

Perrin Conferences Cutting-Edge Issues in Asbestos Litigation Conference

March 12-13, 2024



The Rapidly Developing Science and Medicine on Genetic Cancer Treatments



Jennifer Alesio, Esq.
Simmons Hanly Conroy
San Francisco, CA



Timothy L. Krippner, Esq.
MG+M The Law Firm
Chicago, IL



An Update on Genetic-based Defenses in Mass Tort Cases

March 12, 2024

Timothy L. Krippner

Revolutionary Change Is Occurring

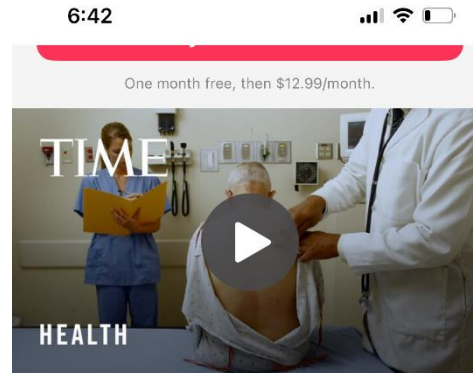
- + The science and medicine involved in genetics, and the human genome is changing at a mercurial pace.
- + It has entered the mainstream through a wide array of immunotherapies, now being actively marketed to the public.
- + Changes are driving a new era of treatment for cancer among many other conditions.
- + We used to use the term idiopathic, is it appropriate now?
- + We are obligated to understand and accept these developments when presenting medical theories to juries in a public forum.



Wake Up

- + Your jurors are changing as they observe the marketing, or encounter these treatments with family members, friends or themselves.





Scientists Have Reached a Key Milestone in Learning How to Reverse Aging

The finding involves mice, but represents an important milestone in understanding what causes cells to age—and potentially how to reverse the process in people

ALICE PARK
VIDEO BY ANDREW. D JOHNSON
JAN 12, 2023 9:38 AM PST

ALICE PARK IS A SENIOR HEALTH CORRESPONDENT AT TIME. SHE COVERS THE COVID-19 PANDEMIC, NEW DRUG



2:49

LTE

Novel Treatment For Damaged Corneas: Cell Therapy

William A. Haseltine Contributor

Feb 17, 2024

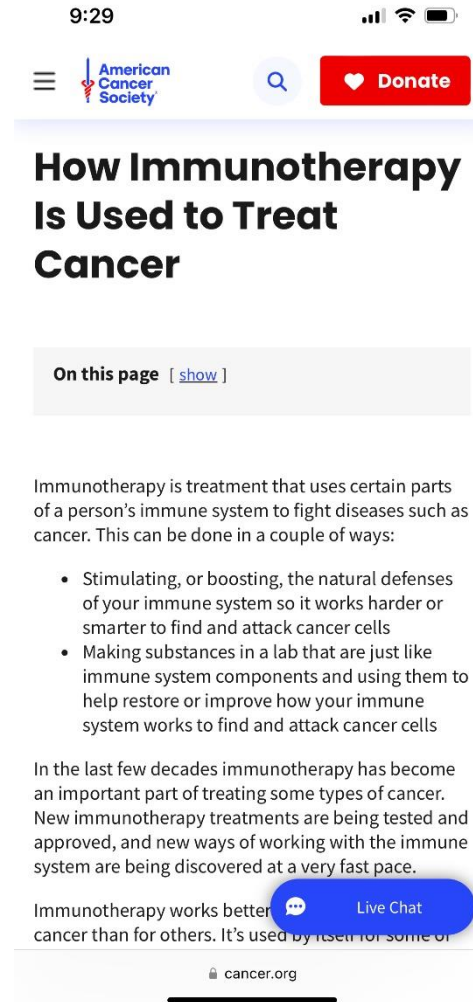


macro close up of eye
IMAGE BY SVSTUDIOART

This story is part of a series on the current progression in Regenerative Medicine. This piece is part of a series dedicated to the eye and improvements in restoring vision.

In 1999, I defined regenerative medicine as the collection of interventions that restore tissues and organs damaged by disease, injured by trauma, or worn by time to normal function. I include a full spectrum of chemical, gene, and protein-based medicines, cell-based therapies, and biomechanical interventions that





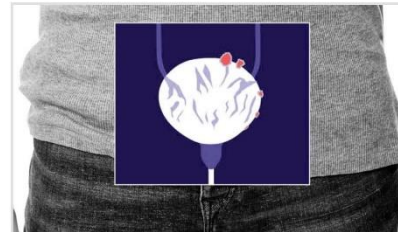
9:31



Watch Now: CRI's Patient Immunotherapy Summit



DONATE






Bladder Cancer





The first FDA-approved immunotherapy treatment—Bacillus Calmette-Guérin cancer vaccine—was for bladder cancer in 1990.





cancerresearch.org

9:31   

Watch Now: CRI's Patient Immunotherapy Summit


   [DONATE](#) 






