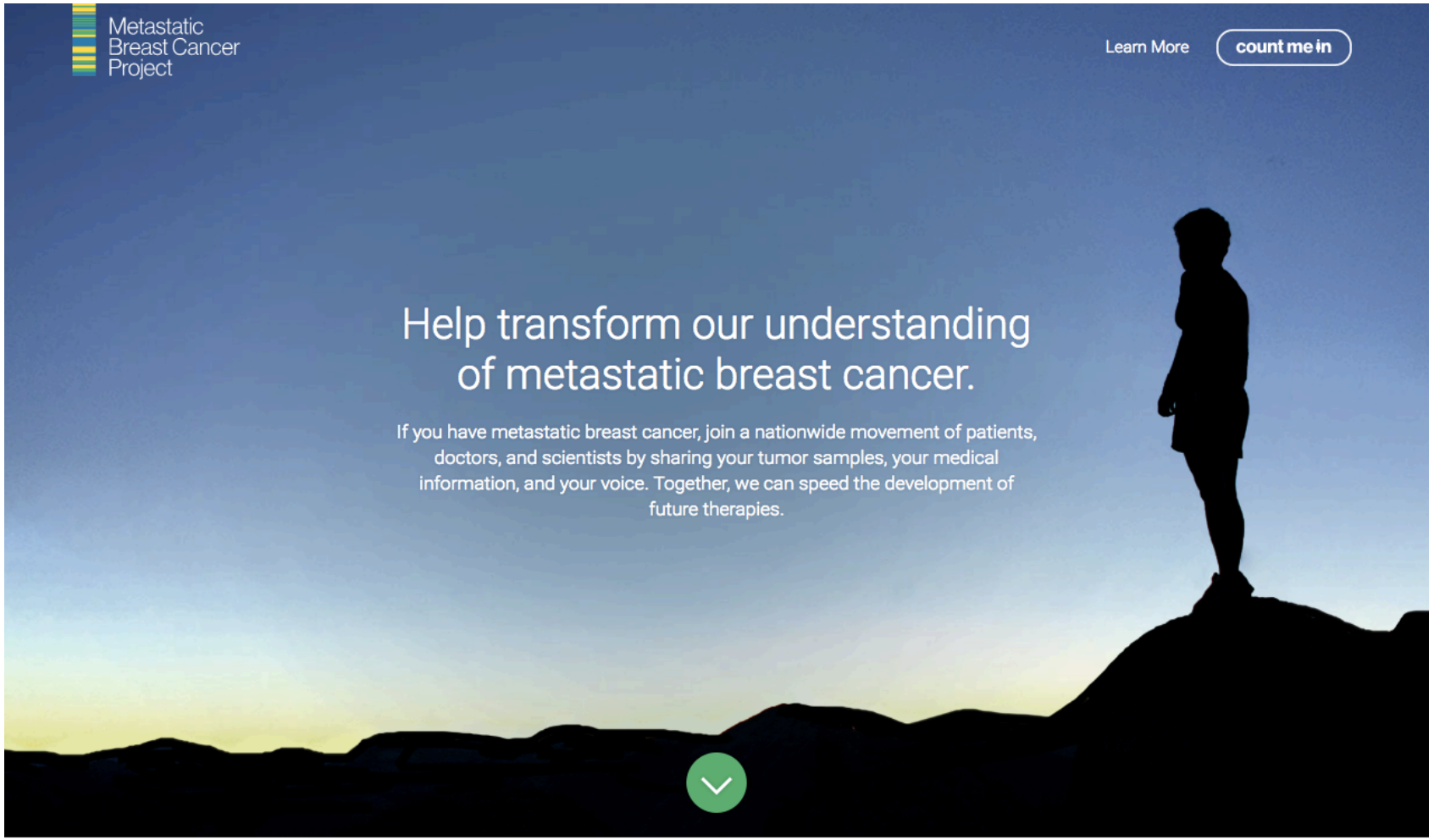
*Only 5% of U.S. cancer patients are enrolled in clinical trials*

*85% of U.S. cancer patients are treated in community settings*

**Most patients have not been readily available for study**


*Social media can now provide a new opportunity to engage cancer patients and directly partner with them in this research*

# The Metastatic **Breast Cancer** Project MBCproject.org

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Metastatic Breast Cancer Project

Learn More | count me in

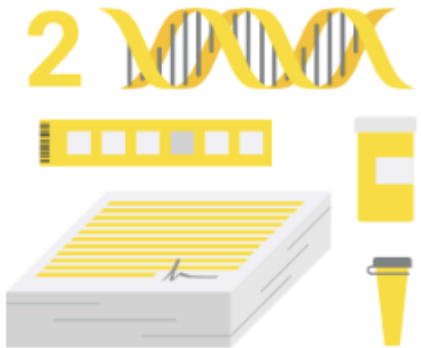
# Become part of the research movement. Have a direct impact on the future.

By saying "Count Me In", you will partner with leading research institutes, hospitals, and patient advocacy groups by sharing part of your stored tumor tissue and copies of your medical records.

## Here's how you can participate


**Step 1. Tell us about yourself**

Click "Count Me In" and complete a simple online form to tell us about yourself and your cancer. Our goal is to perform many different studies within the metastatic breast cancer community, so allowing us to know a little bit about your experience will help us design future




**Step 2. Give us permission to collect your samples and data**

When we start a study that matches what you have told us about yourself, we will ask you to fill out an online consent form that requests your permission to obtain copies of your medical records and some of your stored tumor tissue. We will do the rest - we'll contact

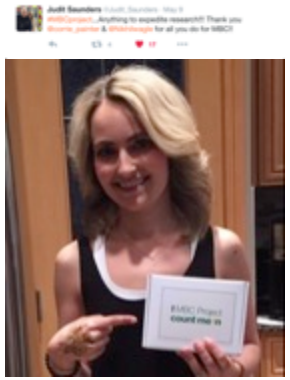

**Step 3. Learn with us along the way**

We are excited to learn with you! Throughout the project, we will provide you with regular updates about the status of the project and share any discoveries that you have enabled us to make. We also may ask you additional questions about your experience to help with

