



Department of Otolaryngology

HEAD AND NECK SURGERY



World Trade Center first responders were exposed to numerous environmental toxins, including flame retardants, asbestos, and benzene.

Are Environmental Toxins Harming Our Thyroids?

After documenting a high incidence of thyroid cancer among World Trade Center (WTC) first responders, researchers at the Mount Sinai Health System—along with Johns Hopkins University and the Universidade Federal de São Paulo—began investigating the reasons for this excess risk.

According to the American Thyroid Association, 20 million Americans have some form of thyroid disease, and cases of thyroid cancer have tripled between 1975 and 2013. Though epidemiologists have cautioned that the primary cause of the increase in diagnoses is due to improved

screening tools, recent studies have begun to investigate a possible association with environmental toxins, including known endocrine disruptors like pesticides and insecticides.

Investigating Thyroid Cancer in WTC First Responders

Led by Emanuela Taioli, MD, PhD, Principal Investigator, Director of the Institute for Translational Epidemiology at the Icahn School of Medicine at Mount Sinai, and Associate Director for Population Science at The Tisch Cancer Institute, researchers questioned whether the excess in thyroid cancer cases was associated with WTC-related

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MESSAGE FROM THE CHAIR



Eric Genden, MD, FACS

On the heels of last year’s 50th anniversary of the Icahn School of Medicine at Mount Sinai and a record-breaking number of research activities at the

Head and Neck Cancer Research Program, fresh developments have transpired in the areas of thyroid cancer investigation, environmental policy, immunotherapy for oropharyngeal cancers, and technology to enhance robotic accuracy. Last year also marked the inaugural year of our Rhinology Fellowship, spearheaded by Satish Govindaraj, MD, Chief of Rhinology and Skull Base Surgery at the Mount Sinai Health System. Fellows of the program will study at The Mount Sinai Hospital —which is ranked No. 28 nationally for Ear, Nose and Throat by *U.S. News & World Report* — as well as New York Eye and Ear Infirmary of Mount Sinai and Elmhurst Hospital in Queens.

Advancements in novel therapeutics and immunotherapy at Mount Sinai are accelerating rapidly. Thomas Marron, MD, PhD, Assistant Director of Early Phase and Immunotherapy Clinical Trials at The Tisch Cancer Institute (TCI), is exploring the efficacy of the use of cemiplimab in destroying residual micro-metastatic disease. Nina Bhardwaj, MD, PhD, Ward Coleman Chair in Cancer Research and Director of Cancer Immunotherapy at TCI, is concentrating on the use of neoantigens to reduce tumor growth for oropharyngeal cancer, as well as glioblastoma and bladder cancer.

On behalf of our faculty, researchers, and trainees, thank you for reviewing the material in this year’s Specialty Report. We are excited about the future of otolaryngology research breakthroughs and hope you share our enthusiasm. ■

For a digital version of this report: mountsinai.org/2020ent

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Icahn School of Medicine Launches Immersive Rhinology Fellowship

In July 2019, the Icahn School of Medicine at Mount Sinai began its immersive Rhinology and Skull Base Surgery Fellowship—a one-year concentration in the management and treatment of complex sinus disorders and advanced skull base pathology. Focused on one fellow per year, the program offers a broad education, including in-office experience and treatment planning.

Led by Satish Govindaraj, MD, FACS, FARS, the Division of Rhinology is one of the busiest rhinology services in the country. In 2018 alone, it had a case volume of more than 1,200. Its faculty, comprising six fellowship-trained rhinologists, is the largest fellowship-trained division of its kind in the county. The team is leading the way in using virtual reality in the classroom, in the operating room, in surgical planning, and for pain control for outpatient rhinology procedures. This combination of high volume and unique expertise lends itself to the Division staking its claim as a highly regarded training ground.

“The fellowship is an exciting milestone and natural academic extension of the Division,” says Dr. Govindaraj, Chief of the Division, and Associate Professor of Otolaryngology. “It is an honor leading this team along with my colleagues Calvin Chen-Hwan Wei, MD; Patrick M. Colley, MD; Anthony G. Del Signore, MD; Alfred M.C. Illoreta, Jr., MD; and Madeleine R. Schaberg, MD, as we train the next generation of rhinologists.”