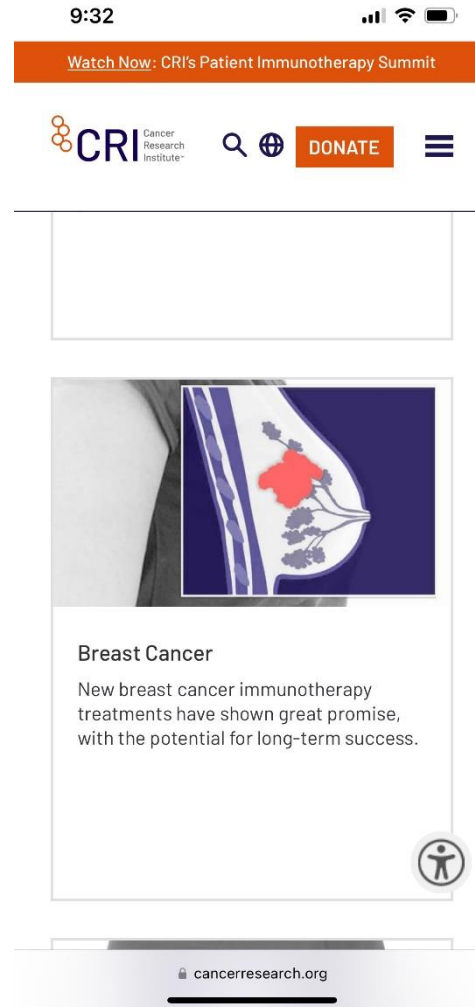
Brain Cancer

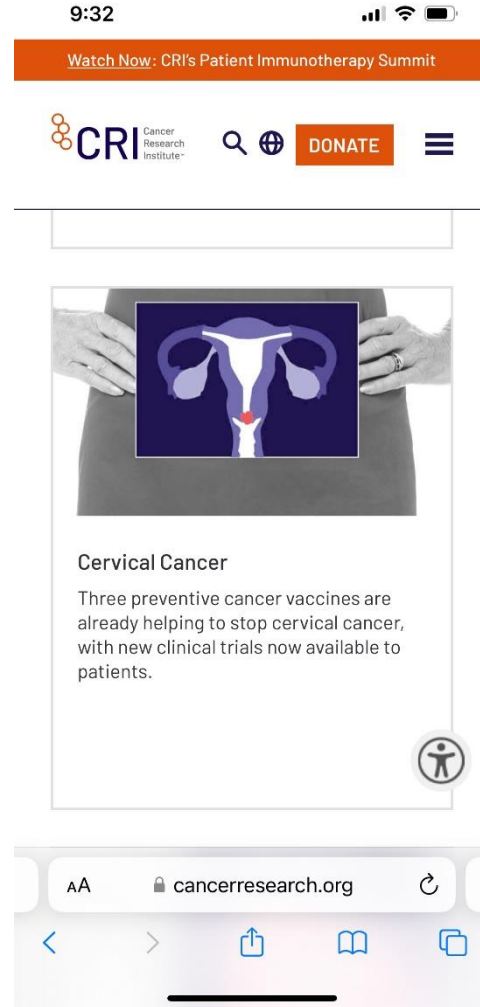
Cancers of the brain and nervous system are relatively rare but very serious. Immunotherapy is showing significant promise.

