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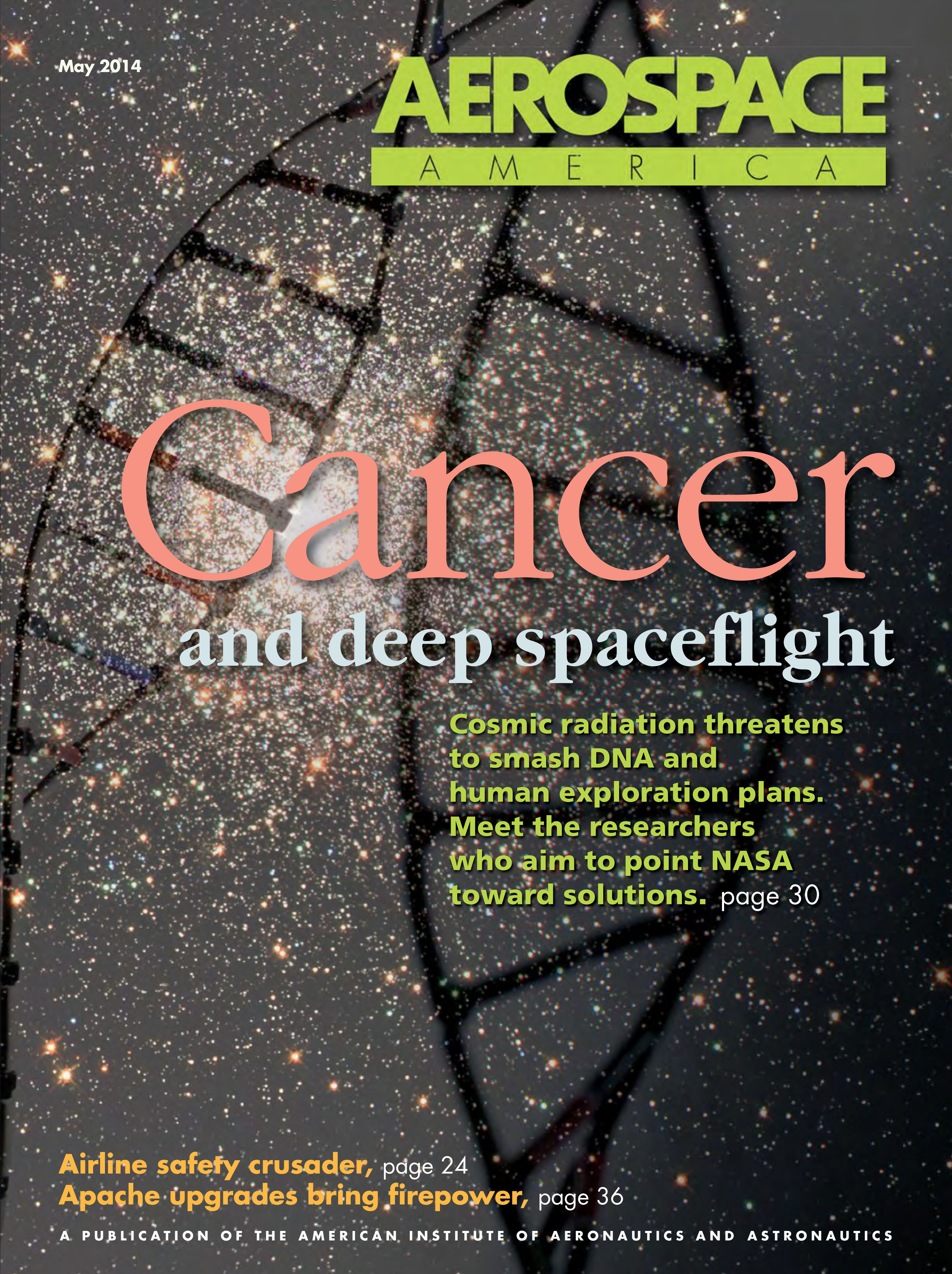

Cancer and deep spaceflight

Cosmic radiation threatens to smash DNA and human exploration plans. Meet the researchers who aim to point NASA toward solutions. page 30