The fellow is schooled in open and endoscopic techniques to treat pathologies within the sinus orbit, intracranial compartments, and external facial components. Todd Spock, MD, the first Rhinology Fellow, chose this program because of its exceptional exposure to advanced surgical and minimally invasive techniques.

Says Dr. Spock, “The fellowship has exceeded my expectations, greatly expanded my rhinology repertoire, and prepared me for a successful future.” ■



Todd Spock, MD, (front) examines a patient under the guidance of Satish Govindaraj, MD, (rear).

Visualizing Head and Neck Tumors With Optical Technology

Resecting head and neck cancers can be particularly challenging for surgeons. There is currently no reliable way to visualize tumors in the larynx, tongue, throat, or palate during surgery. Because of this limitation, it is difficult to confirm that all malignant tissue has been removed. An error in excising the delicate tissue involved can affect patient quality of life and increase the risk of cancer recurrence. Brett A. Miles, DDS, MD, Co-Chief of the Division of Head and Neck Oncology Surgery within the Department of Otolaryngology at the Mount Sinai Health System, and his colleagues at the Head and Neck Cancer Research Program at the Icahn School of Medicine at Mount Sinai, are working to address this issue through the Optical Imaging Program.

“Although we have a range of state-of-the-art imaging technologies we can use preoperatively, there has not been a major breakthrough in visualizing cancer in these functionally sensitive areas,” says Dr. Miles. “The current standard of care is visual inspection of the tumor and sending frozen sections to the lab for pathological confirmation, but we need tools that enable us to verify that we have removed all malignant tissue at the time of resection.”

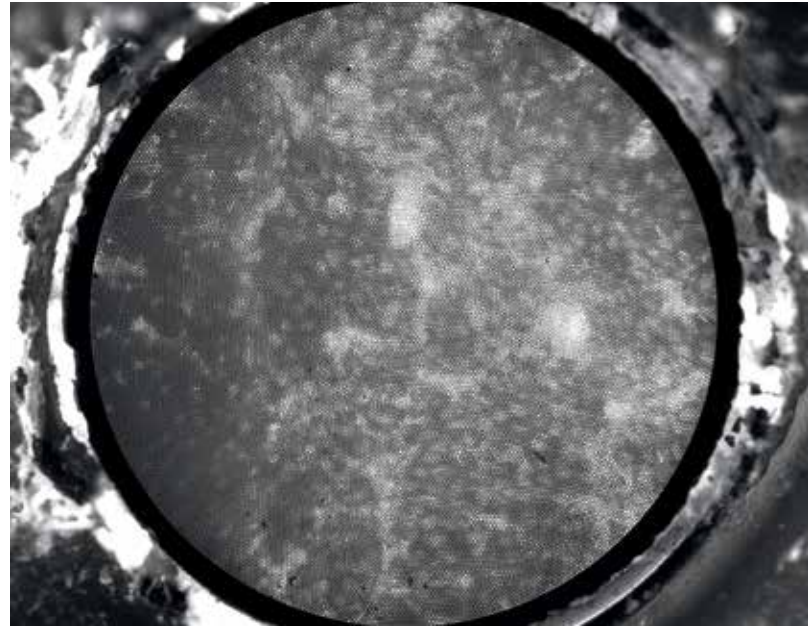
Launched in 2014, the Optical Imaging Program is exploring and assessing the efficacy of optical technologies to improve surgeons’ operative margin control, thus facilitating clear resections *in vivo* and better preservation of normal tissue. Mount Sinai is uniquely positioned to study head and neck cancer—a comparatively rare form of oncological disease—due to its robust referral patterns. The Health System serves a catchment area in New York City where tobacco and alcohol use are common. Additionally, many among the area’s sizable immigrant population experience tobacco exposure as a common feature within their country of origin. This allows for a larger cohort to facilitate the evaluation of optical imaging platforms.

“Although we have a range of state-of-the-art imaging technologies we can use preoperatively, there has not been a major breakthrough in visualizing cancer in these functionally sensitive areas.”

— Brett A. Miles, DDS, MD

“Essentially, we develop scientific protocols to test existing imaging technologies in the field of head and neck cancer,” says Dr. Miles, who is also a Professor of Otolaryngology at the Icahn School of Medicine. “We also have collaborations in place to build new platforms, so we are not only validating technologies that companies are bringing to us but also helping to develop the next generation of imaging tools to enable more precise resection of malignant tissue.”

