Genomic Instability

...and other ruminations on the nature of awards

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Thank you. It's an honor to be here.

Genetics have been on my mind a lot lately.

A few months ago we finalized my daughter's adoption and about a month after that we parted ways with my foster son when he was reunited with biological family.

The adoption of my children means that my spouse and I have started to plan ahead for the challenges of inevitable family tree assignments and from the beginning we've found ourselves reframing questions about who their "real" parents are.

Genetics are everywhere, these days, aren't they?

Ancestry.com and 23&me have taken over advertising spots on Hulu and holiday shopping displays.

Even while I pondered initial ideas for these remarks, the ethics of gene-editing human embryos were being hotly debated on NPR.

For me, though, nearly daily musing on genetics started in earnest about a year and a half ago, when my father unexpectedly passed away.

Garth Richard Anderson was an oncologist - a cancer researcher dedicated to exploring genomic instability.

“Genomic instability [I’ll quote from *Nature*] is a characteristic of most cancers. In hereditary cancers, genomic instability results from mutations in DNA repair genes and drives cancer development.”

Until I was in high school and interned with a genetic counselor in the research hospital where my father worked, I don’t know that I could have told you what he actually did. I often said simply, he “worked in a lab.”

https://www.nature.com/articles/nrm2858

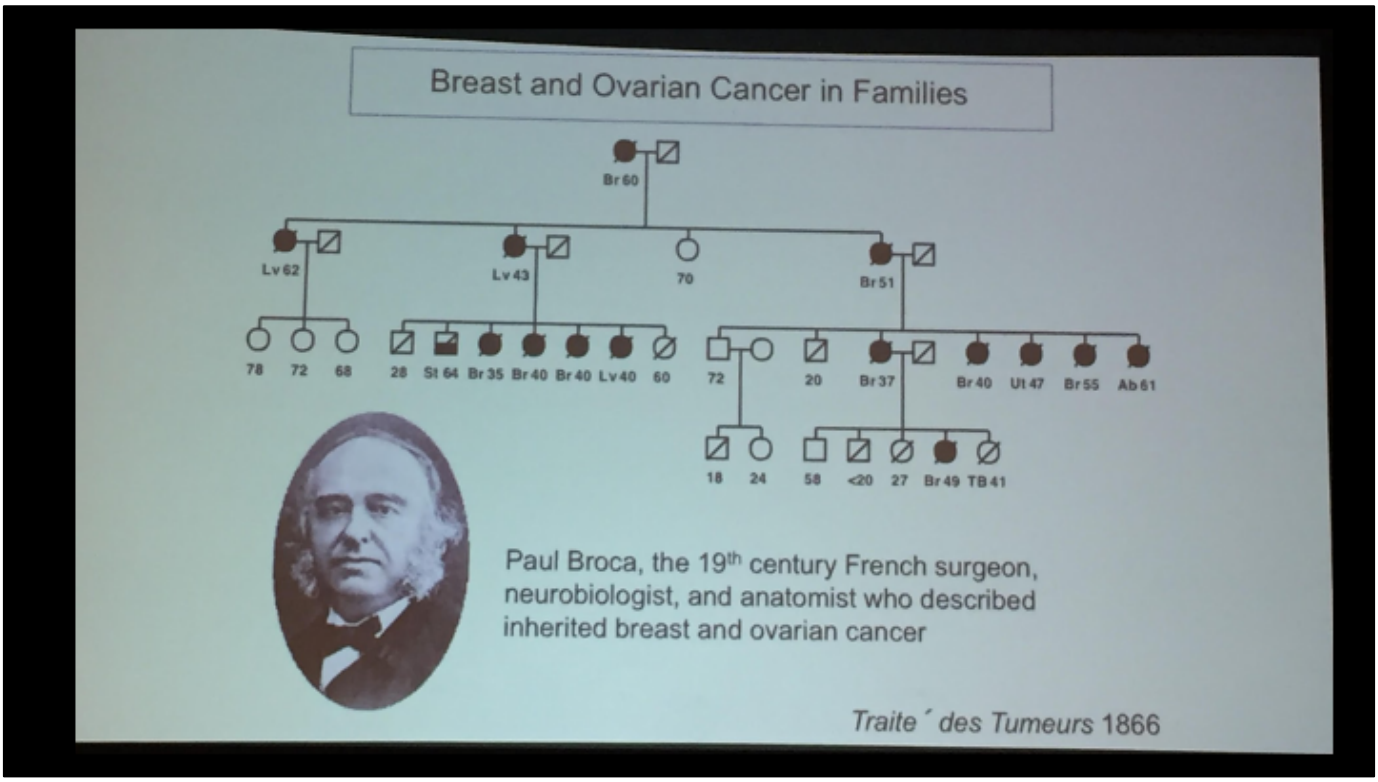
Because most of all, he was just my dad. He loved learning and he loved teaching, as evidenced by this photo when he came to teach my kindergarten class about projectile rockets (like you do).