# The Metastatic Breast Cancer Project


*Over **4200 women and men** with metastatic breast cancer from all 50 states have joined the MBCproject since our launch in October 2015*

# The Metastatic Breast Cancer Project



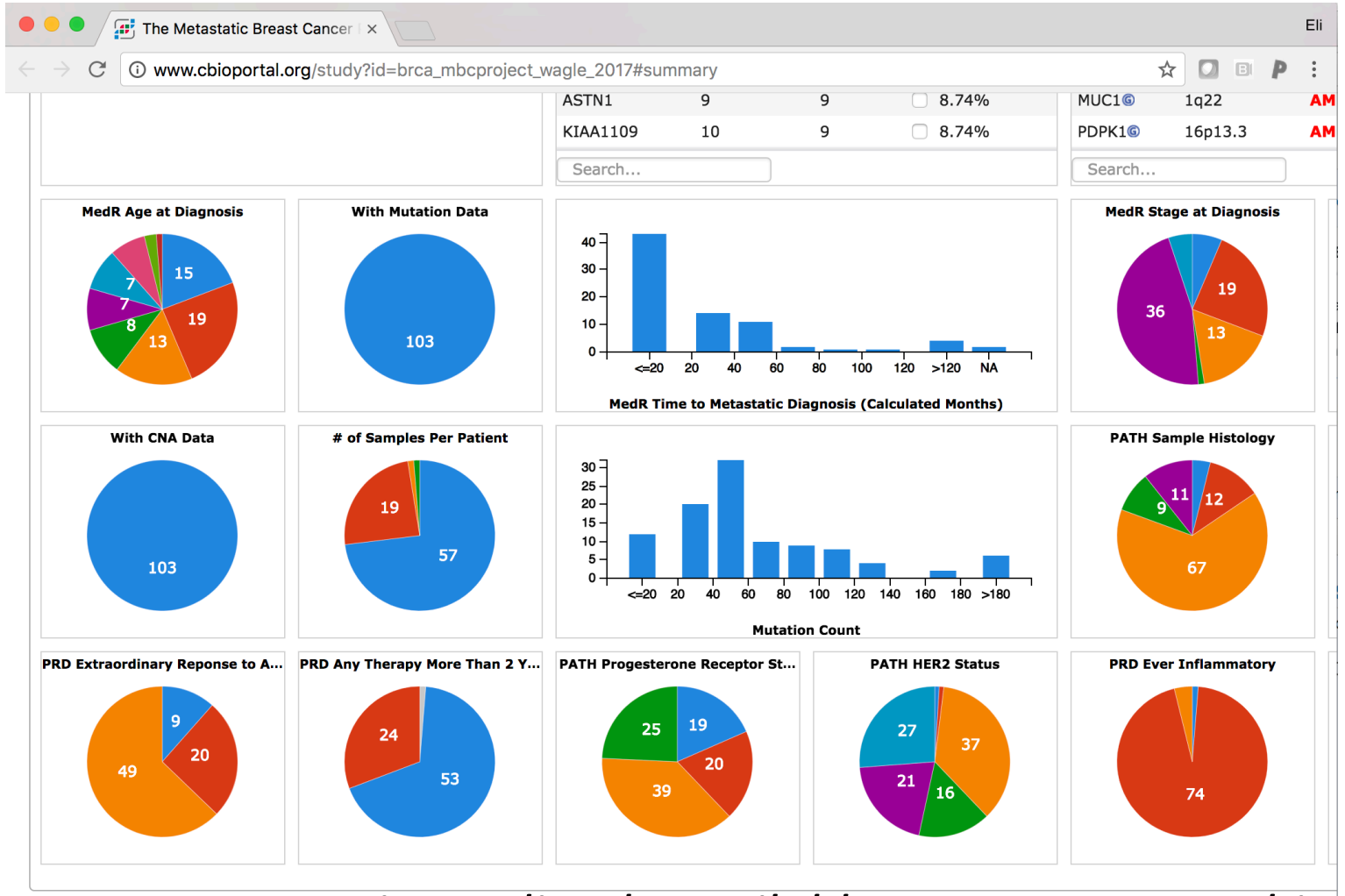



"I want to live and watch my children grow up, but if I can't, then I want to leave a legacy and a cure."
**—Houston, TX**

"As someone who does not live near a research center and therefore cannot easily participate in trials, I finally feel like I can contribute."
**—Lake Tahoe, CA**

"Giving us HOPE for the future and if not for some of us, for our families."
**—Scottsdale, AZ**

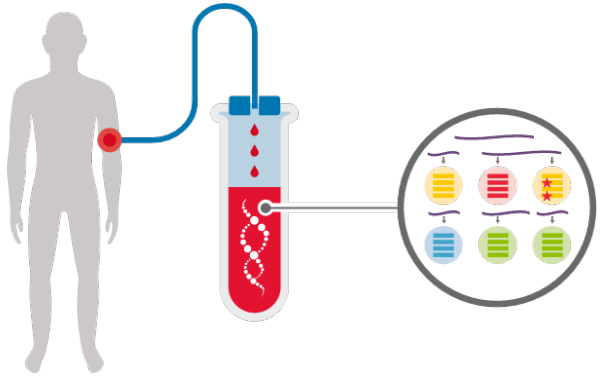
# The Metastatic Breast Cancer Project




*First 100 cancer genomes immediately available to everyone on cbioportal.org*

# Introducing the Metastatic Prostate Cancer Project

*Objective: To generate a publicly available database of clinical, genomic, and patient reported data in MPC to accelerate discoveries and new treatments*



# Prostate cancer patient working group



- Many clinical entities, creating different segregated communities
- Enhancing education in the prostate cancer community
- Men do not like to talk about prostate cancer openly

# The Metastatic Prostate Cancer Project MPCproject.org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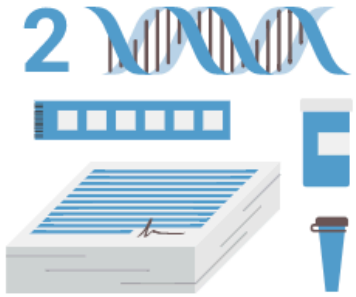
# The Metastatic Prostate Cancer Project MPCproject.org

## Here's how you can participate


### Step 1
Tell us about yourself

Click "Count Me In" and complete a short online form to tell us about yourself and your prostate cancer.




