Hereditary Breast and Ovarian Cancer 2015

Rebecca Sutphen, MD, FACMG


New Details
Angelina's
DOUBLE MASTECTOMY
Inside
HER BRAVE
CHOICE
THIS WAS THE RIGHT
THING TO DO
The IRS Mess / Syria's Youtube War / The End of Al
THE
ANGELINA
EFFECT

JAMA Oncology

Original Investigation | October 01, 2015

Utilization and Outcomes of *BRCA* Genetic Testing and Counseling in a National Commercially Insured Population

The ABOUT Study

OPEN ACCESS ONLINE FIRST

Joanne Armstrong, MD, MPH[1]; Michele Toscano, MS[1]; Nancy Kotchko, MA[1]; Sue Friedman, DVM[2]; Marc D. Schwartz, PhD[3]; Katherine S. Virgo, MBA, PhD[4]; Kristian Lynch, PhD[5]; James E. Andrews, PhD[6]; Claudia X. Aguado Loi, MPH, PhD[7]; Joseph E. Bauer, PhD[8]; Carolina Casares, MD, MPH[8]; Elizabeth Bourquardez Clark, BA[5]; Matthew R. Kondoff, BS[5]; Ashley D. Molina, BS[5]; Mehrnaz Abdollahian, MS[9]; Gregg Walker, MBA[8]; Rebecca Sutphen, MD[5]

- Among a consecutive series of 11,159 women requesting BRCA testing over one year, 3874 responded to a mailed survey.
- Most respondents (61.8%) did not receive pretest genetic counseling from a genetics clinician.
- Lack of physician recommendation was the most commonly reported reason for not receiving counseling from a genetics clinician.
- Respondents who received genetic counseling from a genetics clinician demonstrated greater knowledge about *BRCA* ($P < .001$) and understanding of the information received ($P < .001$) and expressed greater satisfaction ($P < .001$).

UnitedHealthcare®

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UnitedHealthcare Commercial
Genetic Counseling Requirement Effective Jan. 1, 2016

Effective Jan. 1, 2016, UnitedHealthcare commercial members with medical necessity benefit plans will be required to receive genetic counseling before we will approve prior authorization requests for testing for BReast CAncer (BRCA) mutations for hereditary breast and ovarian cancer. A genetic counseling visit will help our members understand the advantages and limitations of BRCA mutation analysis so they can make informed health care decisions. Genetic counseling, which is recommended by the United States Preventive Services Tasks Force as well as the National Comprehensive Cancer Network (NCCN), will help our members understand if the test is right for them as well as help them interpret the results after testing.

The counseling can be done over the phone or in an office setting. All care providers administering the BRCA laboratory test will be required to show evidence that the requirement has been fulfilled in order to receive prior authorization for the test.

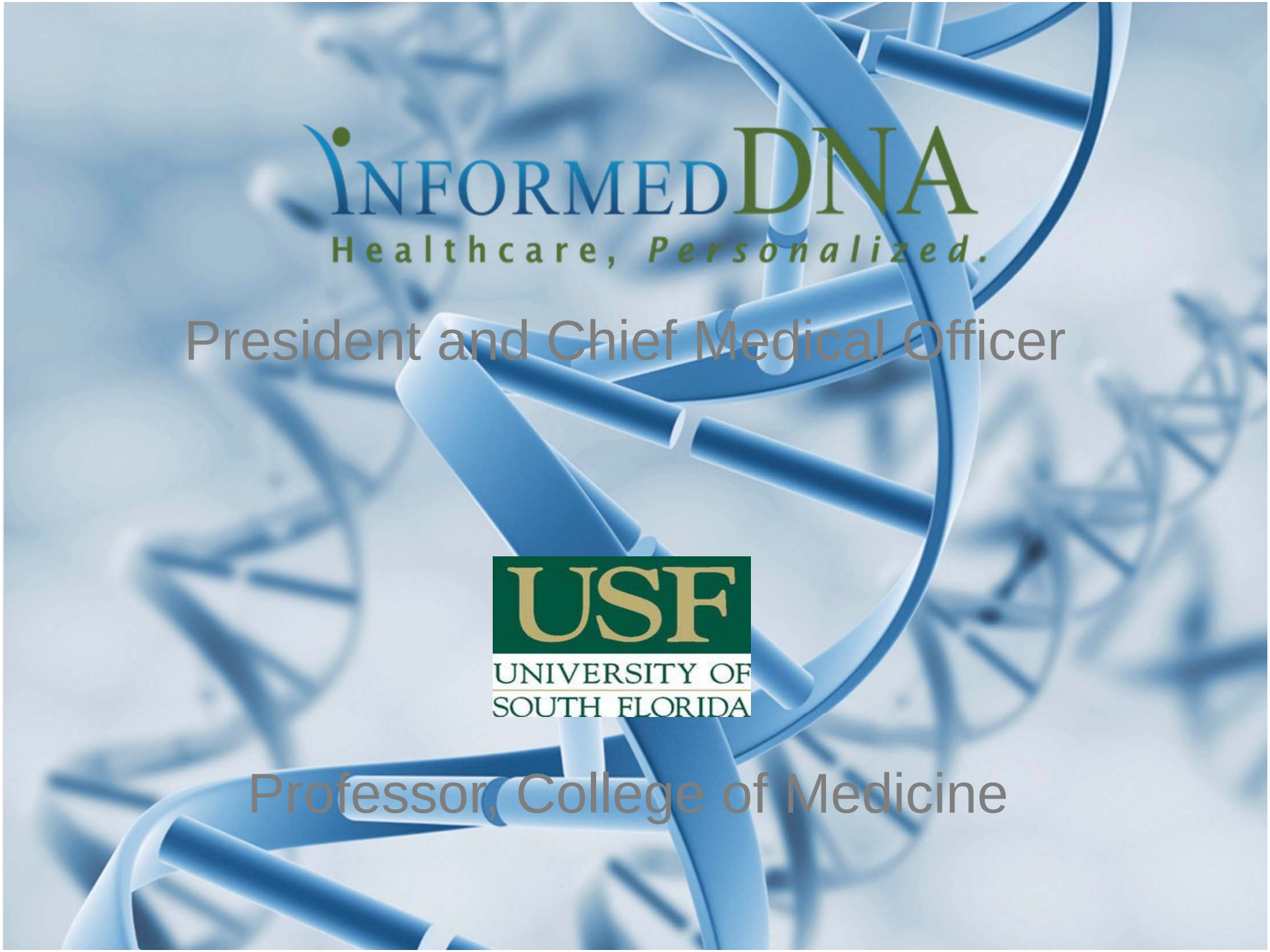
The genetic counseling must be administered by an independent genetics care provider who is not employed by a genetic testing lab. Genetics care providers employed or contracted with a laboratory who are part of an integrated health system that routinely delivers health care services beyond laboratory testing are considered independent. Genetic testing for BRCA mutations requires documentation of medical necessity by one of the following who has evaluated the individual and intends to engage in post-test follow-up counseling:

- Board-eligible or board-certified genetics counselor
- Genetics clinical nurse
- Advanced practice nurse in genetics
- A board-eligible or board-certified clinical geneticist
- A board-certified care provider with experience in cancer genetics who provides cancer risk assessment on a regular basis and has received specialized ongoing training in cancer genetics.

You can use one of the following methods to locate an independent genetics counselor:

- Visit informedDNA.com or call InformedDNA at 800-975-4819 to access nationwide in-network telephone genetic counseling.
- Call UnitedHealthcare at the number on the back of the patient's health care identification card.
- Visit myuhc.com and search for genetics counselors.
- Visit the National Society of Genetic Counselors at NSGC.org. Check the "Genetic Counselor Certified" box at the bottom of the page. This list may however include genetic counselors that are non-participating or employed by the lab.