My dad was a smart guy and I wish I'd told him I thought so more often.

This is my little sister, Robin.

Life went on after we lost our dad, as it does, until last spring when Robin was diagnosed with stage 2B triple negative breast cancer at the age of 32. She's given me permission to include her in this story and spoiler: she's doing fine now, all done with chemo, radiation, and multiple surgeries as we wait out these first critical five years following her diagnosis.

Such an early diagnosis is unusual until you begin to put together a family history like mine.



My family cancer history is not so dissimilar from this famous pedigree published in 1866 by Paul Broca, a French physician who provided the first detailed scientific description of inherited breast-ovarian cancer.

For those who aren't used to reading pedigrees, you can see four generations affected by cancer - this is Broca's wife's extended family. Circles are females, squares are males. Dark coloration means affected by cancer.

A diagonal line indicates that the person is deceased - here at the ages such as 35, 40, 37, 47 and so on.

So last spring my DNA was analyzed, as my sister's had been. And for almost a year to the day, I've been dealing with the consequences of a BRCA1 mutation diagnosis, myself.

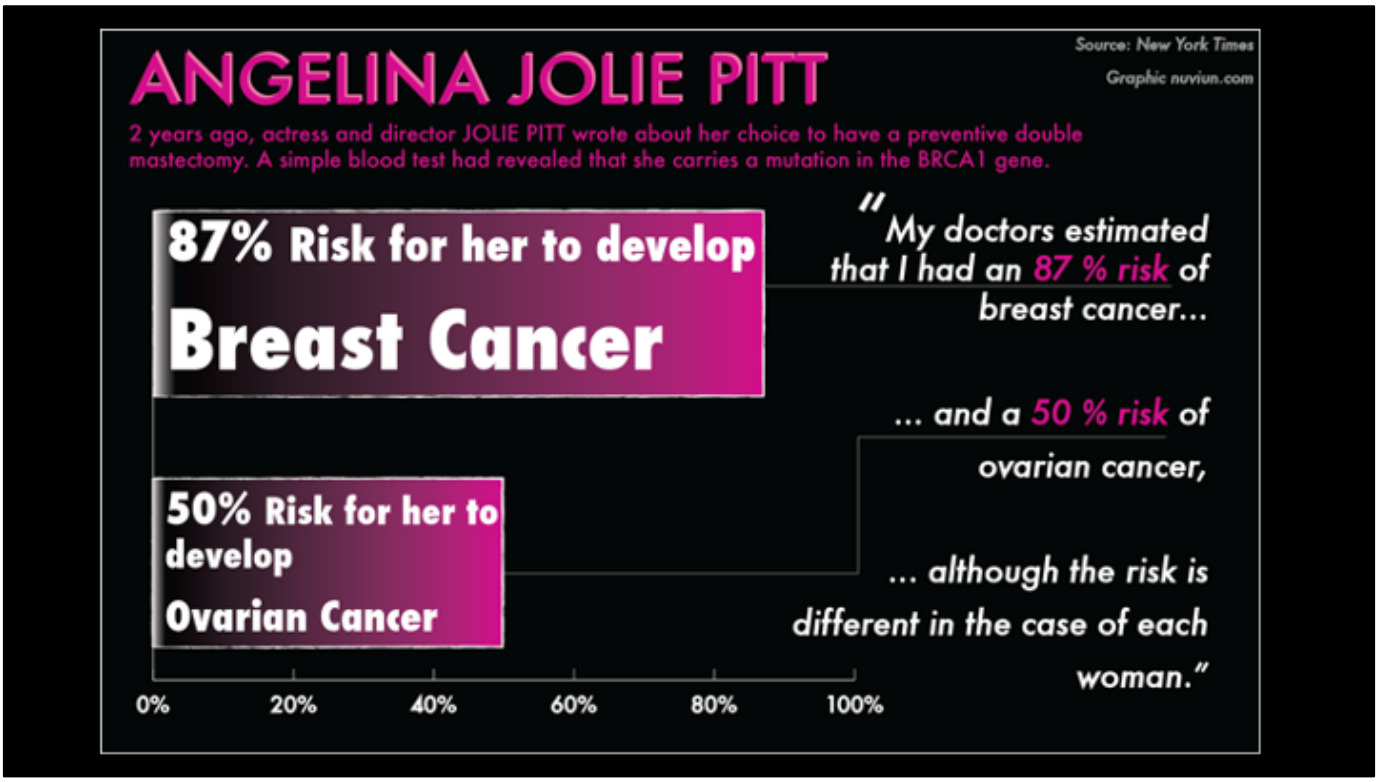
You've likely heard of BRCA1 - it's the Angelina Jolie genetic mutation. Angelina Jolie, yes, and millions of other women *and men*. I hope you'll indulge a brief overview from me, a theater professor, when there are so many who are more qualified to explain in this room.