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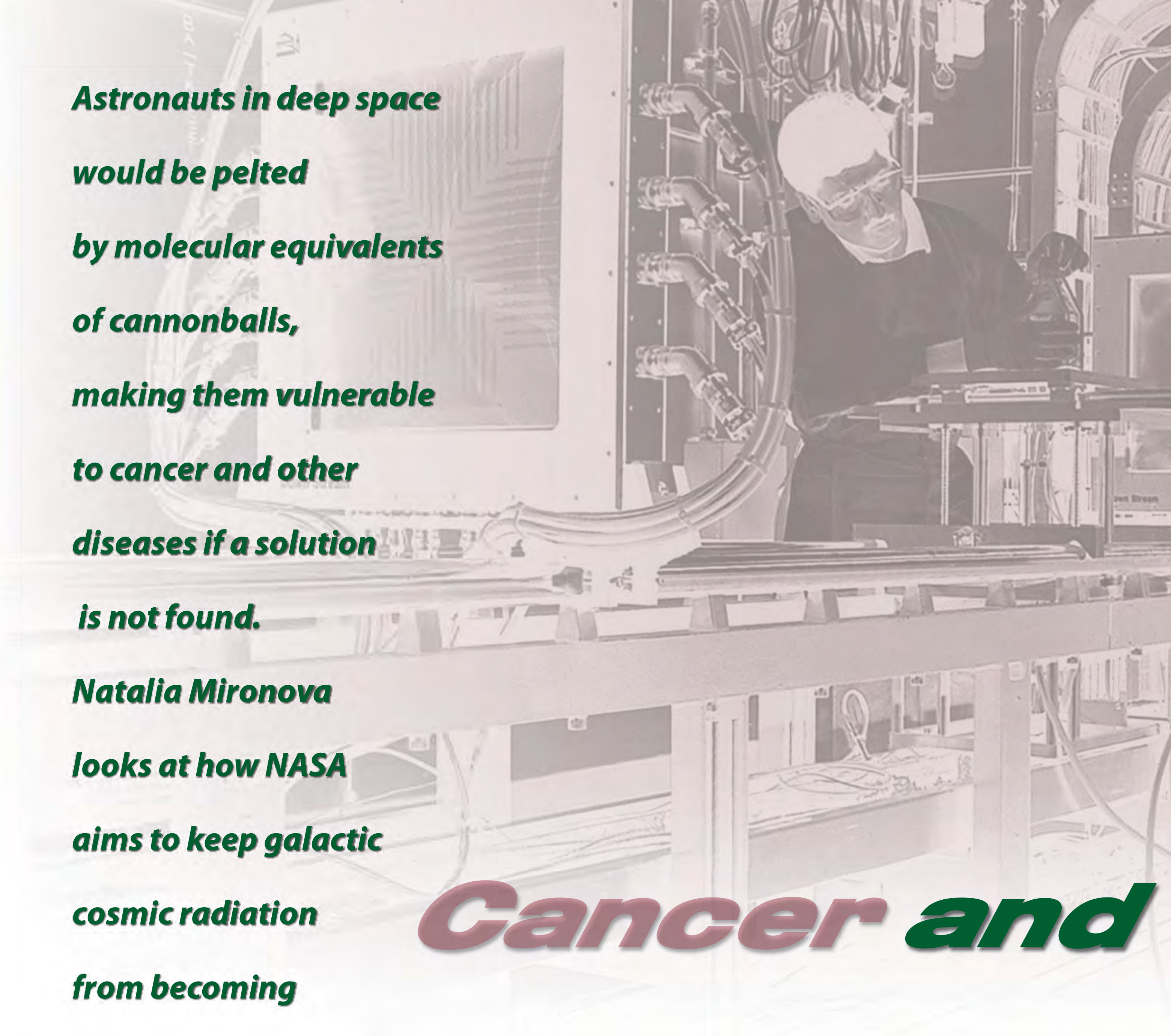

Cancer and

Astronauts in deep space would be pelted by molecular equivalents of cannonballs, making them vulnerable to cancer and other diseases if a solution is not found. Natalia Mironova looks at how NASA aims to keep galactic cosmic radiation from becoming a showstopper.

by Natalia Mironova

A boxy, unassuming piece of equipment sits in a climate- and humidity-controlled room in a basement at Georgetown University Medical Center in Washington, D.C. It's a million-dollar device that researchers are using to analyze tissue samples taken from mice irradiated at a NASA lab on Long Island. Washington is a long way from the astronaut training facilities at the Johnson Space Center in Houston, but the work performed here at Georgetown's Lombardi Cancer Center may help shape the future of human spaceflight. Dr. Albert Fornace Jr. and his team have been working to determine how galactic cosmic radiation affects mice tissue. He hopes the findings will help gauge the risks of certain cancers and point NASA toward strategies for coping with those risks.