For more information about this requirement, please go to UnitedHealthcareOnline.com > Clinician Resources > Oncology > Programs, Tools & Resources > BRCA Testing > Tools & Resources > BRCA Genetic Counseling Requirement Frequently Asked Questions. If you have additional questions or need more information, please email us at unitedoncology@uhc.com. Thank you.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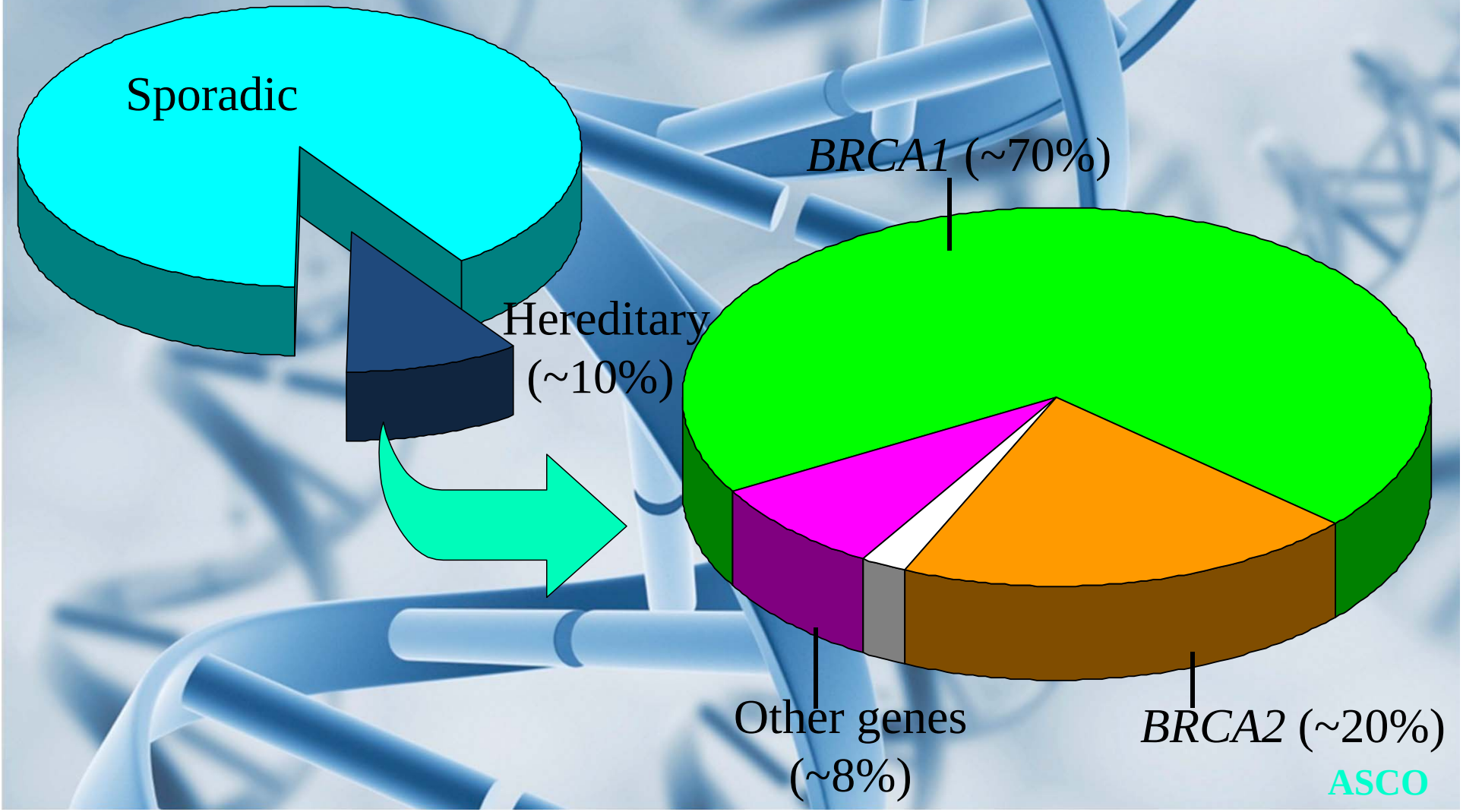
Healthcare, Personalized.
President and Chief Medical Officer
USF
UNIVERSITY OF
SOUTH FLORIDA
Professor, College of Medicine

Outline

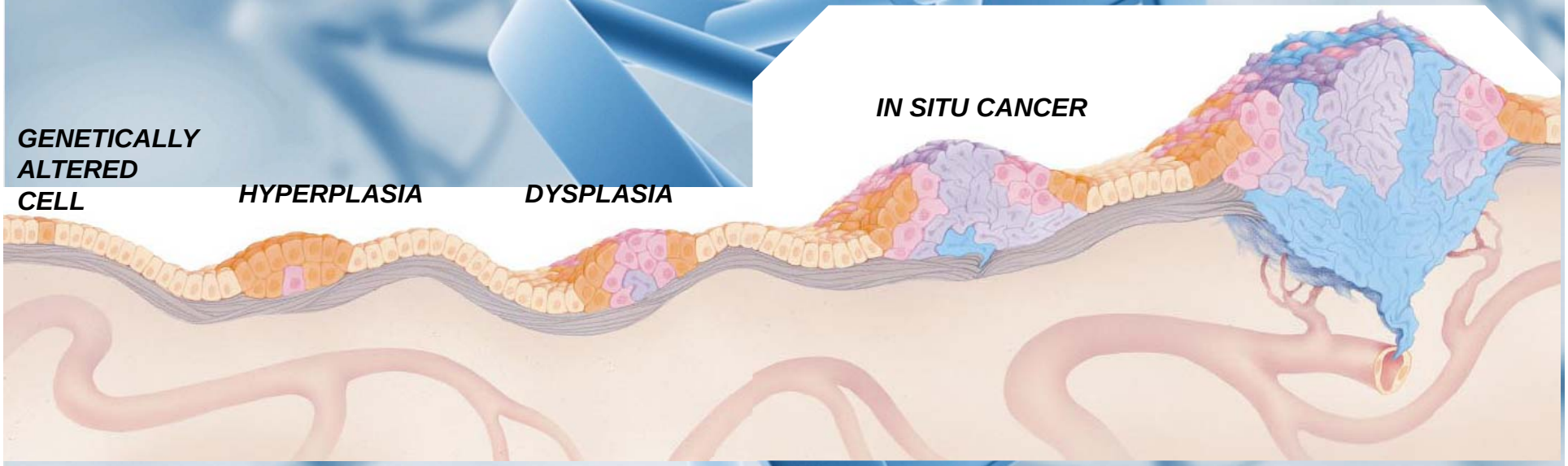
- Features of hereditary breast cancer – how and why is it different from “sporadic” cancer
- The *BRCA1* and *BRCA2* genes
  - Inheritance
  - Prevalence
  - Associated risks
- Approach to Genetic Counseling and Testing
- Screening and Prevention Recommendations
- Treatment Implications