### Step 2
Give us permission to collect your samples and data

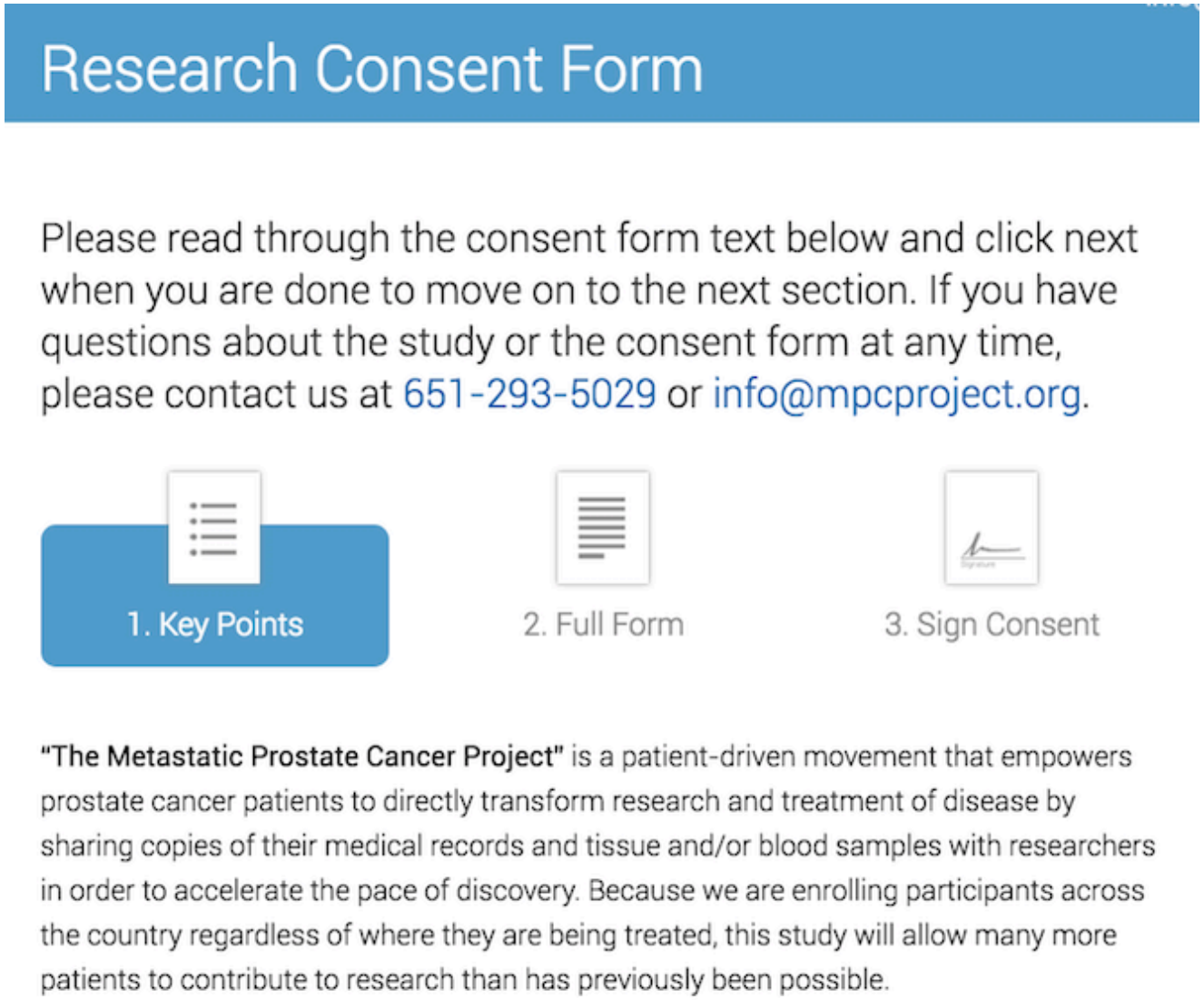
You will be directed to an online consent form to get your permission to collect your samples and data. We will send you a saliva kit and a blood kit. We will do the rest--we'll contact your doctors and hospitals to securely obtain copies of your medical records and a portion of your stored tumor samples.