From NationalBreastCancer.org:
The name "BRCA" is an abbreviation for "BReast CAncer gene." BRCA1 and BRCA2 are two different genes that have been found to impact a person's chances of developing breast and ovarian cancer.

Every person has both the BRCA1 and BRCA2 genes. Despite what their names might suggest, BRCA genes do not cause breast cancer. In fact, these genes normally play a big role in prevention. They help repair DNA breaks that can lead to cancer and the uncontrolled growth of tumors. Because of this, the BRCA genes are known as tumor suppressor genes.

However, in some people (about one in 400), these tumor supression genes do not work properly: a gene mutation.

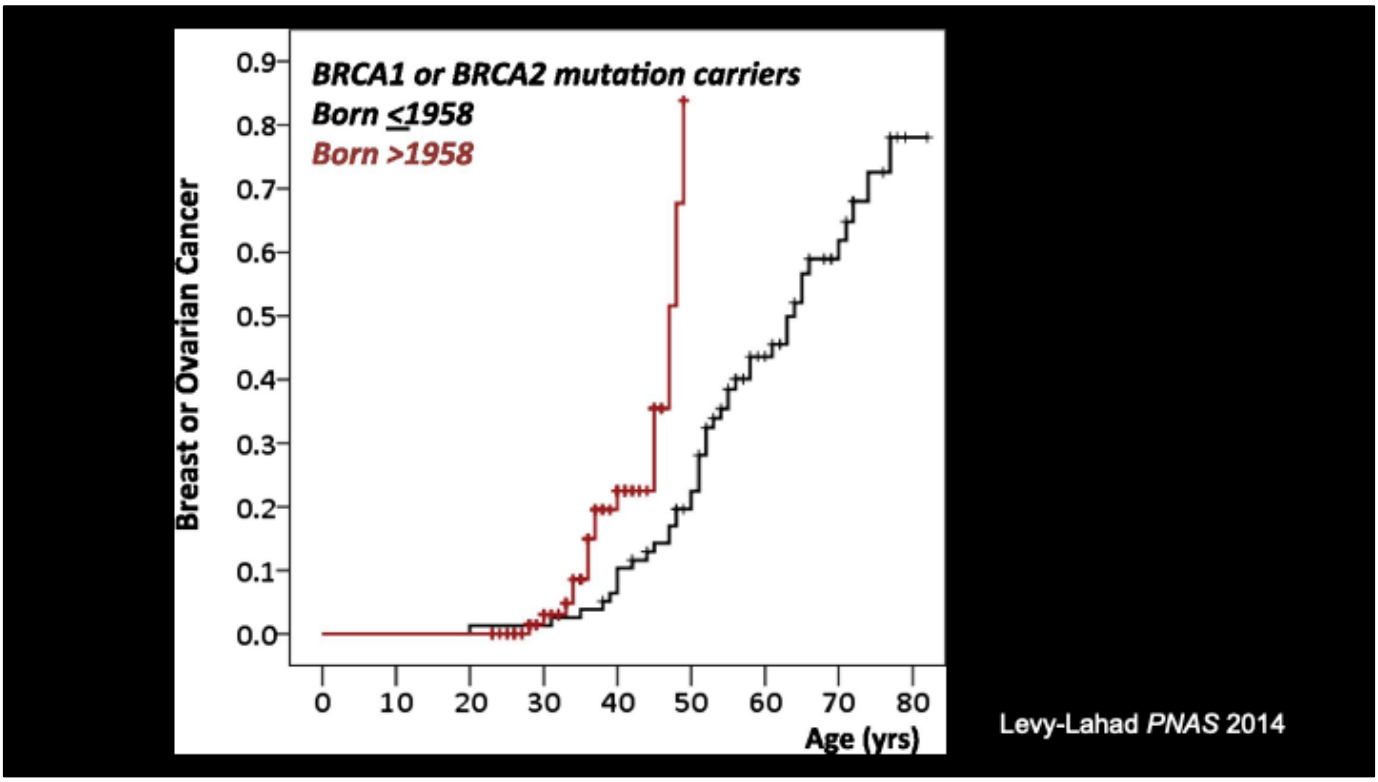
https://www.nationalbreastcancer.org/what-is-brca