Causes of Hereditary Susceptibility to Breast Cancer



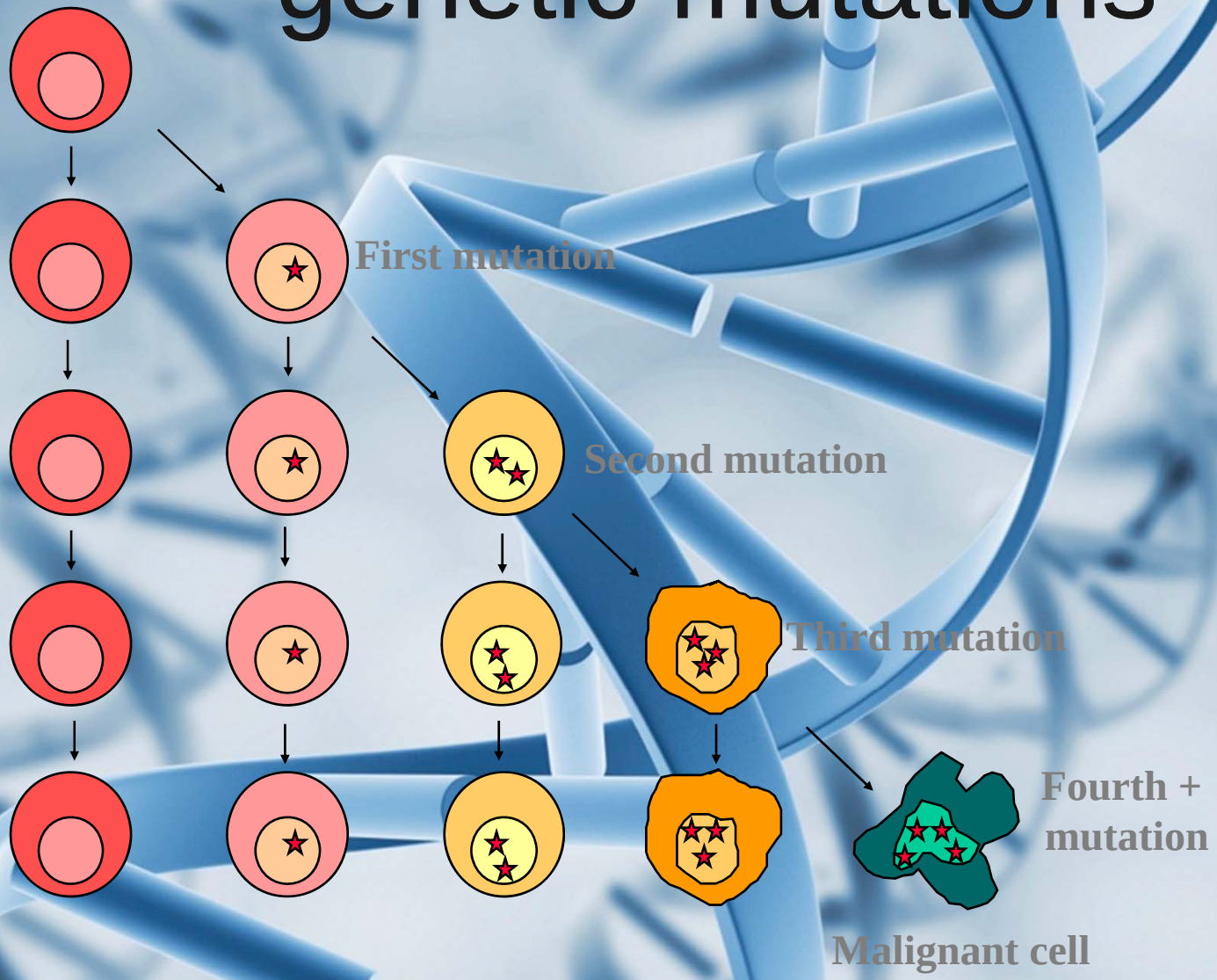
ASCO

All cancers are the result of genetic mutations



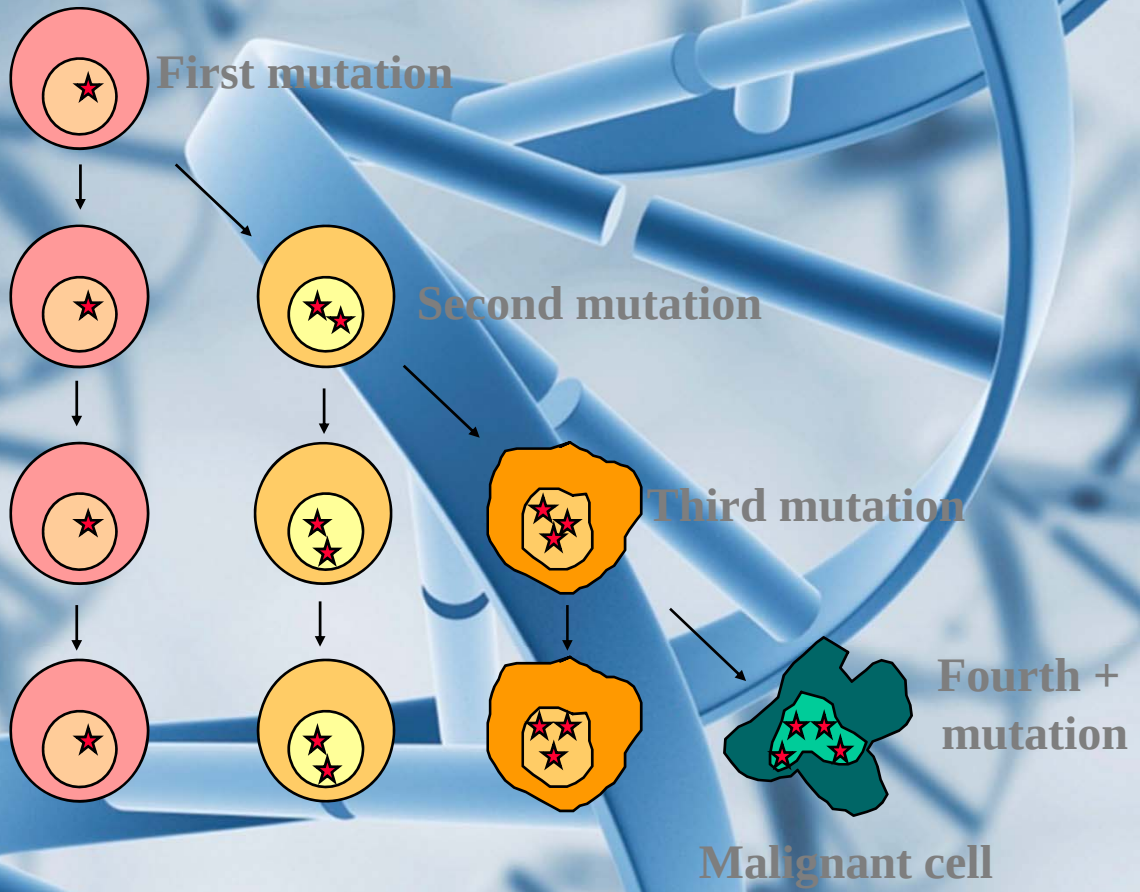
Weinberg RA, *How Cancer Arises*
Scientific American, 1996

All cancers are the result of genetic mutations



NCI

Hereditary cancers are also the result of genetic mutations



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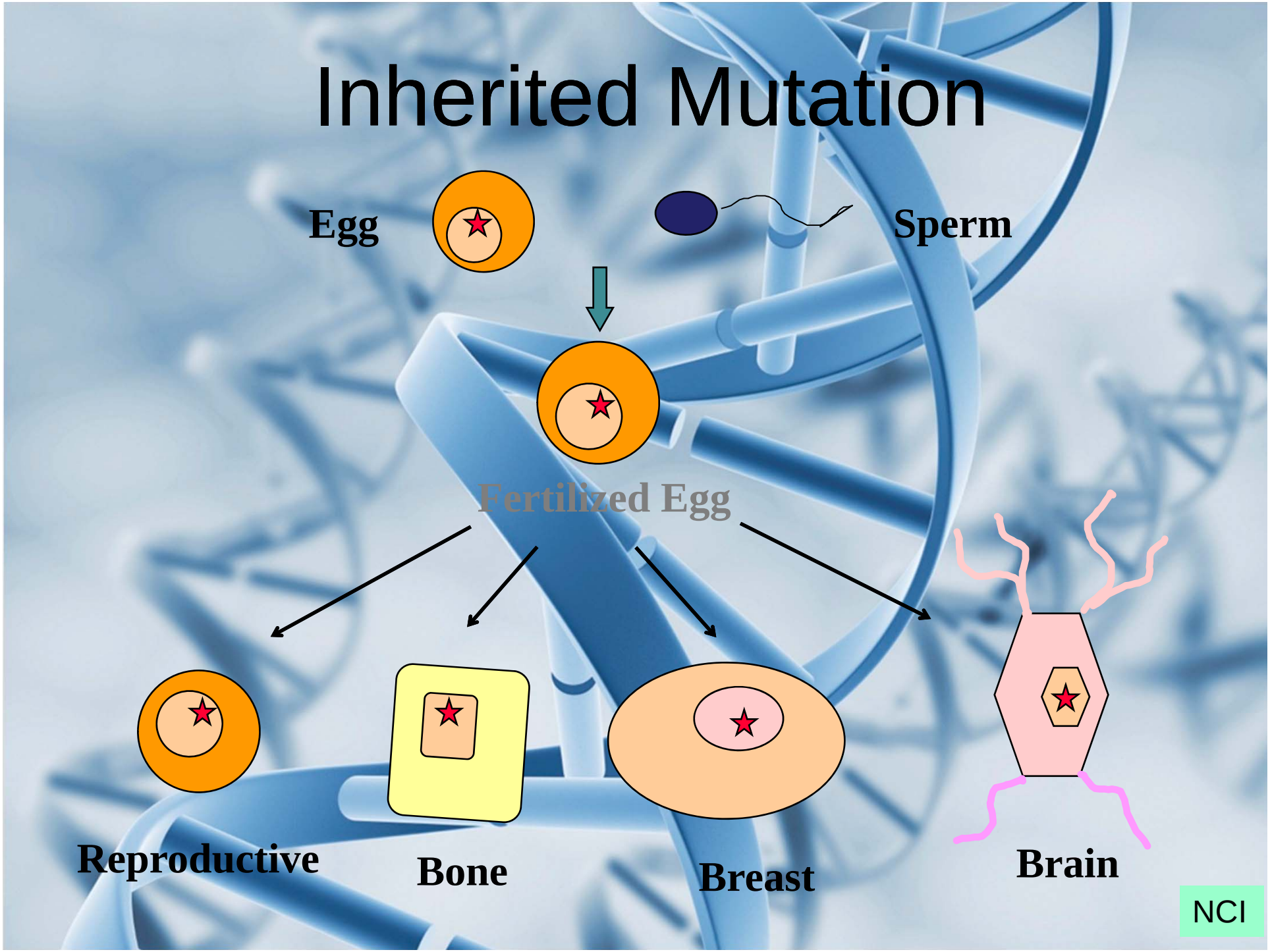
Inherited Mutation