Whether in mice or men, radiation can short circuit cellular metabolism, damage the DNA code that governs how long cells live and how fast they reproduce, which can lead to cancer. So far, there is no evidence that astronauts run a higher risk of developing cancer than the general population. But exposure to galactic cosmic radiation has been limited by the relatively short duration of missions and the fact that astronauts in low Earth orbit are protected by Earth's magnetosphere, which deflects

The NASA Space Radiation Lab

spaceflight

most of the cosmic radiation. With Mars being touted as the new frontier, NASA is worried about the length of the trip through a radiation environment much harsher than Earth's. Early findings from the research at Georgetown suggest those worries are valid. There are proposed medical solutions, but experts say a lot more work should be done before a crew bound for Mars heads to the launch pad.

NEW RADIATION ENVIRONMENT

A long-term, deep space mission would expose astronauts to galactic cosmic radiation on levels never experienced by humans. In deep space, astronauts would have to worry about two types of radiation — solar particle events, or SPEs, which are primarily streams of high-energy protons belched by the sun, and galactic cosmic radiation, or GCR, which consists mainly of higher energy ions plus some protons and gamma rays, which are the small-wavelength, high-energy rays emanating from the hottest region of the universe.

SPE radiation levels vary based on solar activity — they are lower during "solar minimums" and peak

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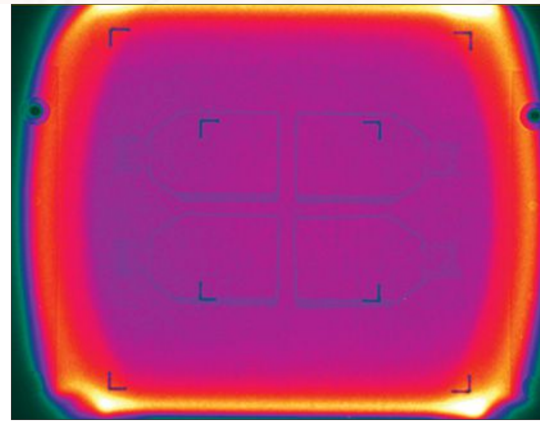
>
> **— Dr. Albert Fornace Jr., Georgetown University**



Brookhaven National Laboratory

Mimicking deep space: Live mice were exposed to heavy ion radiation by placing them in the beam line at Brookhaven National Laboratory, home to the NASA Space Radiation Lab. This researcher is working with unspecified cells, not mice.

Perfect beam: The purple, right, indicates evenly distributed radiation across specimen flasks.

during "solar maximums." A mission could be scheduled during the solar minimum period to lessen the exposure to SPE. But the galactic cosmic radiation is a constant presence in deep space. Dr. Fornace likens the effect of the heavy ions to heavy artillery: "If we think of gamma rays and X-rays which we have here on Earth — and we have good risk estimates — as maybe a BB, then these heavy ions when they hit the cell are like a cannonball. And they are going very fast," he says.

Fornace and his team set out to find out just what kind of damage such a "cannonball" can do to live tissue. For the past four years, they have been using NASA funds to study the effects of space-based radiation on colorectal tumor development. Fornace chose to focus on this particular type of cancer for two reasons: Having been affiliated with NASA since the 1990s, he was aware of the agency's efforts to fund studies on leukemia, breast and lung cancer, and he felt not having any studies of intestinal tumors was a gap in the program. Secondly, he says, "We know that colorectal cancer is increased by radiation. And if radiation caused a modest increase, that could be very bad since it's already the third most common kind of tumor. Whereas if you increase a risk for a rare tumor, two times rare is still rare; two times this would be a big problem."