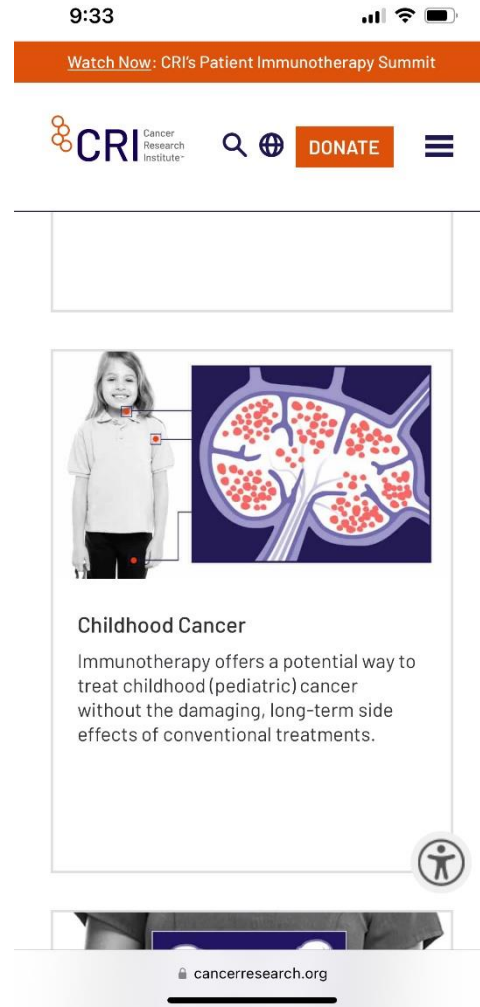


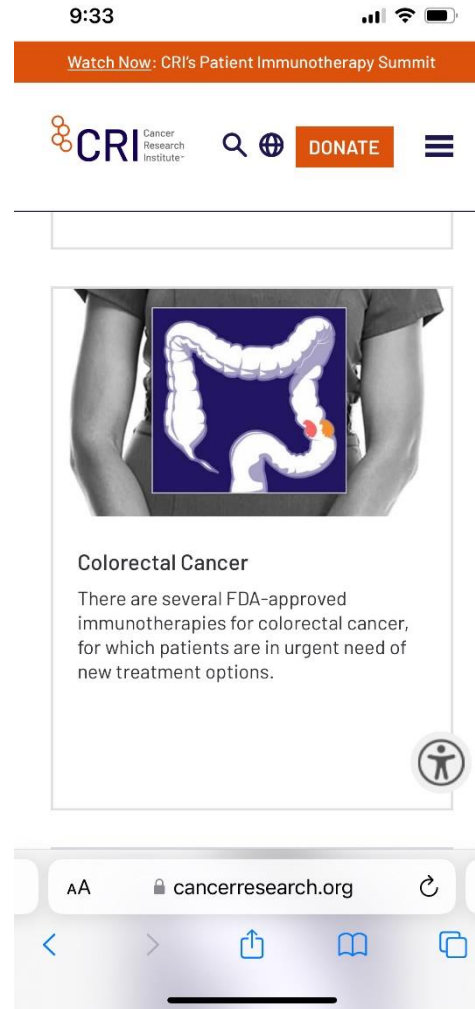


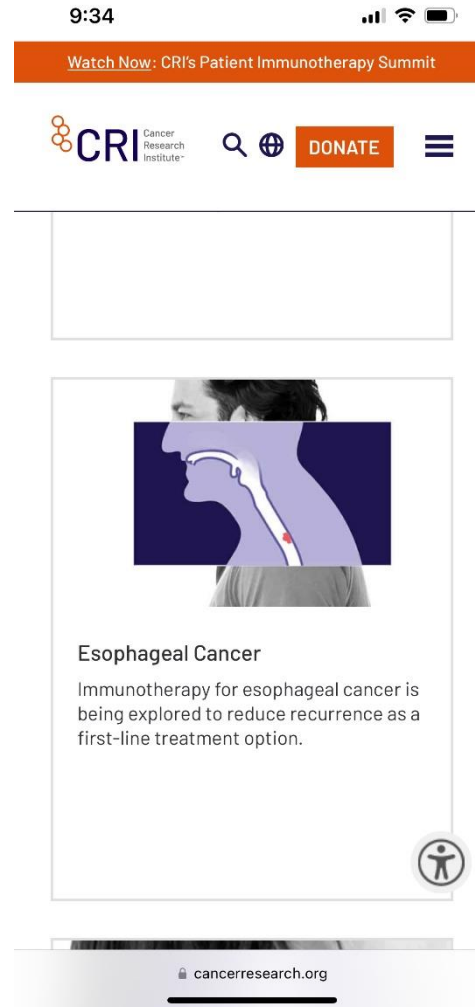
cancerresearch.org

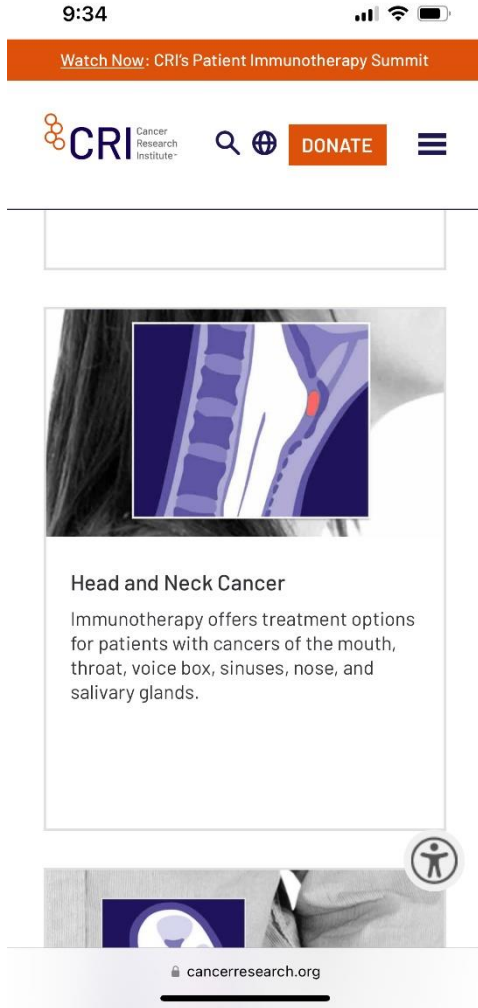


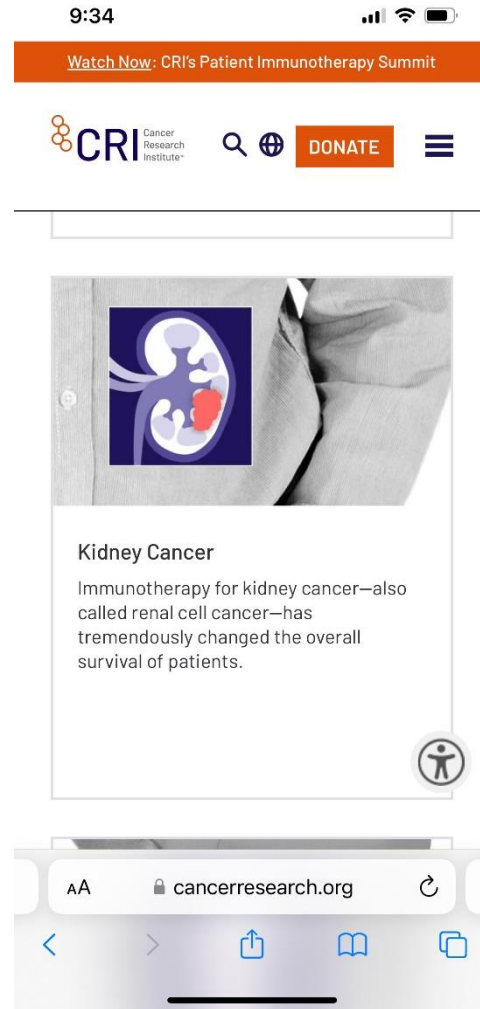


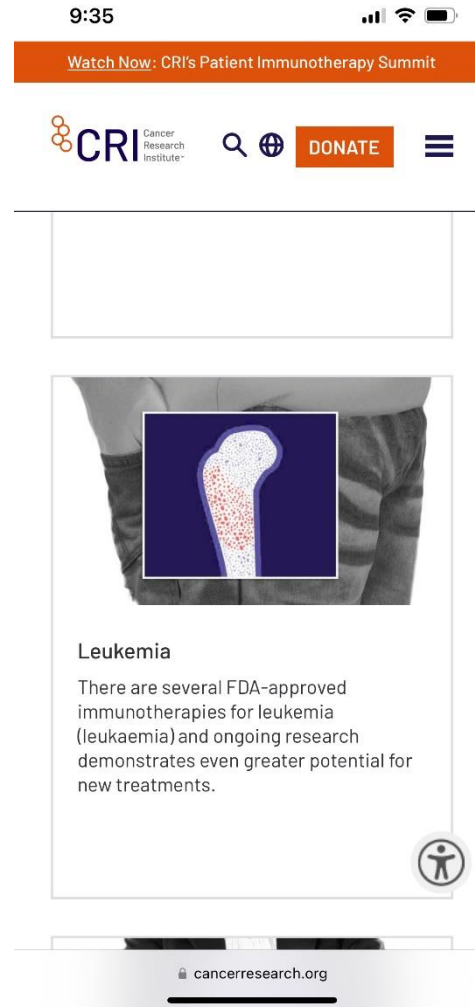




















9:35   


Watch Now: CRI's Patient Immunotherapy Summit

   [DONATE](#) 



Liver Cancer

In addition to the first FDA-approved hepatitis B cancer vaccine, immunotherapy increases the immune response to liver cancer.