Here's what it meant for Jolie (and for many of us with a BRCA1 mutation). [go over statistics on slide]

This is compared to an 8% lifetime risk in a control population.

This genetic mutation had been one area of my father's research. It is also what he unknowingly passed on to my sister and me.



Six days ago - last Tuesday - I had the last of several surgeries that drastically reduce my chances of developing particularly virulent forms of breast/ovarian cancer.

The odds, I'm told, have dropped from approximately 85% to less than 5%.

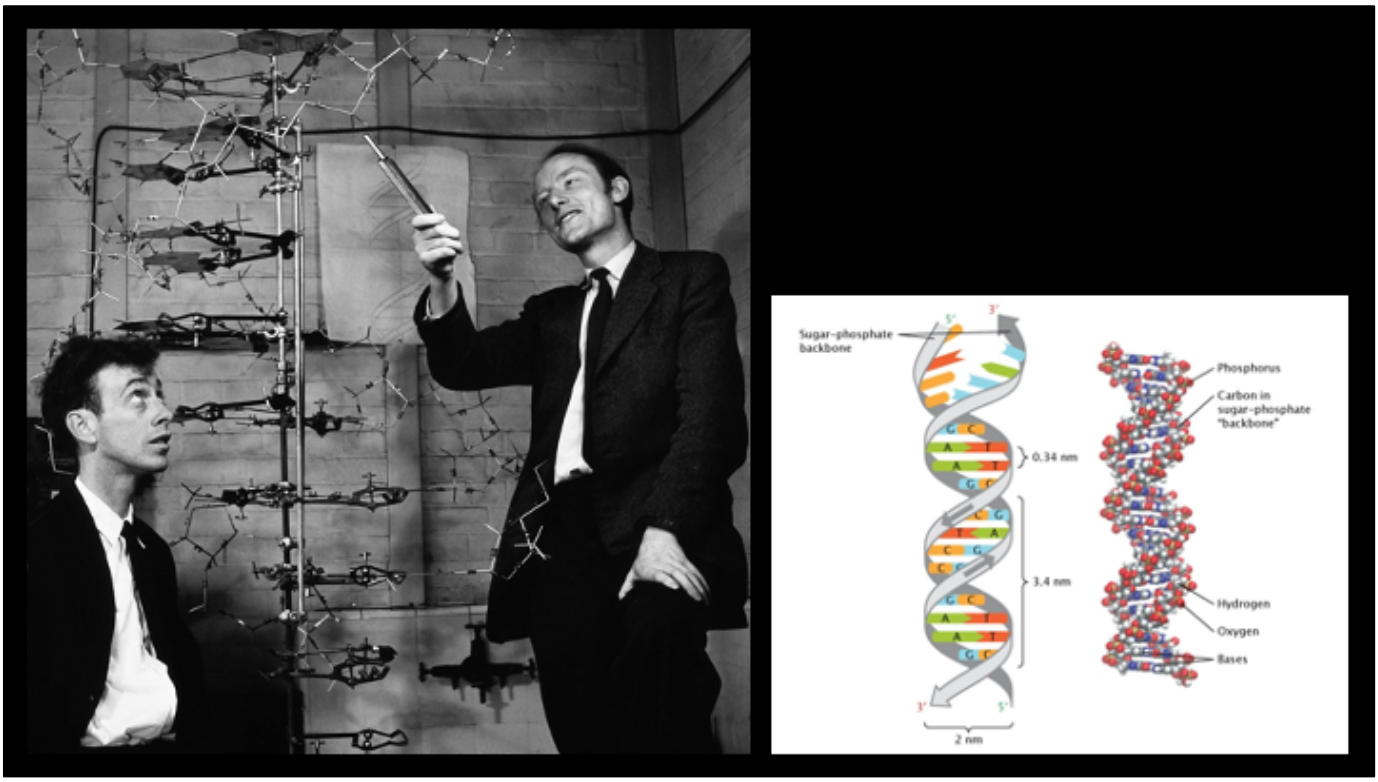
That's still not perfect, but, when you look at this graph, given that I was born after 1958 (the median age in this study) and the fact that I turned 40 last summer, I didn't hesitate.