### Step 3
Learn with us along the way

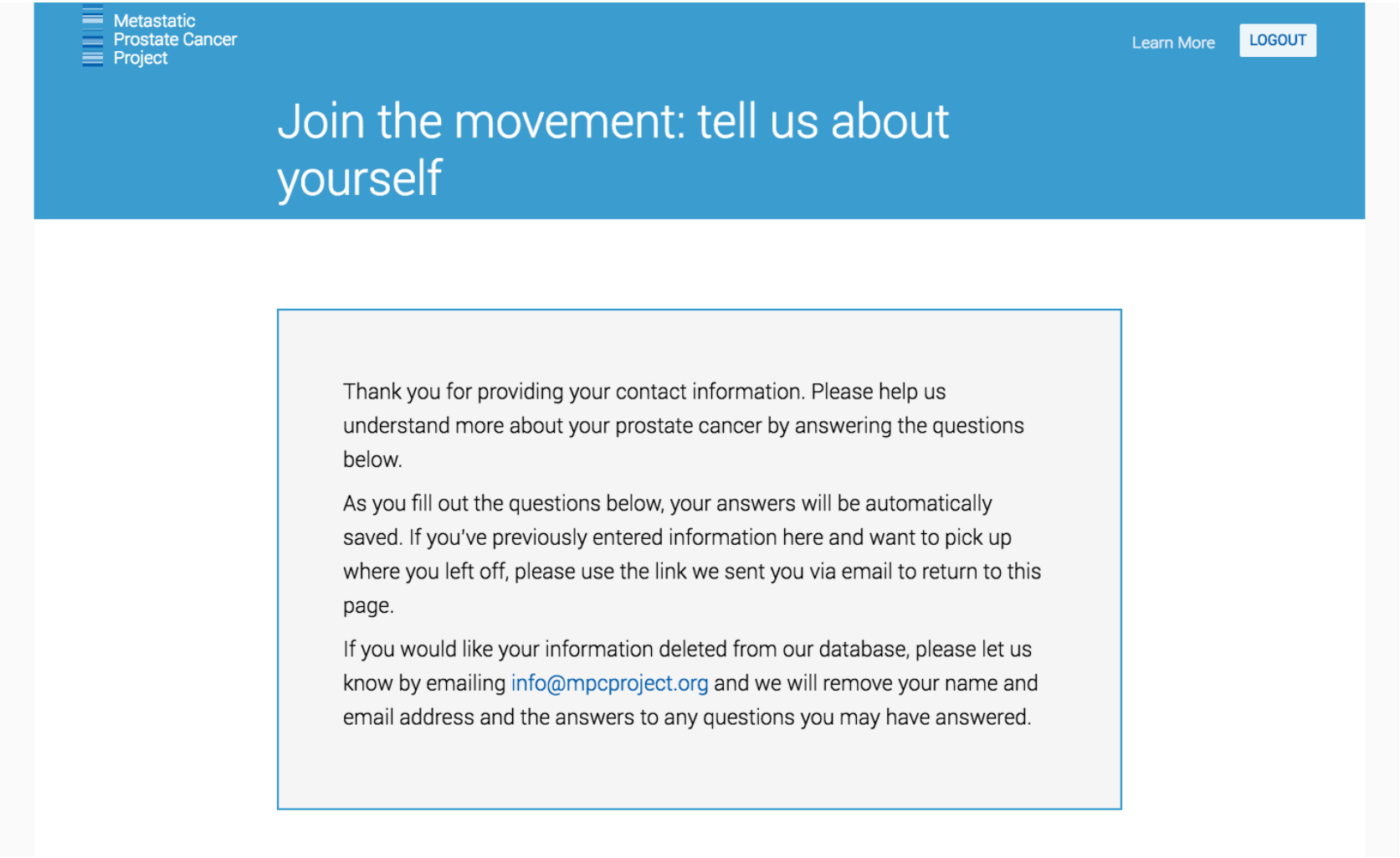
As we learn, we will provide you with regular updates and share any discoveries coming out of the project. We also may ask you additional questions about your experience to help with future studies.

count me in

# Consent process



# Questionnaire process



# Questionnaire process, cont.

## About you

Please fill out as much as you can. All questions are optional. You can return at any time with the link sent to you by email.

1. **When were you first diagnosed with prostate cancer? If you do not remember the month, you can enter just the year.**

   Choose month... | Choose year...

2. **When you were first diagnosed, were you diagnosed with advanced or metastatic prostate cancer (prostate cancer that has spread beyond the prostate, including biochemical recurrence)?**

   - ○ Yes
   - ○ No
   - ○ I don't know

# Questionnaire process, cont.

5. **For your advanced prostate cancer** (prostate cancer that is outside of the prostate), **please check off all therapies that you have previously received or are currently receiving** (Check all that apply)

**Hormones**

- ☐ Lupron (Leuprolide)
- ☐ Zoladex (Goserelin)
- ☐ Casodex (Bicalutamide)
- ☐ Drogenil (Flutamide)
- ☐ Nilandron (Nilutamide)
- ☐ Xtandi (Enzalutamide)
- ☐ Zytiga (Abiraterone)
- ☐ Prostap (Leuprorelin)
- ☐ Firmagon (Degarelix)
- ☐ Suprefact (Buserelin)
- ☐ Decapeptyl (Triptorelin)

**Chemotherapy**

- ☐ Taxotere (Docetaxel)
- ☐ Taxol (Paclitaxel)
- ☐ Paraplatin (Carboplatin)
- ☐ Etopophos / Toposar (Etoposide)
- ☐ Novantrone (Mitoxantrone)
- ☐ Emcyt (Estramustine)
- ☐ Jevtana (Cabazitaxel)

**Other Therapy**

- ☐ Provenge (Sipuleucel-T)
- ☐ Opdivo (Nivolumab)
- ☐ Keytruda (Pembrolizumab)
- ☐ Yervoy (Ipilimumab)
- ☐ Tecentriq (Atezolizumab)
- ☐ Lynparza (Olaparib)
- ☐ Rubraca (Rucaparib)
- ☐ Xofigo (Radium-223)
- ☐ Zometa (Zoledronic Acid)
- ☐ Xgeva / Prolia (Denosumab)
- ☐ Quadramet (Samarium SM 153 lexidronam)
- ☐ Metastron (Strontium-89)

**Experimental/Clinical Trial**

- ☐ Experiment/Clinical Trial
- ☐ Other

6. **Please list additional medications, alternative medications, you've taken or lifestyle changes that you've made since your diagnosis with prostate cancer.**

7. **Have you had any other types of cancer?**

- ○ Yes
- ○ No
- ○ I don't know

8. **Do you have any family history of prostate and/or breast cancer?**

- ○ Yes
- ○ No
- ○ I don't know

9. **How did you find out about this project?**

10. **Is there anything else you would like us to know about your prostate cancer?**

