Perlmutter Cancer Center

Winter 2023 Report

BEST HOSPITALS U.S.News & WORLD REPORT CANCER 2022-23

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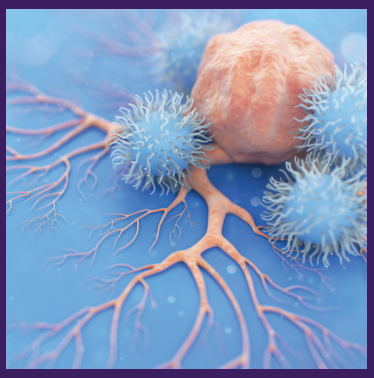

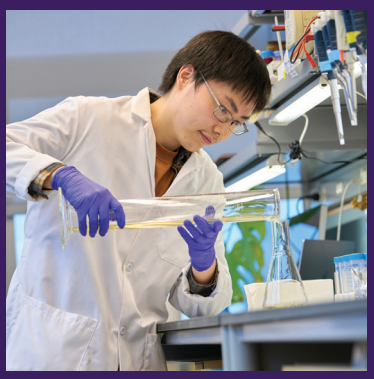

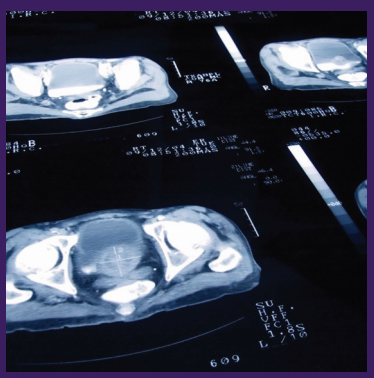


Speak to a live representative: 833-698-5722 (833-NYUL-PCC)

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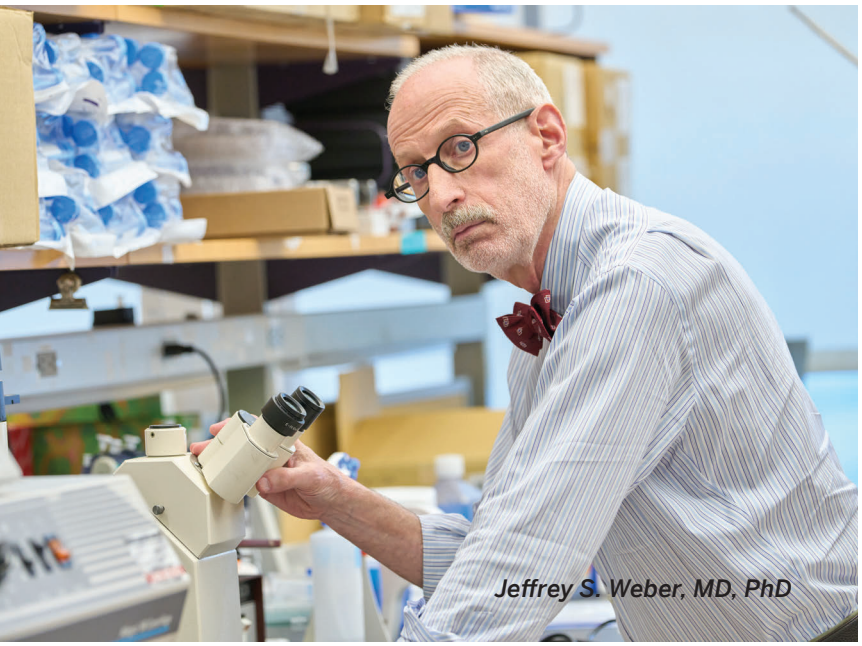
A Personalized mRNA Vaccine Reduces Melanoma Recurrence Risk

Following resection of advanced melanoma, combining a personalized mRNA vaccine with pembrolizumab was shown to reduce the risk of recurrence or death by 44 percent compared to pembrolizumab alone, according to results from the KEYNOTE-942 trial.