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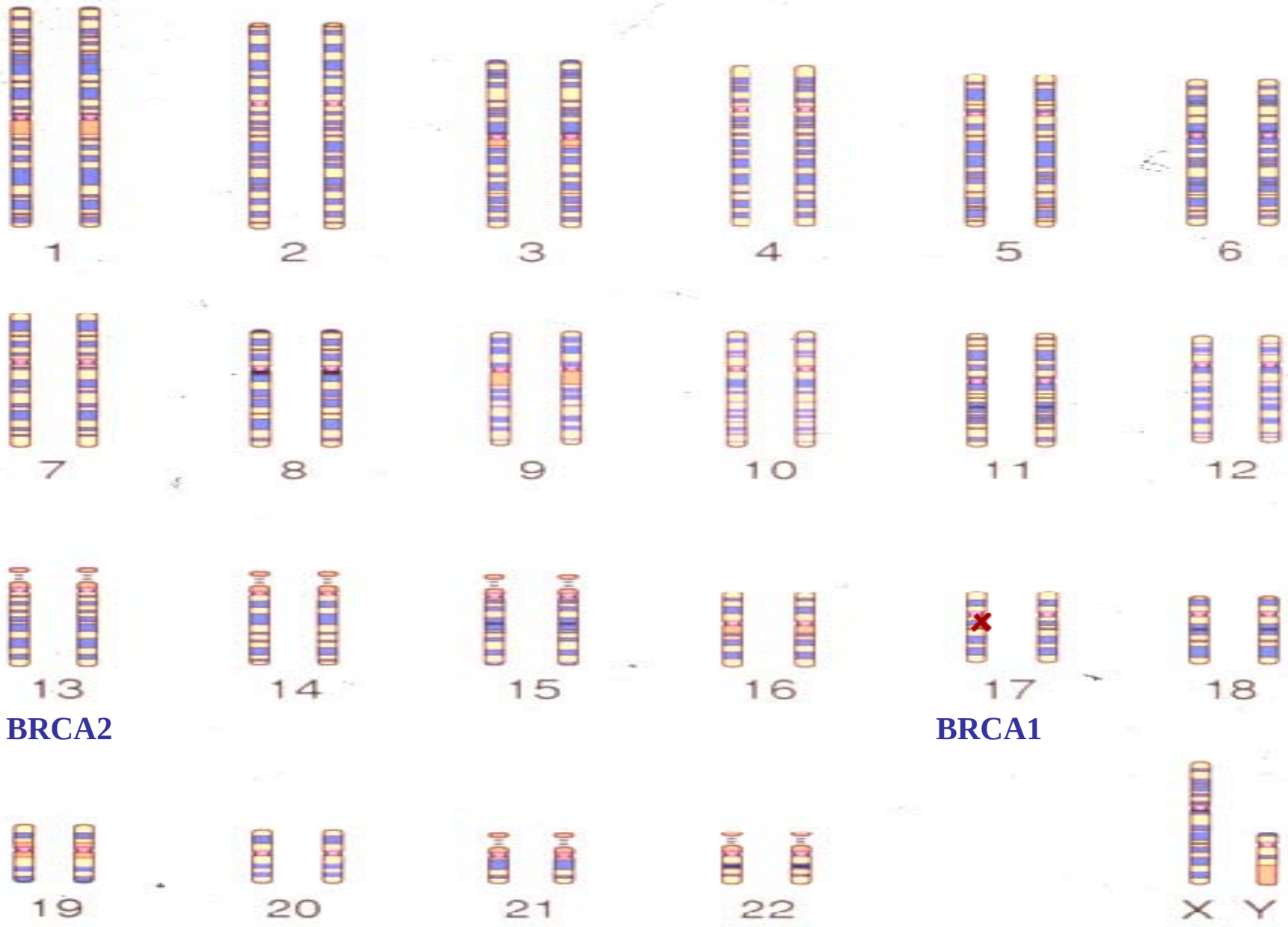
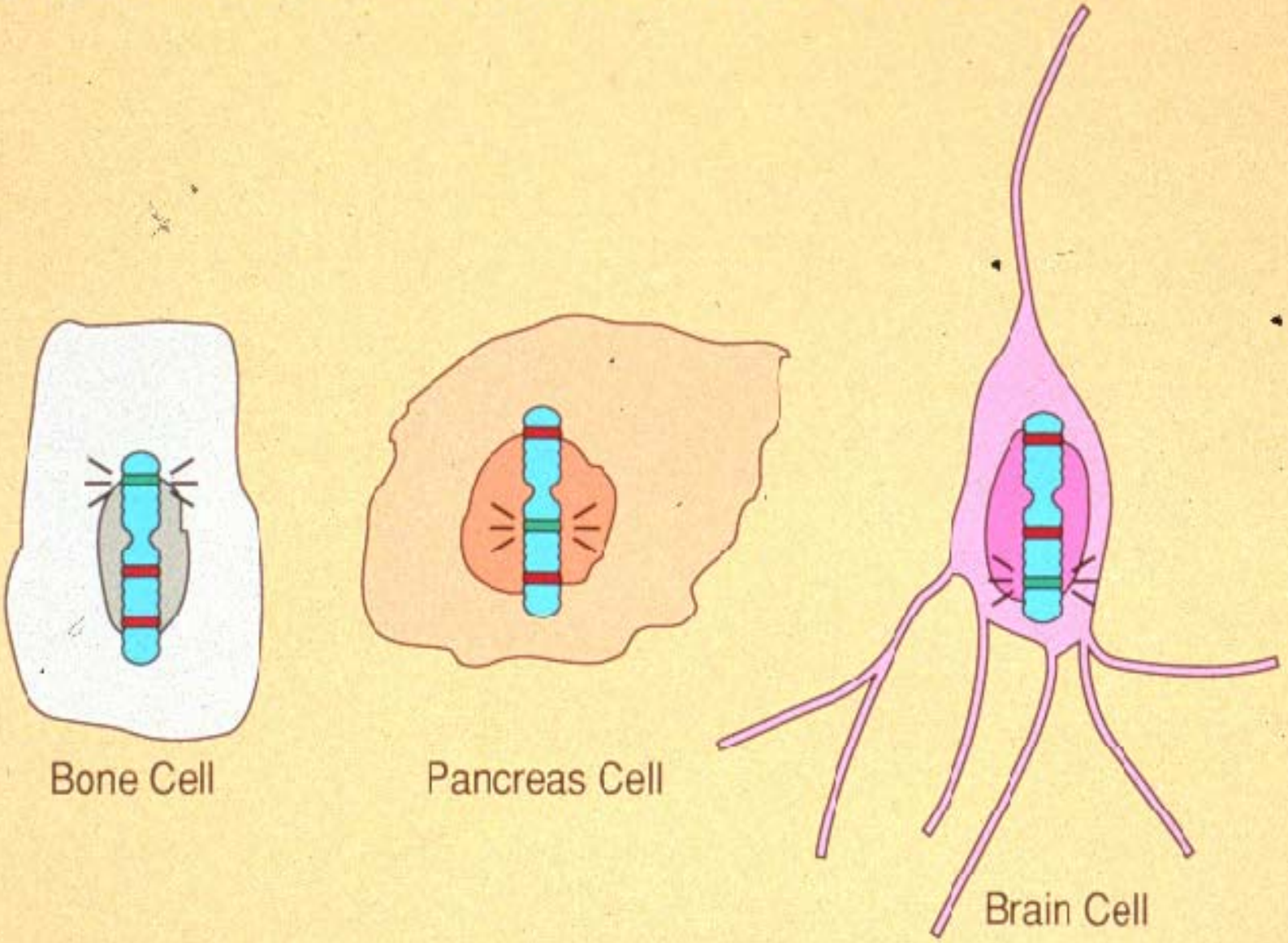
Human Chromosomes



BRCA2

BRCA1

Different Genes-Different Functions



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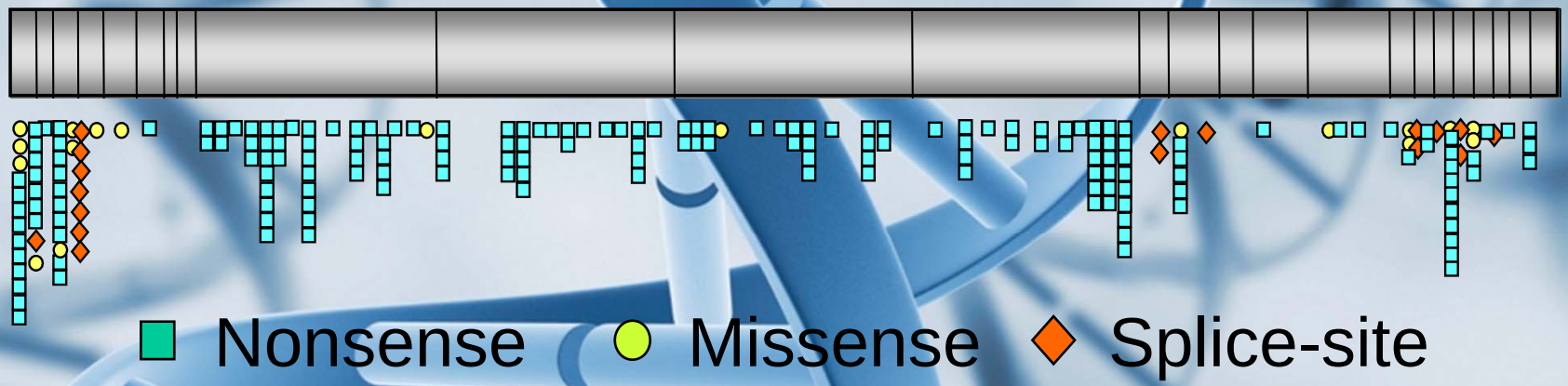
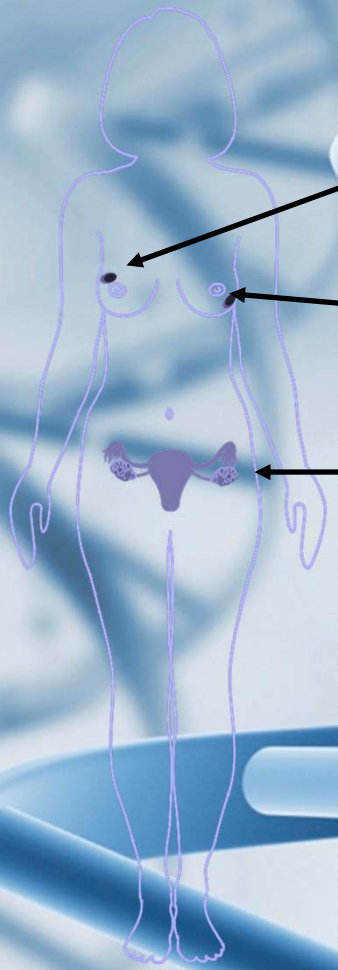
BRCA1

- Tumor suppressor gene on chromosome 17
- Important function in breast and ovary