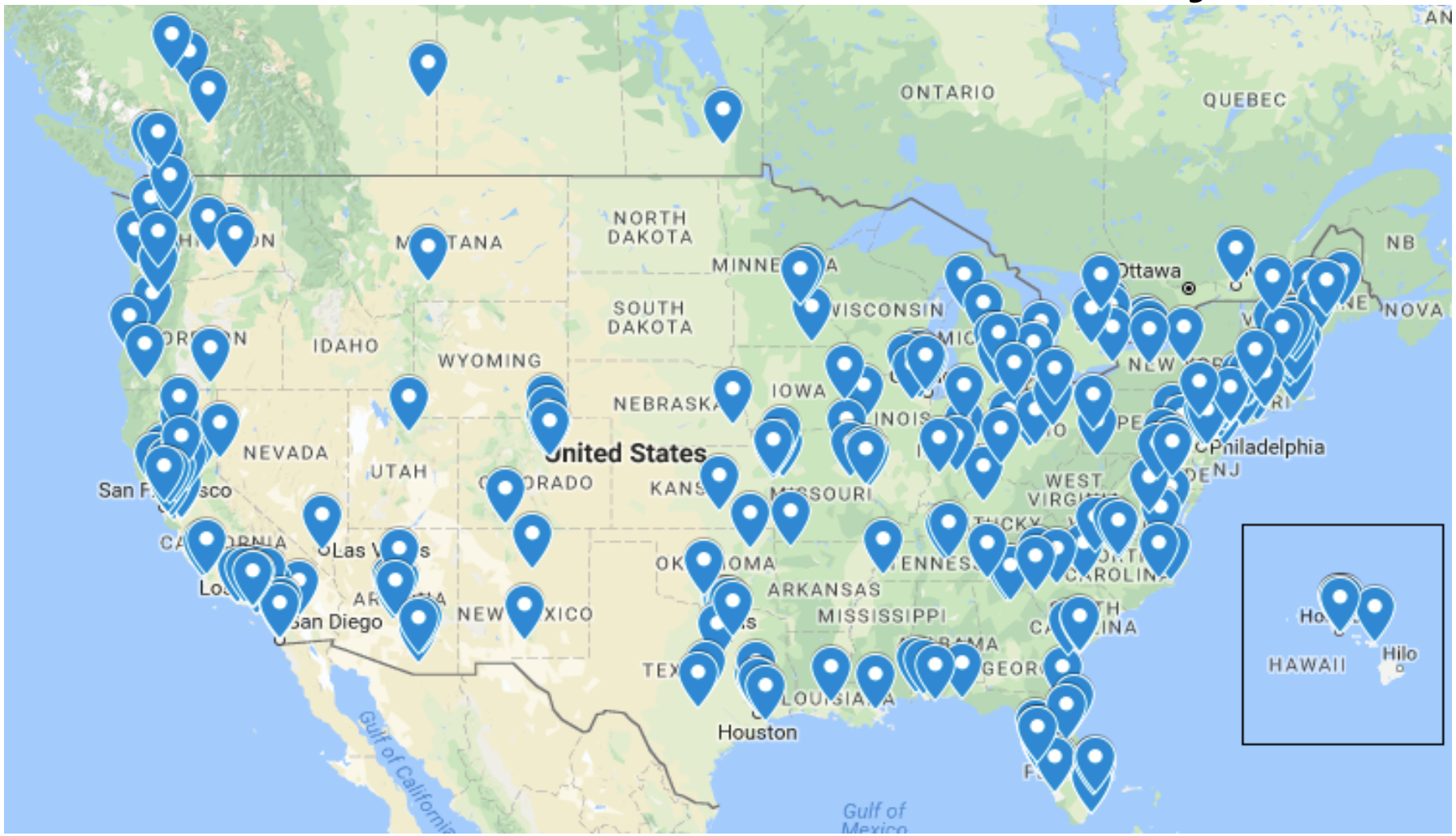
# ”The kit is in the mail”




*No mention of prostate cancer on external facing box after patient feedback*

# Progress to date

# The Metastatic Prostate Cancer Project



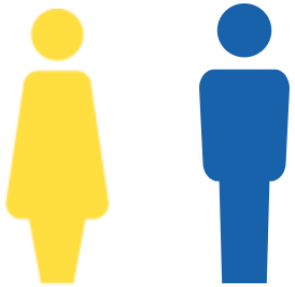

*Over **375 men** with metastatic prostate cancer have joined the MPCproject since our launch in January 2018*

# “Count Me In”

Metastatic Breast Cancer Project

“I want to live and watch my children grow up, but if I can’t, then I want to leave a legacy and a cure.”
**—Houston, TX**

“As someone who does not live near a research center and therefore cannot easily participate in trials, I finally feel like I can contribute.”
**—Lake Tahoe, CA**



Metastatic Prostate Cancer Project

“My doctor told me to do this.”
**—USA**

# Patient Engagement

# Our Advocacy Partners

Prostate Cancer Foundation
Curing Together.

