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How 'Inflammaging' Drives Cancer— And Points Researchers to Treatments

Inflammation fuels the high rate in people over 50, leading scientists to test anti-inflammatories to fight the disease

By Betsy McKay

People are more likely to get cancer as they age. Dr. Miriam Merad has an unconventional idea of how that might be reversed: using allergy drugs and other seemingly unlikely medications to damp a condition known as "inflammaging."

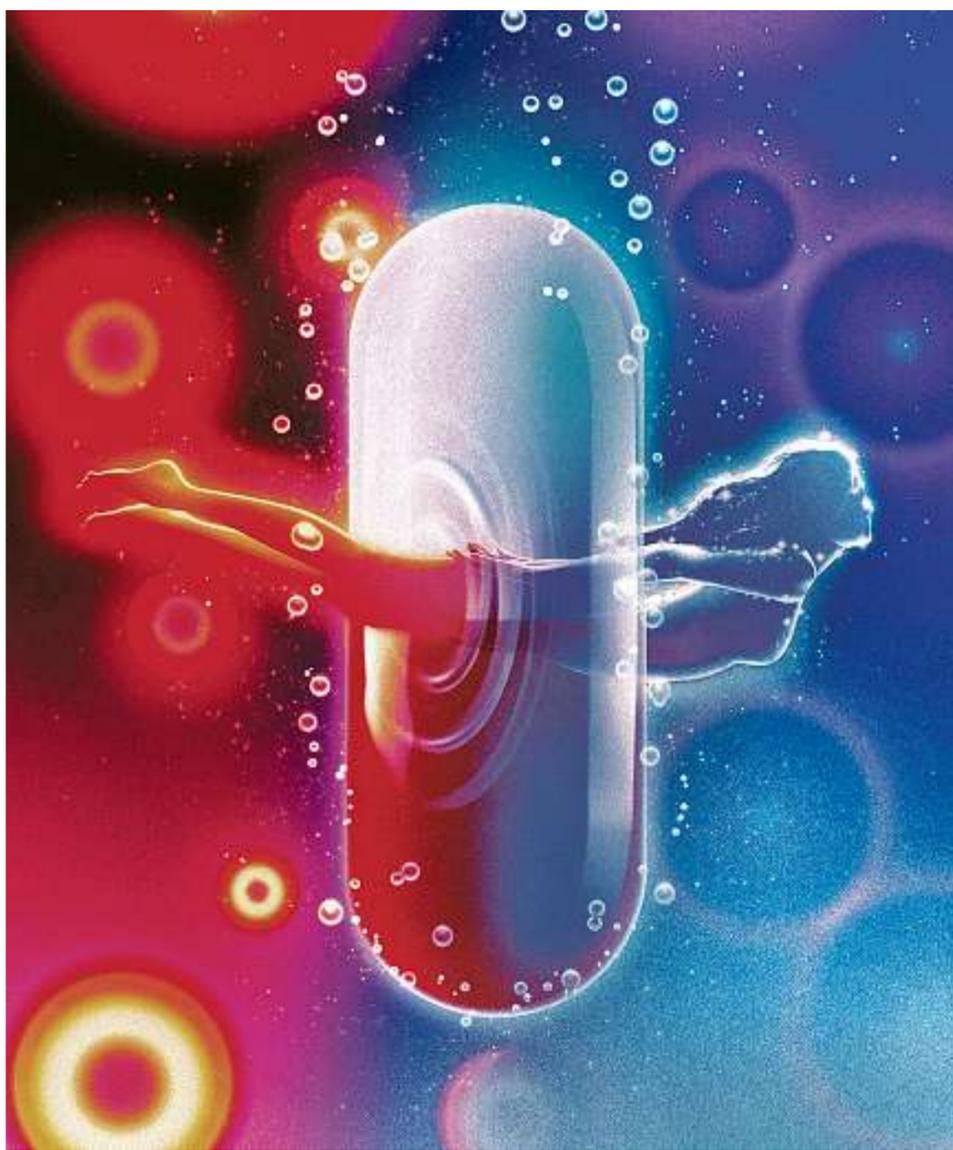
The immunologist and oncologist has spent years examining malignant tumors to learn why people over age 50 account for nine in 10 cancer diagnoses in the U.S. She and her research team at the Icahn School of Medicine at Mount Sinai in New York City have homed in on an answer: the aging immune system. Their studies of individual immune cells in human lung tumors, as well as in old mice, have revealed how chronic, or pathogenic, inflammation in older people—dubbed inflammaging—interferes with the immune system and fuels cancer growth.