BRCA1-Associated Cancers: Lifetime Risk



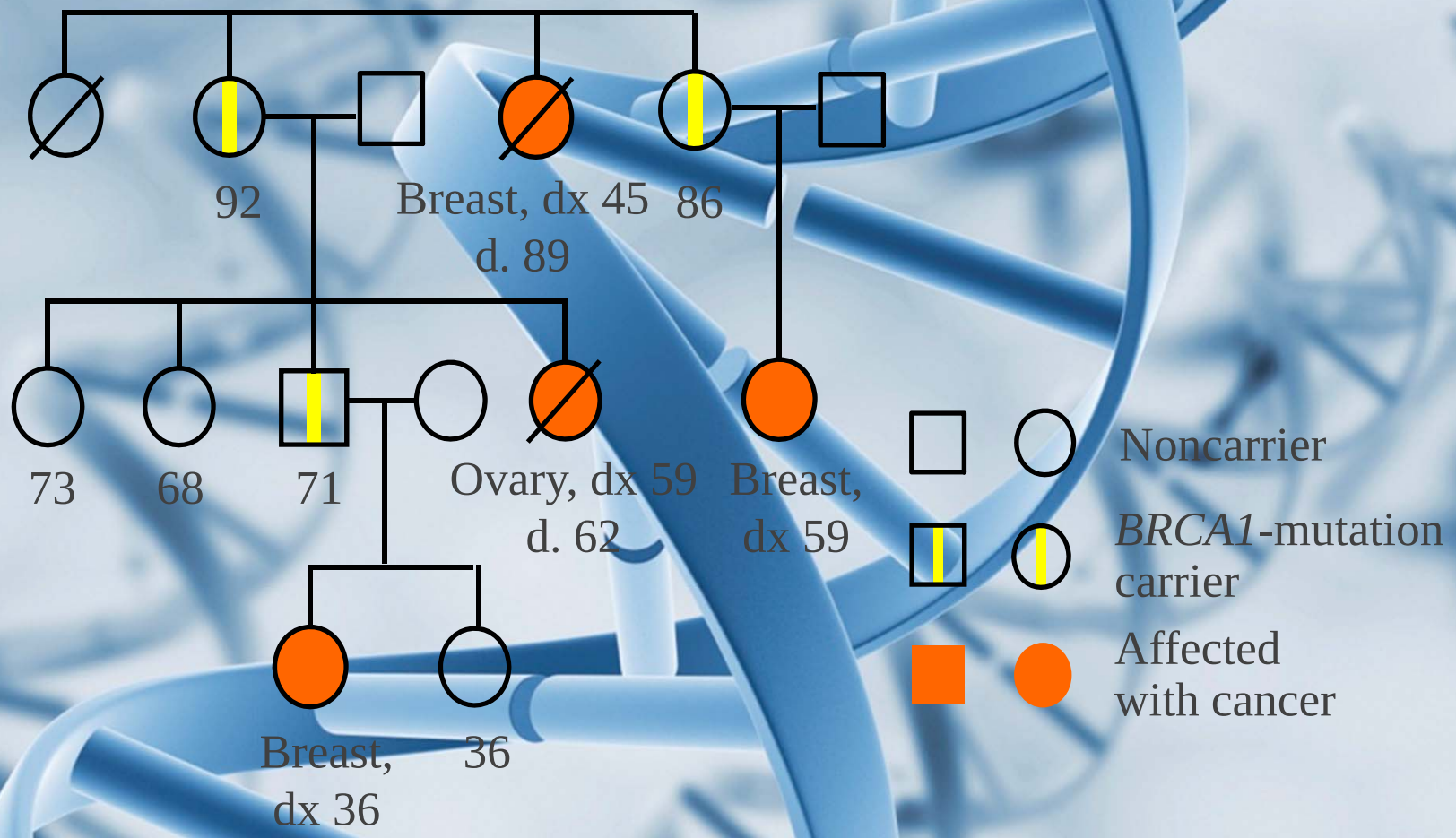
Breast cancer 34%-86% (early age)

Second primary breast cancer 40%-60%

Ovarian cancer 42%-67%

ASCO

BRCA1-Linked Hereditary Breast and Ovarian Cancer



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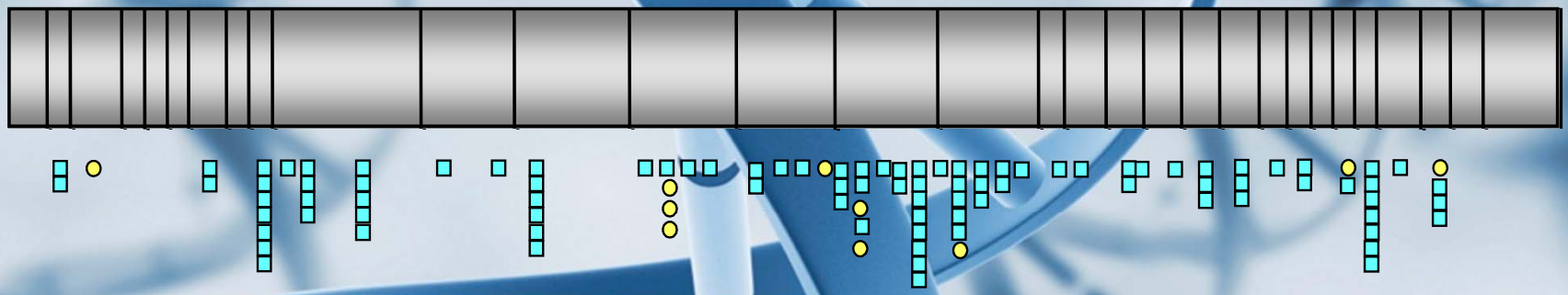
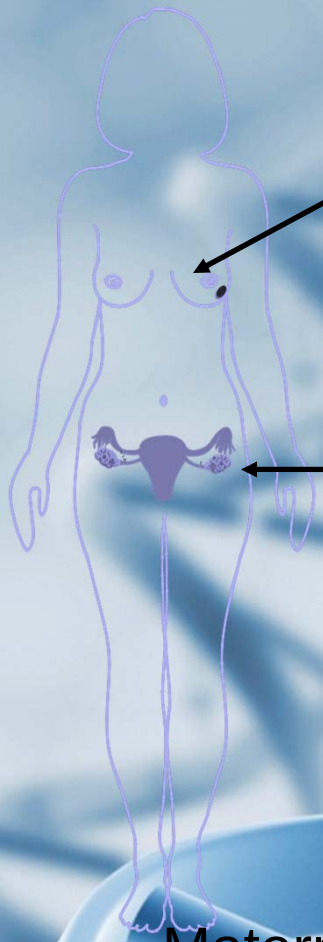
BRCA2

- Tumor suppressor gene on chromosome 13
- Important function in breast and ovary



Nonsense Missense Splice-site

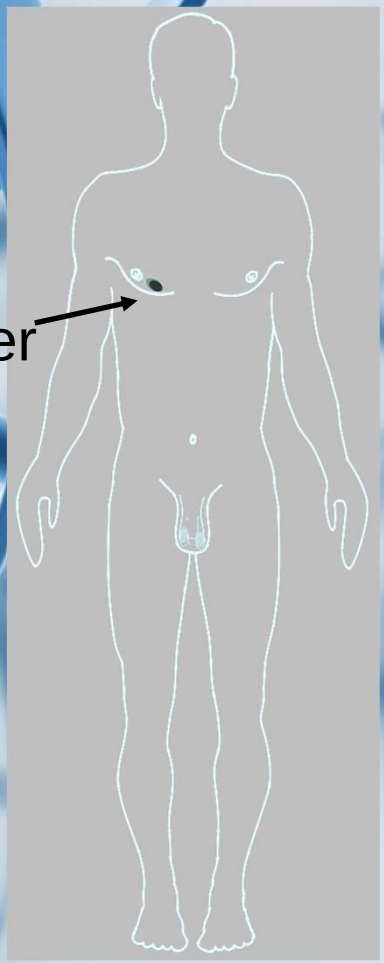
BRCA2-Associated Cancers: Lifetime Risk



breast cancer (24%-83%)

ovarian cancer (16%-51%)

male breast cancer (6%)



Maternal and paternal co-inherited BRCA2 mutations cause recessive Fanconi anemia