cancerresearch.org

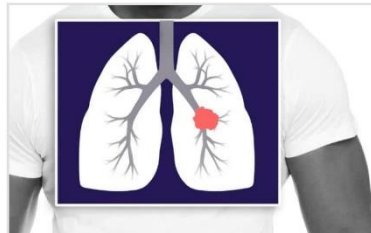
9:36



Watch Now: CRI's Patient Immunotherapy Summit



DONATE

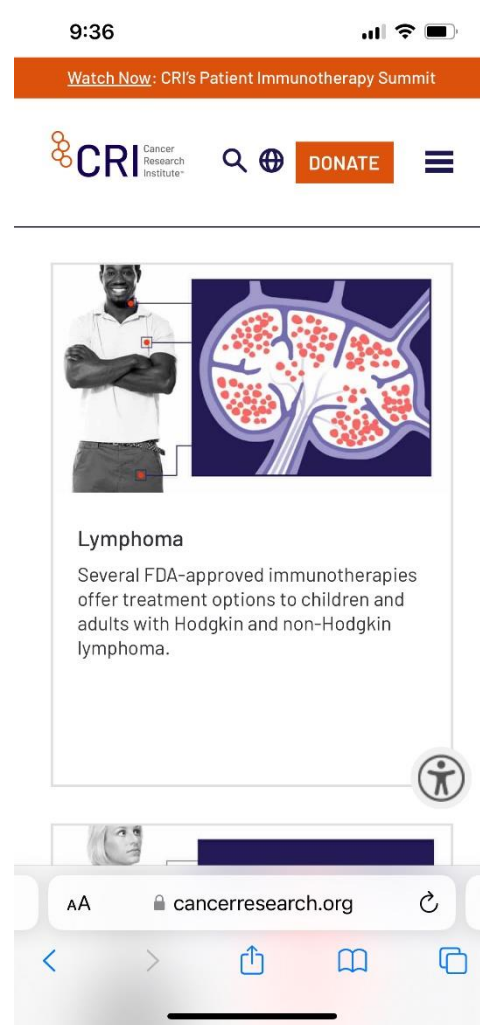


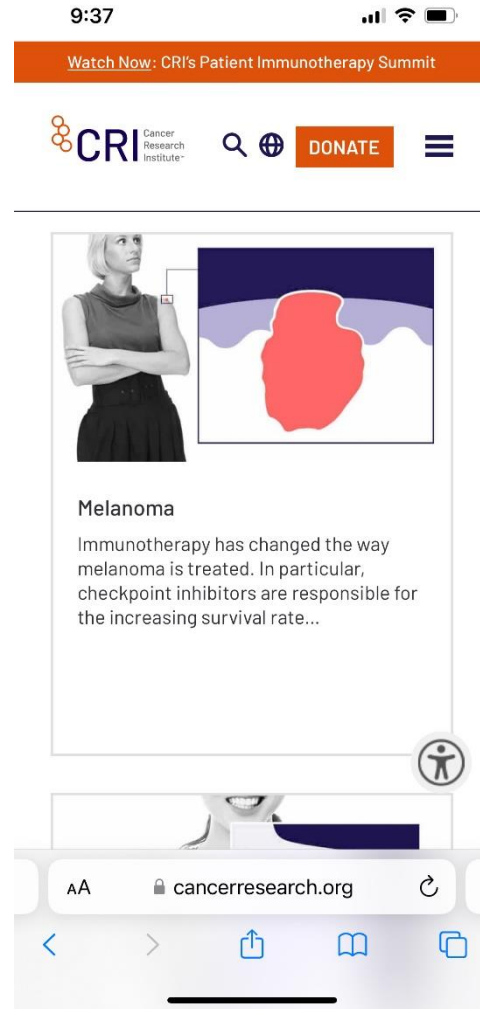
Lung Cancer

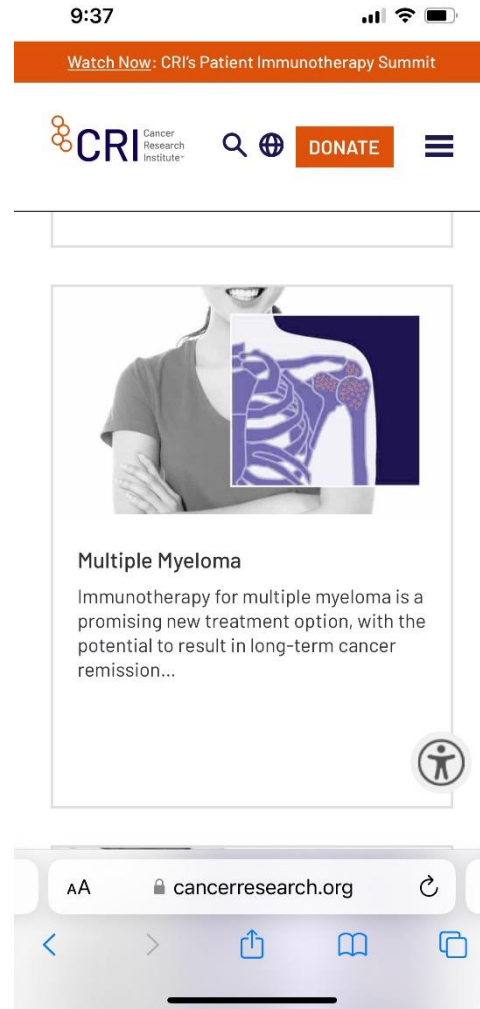
Immunotherapy is a promising option for advanced lung cancer, alone or in combination with treatments like chemotherapy or surgery.

