

HeadLines



JOHNS HOPKINS
MEDICINE

NEWS FROM JOHNS HOPKINS OTOLARYNGOLOGY-HEAD AND NECK SURGERY

WINTER 2020

Raising Awareness of AERD

To help fund research into aspirin-exacerbated respiratory disease, patient Shadi Baniani and friends organized a charity event.

When 38-year-old Shadi Baniani moved to the Northern Virginia area from her native California in 2008, she got the flu for the first time.

Rather than feeling better in a week or two, as most patients do, her illness dragged on, morphing into asthma and a series of sinus infections.

Baniani, who works in the U.S. Patent Office as a patent quality assurance specialist, visited doctor after doctor, and remembers hearing the same diagnosis again and again: “This is just allergies. Everything will be okay.”

As time passed, she felt only worse, losing her sense of balance, developing intense migraines, and gradually losing her ability to breathe sustainably. Eventually, Baniani landed at Johns Hopkins in the office of otolaryngologist-head and neck surgeon **Jean Kim**, where she delivered a stunning diagnosis: a condition called aspirin-exacerbated respiratory disease, or AERD, a triad that includes a proliferation of nasal polyps, intense asthma and a sensitivity to aspirin and its derivatives that can trigger respiratory distress.

“If we can understand what sparks these polyps and propels their growth, we might identify new drug targets that could make a huge difference for patients with this condition.”

—JEAN KIM



After an initial surgery to clear her nose and sinuses of polyps, Baniani’s asthma and other lower respiratory symptoms dramatically improved. Though she described the procedure as life-changing, it wasn’t permanent. Polyps caused by AERD gradually grow back after surgery, explains Kim, necessitating follow-up procedures to keep them in check. Respiratory symptoms must also be managed with a regimen of inhalers and oral steroids, drugs that cause a host of dangerous side effects.

With each exacerbation of her disease, Baniani’s friends and family members began to ask more questions about the disease, and she recalls that none of them had heard about the condition. Kim explains that the disease is underfunded by agencies in the U.S. and there are few resources for research showing progress toward a cure.

To raise awareness and funding for research into the disease, Baniani and her friends organized a charity event at a restaurant in Falls Church, Virginia. Some of her friends are in a band called Feel My Tips, so they performed, and the restaurant owners donated the space. Local businesses gave gift cards to raffle off at the charity; friends and family donated directly to Kim. Baniani raised an approximate total of \$7,000. She hopes to replicate this success at an upcoming dinner in California.

After being treated at Johns Hopkins by Jean Kim, left, patient Shadi Baniani was compelled to raise awareness of AERD and to raise funds to fuel future research.

All monetary donations that were raised went to Kim’s continuous research for AERD, which has been ongoing for decades in search of a cure. Kim’s and her colleagues’ works suggests that AERD’s nasal polyps are driven by a characteristic pattern of inflammation, “If we can understand what sparks these polyps and propels their growth, we might identify new drug targets that could make a huge difference for patients with this condition,” Kim says. Baniani’s ultimate wish is that one day Kim and her colleagues will find a cure for AERD. However, for now, Baniani is happy that any funding and awareness that can be raised for this disease is a possible step toward a cure. “Even though it’s such a small amount, this money could help patients like me have a treatment that’s a little more permanent than the options we have now. I have a lot of hope.” ■

 To support this research call 410-287-2124.