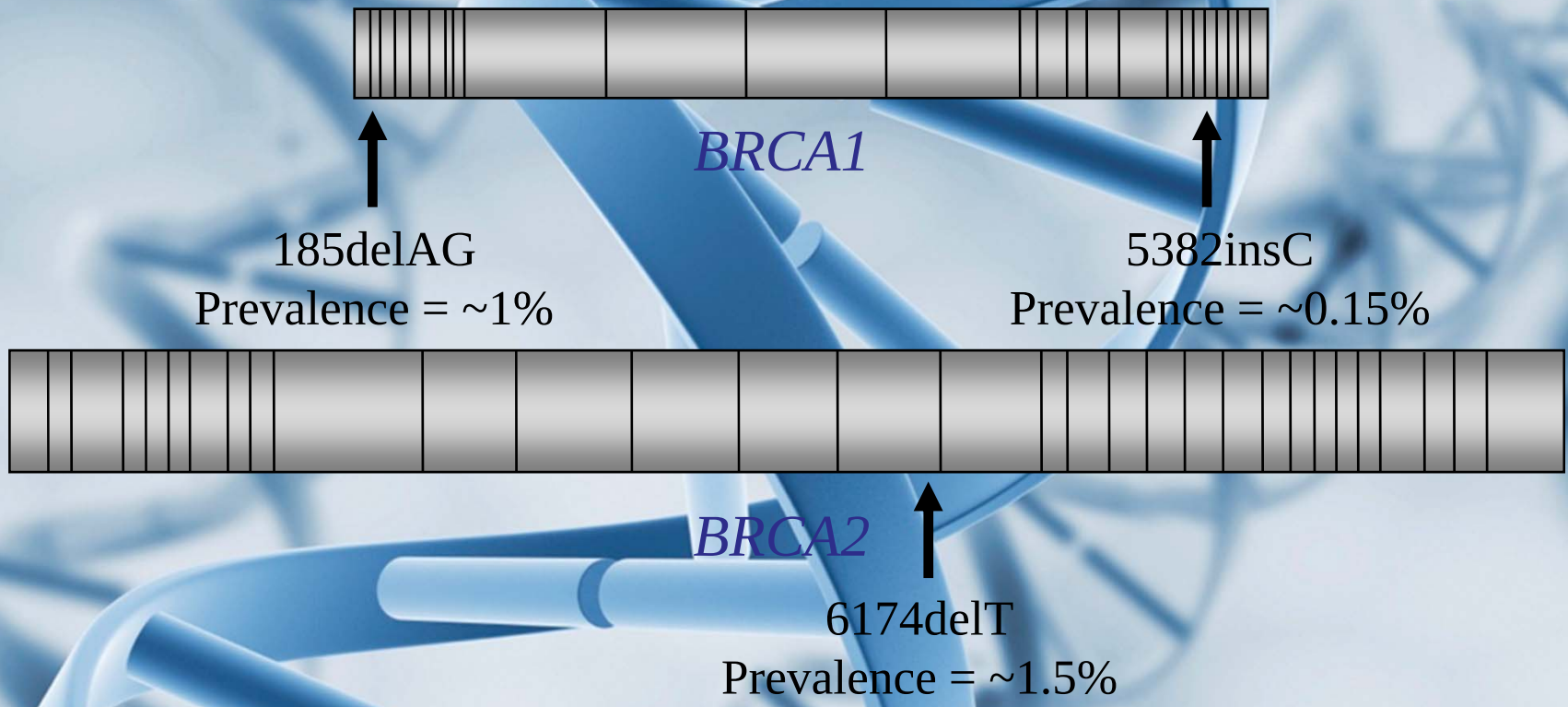
ASCO

Other Cancer Risks

Cancer Type	***BRCA1* Mutations**	***BRCA2* Mutations**
Breast	70-80% lifetime risk	50-60% lifetime risk
Ovarian	50% lifetime risk	30% lifetime risk
Prostate	Ashkenazi mutations associated with increased risk	20-fold increased risk
Pancreatic	Likely increased	10-fold increased risk
Melanoma	Unlikely increased	20-fold increased risk
Gastric	None reported	Limited reports
Others	Unlikely increased	Case reports

BRCA1 and *BRCA2* Mutations in the Ashkenazi Jewish Population

An estimated 1 in 40 Ashkenazi Jews carries a *BRCA1* or *BRCA2* mutation



Features That Indicate Increased Likelihood of BRCA Mutation

- Multiple cases of breast cancer
- Premenopausal breast cancer (≤50)
- Ovarian cancer (fallopian tube, primary peritoneal)
- Breast *and* ovarian cancer on one side of family
- Bilateral breast cancer
- Ashkenazi Jewish heritage
- Male breast cancer
- Triple negative breast cancer (ER-/PR-/*Her2*-) (≤60)
- Pancreatic cancer
- Aggressive prostate cancer (Gleason score ≥7)

NCCN

Genetic counseling – personal consultation with a genetics specialist (e.g., board certified genetic counselor)

- Personalized pedigree assessment - cancer pattern in the family and likelihood it may be hereditary
- Discussion of hereditary cancer risks and genetic testing benefits and limitations
- Determination of appropriate test(s) and appropriate first person in family to be tested
- Assistance with insurance coverage of testing
- Clarification of options for risk management
- Information and resources - follow-up care, peer support, available research protocols

Telephone Genetic Counseling Effective


Telephone Genetic Counseling for High-Risk Women Undergoing *BRCA1* and *BRCA2* Testing: Rationale and Development of a Randomized Controlled Trial

- Nearly all aspects of telephone genetic counseling parallel face-to-face counseling
- Telephone genetic counseling allows for comprehensive service delivery

Peshkin et al. (2008) *Genetic Testing* 12(1): 37-52.


Telephone *BRCA1/2* Genetic Test Results: Prevalence, Practice, and Patient Satisfaction

- When given an option, patients often chose to receive genetic counseling over the phone rather than in person
  - ✓ No difference in satisfaction
  - ✓ Higher satisfaction associated with shorter wait time

Baumanis et al. (2009) *J Genet Counsel* 18:447-463.


Randomized Noninferiority Trial of Telephone Versus In-Person Genetic Counseling for Hereditary Breast and Ovarian Cancer

- Randomized controlled trial showed equivalence on all primary outcomes
- Telephone genetic counseling lowered out-of-pocket costs for patients

Schwartz et al. (2014) *J Clin Oncol* 32(7): 618-26.

Genetic Counseling Overview

1 Referral From Provider

Healthcare Provider

InformedDNA

2 Family History Collection

3 Pre-Test Consultation

4a

If genetic testing is not appropriate for patient...

4b Genetic Testing Coordination

If genetic testing is appropriate for patient...

5 Post-Test Consultation

6 Summary Report

★ Provider to Provider Consultation

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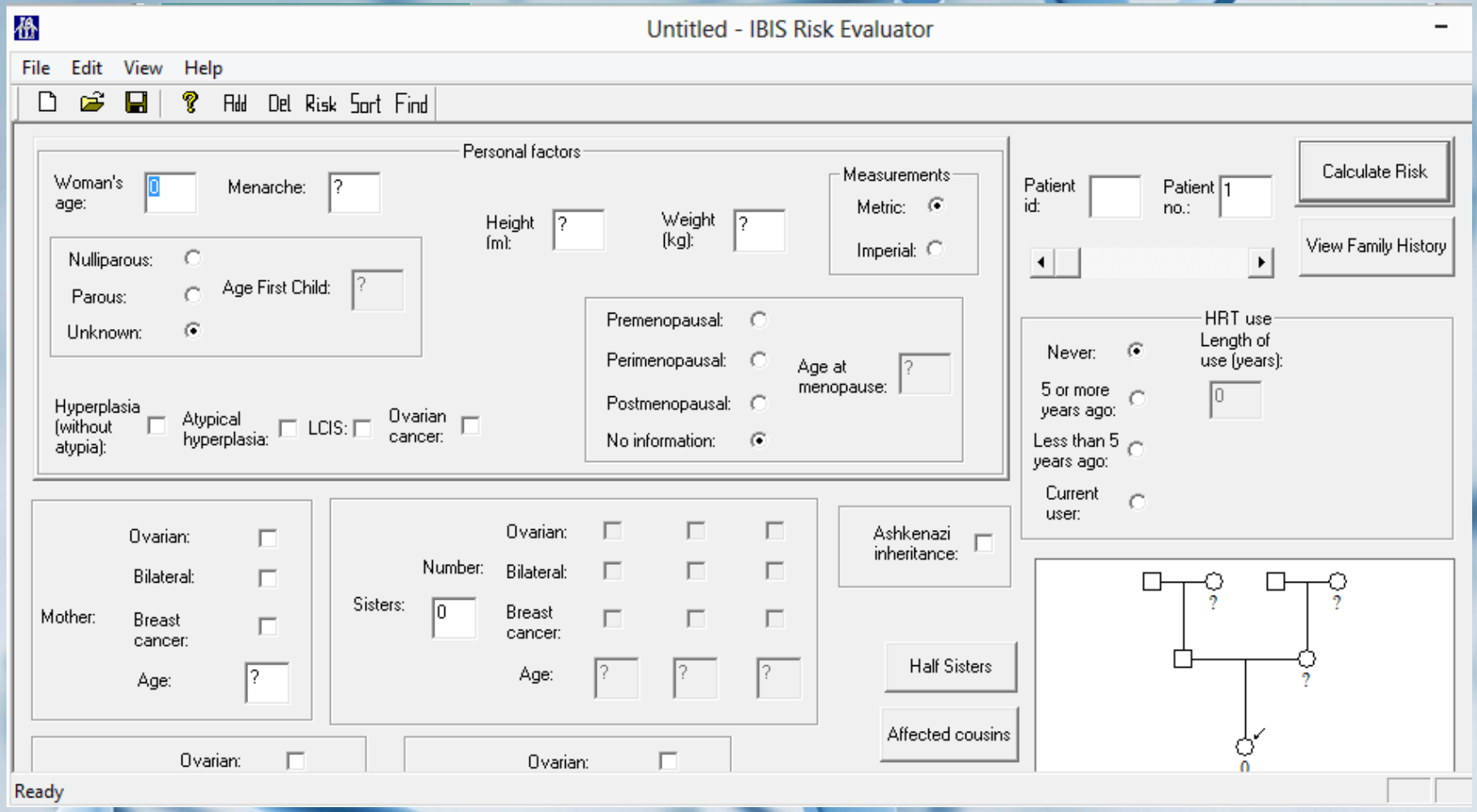
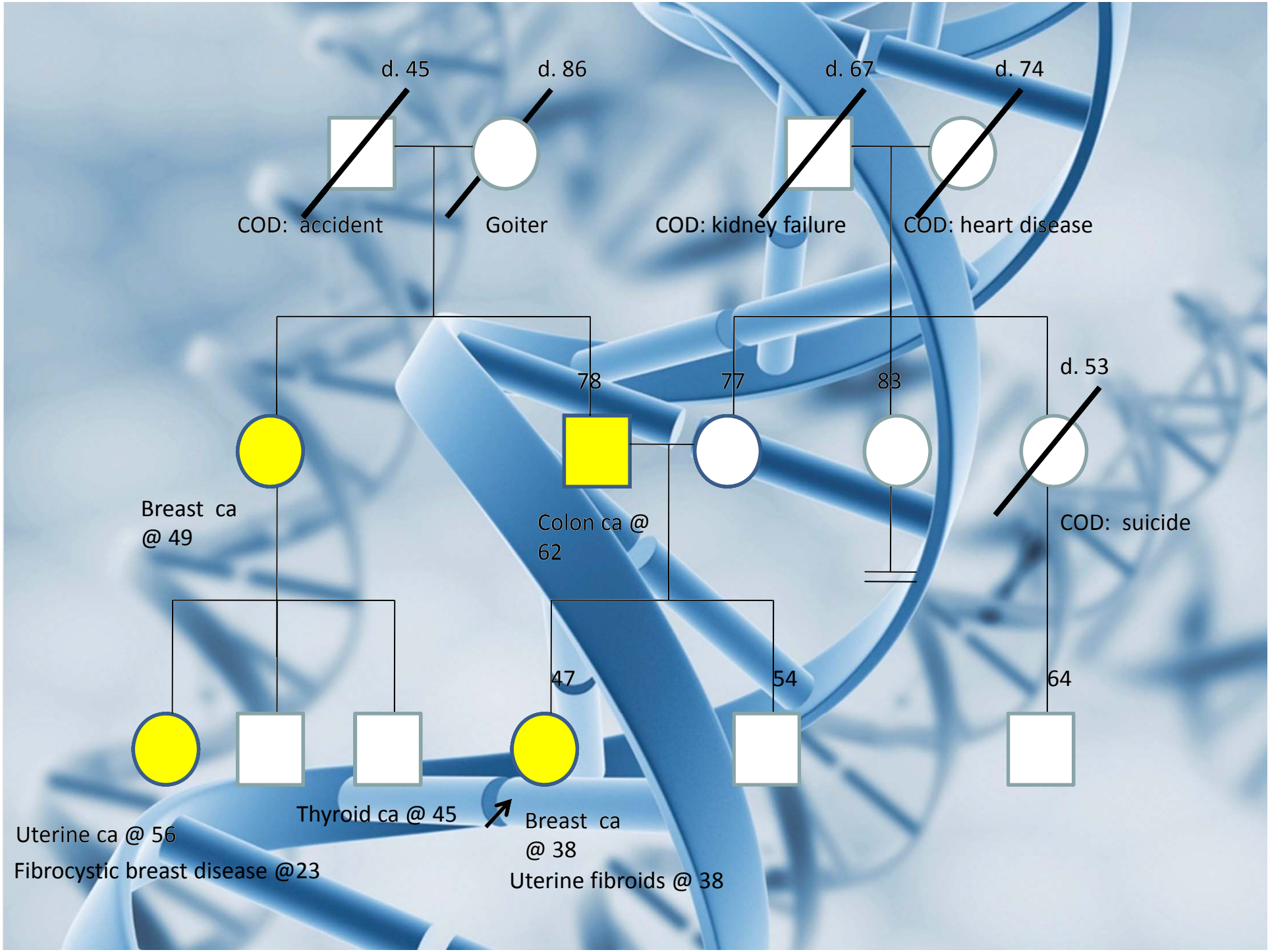
Calculating Risks for Breast Cancer and *BRCA* Mutation