Supported by funding from a National Institutes of Health Bioengineering Research Partnership grant, the ReMission Foundation, and the Ronald I. Dozoretz Foundation, the program has engaged in several studies of optical imaging technologies to date. These include a clinical trial to determine the effectiveness of high-resolution microendoscopy (HRME) in evaluating mucosal malignancy of the oral cavity as well as oropharynx and margin detection; a partnership with the Department of Physics at Fordham University evaluating



This high resolution microendoscopy of a patient with oral cavity cancer shows normal cells (left) and potentially malignant cells (right).

holographic microscopy and spectroscopy to differentiate cancer cells from adjacent normal cells; and collaborations with Rice University on several scientific publications examining the use of optical technologies in head and neck surgery.

Although each of these technologies offers advantages in identifying and evaluating malignant tissue, they all have limitations. “There is no single platform that is going to be the answer,” Dr. Miles says. “That means some combination of platforms may be the way forward, such as pairing HRME with optical coherence tomography, or surface imaging technology combined with fluorescent-lifetime imaging and an ultrasound to measure depth.”

Currently, the program is engaged in two new collaborative efforts that could add innovative imaging tools to the armamentarium of head and neck surgeons. Researchers are collaborating with Rensselaer Polytechnic Institute (RPI) and the ICube lab at the University of Strasbourg in France to develop and validate a multimodal optical imaging platform that combines available robotic technologies to enable real-time assessment of intraoperative tumors. Additionally, Mount Sinai researchers—in partnership with Canada-based Perimeter Medical Imaging—are conducting a clinical trial of an optical coherence imaging solution used for breast cancer resections to see if it can successfully be adapted for head and neck cancer.

“The platform will enable scanning of the autofluorescence of tumor cells, which will help us determine the depth of the tumor in real time during robotic surgery,” says Dr. Miles, who cautions that there is still much work to do to translate the technically complex platform into a usable format. “On the other hand, the Perimeter Medical Imaging could be easily translated to the operating room if successfully validated. This would be significant because it would enable surgeons to confirm that the margins of a resected tumor are clear without having to wait for final pathology.” ■

exposures or if routine surveillance had resulted in an overdiagnosis of malignancies. Mount Sinai colleagues and Co-Investigators Eric M. Genden, MD, Chair of Otolaryngology – Head and Neck Surgery at Mount Sinai, and Maaïke A. G. van Gerwen, MD, PhD candidate, Assistant Professor of Otolaryngology – Head and Neck Surgery, and Research Associate at the Institute for Translational Epidemiology, supported Dr. Taioli in her study.

The results of the study, which were published in the *International Journal of Environmental Research and Public Health* in May 7, 2019, did not show that enhanced screening led to an excess of false-positive malignancies due to the detection of benign tumors. In fact, all samples tested using the antibody-based cancer panel were determined to be true malignant disease. Former studies found that carcinogens were widespread at the WTC site. Among the most numerable compounds were asbestos, silica, and dust fibers, as well as soot, benzene, and organic compounds from burning jet fuel. Despite this, none of these carcinogens correlated to thyroid cancer, and risk factors like exposure to radiation or iodine were not reported. Analysis of WTC dust did show evidence of the presence of endocrine disruptors such as flame retardants, but so far their role in the excess of thyroid cancer in WTC responders is unknown.

Prior to the Mount Sinai Health System's studies in WTC first responders, the European Parliament posed the question of to what degree endocrine disruptors affect health outcomes. In 2011, the body published "State of the Art Assessment of Endocrine Disrupters," and soon after, in 2012, the World Health Organization and United Nations Environment Programme published the "State of the Science of Endocrine Disrupting Chemicals." Both reports cited reproductive health, hormonal cancers, and obesity as potential side effects of increased use of endocrine disruptors. Just three years later, an Endocrine Society report cited more than 1,300 references to different aspects of endocrine disruption. In March 2019, the European Parliament released a follow-up to the important 2011 study by its Policy

Department for Citizen's Rights and Constitutional Affairs. The goal of this new study was to highlight evidence that links endocrine disruptors with negative health impacts and to better protect human health through European Union regulations.