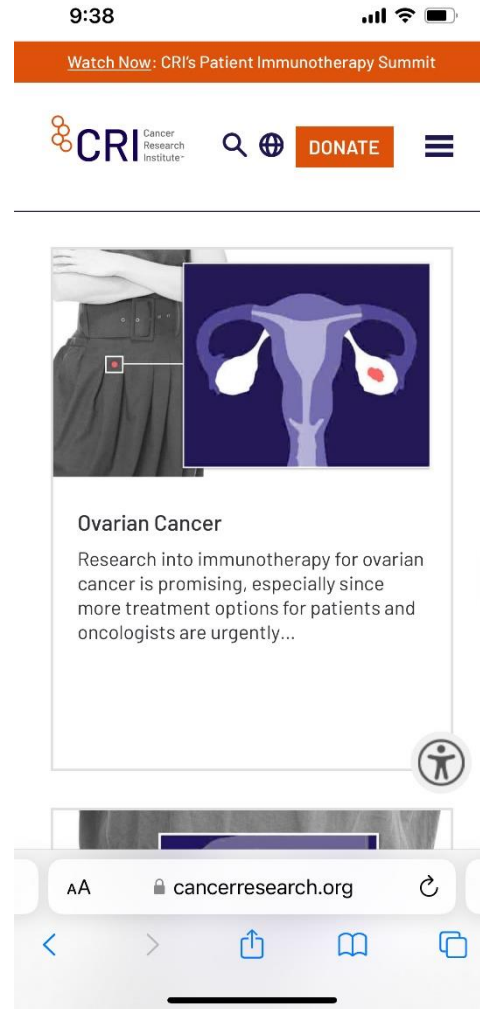


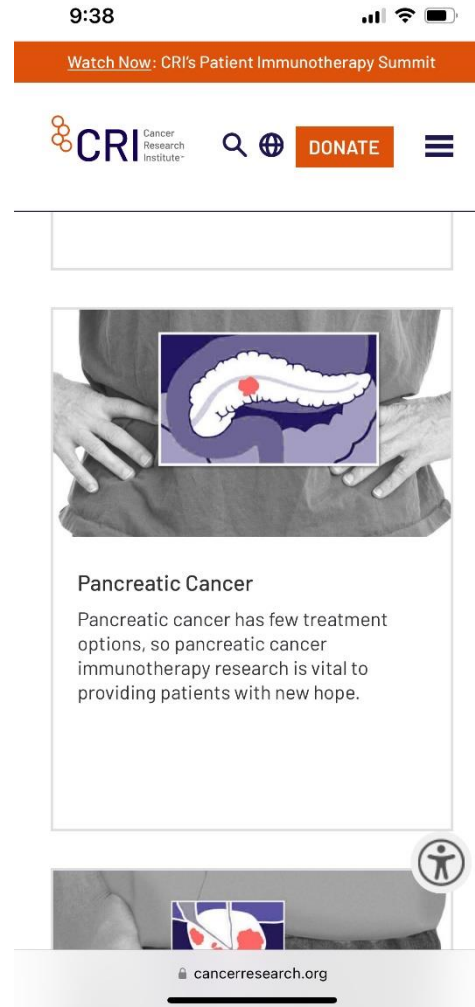
cancerresearch.org

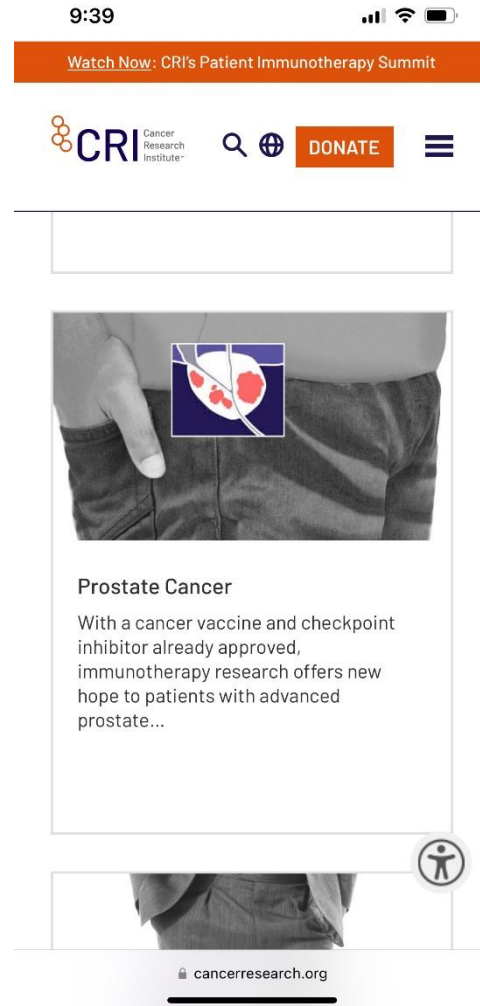


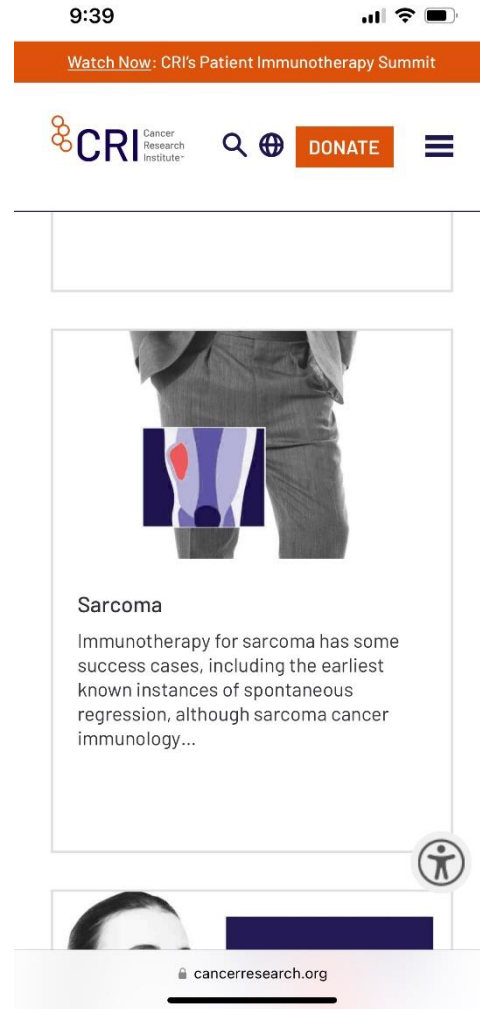


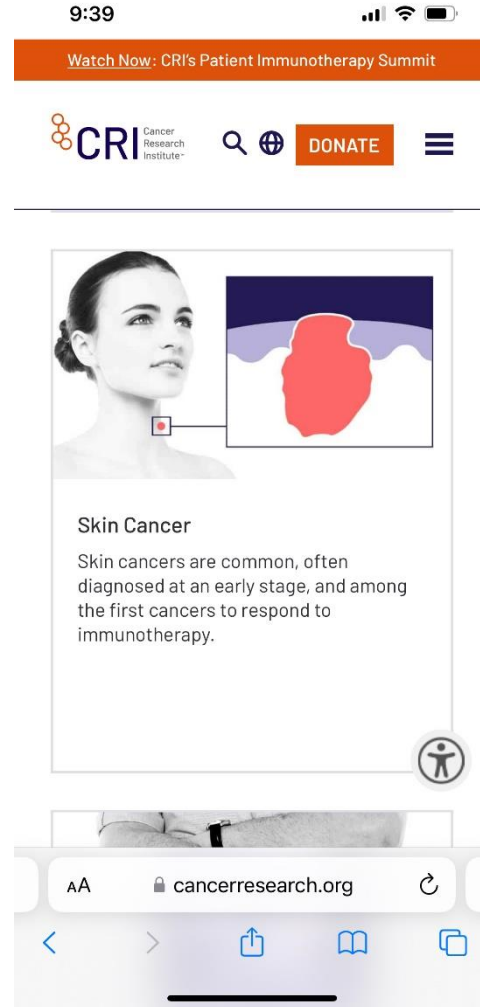




















9:40   


Watch Now: CRI's Patient Immunotherapy Summit

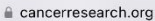
   [DONATE](#) 

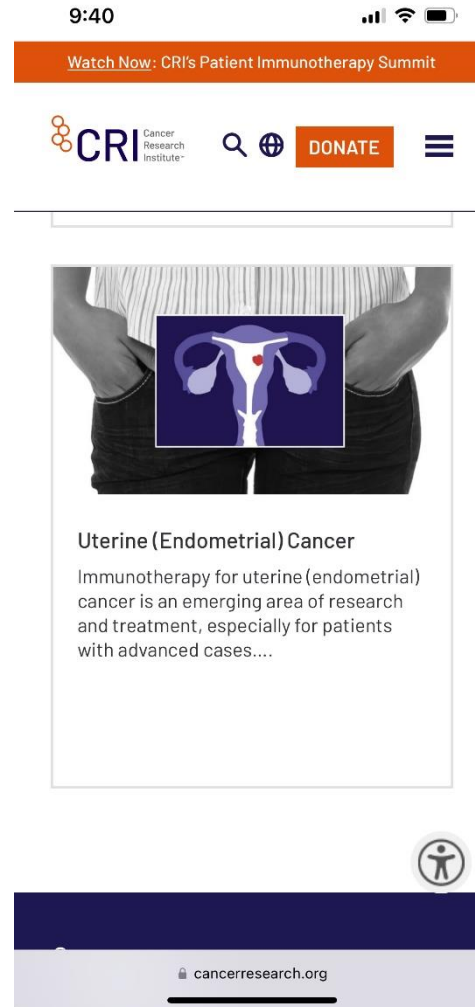


Stomach Cancer

Immunotherapies, including checkpoint inhibitors and targeted antibodies, offer promising new treatment options for stomach (gastric) cancer patients.











What Has Changed?

+ Recent Publications

- Cheung, Testa (2021)
- Carbone (2022)
- Moolgavkar (2023)
 - Revisits Kadarya (2016) among other issues
 - Animal studies
- Belcaid (2023)
- Nair (2023)
- Szlosarek (2024)

+ Dr. Brody testimony in Hofius v. Advanced Auto Parts

- Mesothelioma can result from inherited genetic mutations

+ Dr. Testa testimony in Watts v. Ashley Lumber (2022)

- Position is evolving with science
- Genetic cause of mesothelioma
- Animal studies



Brody Testimony (Genetic Caustation)