The study represents a landmark in the advancement of personalized cancer vaccines, being the first randomized clinical trial to show that a personalized mRNA vaccine improved clinical outcomes compared to an existing treatment.

"These data provide the first evidence that we can improve upon the rates of recurrence-free survival achieved by PD-1 blockade in resected high-risk melanoma," said Jeffrey S. Weber, MD, PhD, principal investigator of the study and deputy director of NYU Langone Health's Perlmutter Cancer Center.

"These findings also provide the first randomized evidence that a personalized neoantigen approach may be beneficial in melanoma."



Jeffrey S. Weber, MD, PhD

Directing T cells to the tumor

With the capacity to encode a tailored combination of up to 34 neoantigen sequences, the mRNA vaccine is designed to initiate an immune response to cancer based on a patient's unique tumor mutations. According to vaccine developers, the optimal combination of neoantigen sequences is identified in only 2 hours using an algorithm that analyzes DNA and RNA sequencing data, and roughly 6 weeks is required for vaccine manufacturing.

Once administered, the neoantigen sequences are translated and undergo antigen processing and presentation, directing T cells to attack the cancer.

Improved outcomes, well tolerated

The study enrolled 157 patients with cutaneous melanoma metastatic to a lymph node and at high risk of recurrence. All patients underwent complete resection and were randomly assigned 2:1 to receive either the combination treatment or pembrolizumab alone, with the mRNA vaccine administered as a total of 9 doses.

In addition to improved recurrence-free survival, the mRNA vaccine was well tolerated, and the adverse event profiles for both the vaccine and pembrolizumab were consistent with past trials. Less than 15 percent of patients receiving both the vaccine and pembrolizumab experienced serious treatment-related adverse events compared to 10 percent who received pembrolizumab alone.

Based on the promising findings, a phase 3 trial will open in 2023 for patients with melanoma, with plans to launch trials of the vaccine in other cancer types soon.

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Raman Spectroscopy Aids Detection of Lung Cancers

Current techniques for evaluating small bronchoscopic biopsies on-site are resource intensive and may compromise the integrity of samples for later analysis.

Jamie L. Bessich, MD, assistant professor of medicine and cardiothoracic surgery at NYU Grossman School of Medicine, is working to incorporate stimulated Raman histology (SRH) microscopy, a novel optical imaging modality, into clinical workflows to help facilitate real-time tissue assessment while preserving samples for downstream analysis. The project builds on the research of Daniel A. Orringer, MD, associate professor of neurosurgery and pathology, which focuses on the use of SRH for brain tumor diagnosis, and is in collaboration with Invenio Imaging.

Putting the tech to the test

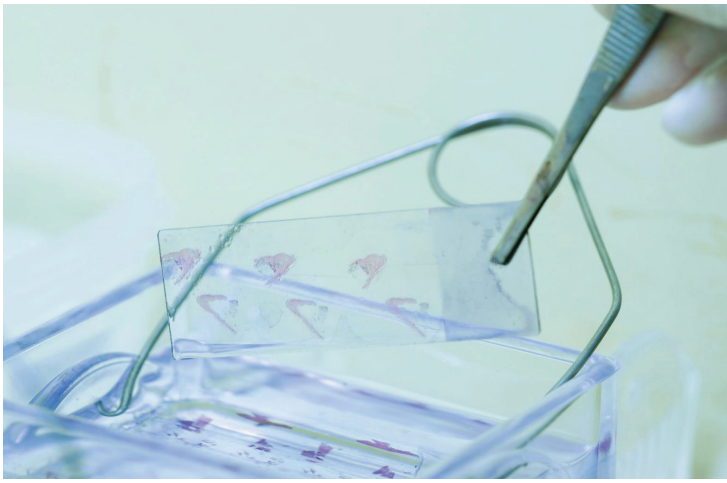
Raman spectroscopy is a common nondestructive imaging technique with several biosensing applications, but it had not been previously assessed in lung biopsies.