PCaFi

ADIRONDACK HIKE FOR HOPE
ADKHIKEFORHOPE.ORG

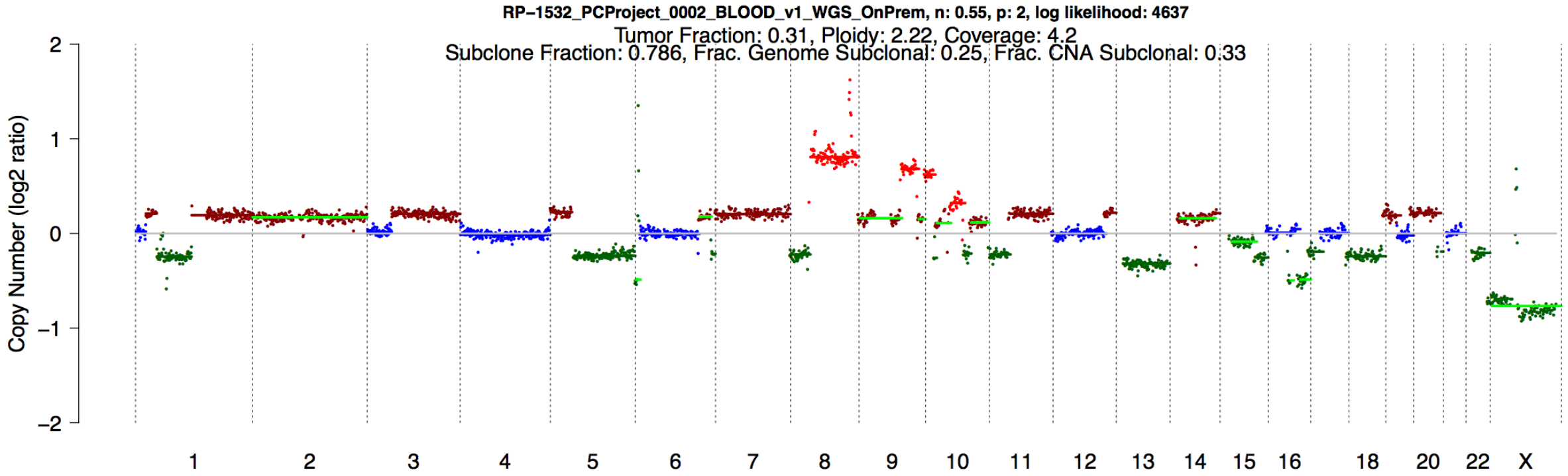
CANCER ABCs™
FROM SURVIVING
TO THRIVING

Us TOO
Prostate Cancer
SUPPORT - EDUCATION - ADVOCACY

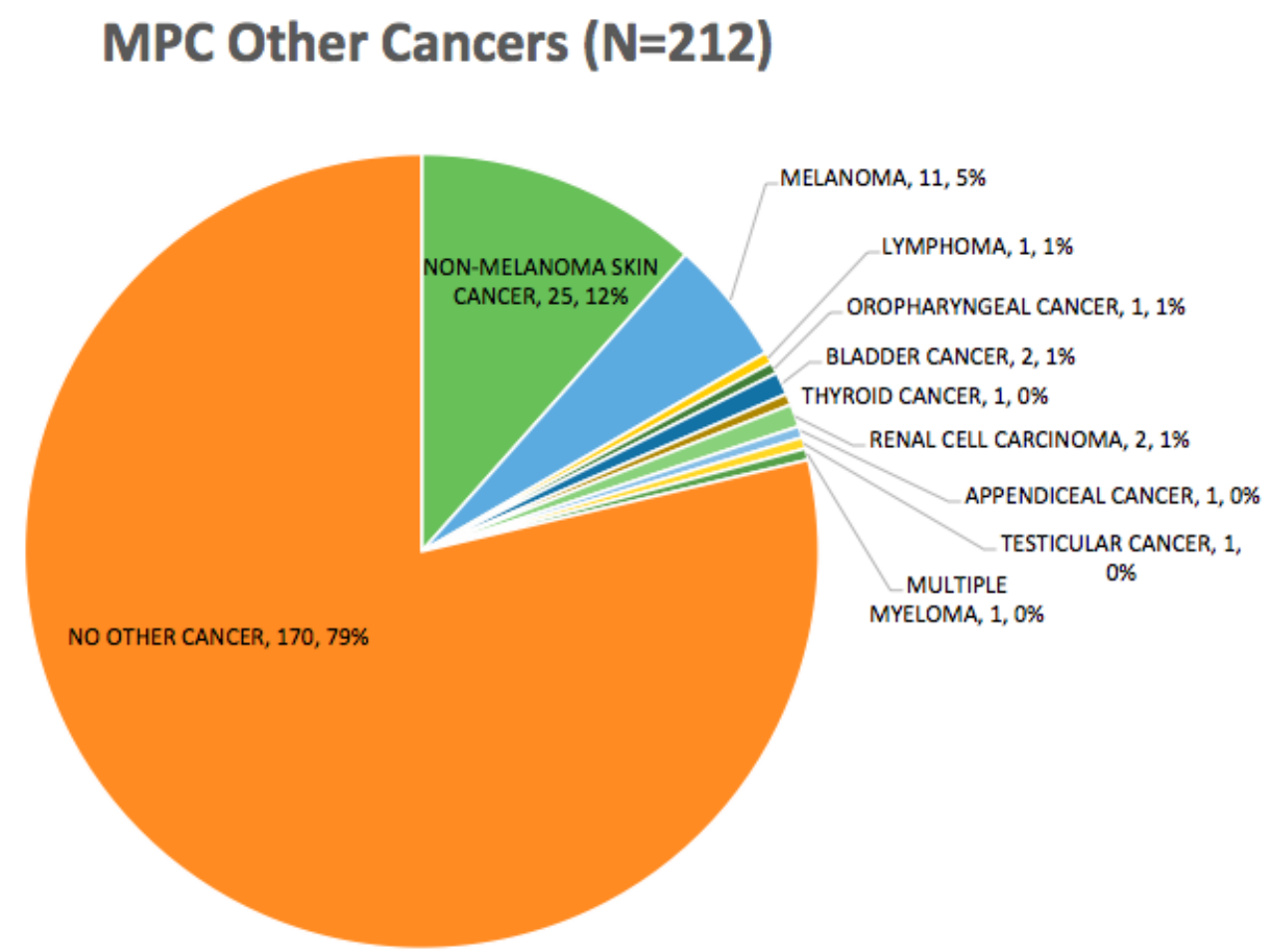
ANSWER CANCER FOUNDATION
Advocacy • Navigation • Support