- + Q: Mesotheliomas can also result from inherited genetic mutations that allow for uncontrolled cell growth, correct?
- + Yes.,
- + Hofius v. Advanced Auto Parts, Inc.



Dr. Testa Conceded Genetics Alone Can Cause Mesothelioma

+ Dr. Testa, in deposition, testified:

- 4 You agree that genetics alone can cause
- 5 mesothelioma independent of environmental factors?
- 6 A I believe it's possible in rare cases.

+ Dr. Testa also acknowledged that there are in fact genetically linked spontaneous cancers:

- 14 Doctor, you believe that there can be genetically linked spontaneous cancers?
- 15 (Objection)
- 16 Yes.



Testa Testimony (Spontaneous Mesotheliomas)

- + Q: And in that paper it indicates that experimental mouse models have allowed researchers, like you, to show the inactivation of single genes or combinations of specific genes – such as BAP1, TSE1, TP53, CDKN2A, and/or NF2 – and **spontaneously initiate or cause and drive mesothelioma tumorigenesis without asbestos exposure, right?**
- + That is correct.
- + Watts v. Ashby Lumber Company



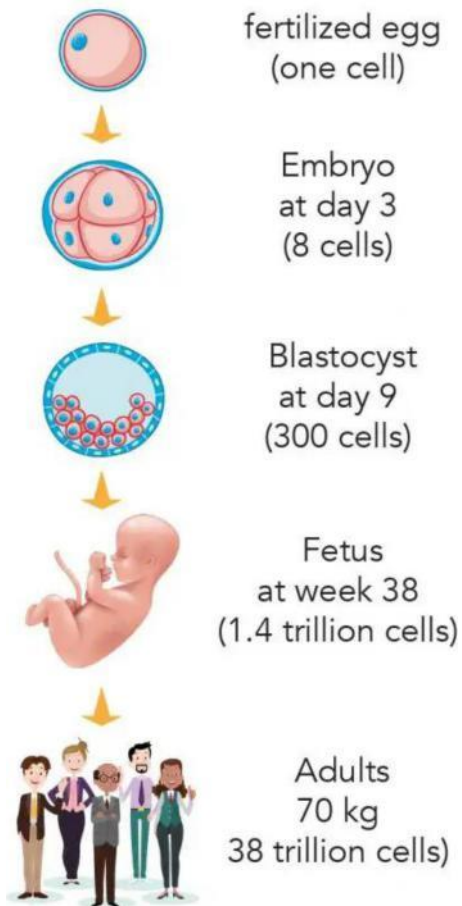
You Tube

- + Oncogenetics – Mechanism of Cancer (Tumor Suppressor Genes and Oncogenes)