Its application to intraprocedural diagnosis has many potential benefits, including reduced procedure time, decreased total biopsies, and improved yield, and could allow for intraprocedural therapeutics to be applied, especially in cases of peripheral nodules.

Says Dr. Bessich, "We wanted to know if this technology could enhance the role of the pulmonologist or thoracic pathologist in the diagnosis or characterization of primary lung cancers."

The team imaged specimens using SRH in the procedure room and submitted them to pathology. After collection, they created a training set of 50 cases from bronchoscopic and surgical lung biopsies. A thoracic pathologist used this training set to interpret the SRH images, referenced against a surgical pathology hematoxylin and eosin (H&E) image with the final diagnosis.

In a prospective validation, the researchers acquired SRH images from 19 cases,



which included 6 benign cases and 13 lung malignancies. The samples were processed sequentially, first with SRH, followed by conventional H&E staining. The pathologist then evaluated the images and provided a diagnosis.

Promising results

For the presence of diagnostic, neoplastic tissue, there was strong case accuracy, sensitivity, and specificity. Further, almost all of the images were considered adequate for diagnosis and downstream analysis.

Dr. Bessich cautioned that "the data are based on a very small number of cases, and future studies need to be conducted to assess the feasibility of the system on a larger scale."

Clinical applications

Dr. Bessich and her team believe that clinical use of SRH microscopy has the potential to shorten the time to delivery of therapy for patients.

"In the clinic, we're often waiting for weeks to receive molecular results from tissue," says Dr. Bessich. "If we could obtain them in real time, we could initiate appropriate therapy sooner."

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Leveraging AI in Breast Imaging

NYU Langone Health (NYULH) researchers have developed a machine learning model for DCE-MRI, the latest tool from data scientist Krzysztof J. Geras, PhD, and colleagues, who are applying artificial intelligence (AI) to improve breast imaging accuracy and reduce unnecessary biopsies.

The team had previously created an AI model for breast ultrasound. A suite of models will ultimately be combined into a larger AI system, with the goal of making predictions and learning from multiple imaging modalities simultaneously. Postdoctoral fellow Jan Witowski, MD, PhD, is first author of the new report.

AI for breast MRI

While mammography is most often relied on for breast cancer screening, MRI can better detect small lesions. Yet, a high rate of false positive findings has limited its use.

To improve breast MRI specificity, Dr. Geras and colleagues, including imaging specialist Linda Moy, MD, a professor of radiology, used over 21,000 bilateral dynamic contrast-enhanced breast MRI exams from NYULH patients to develop a machine learning model and then evaluated the model on three external datasets.

"The model is sufficiently robust that it generalizes to other populations," Dr. Geras says.

In a study published in *Science Translational Medicine*, the AI-based system was shown to be on par with radiologists in detecting breast cancer; a simulation indicated that the model may help to avoid unnecessary biopsies in patients with BI-RADS 4 lesions, for which a "biopsy-all" strategy is currently recommended.

AI for breast ultrasound

In another, largest-of-its-kind study, the team developed an AI model for breast ultrasound, with nearly 5.5 million ultrasound images from over 143,000 NYULH patients. As with MRI, difficulty in interpreting images leads to false positive findings and unneeded biopsies.

Not only was the AI model as accurate at generating diagnoses as experienced radiologists are, but when used to assist in diagnosis, false positive rates decreased by 37 percent, and the number of requested biopsies dropped by 27 percent.

"If our efforts to use machine learning prove successful, ultrasound could become a more effective tool, especially as an alternative to mammography, and for those with dense breast tissue," Dr. Moy says.

Further refining the models

Dr. Geras notes that while initial results are promising, clinical trials among current patients and in real-world conditions are needed before they can be routinely deployed.

He also has plans to refine the AI software to include information such as a patient's added risk from a family history or a genetic mutation tied to breast cancer.