"These findings, germane to WTC responders who were exposed to high level of toxins in the air, prompted us to further explore the effect of environmental exposures on thyroid cancer," notes Dr. Genden. "If pesticides such as the now-banned dichlorodiphenyltrichloroethane (DDT) have already demonstrated a correlation, we aimed to answer what other exogenous compounds contributed to thyroid malignancies, and what, if any, was the impact on tumor aggressiveness?"

"If our study discovers concrete links to thyroid cancers, we— as a nation— will need to question how legislation and regulations can remove them from our food chain."

— Maaïke A. G. van Gerwen, MD, PhD

Mount Sinai Launches Thyroid Cancer Study

In pursuit of answers, a research team composed of Dr. Taioli, Dr. Genden, and Dr. van Gerwen, as well as Catherine Sinclair, MD, Associate Professor of Otolaryngology, and Mark L. Urken, MD, Professor of Otolaryngology, was formed at Mount Sinai to create a thyroid cancer database. Launched in 2019, the investigation aims to assemble a cohort of diagnosed patients at The Mount Sinai Hospital, Mount Sinai West, and Mount Sinai-Union Square; expand the Head and Neck Cancer Research Program to include environmental factors contributing to thyroid cancer risk; and spearhead patient-centered research on quality of life after thyroid cancer surgery.

With the launch of this study, investigation into the potential causal links between thyroid cancer and environmental toxins, specifically in the WTC responders, continues. The presence of known endocrine disruptors like polychlorinated biphenyls (PCBs), phthalates, and pesticides, as well as flame retardants, in the dust at the WTC site served as a baseline of toxins being queried among Mount Sinai patients. These and other endocrine disruptors can be found in products used daily. For instance, PCBs are detectable in insulation and as plasticizers; per- and polyfluoroalkyl substances (PFAS) are in food packaging, stain- and water-repellent fabrics, nonstick products, polishes, waxes, paints, and cleaning products; and bisphenol A is ubiquitous in plastics. Additionally, pesticides used for agricultural purposes may enter the food chain and be consumed, as we know that food and beverages contain pesticide particles.

"If our study discovers concrete links to thyroid cancers, we— as a nation—will need to question how legislation and regulations can remove them from our food chain," says Dr. van Gerwen, who notes that banning specific pesticides or limiting the amount of toxins sprayed onto farms may be necessary. "The increased demand for organic foods is a telling sign that consumers are already quite conscious of food and beverage ingredients, but it comes with the opportunity cost of hefty expenses. If we proactively tackle disruptors legislatively, we can dynamically improve overall endocrine health and reduce health care costs associated with thyroid cancers." ■



Used to monitor and water crops, agricultural drones can also spray pesticides, which can then enter the food chain.

Mount Sinai Researchers Identify Head and Neck Cancer Biomarkers Using Preoperative Immunotherapy

Although physicians know that immunotherapy works for a subset of head and neck cancers, there is still much to learn about why it works and for which patients. Thomas Marron, MD, PhD, Assistant Director of Early Phase and Immunotherapy Clinical Trials at The Tisch Cancer Institute (TCI), and a team of researchers are examining this question with an exclusive phase I study of cemiplimab, a preoperative immunotherapy treatment. Sponsored by Regeneron Pharmaceuticals, Inc., the study will focus on patients with head and neck squamous cell carcinoma lesions (HNSCC); to date, cemiplimab has been studied as a treatment for resectable non-small-cell lung cancer and hepatocellular carcinoma.

TCI investigators within the Novel Therapeutics Unit will capitalize on the “window of opportunity” before a tumor is removed to determine the clinical activity and safety of cemiplimab as well as pinpoint biomarkers that may in the future help predict which therapies will work in which patients. Researchers will focus on responders and nonresponders, as well as on recurrence of disease.

“The idea behind cemiplimab is that it recruits and provokes the immune system to learn there is a tumor, recognize it as foreign, and ultimately kill any residual cells—termed micro-metastatic disease—that have escaped the primary tumor and would not be removed during surgery,” says Dr. Marron, Principal Investigator of the study.



Led by Thomas Marron, MD, PhD, the Early Phase and Immunotherapy Clinical Trials team aims to better identify biomarkers using an immune checkpoint inhibitor.

“We want to use the macroscopic tumor to tell the immune cells what to target in terms of microscopic disease.”

In the study, 21 participants will receive three to six weeks of cemiplimab prior to surgery, followed by standard adjuvant chemotherapy/radiation treatment (based on stage) as well as eight additional cycles of immunotherapy. Throughout treatment, researchers will examine and compare tissue, blood, and stool samples.