Merad and other researchers are testing whether existing anti-inflammatory medications usually used to fight rheumatoid arthritis or allergy conditions like asthma or eczema can slow cancer in older patients. They are also searching for new drugs. "Aging is something that we think we can transform," says Merad, director of the Marc and Jennifer Lipschultz Precision Immunology Institute at Mount Sinai.

Inflammation is the immune system's reaction to a threat. Immune cells circulate in the body, attacking invaders such as viruses and cancer and calling for backup—more immune cells—when necessary. Working correctly, they can beat back Covid-19 or heal a cut on the finger. But the immune system can also overreact, fueling inflammation that gets in the way of healing or leads to disease. It misfires like this more as people age.

"A big focus of the field right now is to separate beneficial inflammation, the one that protects us from microbes and from tumors, from the pathogenic inflammation that is enhancing cancer progression, promoting atherosclerosis, promoting damage in the older brain," Merad says.

The idea of using drugs on cancer patients that damp inflammation is counterintuitive, says Dr. Andy Minn, who is scheduled to become chair of a new immuno-oncology program at Memorial Sloan Kettering



Dr. Thomas Marron and Dr. Miriam Merad at the Icahn School of Medicine at Mount Sinai in New York.

Cancer Center in August. Immunotherapies, which rev up the immune system to attack tumors, have transformed cancer care over the past several years. "The common wisdom is that we want

to ramp up inflammation as much as possible so that inflammation can be harnessed by the immune system to kill the cancer," Minn says. "The blind spot has been that there are different types of inflammation."

Often the assumption is that older people get sick more easily because their immune systems weaken, says Dr. Thomas Marron, a thoracic medical oncologist who heads the early-phase trials unit at Mount Sinai's Tisch Cancer Institute. That does happen, he says, but at the same time, "we really are seeing this sort of hyperactivation."

"The body is just basically like a flower bed primed to grow cancer as you get older," he says.

As a person ages, the immune system has to work harder to kill infections or mutations, like cancer. But the immune system itself is aging and produces fewer of the type of immune cell that targets and kills cancer cells. At the

same time, it makes more of a type of immune cell that responds initially to infections. Known as myeloid cells, with aging they become more inclined to overreact and create inflammaging. These inflammatory cells may provide a "hit" necessary for older cells with mutations to turn cancerous, says Merad of Mount Sinai.

A study of 72-week-old mice at Mount Sinai—correlating to about 65 years of age in humans—showed how an aging immune system drives cancer. Matthew Park, a medical student who led the research in Merad's lab, discovered that myeloid cells in lung tumors of the older mice churned out interleukin-1, or IL-1, a protein long linked to inflammaging. The IL-1 summoned more myeloid cells to the lungs, leading to more inflammation and tumor growth.

When Park put young immune systems in the mice, their lung cancer came under control.

He also gave the mice a rheu-

matoid-arthritis drug called anakinra that blocks IL-1. It slowed tumor growth when given early. That suggests that anti-inflammatory treatment would work best for older people at high risk of cancer, or with early-stage disease, according to the study, although research findings on mice can't always be generalized to humans. "We can potentially prevent lung cancer," Park says.

Drugs known as JAK inhibitors—used to treat inflammatory diseases like eczema or ulcerative colitis—have similar potential for treating cancer in older patients, two studies published in June

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2024 suggest. One study examined patients with lung cancer. The other showed that a drug called ruxolitinib stopped Hodgkin lymphoma from progressing in 46% of patients who were also on immunotherapy.

Treatment in the future will involve using technology to figure out when to fire up the immune system or quiet it, says John Tejjaro, professor of immunology and microbiology at the Scripps Research Institute in La Jolla, Calif. "It's not as simple as you either turn on the gas or hit the brake," says Tejjaro, co-senior author of the ruxolitinib study.

Marron at Mount Sinai is testing another type of medication in older cancer patients—an antiviral—to combat inflammaging. The hope is to calm inflammation that flares up when ancient viruses that are integrated into the human genome reactivate, which can happen during aging.