Multi-Celled Organisms like Humans

Multi-Celled Organisms

Growth

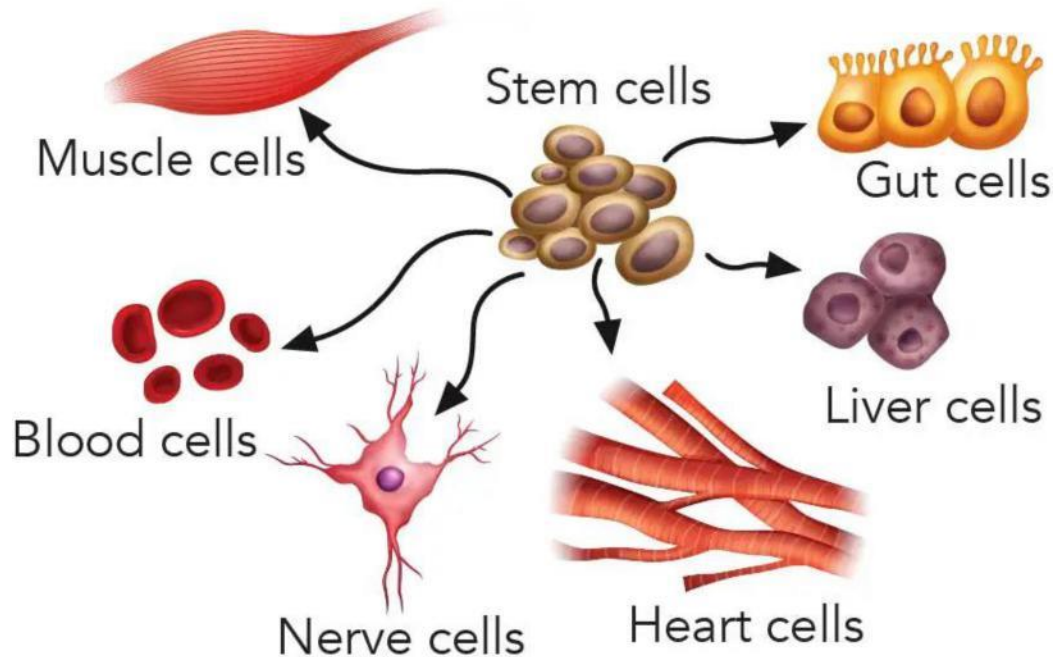


*“Our bodies are made up of trillions of cells, which must work together to keep us healthy. Our cells need to be able to divide to make new cells to help the body grow, or to replace cells that have died. **At the same time, cell growth and division need to be controlled, so the cells don’t grow too much and crowd out the cells around them.**”*

“It may be helpful to think of a cell as a car. For it to work properly, there need to be ways to control how fast it goes – that is, ways to speed up cell growth and division if it’s needed (like a gas pedal), and ways to keep this growth under control or slow it down (like a brake pedal). There also need to be ways to fix parts of the car if they break down.”

Multi-Celled Organisms like Humans

Replenishment



“The stem cells, which have the capability to become several cell types, consistently divide to replenish the loss of old cells.

Different cell types have various turnover rates. For example, cells that protect the inner surface of our stomach and gut need to change every 2-5 days. Our skin cells need to be replenished every other week. Liver cells can work for a year before retirement. About 1-10% of heart muscle cells renew every year. However, nerve cells in the brain and lens cells in the eyes have to work for the entire lifetime.”



What Does This mean For Us?

- + The genetic issue presents an ongoing dynamic and not a latent condition.



Egg Shell Plaintiff

- + A defendant takes a plaintiff “as they find them” and is responsible for all damages, resulting from conduct “Even though, because of the plaintiff, pre-existing frailty of health, they proved to be more severe than they would have been in a “normal person”.
- + Elderly Plaintiff



An Issue of Causation

- + The Genetic issue presents a dynamic process that is occurring independently from alleged somatic (i.e. environmental or “exposure”) potential causes.
- + Did the conduct of the defendant or defendants cause (“but for” or “substantial contributing factor”) the cancer to occur?



Spectrum of Cause

- + Heavy and lengthy occupational exposure -> Employment/paraoccupational -> Take Home -> Questionable or Unknown
- + Genetic issue? Identified? Treatment? Cancer syndrome in individuals or families.
- + This issue is redefining our knowledge in a significant way and is fundamental to cancer treatment. It is not going away.