The effectiveness of the antitumor agent will be measured by evaluating the immune cells in tumor biopsies before treatment, and in the treated tumors that are resected. Dr. Marron believes the best way to identify biomarkers is to observe the dynamic changes that occur over the three to six weeks of cemiplimab treatment.

“Studies like this are essential to identifying specific changes in people’s tumors and immune system. We can use our findings to develop an effective algorithm for first-line treatment that makes a difference for people living with cancer.”

Cemiplimab—trade name Libtayo—is an immune checkpoint inhibitor that augments the body’s ability to recognize and kill cancer cells. Previously, it was studied by Mount Sinai researchers in patients with metastatic gastrointestinal cancers. The U.S. Food and Drug Administration (FDA) has approved its use in those with metastatic cutaneous squamous cell carcinoma.

The treatment works by inhibiting the interaction between PD-1 on T cells and PD-L1 on a tumor; PD-L1 acts as a “stop” sign, blocking successful detection and elimination of cancer cells by T cells. There are six FDA-approved drugs disrupting this interaction, but there are dozens of additional on/off “switches” in the immune system that cancers can hijack to evade the immune system. Based on preclinical data, there are now more than 3,400 other immunotherapy drugs in development targeting these other immune pathways. While all these potential treatment options are exciting, little is known about which medications will work for which patients.

Advances in Immune Monitoring Techniques

Mount Sinai is one of four institutions—alongside the Dana-Farber Cancer Institute, Stanford University, and MD Anderson Cancer Center—to receive a large grant to establish a Cancer Immune Monitoring and Analysis Center, part of the National Cancer Institute’s Cancer Moonshot initiative. These prestigious centers are charged with standardizing the use of new immune monitoring platforms and analyzing biospecimens from all cancer trials sponsored by the National Institutes of Health. This Cancer Moonshot grant further

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Psychosocial Interventions Provide Novel Treatment for Neurogenic Laryngeal Hypersensitivity

Researchers at the Department of Otolaryngology – Head and Neck Surgery at the Icahn School of Medicine at Mount Sinai have found that principles gleaned from cognitive behavioral therapy are beneficial for patients with neurogenic laryngeal hypersensitivity (NLH) symptoms. The condition, which is defined by a constellation of symptoms such as coughing, throat clearing, and vocal cord dysfunction, often requires multidisciplinary evaluation and management. This novel psychosocial intervention was initially developed to help World Trade Center first responders. Subsequently, researchers found the approach to be beneficial for patients newly diagnosed with NLH as well as those previously nonresponsive to traditional therapies.

“Our anecdotal evidence showed that patients with NLH were demonstrating overwhelmingly consistent positive results to this new therapy technique without the need for medical or surgical interventions,” says Mark S. Courey, MD, Director of the Grabscheid Voice and Swallowing Center at Mount Sinai, and Chief of the Division of Laryngology within the Department of Otolaryngology – Head and Neck Surgery. “We launched this study to measure the effects of an interdisciplinary approach and to determine if the data supported our observations. The hypothesis was that positive results would establish an innovative protocol for future treatment of patients with NLH.”

Mount Sinai researchers retrospectively reviewed the charts of patients diagnosed with NLH over a 12-month period. Patients were diagnosed with NLH after a negative pulmonary and gastroenterology workup followed by a joint clinic visit with a laryngologist and speech-language pathologist. Patients were included in the retrospective if they had participated in a minimum of three therapy sessions with a speech-language pathologist who assessed their symptoms and triggers, educated them about NLH, and provided them with intervention techniques and retraining to help manage symptoms. Speech-language pathologists taught cough suppression techniques that patients would use when experiencing a sensation prior to a cough or

throat clear. Additionally, patients received instruction in pursed-lip breathing and semi-occluded vocal tract tasks to address inefficient respiratory and voicing patterns.

“Because many patients with NLH feel they do not have control over their symptoms, we established a distinct protocol provided by trained speech-language pathologists, with a heavy emphasis on patient understanding of the diagnosis,” says Leanne Goldberg, MS, CCC-SLP, Director of Speech-Language Pathology at the Department of Otolaryngology, and Clinical Specialist, Voice, Swallowing, and Cough Therapy at the Grabscheid Voice and Swallowing Center. “The education encompassed the physiology and psychological contributions of the disorder and enabled patients to see that they can manage, or even relieve themselves of, their symptoms.”