I would do whatever I could to ensure that I would be around for my kids for as long as possible.

As I said, genetics have been on my mind a LOT. By now I'm sure you're wondering what serious genetic mutations have to do with awards, especially on your award night!

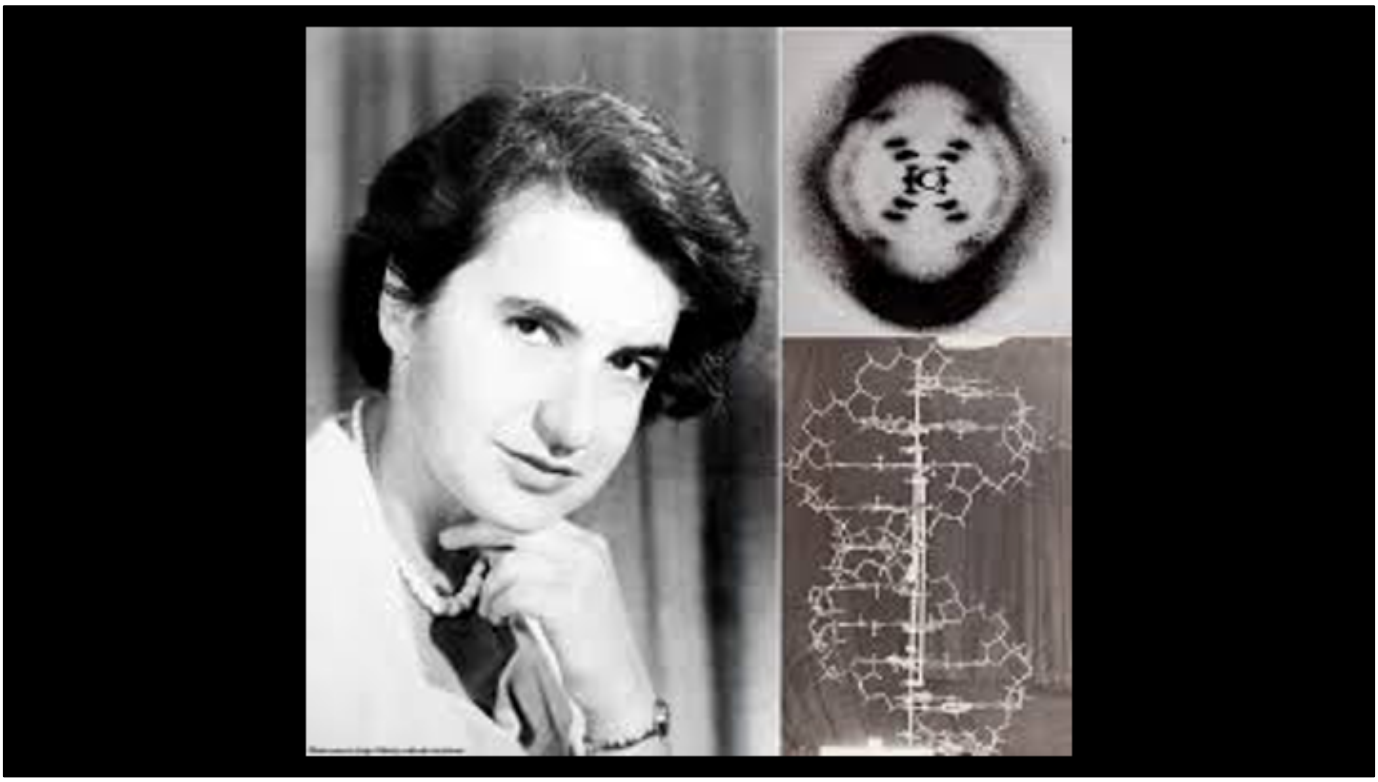
Okay. Let's talk awards.