The State of The Art





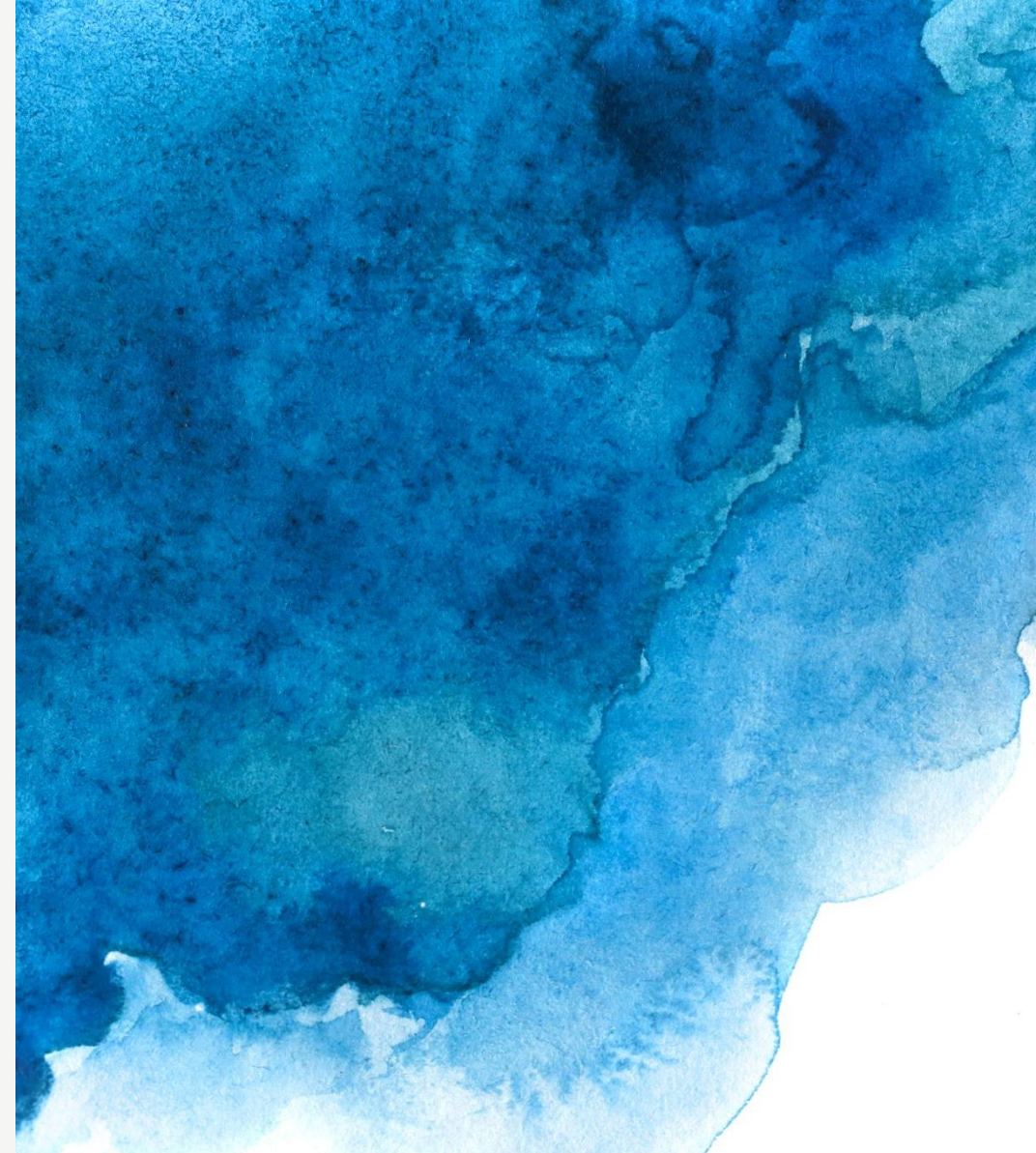
Thank You

Science and Medicine of Genetic Cancer Treatments

Jennifer L. Alesio



SIMMONS HANLY CONROY
A NATIONAL LAW FIRM



Immunotherapy

Check Point Inhibitors

CAR-T Therapy



The “mabs”

Pembrolizumab (Keytruda)

Nivolumab (Opdivo)

Ipilimumab

Currently in clinical trials

Durvalumab

Tremelimumab

The logo for Keytruda, featuring the word "KEYTRUDA" in green capital letters. The letter "Y" is stylized with a dark blue vertical bar and a green diagonal bar.The logo for Opdivo, featuring the word "OPDIVO" in bold blue capital letters with a registered trademark symbol. Below it, the word "(nivolumab)" is written in a blue script font. The logo is accented with orange and blue diagonal lines.

The top of the slide features a decorative header with a dark teal background. It contains several overlapping semi-circular shapes. Some are solid dark purple, while others are filled with concentric arcs or radial lines in a lighter purple shade.

Oh, and while I'm up here

Dr. Testa did not “recant” anything.

2 Q. All right. So I understand it is your
3 hypothesis that the genetic modification that the Watts
4 family, unfortunately, has inherited in and of itself

5 17 THE WITNESS: That's correct, I believe that
18 you have to have other genetic alterations that occur
19 during the lifetime of that individual that are
20 contributed by exogenous forces such as especially
21 asbestos and that are known to be causes of
22 mesothelioma.

What actually happened in Watts . . .

Past medical bills (by stipulation):	\$319,970
Future medical expenses:	\$250,000
Lost Income:	\$2,091,228
Loss of household services:	\$273,455
Past Pain and Suffering:	\$3,750,000
Future Pain and Suffering:	\$3,000,000
Loss of Consortium:	\$1,000,000

\$10,684,653 Verdict for the Plaintiffs

**But even in a
case that ended
in a defense
verdict . . .**

Defendant withdrew Dr.
van Zyl as witness following
a motion to strike his
testimony in its entirety

Jurors ultimately found for
the defense, but said they
thought the BAP-1
“defense” was a “smoke
screen”

**WE'RE ON A
ROAD TO NOWHERE**



CHEK2? Check, please.

14 Q. For example, none of these papers, not the
15 two you cited to me or any of the rest we're going to
16 spend our time talking through here today, says that
17 the CHEK2 mutation by itself in the absence of
18 asbestos exposure is capable of causing that
19 pathogenic response, right?

20 A. Correct.

A. Yeah, I -- I think that's -- that's true.

Q. To a reasonable degree of medical and scientific certainty, somebody might one day prove it is a cause.

A. I think that they've got very good preliminary data that -- that highly suggests it, but it hasn't been totally proven yet.

Q. Okay. And the preliminary data that highly suggests it are the three papers you have just indicated to me, and not a single one of the authors of those papers have made a statement akin to that CHEK2 is an independent cause of malignant mesothelioma, correct?


A. I've already went through that with you

before, and I stick by my original answer.

Q. Okay. So then let's be very clear.

None of those papers indicate anywhere in them that CHEK2 is an independent cause of malignant mesothelioma, correct?

A. They -- they do not.

The top of the slide features a decorative header with a dark blue background. It contains several overlapping semi-circular shapes in a darker blue shade. Some of these shapes are filled with concentric red lines, while others are filled with a pattern of small red dots.

We have reached the portion of this afternoon's program wherein I will moralize at you in my characteristically annoying way . . .



HACKERY IS NOT SCIENCE



CROSSFIRE

AMERICA VOTES 2004

SCIENCE IS SCIENCE

Our study has several limitations. First, obviously, like so many other related studies, the expression of the 48-gene mesothelioma prognostic signature, including the CCNB1 gene, is just associated with patient survival, and any possible causal relations remain to be further studied. Second, the SELECT anal-

Nair et al, 2023.

WHAT CAN GENOMIC TESTING TELL US RIGHT NOW?

WILL IT TAKE LONGER
TO DIE FROM
MESOTHELIOMA?

TREATMENT



INDEPENDENT
ENDPOINT
OF M
CAUSE
PEOPLE
ESTO