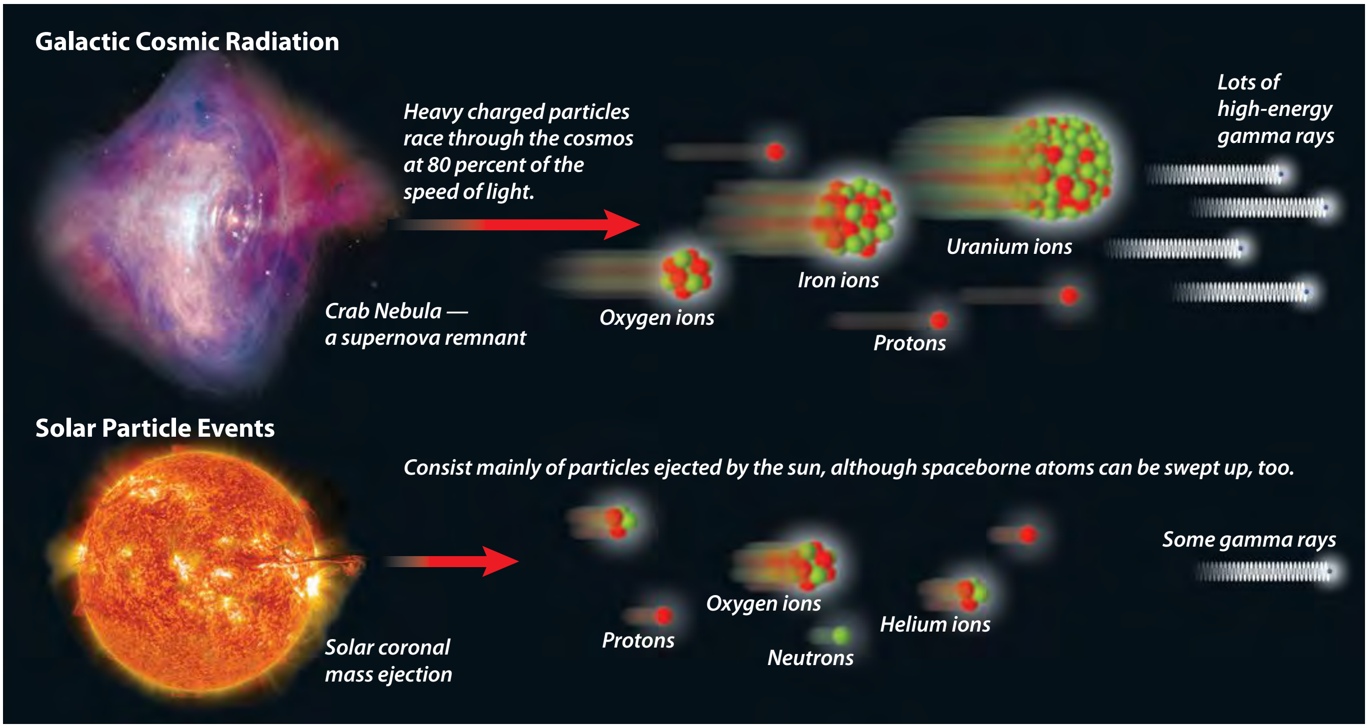
In 2013 Fornace and his colleagues, Dr. Kamal Datta and Dr. Shubhankar Suman, published a paper detailing how cosmic radiation increases colorectal cancer in mice. The team used specialized mutant mice predisposed to colorectal tumors; the mice were irradiated with both gamma radiation and heavy ion radiation. Sending research mice to deep space is an expensive and complex proposition; so the Georgetown team found a way to expose them to heavy ion radiation here on Earth, at NASA's Space Radiation Lab on the grounds of Brookhaven National Laboratory. A large apparatus called the cyclotron can strip any atom down to the nucleus, and then with magnets spin it around, getting it close to the speed of light; magnets then direct the particles down the pipe that leads to the research laboratory where lab mice are treated.

"These mice are well studied. This mouse model has been used to study colorectal cancer before. Once we expose these mice to different types of radiation, we do a quantitative as well as qualitative analysis — count the tumors and grade the tumors," says Datta.