d. 45
d. 86
d. 67
d. 74
COD: accident
Goiter
COD: kidney failure
COD: heart disease
78
77
83
d. 53
Breast ca @ 49
Colon ca @ 62
COD: suicide
47
54
64
Thyroid ca @ 45
Uterine ca @ 56
Fibrocystic breast disease @23
Breast ca @ 38
Uterine fibroids @ 38

Cowden syndrome – PTEN

- Breast cancer – 25 to 50% risk
- May occur at younger age
- Some male breast cancer
- Thyroid cancer – 10%
- Endometrial (uterine) cancer – 5 – 10%
- Kidney cancer – unknown risk level
- Colon cancer – unknown risk level
- Skin cancer – unknown risk level

Other features of PTEN

- Fibrocystic breast disease
- Uterine fibroids
- Thyroid – goiter, thyroiditis
- Lipomas
- Hemangiomas
- GI polyps

50% chance to pass down the mutation to each child

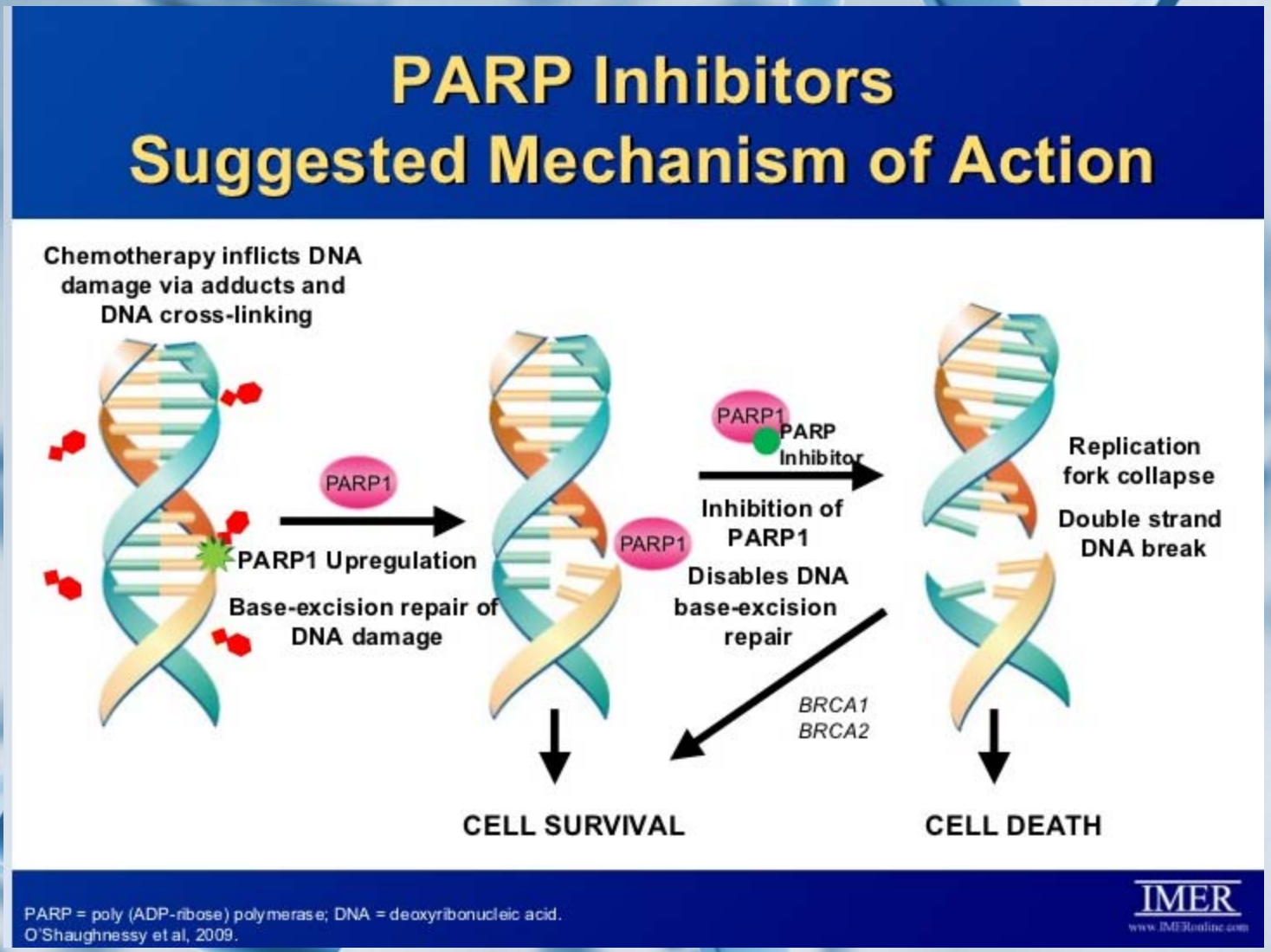
Hereditary Breast Cancer Genes

Genes	Syndromes	RR of breast cancer	Cancer risk by 70
BRCA1	HBOC	14-32X	34%-86%
BRCA2	HBOC	10-19X	24%-83%
P53 (TP53)	Li-Fraumeni	2-6X	>90%
PTEN	Cowden	2-4X	25%-50%
STK11	Peutz-Jehgers	3.5-4X	44%-50%
CDH1	Hereditary Diffuse Gastric Cancer	3-4X	39%-82%
Breast MRI recommended by NCCN			
PALB2	Fanconia Anemia		
ATM	Ataxia-Telangiectasia		
CHEK2	CHEK2		

BRCA Management Options

- Increased surveillance
  - Annual breast MRI @ 25 – 29
  - Annual breast MRI and mammogram @ 30 – 75
  - Males: annual prostate screening @ 40
- Prophylactic surgery
  - Offer bilateral mastectomy
  - Recommend bilateral salpingo-oophorectomy @ 35 - 40
- Chemoprevention
  - Tamoxifen or if postmenopausal Raloxifene, Aromatase Inhibitors
  - Oral contraceptives prior to oophorectomy