Johns Hopkins Launches Center for HPV-Related Head and Neck Cancer

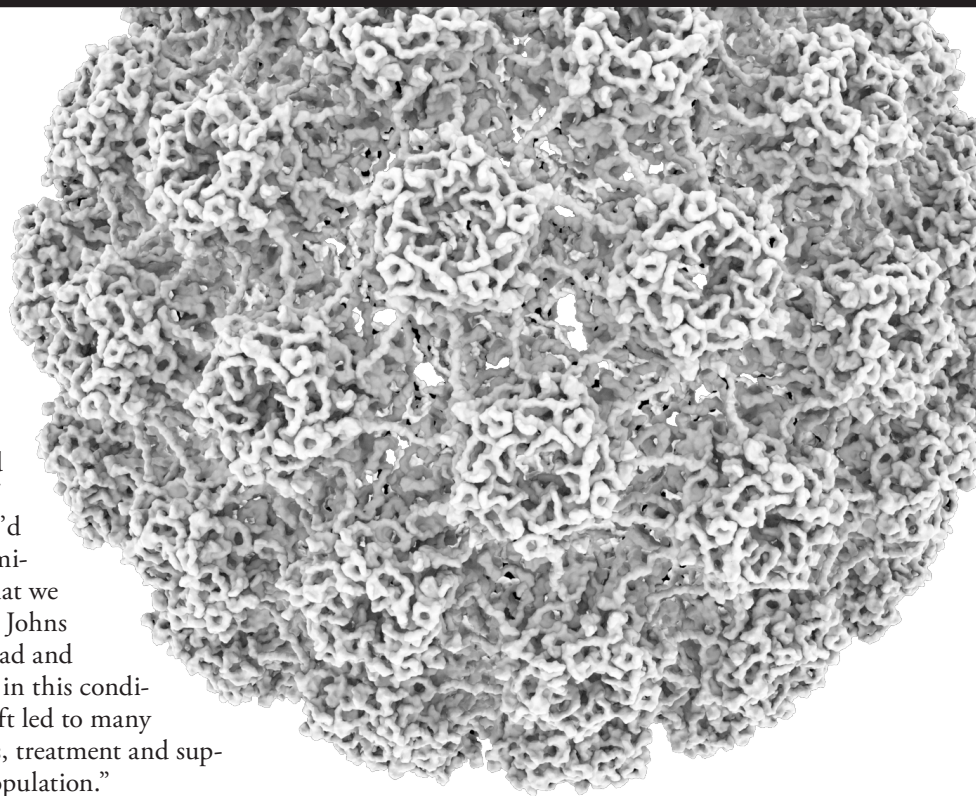
More than a decade ago, physician-researchers at Johns Hopkins began noticing and documenting a wave of head and neck cancers that differed from traditional presentations. Patients with these tumors were often missing the usual risk factors that doctors had been taught to expect, such as smoking and alcohol use, and they tended to be significantly younger than those usually diagnosed with these cancers — in their forties and fifties, rather than their sixties and beyond. The malignant cells even looked different under the microscope. Doctors here were among the first in the world to link these tumors with human papilloma virus (HPV), the virus that also causes genital warts and the overwhelming majority of cervical cancers.

Since then, Johns Hopkins has continued to be a pioneer in learning the unique features of HPV-associated head and neck cancers and finding new ways to treat them. Recently, physicians here decided to pool their expertise to launch the Center for HPV-Related Head and Neck Cancer, part of the Sidney Kimmel Comprehensive Cancer Center, bringing multidisciplinary experts together to provide care

specifically focused on this disease.

“HPV-related cancers used to make up only a fraction of the head and neck tumors we’d diagnose. Now it’s the predominant head and neck cancer that we see,” says **Carole Fakhry**, a Johns Hopkins otolaryngologist–head and neck surgeon who specializes in this condition. “Recognition of this shift led to many questions regarding diagnosis, treatment and support of this unique patient population.”

Fakhry says that unlike traditional head and neck cancers, HPV-related tumors respond more readily to treatment, including surgery, radiation and chemotherapy. As a result of this, the question of whether or not patients can achieve similar outcomes with greatly reduced treatment intensity has emerged as a question of great interest. Johns Hopkins will soon launch a treatment deescalation trial in which eligible patients are offered immunotherapy followed by surgery and nearly half the doses of chemotherapy and radiation delivered to



Johns Hopkins will soon launch a treatment deescalation trial in which eligible patients are offered immunotherapy followed by surgery and nearly half the doses of chemotherapy and radiation. Image shows 3D rendering of HPV.

those with traditional disease. With careful monitoring, she says, these patients may be able to avoid lifelong side effects caused by collateral damage from these treatments.