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Salvage Cryoablation Following Radiation Therapy Failure

For individuals with locally recurrent prostate cancer, salvage cryotherapy has become a preferred treatment option with curative potential.

Aaron E. Katz, MD, professor of urology and an early pioneer of the technique, explains that while therapy for patients with radiation-recurrent disease needs to be individualized, salvage cryoablation is often a treatment of choice for patients in this setting.

Cryotherapy ablates all tissue in a targeted area, which allows for the freezing and destruction of tissue beyond the confines of the prostate gland, offering a potential advantage compared to other treatment options.

Importance of PSA monitoring

Monitoring prostate-specific antigen (PSA) after treatment of localized disease can lead to the detection of biochemical recurrence. In many cases, rises in serum PSA above baseline do not co-occur with symptoms of recurrence.

"For patients with a confirmed rise in serum PSA after prior definitive RT, careful assessment is required to rule out distant metastases," says Dr. Katz.

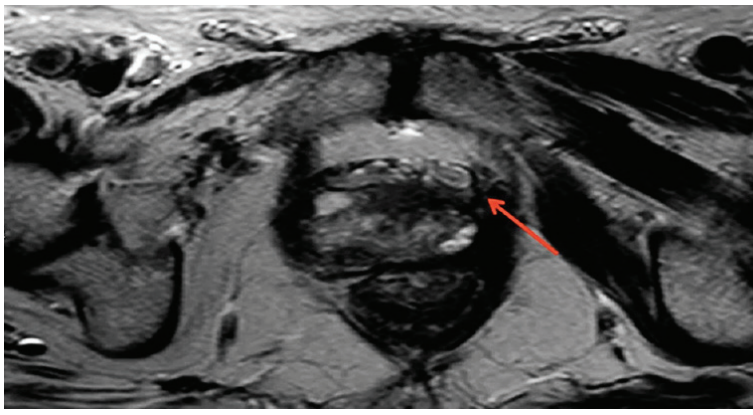
In the last five years, the use of novel PET/CT imaging modalities and agents has dramatically improved the detection of recurrent disease.

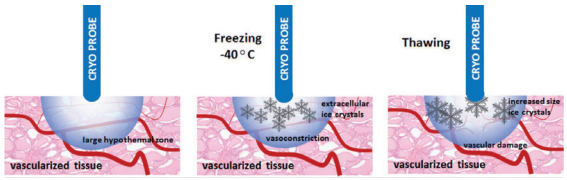
"After such detection, the goal of salvage cryotherapy is to delay initiation of androgen deprivation therapy (ADT), which can have deleterious side effects," explains Dr. Katz.

Benefits versus other treatment options

Other salvage treatment options for patients with a positive biopsy, without evidence of metastatic disease, include radical prostatectomy and brachytherapy.

Cryotherapy offers unique advantages compared to these approaches. Benefits include no delayed/long-term complications, low rates of incontinence, and no risk of secondary malignancy. Magnetic resonance (MR)-guided cryotherapy has proved to allow for real-time imaging of the ablated zone by active monitoring.





Current guidelines from the American Urological Association (AUA) support cryotherapy as an option in this setting.

The procedure is covered under Medicare for patients with localized disease who have failed a trial of radiation therapy as primary treatment and meet one of these conditions: Stage T2B or below, Gleason score < 9, or PSA < 8 ng/mL.

Potentially curative option

In addition to the benefits noted above, for patients with locally recurrent prostate cancer, there is the potential for cure. The 5- and 10-year disease-specific survival rates following salvage cryoablation are 91 percent and 79 percent, respectively.