BRCA Targeted Therapy



Targeted Therapy in Ovarian Cancer

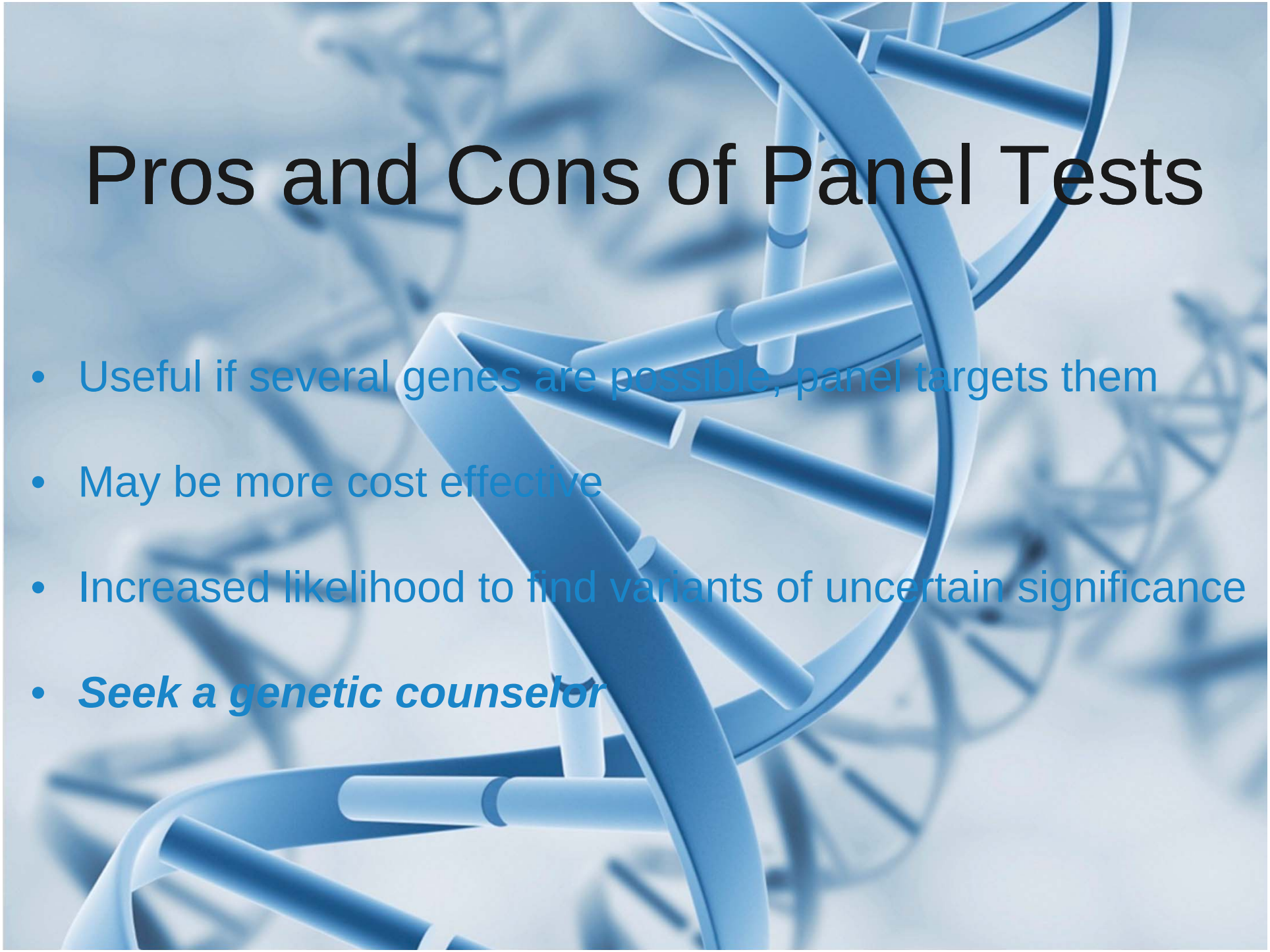
- PARP inhibitor Olaparib (Lynparza)
  - FDA approved in December 2014
  - BRCA mutation carriers only
  - Have had at least 3 lines of chemotherapy

What About Next-Gen Sequencing?

- Different technology/ies
- Facilitates testing for multiple genes in the same test
- Less expensive for the laboratory to perform
- Capable of examining whole exome or whole genome

Testing Panels

- Multiple genes included
- Different labs offer different panels
- Some genes are known to be associated with HBOC
- Some genes are known to be associated with cancer
- Some genes might be associated with cancer
- Some panels cover lots of genes for different health conditions besides cancer



Pros and Cons of Panel Tests

- Useful if several genes are possible, panel targets them
- May be more cost effective
- Increased likelihood to find variants of uncertain significance
- ***Seek a genetic counselor***

JAMA The Journal of the American Medical Association

Viewpoint | September 17, 2014

Population-Based Screening for *BRCA1* and *BRCA2*

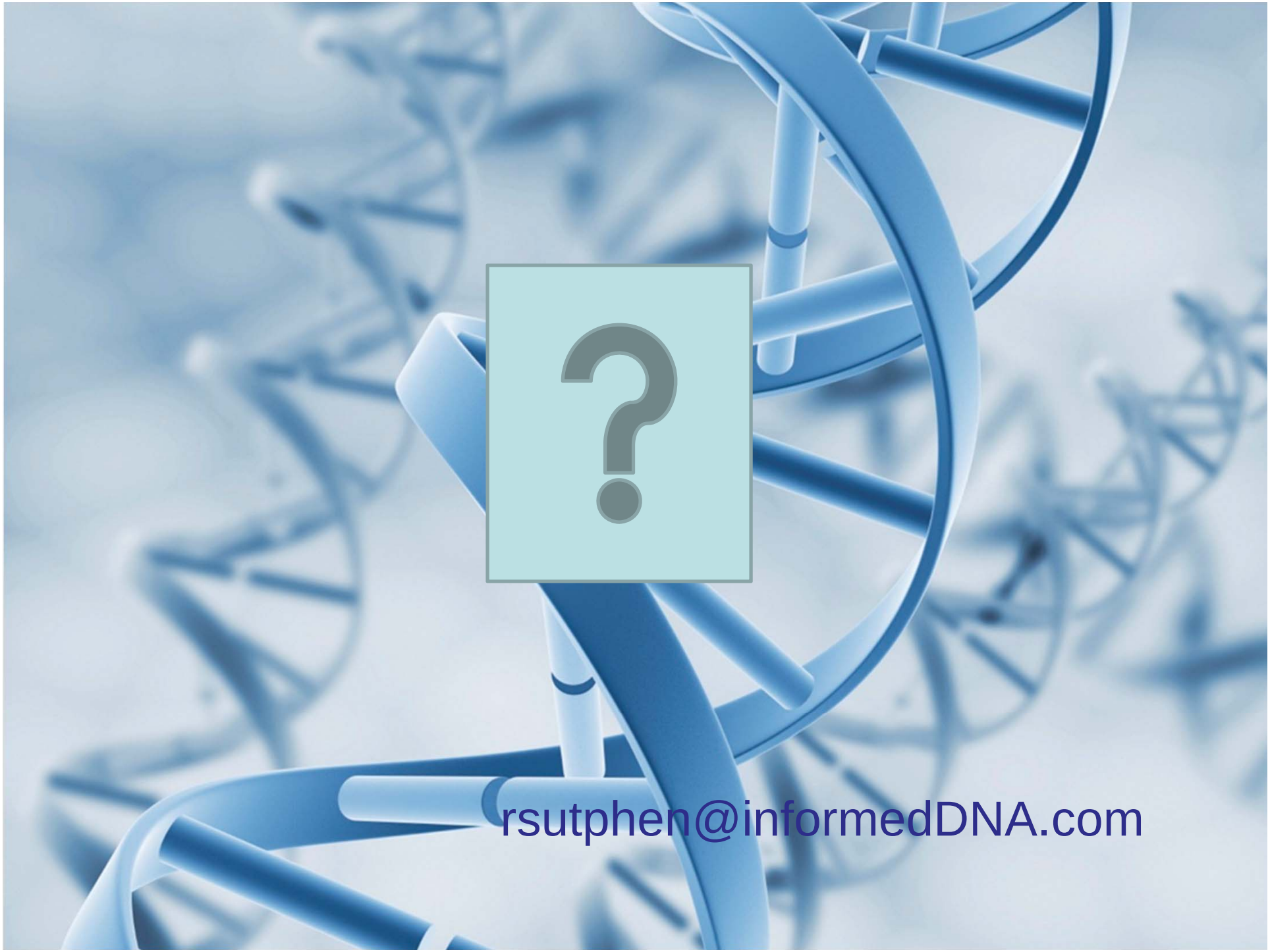
2014 Lasker Award FREE

Mary-Claire King, PhD[1]; Ephrat Levy-Lahad, MD[2,3]; Amnon Lahad, MD, MPH[3,4]

[+] Author Affiliations

JAMA. 2014;312(11):1091-1092. doi:10.1001/jama.2014.12483.

The 2014 Lasker-Koshland Special Achievement Award in Medical Science has been presented to



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