Other clinical trials run through the center focus on the trigger for the disease itself, adds **Tanguy Seiwert**, a Johns Hopkins head and neck medical oncologist who specializes in immunotherapy and HPV-related head and neck cancer. The center’s team will soon be monitoring patients who have finished their treatment protocols for residual traces of HPV in their saliva and blood. Those who test

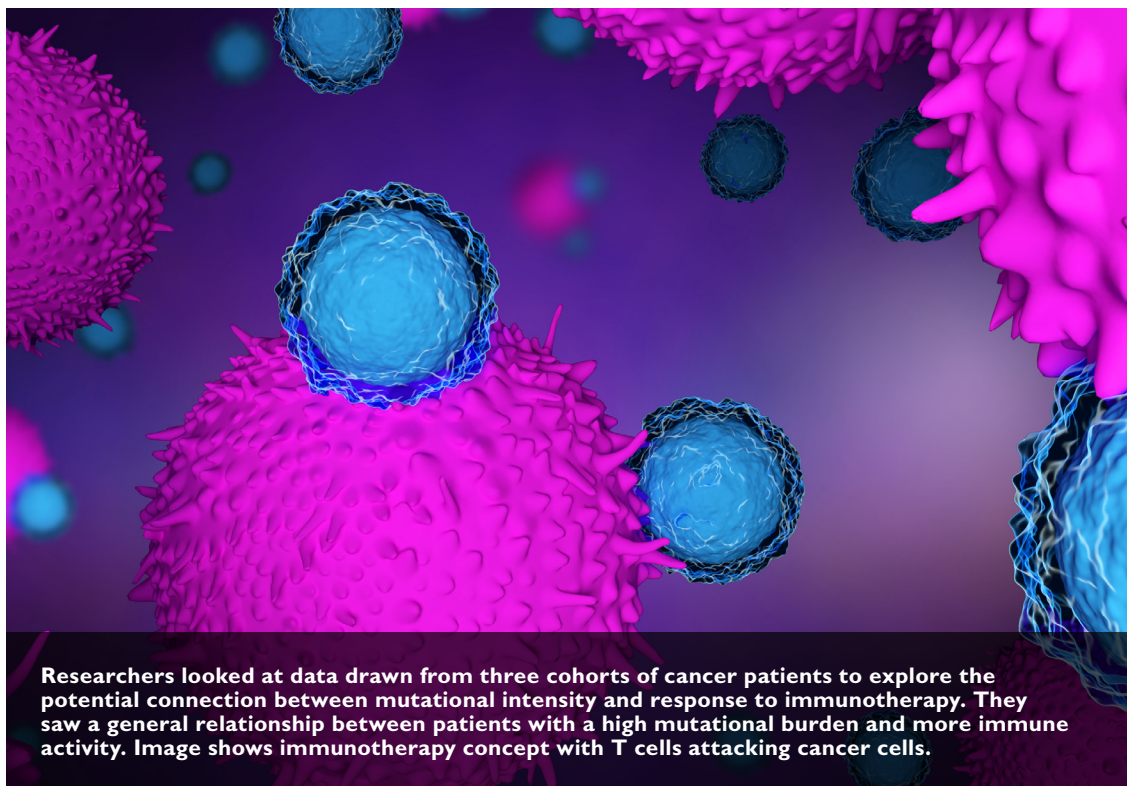
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“HPV-related cancers used to make up only a fraction of the head and neck tumors we’d diagnose. Now it’s the predominant head and neck cancer that we see.”

—CAROLE FAKHRY

RESEARCH



Researchers looked at data drawn from three cohorts of cancer patients to explore the potential connection between mutational intensity and response to immunotherapy. They saw a general relationship between patients with a high mutational burden and more immune activity. Image shows immunotherapy concept with T cells attacking cancer cells.

Predicting Who Will Respond to Cancer Immunotherapy

A new Johns Hopkins study suggests that genetic sequencing could hold key to identifying patients who would benefit from treatments.