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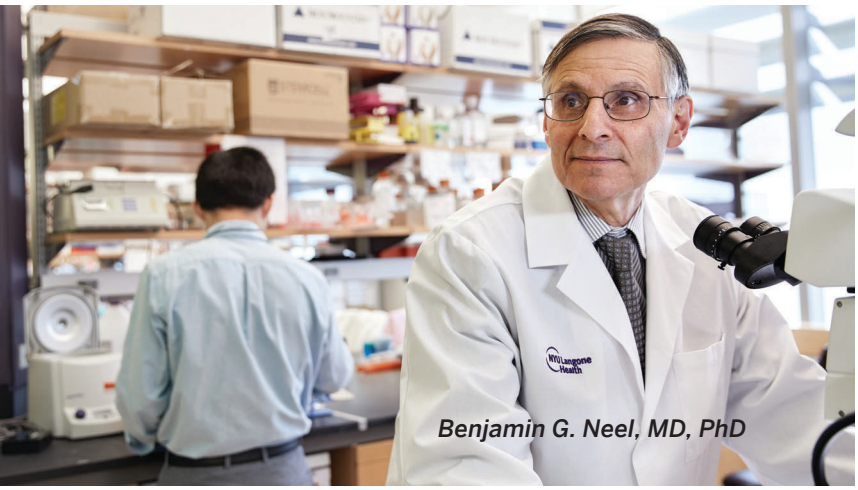
New Biotechnology Combines Targeted and Immune Therapies to Kill Treatment-Resistant Cancer Cells

Targeted therapies attach to and hinder cancer-causing proteins, but cancer cells can quickly evolve to thwart their action. A new study in *Cancer Discovery* led by Perlmutter Cancer Center researchers describes a strategy to overcome these limitations, leveraging the process by which major histocompatibility complex (MHC) molecules present peptides on cell surfaces for immune cell recruitment.

Unmasking cancer cells for immunotherapy attack

The team recognized that covalent inhibitors form stable attachments with oncoproteins and reasoned that once these oncoproteins are broken down into peptides, the unique drug–peptide conjugates could act as an MHC-displayed "flag" recognized by antibodies. The team then engineered such antibodies and joined them to another antibody known to recruit T cells, forming bi-specific antibodies that destroy cancer cells.

"Even when genetic and other changes frustrate targeted therapies, they often still attach to their target proteins; this can be used to label cells for immunotherapy attack," says co-corresponding study author Shohei Koide, PhD, a professor in the Department of Biochemistry and Molecular Pharmacology at NYU Grossman School of Medicine and a member of Perlmutter Cancer Center.



Benjamin G. Neel, MD, PhD

"Further, our system, conceptually, has the potential to increase the efficacy of any cancer drug when attached to the drug's disease-related target where the combination can be displayed by MHCs."