After reviewing pre- and post-intervention responses to the Newcastle Laryngeal Hypersensitivity Questionnaire from 26 participants, researchers found that 85.5 percent achieved an improved score, with 65.4 percent exceeding the minimal clinically important difference for the instrument (1.75 points). The degree of improvement was variable, with the average being 3.2 points. Subscore analysis of the questionnaire’s obstruction, pain/thermal, and throat tickle

subcategories revealed that most of the improvement was related to throat tickle, with the least improvement in the pain/thermal category. Subjects were predominately female (69.2 percent) with an average age of 60.8 (range 34-81). There was no correlation between the scores and age, gender, or number of treatment sessions.

“The results from this patient population reflect our observations regarding the strong impact we are having on patients with this diagnosis,” Ms. Goldberg says. “As a result of our research and data, we are hopeful that this novel approach will be adopted by other institutions that provide treatment for NLH patients.”

Ms. Goldberg says more participants have been subsequently added to the study and the results are consistent with initial findings. The goal now is to conduct prospective multi-institutional studies to gain insights on the effects of this treatment strategy on a larger group of patients with NLH.

“In addition to the effects of the protocol for treatment, we will be looking at other factors such as personality types and other epigenetic factors that may affect response,” she says. “We continue to explore many avenues that will enable us to develop new treatment options to help patients manage their symptoms more effectively.” ■



Leanne Goldberg, MS, CCC-SLP, and Mark S. Courey, MD, examine a patient who has undergone hypersensitivity treatment.

Innovative Personalized Neoantigen Vaccines Target Cancer Tumors

Researchers at the Cancer Immunology Program at The Tisch Cancer Institute (TCI) are building potent tumor-targeting inoculations with personalized vaccines derived from neoantigens. Shown to be immunogenic in animal models, neoantigens have the ability to reduce tumor growth through the education of antigen-specific killer T cells. The first human study of a neoantigen-derived personalized vaccine was completed in several patients with head and neck cancers as well as patients with multiple myeloma and lung, breast, and ovarian cancers. The vaccine proved to be safe, and early evidence of its effectiveness was noted in the patients' blood.

TCI is intensely focused on the development of personalized vaccines for patients who are at high risk of cancer recurrence or who have cancers that require treatment beyond the standard of care. Neoantigens—altered tumor proteins that have not been previously seen by the immune system—are critical actors, as their use allows for the creation of a vaccine based upon an individual patient.

Nina Bhardwaj, MD, PhD, the Ward-Coleman Chair in Cancer Research and Co-Director of Cancer Immunotherapy at TCI, led a team of researchers in the development of a robust pipeline for identifying patient neoantigens using a set of bioinformatic tools called “OpenVax.” One of the only vaccine pipelines in New York, this novel platform has elevated vaccine production and procurement.

“Its development has transformed the operation and the ability to generate a pipeline from the tumor procurement all the way to vaccine production and delivery,” says Dr. Bhardwaj. “It also has given us a great deal of insight into the kind of immune responses these vaccines can generate.”

Additionally, Dr. Bhardwaj’s team created a platform to formulate these neoantigens into a multi-peptide personalized vaccine within the Institute’s Vaccine and Cell Therapy Laboratory—a controlled facility for the testing and manufacturing of immunotherapies. Currently, the team is studying a neoantigen-derived personalized vaccine for both glioblastoma and bladder cancer.



A team led by Nina Bhardwaj, MD, PhD, developed one of the only vaccine pipelines in New York.

Creating Cancer-Specific Vaccines Using Shared Neoantigens and Viral Antigens

Mount Sinai researchers have discovered “shared neoantigens” in certain tumors that would allow for the formulation of “off the shelf” vaccines. While still personalized, these vaccines would be dedicated to a specific cancer as opposed to a specific patient. Future studies will combine these approaches with other immunotherapies, such as checkpoint inhibitors, in order to further enhance the vaccine response.

Researchers are also investigating the role of viral antigens in tumors associated with human papillomavirus (HPV), specifically for head and neck cancers. Antigens derived from the HPV virus itself would allow scientists to prepare vaccine formulations that precisely target the virus. In another approach, investigators are separating killer T cells from patients’ blood and tumor tissue that specifically recognize HPV antigens. These T cells would then be expanded and delivered back to patients whose HPV-associated tumors have not yet responded to conventional therapies.