What the researchers found was concerning. The tumors found in mice treated with heavy ion radiation were not only more numerous, the tumors were also higher grade, meaning they were malignant rather than benign. "All our studies show there is more risk for colorectal cancer," says Datta. There are, of course, still the unknown factors that the Georgetown researchers mention when talking about their results: There is the question of dosage — the radiation dose administered to the mice in hours or days would be spread out over several months for the astronauts. The study can't measure any effects of microgravity or the psychological stress of being on a long space mission. On top of that, there is the species difference. Mice are, after all, not people, but Fornace says they proved to be a good model in previous colorectal cancer studies not related to space radiation. The results, they believe, are telling: "I think we can say with confidence that the risk is not going to be lower than what we know for gamma rays," says Fornace. He views cancer as one of the potential "major hang-ups" in planning deep space missions.

Deep space dangers

Mars explorers will need protection from galactic cosmic radiation, which researchers say would plow into cells like molecular artillery.



Sources: NASA SOHO solar observatory, NASA Hubble and Chandra images

Graphic by John Bretschneider

DEFINING ACCEPTABLE RISK

Currently, NASA limits its astronauts to receiving 3 percent of the estimated fatal lifetime radiation exposure. This is based on science that says exposure to 1 sievert of radiation increases a person's risk for fatal cancer by 5 percent. How many "safe days" in space that translates to depends on the individual astronaut's "age, gender, prior exposure, solar cycle and mission location," according to Dr. Rich Williams, NASA's chief health and medical officer. In an e-mail he says, "For crew with no prior exposure, the number of estimated safe days can range from 180 to 1,600 days, for young females on deep space missions and older males on ISS missions respectively."

This policy limits the number of individuals who would qualify for a long-term deep space mission, like one to Mars. "You don't want to send a total rookie, you want somebody who's been in space and knows what they are doing, that means probably that person already has significant exposure. If you already had exposure in space then you're getting up to where your limit is," says Dr. Dorit Donoviel, deputy chief scientist at the National Biomedical Research Institute in Houston, Texas, a non-profit institute established by NASA in 1997 to address health-related issues of long-term spaceflight. Donoviel points out that this 3 percent policy would preclude women from going on a lot more missions, because women reach their maximal safe days in space sooner than men. That's because women already have higher incidents of radiation-induced cancers, and on average they live five years longer than men, which gives more time to develop cancer.

Donoviel says one of the measures to take to protect the crew from galactic cosmic radiation would be to make the trip shorter. But so far, new propulsion technologies that would achieve that, or techniques to shield the spacecraft from galactic cosmic radiation, remain the stuff of science fiction: "Right now there are no lightweight solutions, in fact no ways to shield from galactic cosmic rays," says Donoviel. The best solution, she says, may lie with pharmaceuticals.

Besides colorectal cancer risk, the Georgetown researchers looked at the

Most days in space

Humans have spent the equivalent of more than two years in Earth orbit with no evidence of higher cancer rates. A Mars mission would instantly propel crew members into the record books and expose them to harsher cosmic radiation.

Soviet Union | Russia | Ukraine | United States

Men

1 Sergei Krikalev
803 days
6 flights

2 Alexandr Kaleri
769 days
5 flights

3 Sergei Avdeyev
747 days
3 flights

4 Gennady Padalka
710 days
4 flights

5 Valeriy Polyakov
678 days
2 flights

6 Anatoly Solovyev
651 days
5 flights

7 Yuri Malenchenko
641 days
5 flights

8 Viktor Afanasyev
555 days
4 flights

9 Yury Usachev
553 days
4 flights

10 Pavel Vinogradov
546 days
3 flights

SOURCES: NASA, Korolev Special Design Center, Gagarin cosmonaut training center, Roscosmos

long-term effects of heavy ion radiation on healthy cells, and what they found was equally worrisome. They've discovered what Fornace calls "the field effect" of heavy ion radiation. A year after radiation exposure, the researchers looked at the metabolism inside exposed cells and found that the mitochondria — the cell's powerhouse, where oxygen is metabolized — were generating unusually high amounts of toxic byproducts, or free radicals.

"Basically a year later we're finding that normal metabolism has been perturbed, normal mitochondrial function has been perturbed so it's generating more of these toxic byproducts, and they can damage DNA. So we're seeing increased DNA damage. And this is not due to radiation per se, the radiation is long gone. But the signaling pathways have been perturbed, and we are getting these long-term events," says Fornace. The extra toxins could lead not just to cancer but to diabetes and heart disease, for instance.

