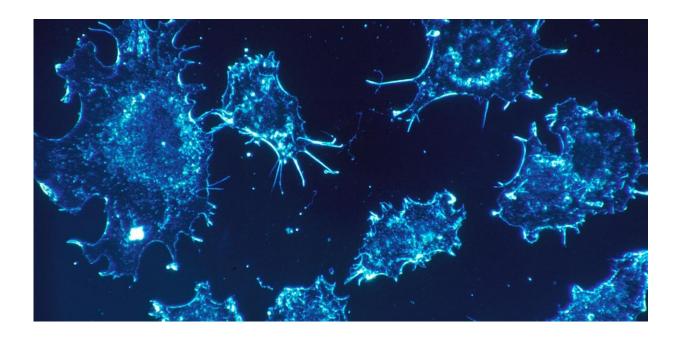


# Five counterintuitive ways scientists are approaching cancer research to improve treatment and prevention

November 2 2023, by Vivian Lam



Cancer cells don't follow the typical rules that allow a multicellular collective to function. Credit: <u>Dr. Cecil Fox/National Cancer Institute</u>

How researchers conceptualize a disease informs how they treat it. Cancer is often described as uncontrollable cell growth triggered by genetic damage. But cancer can also be seen from angles that emphasize mathematics, evolutionary game theory and physics, among others.



Molecular biology has brought significant advances in making it possible to live with <u>cancer</u> as a <u>chronic illness</u> rather than a fatal disease. Alternative frameworks, however, can offer scientists additional insights on how to prevent tumors from spreading throughout the body and becoming resistant to treatment.

Here are a few unconventional lenses through which researchers are viewing cancer with fresh eyes, drawn from The Conversation's archives.

### 1. Evolution and natural selection of cancer

The body is far from a wonderland for cells. Each individual cell competes against trillions of others for finite space and nutrients. If they're able to cooperate in an orderly enough fashion, sharing resources and dividing labor, the collective functions effectively. Cancer cells, however, cheat the system: They hog resources, take up as much space as possible and refuse to die.

In this way, cancer can be thought of as an evolutionary disease—these are cells that have developed the genetic mutations to outcompete their neighbors, and subsequent cell generations inherit this survival advantage. Cancer cells benefit at the expense of the collective until the entire organism collapses.

Oncologist <u>Monika Joshi</u> and pathologists <u>Joshua Warrick</u> and <u>David</u> <u>DeGraff</u> believe that understanding evolution is key to understanding cancer. Screening programs are effective, for example, because removing a nascent tumor is easier than treating one that has evolved the ability to spread. Cancer cells likewise become resistant to treatments because they're pushed to further evolve to survive.

Some researchers are applying the principles of <u>evolutionary game</u> <u>theory</u> to reduce treatment resistance and optimize therapies for



children.

"The fight against cancer is a fight against evolution, the fundamental process that has driven life on Earth since time immemorial," they wrote. "This is not an easy fight, but medicine has made tremendous progress."

## 2. Fluid mechanics of cancer

As much as cancer is a disease that respects no boundaries, tumor cells are still shaped by their environment. Unlike healthy cells that take the hint when their presence isn't wanted, however, tumor cells not only survive but thrive in stressful conditions. Isolated cancer cells able to adapt to harsh settings are the ones that establish metastatic colonies and become resistant to treatment.

While researchers have focused on how biochemical signals direct cells to move from one location to another, a cell's physical environment also affects where it migrates. Mechanical engineer <u>Yizeng Li</u> found that a cell's "solid" and "fluid" surroundings influence its movement.

Cancer cells encounter varying degrees of fluid viscosity, or thickness, as they travel through the body. Li and her team found that breast cancer cells counterintuitively move faster in high viscosity environments by changing their structure. This meant that fluid viscosity serves as a mechanobiological cue for cancer cells to metastasize.

"Cancer patients usually don't die from the original source of the tumor but from its spread to other parts of the body," Li wrote. "Understanding how fluid viscosity affects the movement of tumor cells could help researchers figure out ways to better treat and detect cancer before it metastasizes."



#### 3. Inflammation link to cardiovascular disease

Apart from being leading causes of death around the world, cardiovascular disease and cancer may not initially seem to have much in common. The many <u>risk factors</u> they share, however—like poor diet, smoking and <u>chronic stress</u>—coalesce with chronic inflammation: persistent, low-grade activation of the immune system can damage cells in ways that encourage either disease to develop.

For biomedical engineer <u>Bryan Smith</u>, the developmental parallels between these diseases signal they could be treated at the same time.

Drugs can be repurposed to target diseases for which they weren't originally designed. Certain drugs, for example, can direct immune cells called macrophages to consume both <u>cancer cells</u> and the cellular debris that contribute to cardiovascular plaques.

"As <u>basic science</u> discovers other molecular parallels between these diseases, patients will be the beneficiaries of better therapies that can treat both," wrote Smith.

### 4. Mathematics of cancer

In certain contexts, math has unique strengths in describing the natural world. For instance, epigenetics—where and when genes are turned on or off—plays as much a role in cancer progression as direct changes to the genetic code. Epigenetic changes can alter healthy cells to the point of losing their normal form and function. But the randomness of these changes makes it difficult to tease out pathological from normal genetic activity.

A <u>mathematical concept</u> called stochasticity—or how the randomness of the steps of a process influences how predictable its outcome will



be—lends a logical framework to the <u>epigenetic changes</u> contributing to cancer, clarifying when <u>healthy cells</u> rapidly develop into <u>tumor cells</u>.

Stochasticity is commonly used to study stock market behavior and epidemic disease spread, and researchers quantify it by examining the degree of uncertainty, or entropy, of a particular outcome. Identifying high entropy areas in the genome could offer another approach to cancer detection and drug design.

Cancer geneticist <u>Andrew Feinberg</u> has been using entropy to quantitatively describe the epigenetics of cancer. He and his colleagues found that high entropy regions of the genome in the skin become even more entropic with sun damage, increasing the chance of developing cancer. This offers a potential explanation for why cancer risk significantly increases with age.

"Epigenetic entropy shows that you can't fully understand cancer without mathematics," Feinberg wrote. "Biology is catching up with other hard sciences in incorporating <u>mathematical methods</u> with biological experimentation."

# 5. A public health issue

Cancer is a disease that develops in an individual, but its socially derived causes and societal-wide effects are hardly limited to a single person.

Take the case of lung cancer. It is stigmatized as a disease brought on by poor lifestyle choices—a consequence of a personal decision to use tobacco products. But as thoracic oncologist <u>Estelamari Rodriguez</u> noted, the face of lung cancer has changed.

"Over the past 15 years, more women, never-smokers and younger people are being diagnosed with lung cancer," she wrote. While lung



cancer rates have significantly decreased for men, they have substantially risen for women around the world. Despite being the leading cause of cancer death among women, screening rates remain low compared with other cancers.

More broadly, cancer symptoms are often unrecognized or misdiagnosed, not only for women but also for many marginalized populations, including people of color, transgender patients and the uninsured.

These disparities are due in part to biases in medical education and clinical research that fail to prepare clinicians to care for the diversity of patients they'll encounter. Tenuous access to preventive care and disproportionate exposure to carcinogens among certain populations compound these inequities.

The purview of cancer goes far beyond a single discipline. It takes a village of researchers, policymakers and patient advocates to achieve effective and accessible cancer care for all.

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Provided by The Conversation

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