Who is credited with discovering the double helix - the structure of DNA?



Francis Crick & James Watson - and the Double Helix

Here they are, along with Maurice Wilkins, accepting the Nobel Prize in Physiology or Medicine in 1962.



What about Rosalind Franklin?

I first learned about Rosalind Franklin in high school chemistry. We had to do reports and I chose her name simply because it belonged to one of very few women on a long list of options.

Rosalind Franklin was an English scientist who made X-ray images of DNA. Her work was critical to the discovery of the double helix structure. Franklin died before the structure was discovered, however, and the Nobel Prize can only be given to living people.

We can’t change the history of the Nobel Prize. But we can acknowledge the contributions/work of others… especially women and other historically marginalized groups in STEM fields.

TAKEAWAY #1: Acknowledge the shoulders on which you stand… and those who haven't been invited for recognition.

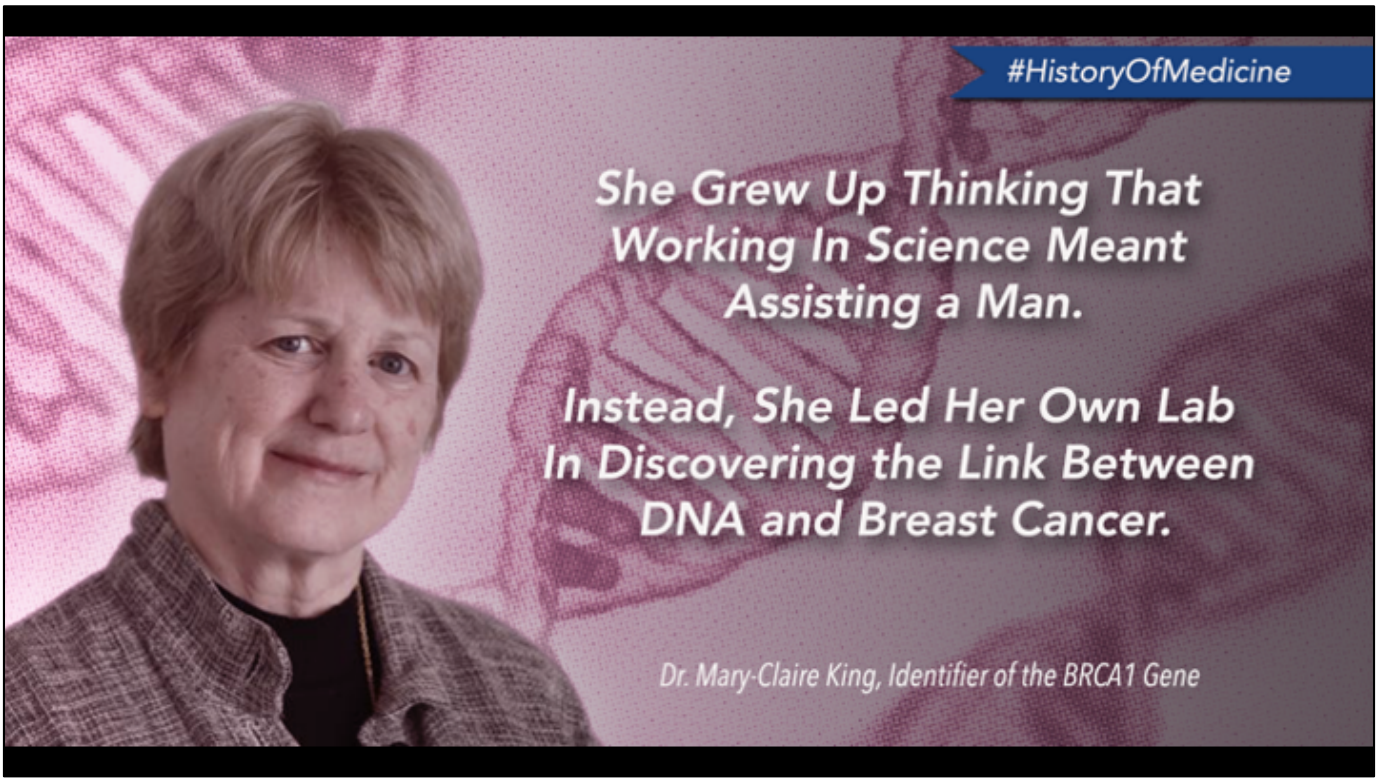
TAKEAWAY #2: Awards should be celebrated, but they don't really matter in the long run. The achievements they recognize do.