Johns Hopkins First in U.S. to Use Radiofrequency Ablation to Treat Thyroid Nodules

Thyroid nodules are ubiquitous — an estimated 80 percent of Americans have these typically benign growths, says Johns Hopkins otolaryngologist–head and neck surgeon **Jonathon Russell**. But in a fraction of individuals, thyroid nodules expand to a size that becomes problematic, leading to troubles with swallowing, breathing or changes in appearance that patients find unsightly.

“Several years ago, the choice on how to respond to benign thyroid nodules was binary: either perform surgery or not,” Russell says. “Because these growths typically aren’t life-threatening, many patients chose to live with them rather than deal with the recovery and scars of surgery.”

But recently, says Russell and his colleague thyroid surgeon **Ralph Tufano**, Johns Hopkins began offering a third option: radiofrequency

ablation (RFA), a technique that destroys unwanted tissue using heat generated from medium frequency alternating current and is offered at just a handful of centers in the U.S. for this indication.

RFA has been used for decades to treat conditions affecting the heart, liver, and other areas. But its use in the neck has been limited due to the close proximity of vulnerable anatomical structures, such as nerves critical for swallowing and speaking, explains Tufano. With better technology and more refined techniques, he adds, RFA has become a popular way to treat benign thyroid nodules elsewhere in the world. Johns Hopkins’ leadership in “scarless” techniques to treat thyroid and parathyroid nodules and cancers made it a fit to be a pioneer for RFA in the U.S.

Russell, Tufano, and their colleagues use ultrasound guidance to insert the RFA probe into a nodule, creating a pattern of damage that’s visible under imaging.

Represented in illustration: Johns Hopkins experts use ultrasound guidance to insert a radiofrequency ablation probe into benign thyroid nodule, creating a pattern of damage that’s visible under imaging. Depending on the size of the nodule, this procedure takes as little as 30 minutes to complete.



Ralph Tufano



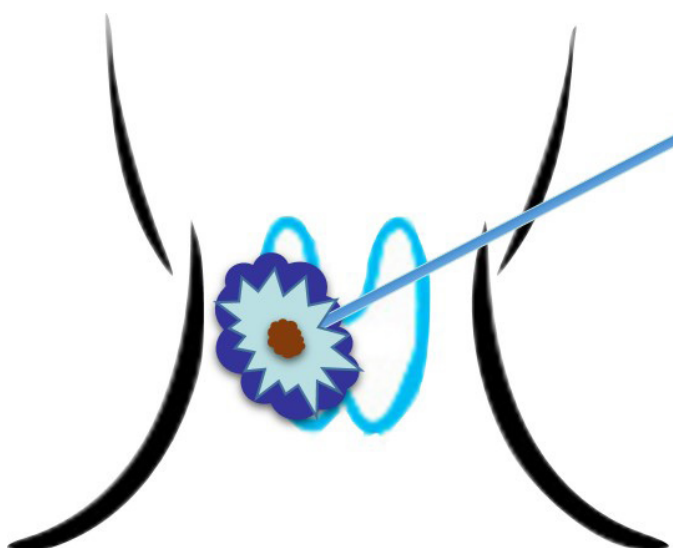
Jonathon Russell

Depending on the size of the nodule, this procedure takes as little as 30 minutes to complete, Russell says. Over the next several weeks and months, the damaged tissue shrinks and disappears, leaving patients with markedly reduced nodule size and related symptoms.

Because RFA is minimally invasive and extremely targeted, says Tufano, there are no scars and patients can avoid the long-term consequences of surgery, such as the need to take thyroid hormones for life.

Right now, he adds, the procedure is limited to benign nodules, in which patients have at least two confirmed biopsies showing no malignancy. But eventually, RFA may be an option for patients with small cancerous tumors. In time, Russell says, he and Tufano plan to also offer this procedure under local anesthesia, performing it right in the clinic.

“Patients whom we’ve already treated with RFA tell us that it’s a relief to avoid surgery and avoid the need for thyroid hormone while still being able to reduce their thyroid nodules’ size and relieve their symptoms,” Tufano says. “We’re pleased to offer them another option.” ■



 To learn more, call 410-287-2124.

Immunotherapy drugs have made remarkable headway in many types of cancers, including melanoma, lung, colorectal, and head and neck.