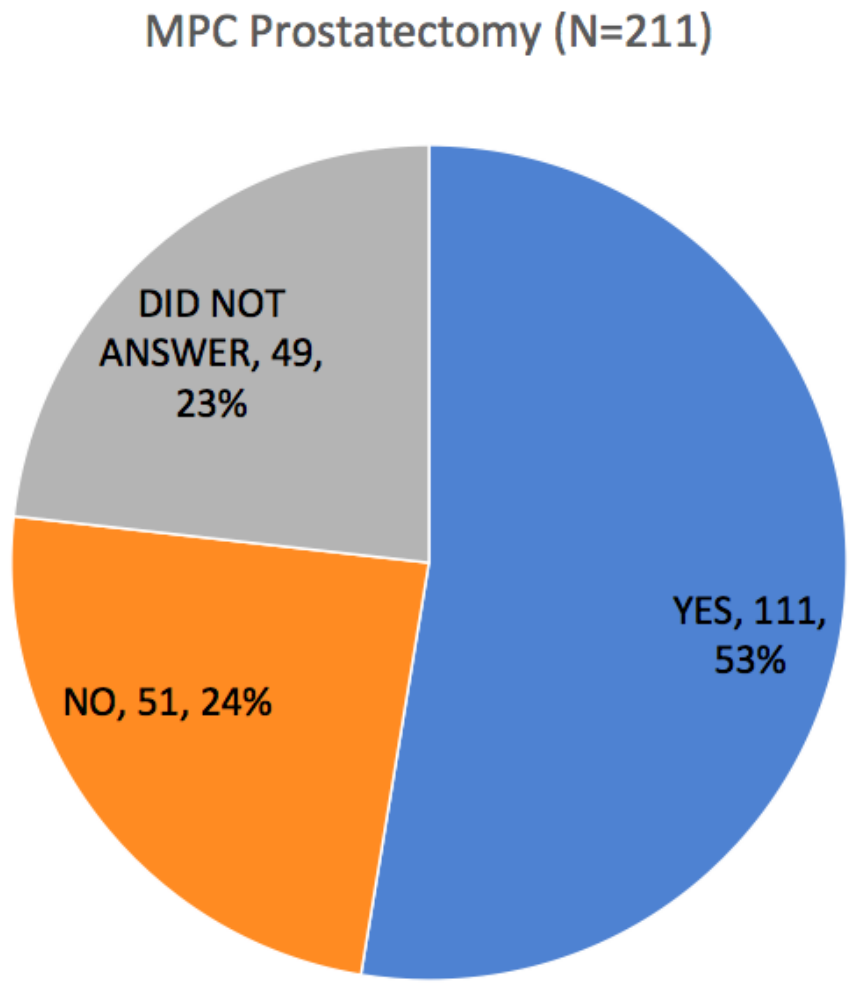
# Both saliva and ”liquid biopsy” kits

# “Liquid” biopsy from a beta-tester

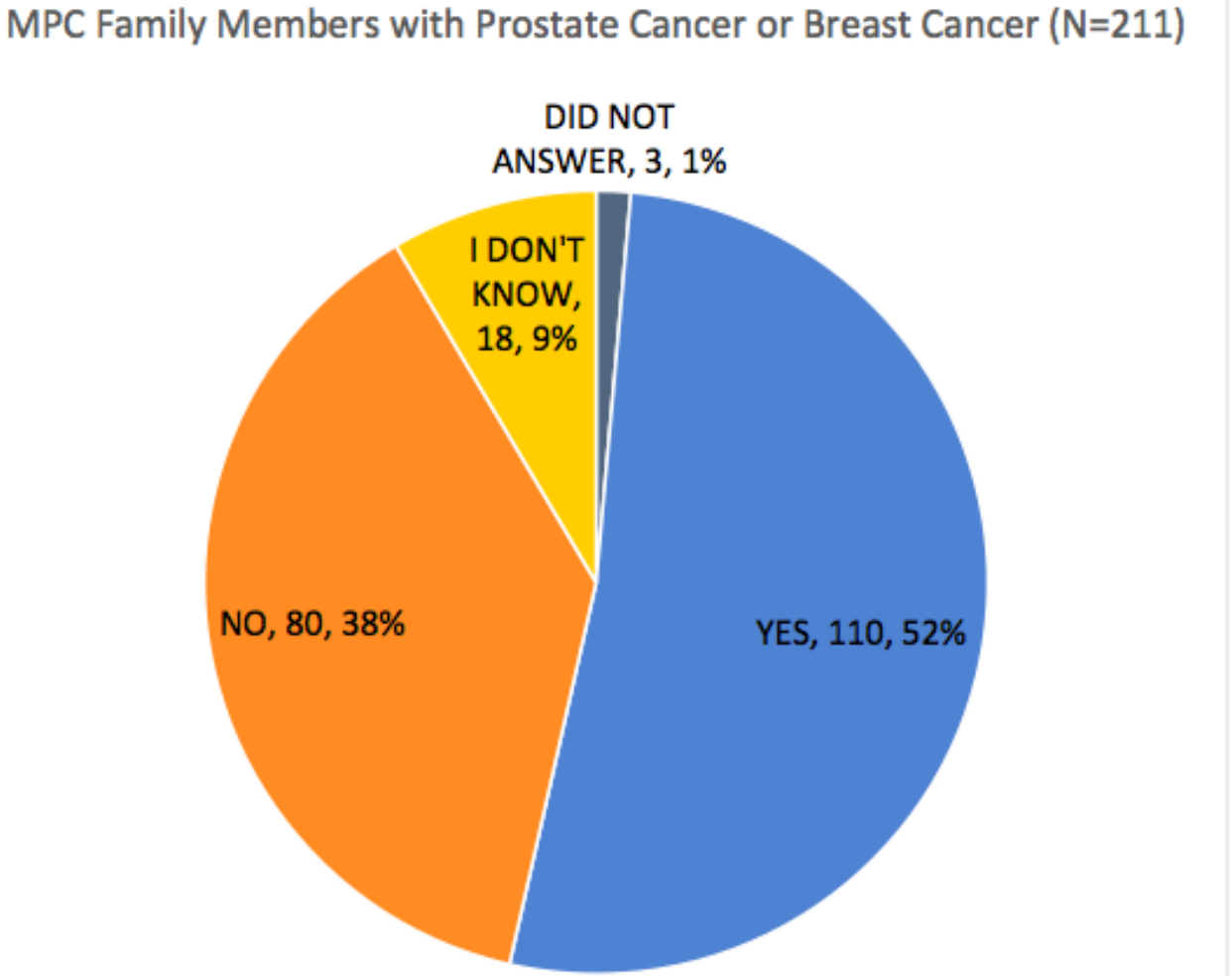


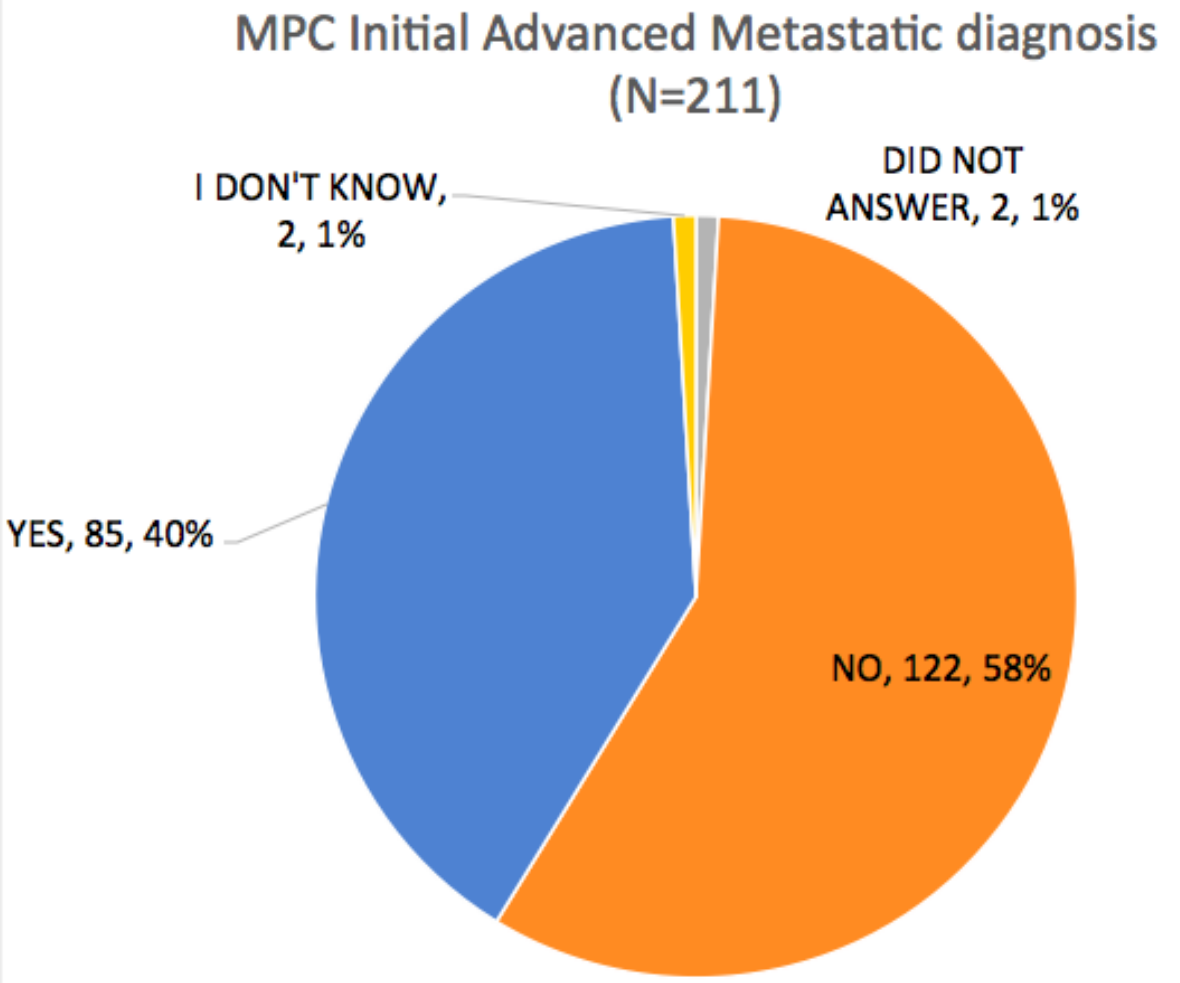
# Patient-reported data



# Patient-reported data, cont.




***New hypotheses driven directly by patient-reported information!***

# Translating discoveries into clinical action

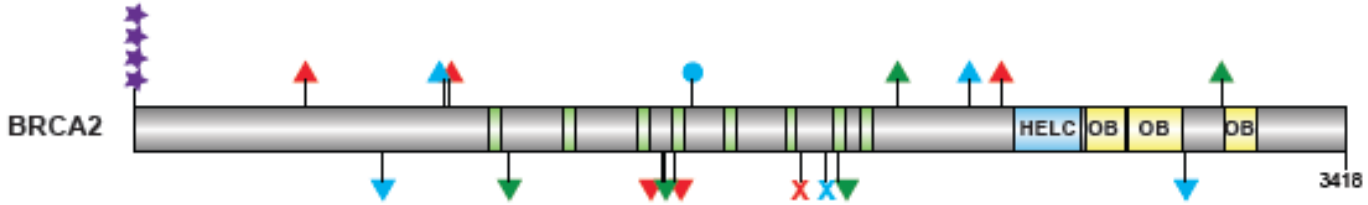
# Currently no individual return of results

4. **Will I benefit from participating?**

   While taking part in this study may not improve your own health, the information we collect will aid in our research efforts to provide better prostate cancer treatment and prevention options to future patients. We will provide you with updates about key research discoveries made possible by your participation.

# Example of research findings that have rapidly changed clinical practice

2015




The NEW ENGLAND JOURNAL of MEDICINE

2016

ORIGINAL ARTICLE

## Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer

C.C. Pritchard, J. Mateo, M.F. Walsh, N. De Sarkar, W. Abida, H. Beltran, A. Garofalo, R. Gulati, S. Carreira, R. Eeles, O. Elemento, M.A. Rubin, D. Robinson, R. Lonigro, M. Hussain, A. Chinnaiyan, J. Vinson, J. Filipenko, L. Garraway, M.-E. Taplin, S. AlDubayan, G.C. Han, M. Beightol, C. Morrissey, B. Nghiem, H.H. Cheng, B. Montgomery, T. Walsh, S. Casadei, M. Berger, L. Zhang, A. Zehir, J. Vijai, H.I. Scher, C. Sawyers, N. Schultz, P.W. Kantoff, D. Solit, M. Robson, E.M. Van Allen, K. Offit, J. de Bono, and P.S. Nelson

2017

PARP inhibitor clinical trials
Platinum chemotherapy

Universal genetic testing

***Regular updates of research findings to participants***

***Bring updates to your physician***

# Summary

- Partnering directly with the MPC community enables *rapid* identification of large numbers of patients willing to share tumors, saliva, and medical records to accelerate research
- Enables study of rare patients, otherwise challenging to find with traditional approaches
- A shared resource: all clinical and genomic data generated in this study will be shared widely with researchers

# Team

## Eli Van Allen

- Assistant Professor of Medicine: Harvard Medical School
- Oncologist: Dana-Farber/Partners Cancer Care
- Associate Member: Broad Institute

## Corrie Painter

- Associate Director of Operations and Scientific Outreach

## Nikhil Wagle

- Executive Director: Count Me In Initiative (Broad Institute)
- Director, Metastatic Breast Cancer Project
- Assistant Professor of Medicine: Harvard Medical School

## Stephanie Mullane

- Associate Computational Biologist: Broad Institute

## Mike Dunphy

- Innovation and Operations Manager: Broad Institute

*Plus many others…*

# Let’s work together!

- **Questions?**

- Emails: info@mpcproject.org
- Twitter: @PrCaProject
- Facebook: https://www.facebook.com/MetastaticProstateCancerProject/