There are a few ideas I hope you'll take away from my remarks this evening:

TAKEAWAY #1: Acknowledge the shoulders on which you stand… and those who haven't been invited for recognition.

Let's not stop there.

TAKEAWAY #2: Awards should be celebrated, but they don't really matter in the long run. The achievements they recognize do. Allow me to explain.



In 1990, decades after the discovery of the double helix, Dr. Mary-Claire King and her lab published a landmark paper in *Science*, proving the existence of the first hereditary breast cancer gene: *BRCA1*.

This was a really big deal, for at the time, virtually the entire medical science community believed that breast cancer was caused by a number of different genes interacting with different environmental factors, and that the search for a unique 'breast cancer gene' was a hopeless cause.

I also want to share that Dr. King had been a math major at a small liberal arts college not unlike this one. Shout out to math majors.

- 2018, Advocacy Award, American Society of Human Genetics (ASHG)[63]
- 2018, Shaw Prize in Medicine, China[64][65]
- 2018, Dan David Prize, Israel[66]
- 2017, TNQ Distinguished Lectures in the Life Sciences, Seventh Annual Cell Press-TNQ India Distinguished Lectureship Series[67]
- 2016, National Medal of Science[68](announced in 2015)[69][70]
- 2016, TUBA Academy Prize in Health and Life Sciences, TÜBA - Turkish Academy of Sciences [71]
- 2014, HudsonAlpha Life Sciences Prize[72]
- 2014, Lasker~Koshland Special Achievement Award in Medical Science[73][74]
- 2013, Paul Ehrlich and Ludwig Darmstaedter Prize[49]
- 2010, CSHL Double Helix Medal Honoree[75]
- 2006, Dr A.H. Heineken Prize for Medicine[12]
- 2006, Weizmann Women & Science Award, Weizmann Institute of Science[76]
- 2005, member, National Academy of Sciences[77]
- 2004, Gruber Prize in Genetics, Gruber Foundation[78]
- 1999, Basic Science Award, Brinker International Awards for Breast Cancer Research, Susan G. Komen for the Cure[79]
- 1996, inaugural Jill Rose Award, The Breast Cancer Research Foundation[80][81]
- 1994, Institute of Medicine (now National Academy of Medicine)[82]
- 1994, G. H. A. Clowes Award, American Association for Cancer Research (AACR) & Eli Lilly and Company[83]
- 1993, Fellow, AAAS[84]
- 1993, Woman of the Year, *Glamour* Magazine
  - 1992, Susan G. Komen Foundation Award for Distinguished Achievement in Breast Cancer, Susan G. Komen for the Cure[83][85]

Dr. King has won numerous awards, prizes, and honors for her extensive scientific and humanitarian work. So many, in fact, they are impossible to contain on just one slide.