However, only a subset of patients benefit from these treatments. To improve the chances for success, researchers have searched for biomarkers that could signal which patients might benefit the most. One such marker, mutations in mismatch repair genes — which affect how well DNA repairs itself when it makes a mistake during replication — boost the odds that immunotherapy will work. However, only 50% of patients with these mutations respond to immunotherapy drugs.

A new study led by Johns Hopkins otolaryngologist–head and neck surgeon **Rajarsi Mandal** suggests that it’s not the mutation itself that makes immunotherapy more likely to work — it’s the number of resulting DNA mismatches that build up in cancer cells over time.

Mandal and colleagues performed several experiments to tease out immunotherapy response in mismatch repair deficient tumors in mice and humans. The researchers purposely created mismatch repair deficient mouse cell lines. They found that those grown for longer developed more mismatch-related

mutations. When these cells were injected into mice, the animals were more likely to respond to immunotherapy drugs to eradicate these cells.

Furthermore, when the researchers extracted the resulting tumors and dissected them, those with a higher mutational burden had a greater infiltration of immune cells, suggesting that the immune system was mounting a stronger attack. After sequencing the DNA of animals treated with immunotherapy, researchers found a lower mutational burden, suggesting that the immune system was specifically

“This could open up a whole new avenue for precision medicine, using science to change people’s clinical care and boost outcomes.”

—RAJARSI MANDAL



targeting cells that carried more mutations.

Building on these findings, the team looked at clinical data drawn from three independent cohorts of cancer patients to see what the relationship might be between mutational intensity and response to immunotherapy in people. The researchers saw a general relationship between patients with a high mutational burden and more immune activity. In a group of 15 patients from Hopkins with mismatch repair deficient tumors, this translated into a better response to immunotherapy among patients with more mutations. This finding held true in a group of 33 patients from Memorial Sloan Kettering.

Mandal notes that these results could lead to better ways to stratify which patients might benefit from immunotherapy or help researchers develop ways to universally improve survival with these drugs.

“This could open up a whole new avenue for precision medicine,” he says, “using science to change people’s clinical care and boost outcomes.” ■

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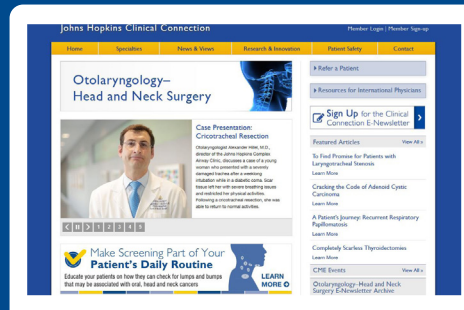
*Center for HPV-Related Head and Neck Cancer
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positive will receive immunotherapy aimed at fighting the virus to potentially prevent cancer recurrence. Similarly, another clinical trial will use immunotherapy as a first-line treatment — a milder therapy that could help patients avoid high doses of harsher treatments.

Patients cared for through the center will have access to a host of experts in this condition, including medical, surgical, and radiation oncologists, physical therapists, and social workers. A patient navigator will help assemble each patient's care team based on their unique needs, maximizing efficiency so patients can be seen and treated quickly.

“We are at an unprecedented point where we can really change outcomes for HPV-associated cancer patients,” says Seiwert. “For these cancers, Johns Hopkins will continue to lead the way.” ■

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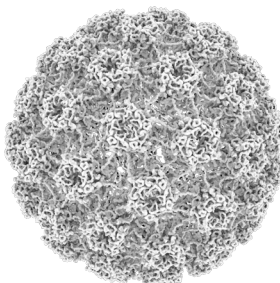


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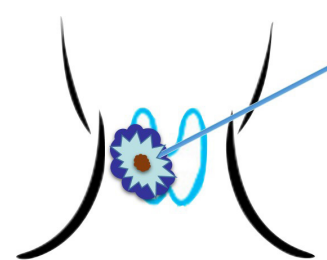
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Awareness of
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Johns Hopkins
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Thyroid Nodules