The research is providing time to find solutions: "I think it's concerning that we're having these long-term changes, but it gives us potential druggable targets that could be used to lessen the chance of cancer and the like," says Fornace. That is exactly what Donoviel and the scientists at the biomedical institute are working on, developing ways to prevent and treat effects of galactic cosmic radiation.

One of the suggested ways to approach the problem is to create a genetic profile of each astronaut and then personalize the drugs. Donoviel described the way the proposed process would go: "You've been selected for flight, and now we're going to [genetically] profile you because we want to understand what kinds of medicines we need to send along with you. If you are more susceptible to let's say de-

Radiation *and risk*

Radiation exposure and subsequent risk of developing cancer have long been on the list of health concerns for those who go to space. Even on a short mission to the International Space Station, astronauts risk exposure from solar flares or from crossing through the South Atlantic Anomaly — the area where the Van Allen radiation belt comes close to the Earth and intersects with the flight path of some spacecraft, sometimes knocking out electronics. So naturally, NASA is keeping a close eye on its astronaut corps.

Since 1989, NASA's Johnson Space Center has been running a Longitudinal Study of Astronaut Health, or LSAH, which in 2010 was renamed the Lifetime Surveillance of Astronaut Health. According to Dr. Rich Williams, NASA's chief health and medical officer until mid-2010, it "was primarily a research study designed to compare the astronauts to a healthy cohort of civil servants." The study found that astronauts do not have a higher total cancer incident rate compared to the U.S. "terrestrial population." But Williams and others point out that the study's data is not very reliable: It's limited by the small number of subjects (fewer than 400, according to Williams) and skewed by the fact that astronauts tend to be healthy individuals who don't smoke, exercise regularly and have access to top-notch medical care. "It is very difficult to determine with certainty if there is an occupational health risk increase in the astronauts due to their spaceflight experience. Further analysis and investigation is needed for specific cancers," said Williams by email.

Women

1 **Peggy Whitson**
376 days
2 flights

2 **Sunita Williams**
321 days
2 flights

3 **Shannon Lucid**
223 days
5 flights

4 **Susan J. Helms**
210 days
5 flights

5 **Tracy Caldwell Dyson**
188 days
2 flights

6 **Catherine Coleman**
180 days
3 flights

7 **Karen L. Nyberg**
180 days
2 flights

8 **Yelena Kondakova**
178 days
2 flights

9 **Shannon Walker**
163 days
1 flight

10 **Sandra Magnus**
157 days
3 flights

Graphic by John Bretschneider

veloping atherosclerosis or heart disease, we're going to put you on preventative measures. If you have a mutation that makes you more predisposed to cancer, we're going to give you a higher dose of anti-oxidants than the guy next to you who doesn't have that. So it becomes a personalized way to prevent and treat."

The idea of genetic screening is a controversial one. According to Donoviel, the astronaut corps is very resistant to the idea of such testing. One can understand why an astronaut who spent years training for a space mission would not want to be excluded based on a genetic test revealing a mutation that may increase his or her risk for a certain type of cancer. Donoviel says that's not what her institute is proposing: "I think the idea is not to use genetics screenings to pre-select people, but really to understand the susceptibilities of the individuals that are selected. And then to apply personalized preventative measures and therapies en route in case something develops."

NASA's Williams says by email that it's entirely too early to broach the subject: "It will take many more years of development by the medical research community and pharmaceutical industry to robustly and reliably determine which genes indicate increased cancer risk, the biological mechanisms involved, and effective pharmaceuticals or life style changes to prevent or mitigate a person's susceptibility to a specific cancer caused by radiation damage. In summary, it is very premature to discuss screening of astronauts based on their genome, because of the current limited understanding and uncertainties involved."

Brookhaven National Laboratory

Cell room: A researcher prepares samples for irradiation as part of NASA's work to assess the biological effects of heavy ions.

The experts seem to agree on two things: One is that more research is needed both in the fields of spacecraft technology and on the medical side before a deep space mission becomes reality; the second is — despite the potential danger — human space exploration is worth the risk and the effort. When asked why we should send humans to space in light of his very worrisome findings, Georgetown's Fornace quoted then-NASA Administrator Michael Griffin in a 2005 interview with the Washington Post: "In the long run, a single planet species will not survive."