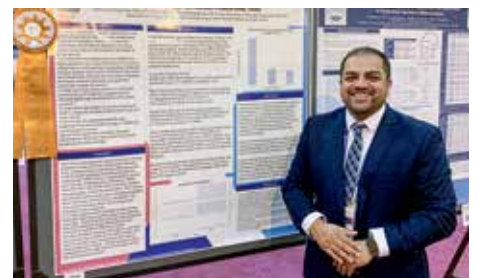
The Centers for Disease Control and Prevention estimate that 19,000 people are diagnosed with oropharynx cancer each year. Seventy percent of these cases are HPV-associated. As these cases rise, Dr. Bhardwaj emphasizes that thorough knowledge of the virus is critical.

Says Dr. Bhardwaj, “We need to understand how the virus is modulating cancer development and altering the microenvironment so that we can intervene to boost the immune system and respond to HPV antigens.” ■

Icahn School of Medicine Resident Wins Poster Award

Ameya Jategaonkar, MD, an Otolaryngology resident at the Icahn School of Medicine at Mount Sinai, was honored with the Best in Head and Neck Surgery poster award at the American Academy of Otolaryngology – Head and Neck Surgery Annual Meeting & OTO Experience 2019. Dr. Jategaonkar received the award for his submission, “Neutrophil to lymphocyte ratio as a prognostic factor for oropharyngeal squamous cell carcinoma

treated with TORS.” He shares credit with fellow researchers, Arvind Badhey, MD, and Kevin Wong, MD—residents at the Icahn School of Medicine—as well as Eric Genden, MD, MHCA, FACS, Isidore Friesner Professor and Chair, Otolaryngology – Head and Neck Surgery; Brett Miles, MD, Co-Chief, Division, Head and Neck Cancer Surgery; and Raymond Chai, MD, FACS Director, Head and Neck Robotic Surgery, Mount Sinai Downtown. ■



Ameya Jategaonkar, MD



Using CyTOF, Dr. Marron and his team can observe up to 50 proteins on individual cancer cells, maximizing the information obtained from each sample.

positions the Health System as a leader in the rapidly growing field of cancer immunotherapy.

As part of a partnership with the cemiplimab study sponsor, Mount Sinai researchers have access to a groundbreaking drug development resource called *VelocImmune*®, a technology developed to rapidly produce antibodies for potential therapeutics. This collaboration allows researchers to study new targets, find smarter ways to manipulate the immune system, and target more proteins at a faster clip.

Additionally, Dr. Marron's team is using a game-changing mass cytometry technology (CyTOF) to study the proteins on cancer cells and immune cells. CyTOF stains proteins on single cells by making antibodies that are stuck to heavy metals. Traditional flow cytometry is a laboratory technique that was used for decades; with it, researchers were able to look at just a handful of proteins on cells and differentiate subsets of immune cells such as T cells and B cells. Akin to graduating from an instant camera to a telephoto lens, researchers using CyTOF can see up to 50 proteins on each individual cell. This allows them to identify the immune cell subtypes and classify the maturation and activation status of the cell as well as some of the regulatory on/off checkpoints.

"The maturation and activation statuses of the cell are what we hope to alter with immunotherapy," explains Dr. Marron. "The idea is to change 'exhausted' immune cells to 'activated' immune cells capable of killing cancer."

For an even higher-resolution view of each individual immune cell within the tumor, Dr. Marron's laboratory collaborators are using Cellular Indexing of Transcriptomes and Epitopes by Sequencing (CITE-Seq), a technique that combines the capabilities of CyTOF and single-cell RNA sequencing to characterize both the RNA and protein in each individual cell.

"These analyses will allow for the ultimate personalized medicine," says Dr. Marron. "We hope to eventually be able to identify not only what drives cancer growth but also how growing tumors are evading detection by the immune system. These advances will allow us to identify the optimal combination therapy to target tumor cells and leave normal cells alone. This is the holy grail of immunotherapy." ■

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The Valley Hospital

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The Mount Sinai Hospital

Hess Center for Science
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Mount Sinai Doctors

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212-844-8775 (Head and
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NYEE – Tribeca

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