Images:
Lasker Award Ceremony 2.) American Cancer Society Legacy and Leadership, 3.) National Medal of Science 4.) Shaw Prize

Cut to last October, when my sister and I attended a conference for the organization, FORCE, or Facing Our Risk of Cancer Empowered. Attendees were asked to wear mardi-gras beads like these to help build community; different colors had different meanings:

- Red was for a health care provider or researcher;
- Pink, teal, and lime green were for survivors of breast, ovarian, and other cancers respectively.
- White, silver, and gold represented the number of years since diagnosis.
- Dark blue was for BRCA1 mutation carriers, dark green for BRCA 2.
- Black indicated a supporter/spouse/partner/relative or friend.

And so on, across the rainbow spectrum. Everyone at the conference - well over 1000 people - wore some combination of these beads, embodying the consequences of our genetic variations.

Dr. King was honored at the FORCE conference with the Spirit of Empowerment Award for Research. I took the photo on the right from my seat at a table in a crowded room much like this one. I wish I hadn't zoomed in, just so you could have a sense of the people in the room.

Dr. King has received dozens if not hundreds of awards. But there in that room, looking around at the rainbow of beaded necklaces worn by hundreds of individuals who were in wrapt attention, it was clear to me that the award wasn't about Dr. King or the statuette she graciously accepted.

It was about the work she did, with so many others, on the shoulders of many, and on which so many developed their own research. This work gave the hundreds of people in that room, gathered in some kind of colorful genetic community, an opportunity to make informed choices about their bodies, to take control of their lives. To survive.

Awards, you see, aren't really about you. They're about your work - work that means something significant to someone else and that goes beyond your very existence.

Thank goodness for this work. Not for the awards that Watson and Crick received that perhaps Rosalind Franklin should have received, or for the awards that King received at any point in her ongoing career.

Their awards won't keep me alive to see my children grow up. But their work will, I trust, as will the work of so many others who have been inspired by them.

Thank goodness for their creativity, determination, and dedication. And thank goodness for yours.

Ruminations in summary....

#1: Acknowledge the shoulders on which you stand… and those who haven't been invited for recognition.

#2: Awards should be celebrated, but they don't really matter in the long run. The achievements they recognize do.

#3: Let people know they've influenced your work. Celebrate the inspirations in your life as well as your own achievements.

I've been invited to speak tonight because, like you, I won an award. The Helen Mulvey teaching award "recognizes an assistant professor who regularly offers classes that challenge students to work harder than they thought they could and to reach unanticipated levels of academic achievement."

So I suppose, in a way, I feel a responsibility to *challenge* you this evening.
The achievements we recognize with awards do not emerge in a vacuum. So I challenge you, award winners, as we recognize each of you tonight, keep these ruminations in mind:

#1: **Acknowledge the shoulders on which you stand… and those who haven't been invited for recognition.** Think of those who paved the way for you, those who made your work possible, and those who championed the recognition of your work. Think, too, of those who are not here, but perhaps should be. How you can pave the way for others?
#2**: Awards should be celebrated, but they don't really matter in the long run. The achievements they recognize do.**
Finally,
#3: **Let people know when they've influenced your work. Celebrate the inspirations in your life.**
Life can be chaotic, and yes, unstable, particularly at this time of year and especially on the brink of major life changes. But every now and then a pause, a remembrance, can be precious.

Thank you

My high school physics teacher, Mr. Mruk, who modeled excellence in teaching.

The Connecticut College students who teach and inspire me every day.

My colleagues.

Researchers and those who fund them.

My siblings, mom, and extended family.

Steve, Oscar, Yelena, and Demetri.

My dad. He was a smart guy.

Thank you for doing the work.

Congratulations, everyone.

It is truly an honor to celebrate your achievements with you this evening.