Anne Martz, a 90-year-old with metastatic lung cancer, participated in a trial last fall of lamivudine, an antiviral for HIV and hepatitis B. It had shown a benefit in the 72-week-old mice in Merad's lab.

Martz, who was born in Denmark and lives in New York City, had a recurrence of lung cancer three years ago and has been receiving immunotherapy. It beat back much of the cancer, she said, but a tumor grew on her adrenal gland and the immunotherapy wasn't working against it.

After she took the lamivudine pills twice a day for six weeks, along with her immunotherapy, a scan showed the tumor stopped growing. She is back on the lamivudine pills now after a more recent scan showed growth again.

She likes that the drug was tested in elderly mice. "I thought if it had been in elderly mice, I'm an elderly person, it might work with me, too," she said.

Printing Error Ruffles Fans Of Mahjong

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"The League."

"It was a kerfuffle. Everyone was talking about it," Oliphant said, quick to swear that's not a complaint.

Once the realm of 80-year-old retirees, mahjong has grown in popularity, with players now including Hollywood stars like Julia Roberts and Mindy Kaling.

In an interview with Stephen Colbert several years ago, Roberts said she plays mahjong once a week with her girlfriends. The game, she said, was "a way to build order out of chaos based on random drawing of tiles."

Participation has exploded over the past two years, according to many players and instructors, and a cottage industry has popped up around the game. There are tile sets selling for upward of \$2,900 and designer jewelry made out of mahjong tiles, not to mention the countless YouTube tutorials and Facebook groups and Reddit threads discussing correct plays, rules and etiquette.

The National Mah Jongg League was founded in New York City in 1937 to standardize the game in America, and its annual card has divided the winners from the losers

for nearly 90 years.

Mahjong—which many American players spell Mah Jongg, thanks to the League—is a showcase of strategy and wits. Four players draw and discard tiles to complete specific tile patterns. The tiles are colorfully adorned with different suits—of dots, crabs, bamboo, as well as other characters like dragons, flowers and winds.

In the American version, the National Mah Jongg League card dictates which patterns win. It is copy-righted and changes every year.

Meanwhile, the League, which donates a portion of its sales, has largely stayed the same.

Its website "is a throwback to a webpage in the late 1990s," said Krista Obitts, a mahjong enthusiast who started playing two years ago.

The phone number listed on the site often goes unanswered; it recently played a recorded apology for the misprint mishap. And while there's been some inflation—the standard-size card now costs \$14, when in 1973 it cost 75 cents—the look, style and feel of the cards is virtually unchanged.

Perhaps, some mahjong players whispered recently but didn't dare say on the record for fear of retribution, the League needs to modernize.

The League said it wouldn't be able to speak about the issue until late August. "Right now we are focused on delivering the annual NMJL card and standard hands," President Larry Unger said, adding the items help the community "enjoy this magical game."

On a recent Wednesday night in



Screenshot, above, of Julia Roberts talking about mahjong on 'The Late Show with Stephen Colbert'; left, instructor Tori Rittinger.



Arlington, Va., more than two dozen women gathered at a local pizza and beer hall to learn and play mahjong with instructor Tori Rittinger. Most had played the game before and were well aware of the misprint fiasco.

The misprint showed one line on both the standard and large-print

tributed over the misprinted line.

Thomas purchased five 2025 cards and said she had stalked her mail earlier this spring waiting for them to arrive. Many players order multiple cards so they have a full set on hand when friends come over to play.

Thanks to her quick-fix stickers, she's not anxiously awaiting the new batch of cards, coming any day now. "Can you imagine having to reprint all those cards?," she said in sympathy with the League.

Some players, often those newer to the game and still getting used to the 55 lines of tile patterns that can crown them winners, played down the misprint.

Martine Kline said she found the mistake in this year's card to be obvious, but acknowledged it could be detrimental for more experienced players. Those players tend to move through games faster and rely on quickly glancing at the color patterns as they collect tiles.

"It did stir up rage among the old guard," said Kline, who lives near Jackson, Miss., and has been playing since 2022.

Oliphant, the Tampa enthusiast, waited on her corrected 2025 National Mah Jongg League card like the rest of the American mahjong community. She didn't let that stop her from playing.

"Where there's a will, there's a way to play mahjong," said Oliphant. She's even made it into a business, founding Destination Mah Jongg, which organizes mahjong tournament vacations.

The card finally arrived last week.