Engineering bi-specific antibodies for multiple drug targets

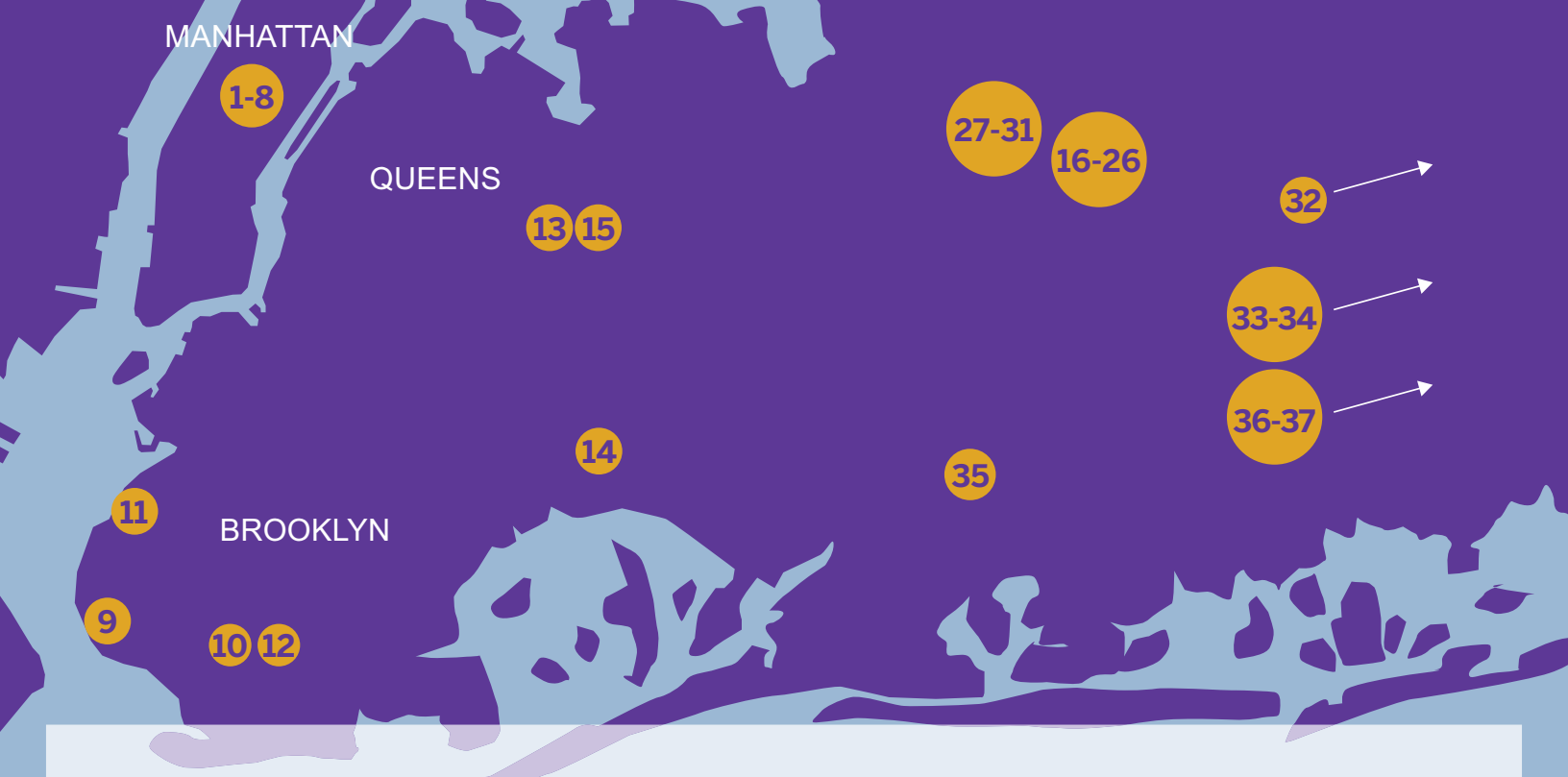
The researchers focused on the targeted therapy sotorasib, developing bi-specific antibodies that recognize the drug bound to its target, KRAS G12C. In sotorasib-treated lung cancer cells grown in culture, the bi-specific antibodies selectively recruited T cells to kill treatment-resistant cells marked with the unique drug–peptide "flag."

Showing the technology's broad potential, the team also developed bi-specific antibodies that recognize osimertinib bound to an altered form of EGFR seen in other lung cancers, and prototypes that recognize ibrutinib bound to its target, BTK.

Potential for lesser treatment toxicity

"Our results further show that the antibodies attach to drug molecules only when presented by MHCs on cells, and so could be used in combination with a drug," says study co-corresponding author Benjamin G. Neel, MD, PhD, director of Perlmutter Cancer Center.

"Used in combination with such antibodies, a given drug would only need to flag cancer cells, not fully inhibit them," he notes. "This creates the possibility of using drugs at lower doses, potentially, for reducing the toxicity sometimes seen with covalent inhibitors."



Perlmutter Cancer Center

Perlmutter Cancer Center comprises **59** centers, programs, and services across **37** sites throughout New York City and Long Island.

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    • Doctor's Office
19. Perlmutter Cancer Center—Mineola
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    • Imaging Services
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    • Radiation Oncology
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26. Perlmutter Cancer Center Radiation Oncology at NYU Langone—Mineola, 264 Old Country Rd.
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