JANUARY 2021

HMH RESEARCH NEWS

Convalescent Plasma for COVID-19 – early and outpatient

Groundbreaking research for convalescent plasma treatment for COVID-19 patients continues at Hackensack Meridian *Health* – now with a new Phase 2 study.

The researchers at John Theurer Cancer Center at Hackensack University Medical Center and their colleagues at the Hackensack Meridian Center for Discovery and Innovation (CDI) continue Phase 2 testing of the clinical treatments – now in an outpatient setting to treat earlier and help the infected avoid hospitalization.

Also required: more plasma donations for COVID-19 survivors.

READ MORE

CDI Awarded NIH Grant for COVID-19 Drug Discovery with Merck

The Hackensack Meridian Center for Discovery and Innovation (CDI) has been awarded $619,850 to continue a key drug-discovery program in pursuit of COVID-19 treatments.

The drug discovery program is focused on the assessment of hundreds of drug candidates in the CDI labs to find the most promising potential therapies.

The funding is aimed at accelerating the partnership at the CDI's NIH Center of Excellence in Translational Research (CETR), helmed by David Perlin, Ph.D., the CDI's chief scientific officer, for "rapid drug development targeting SARS-CoV-2" – and also potential therapies for all coronaviruses ("pan-coronavirus" treatments).

READ MORE

Hackensack Meridian Health Recruits Phase 3 Clinical Trial of Janssen's COVID-19 Vaccine at Jersey Shore University Medical Center

Hackensack Meridian *Health* is now enrolling individuals in the Janssen Pharmaceutical Companies of Johnson & Johnson's Phase 3 COVID-19 vaccine trial.

The Phase 3 international, randomized, double-blind, placebo-controlled ENSEMBLE 2 trial run by Johnson and Johnson is designed to evaluate the safety and efficacy of a two-dose regimen of Janssen's investigational COVID-19 vaccine candidate versus placebo in up to 30,000 adults 18 years old and older.

This ENSEMBLE 2 trial involves a two-dose regimen, administered on day 1 and day 57 of participation. Half of the volunteers will be administered the vaccine, with the other half administered placebo. The total study duration is more than two years.

READ MORE

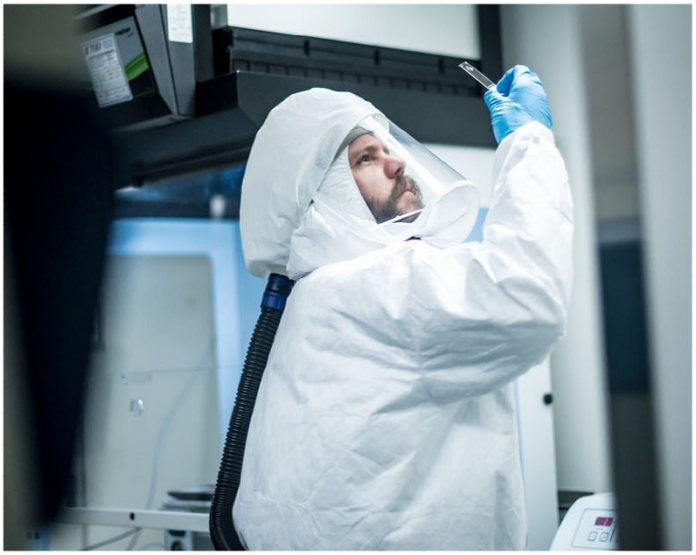
Investigator Training Lecture Series 2021 – Starting Soon!

The series, co-sponsored by the Office of Research Administration and the School of Medicine, is designed for physicians, scientists, nurses, and any other team members that may be involved or interested in research. Its objectives are to guide researchers on getting started in research, including obtaining funding, feasibility, and study design; create awareness regarding regulatory and scientific issues surrounding research; and inform researchers on processes related to managing the project and thereafter, including publishing.

More information about this series and our other educational offerings is available here. You can also find a list of the research education events on our calendar, which is continually being updated: https://events.hackensackmeridianhealth.org/research .

Goodbye to our Retirees!

We will surely miss two of our colleagues who will soon be free from this daily toil called "work". Diana Caulfield retired at the end of 2020 and Roxanne Valasa will be tucking away the last of her study binders by the end of January. Their research experience combined adds up to about fifty years of good clinical practice. We thank them for the role they played in our research family through all these years and wish them all the best.



REGULATORY & PROCESS CHANGES OR REMINDERS

JANUARY 2021

From the Research Integrity Office

HRPP SOPs were updated, effective 12/11/2020:
These can be found within eReseach and on the ORA website:
o Clarification was added to Sections 8, 14, 15, and 17 about who must be notified in the circumstances of protocol suspension/termination and/or serious or continuing noncompliance when relying on an external IRB.
o Section 9.1.3 was revised to clarify that when relying on an external IRB, personnel changes must first be submitted to HMH IRB through eResearch and acknowledged by the Research Integrity Office prior to being submitted to the external IRB of record.

Tracking your eResearch submission:
Once you have submitted your application in eResearch, you're able to track the status by using the following features:
o "Current State" (found in the top left corner of the submission's main page) indicates where in the submission process the application is: Whether it be in 'Department Review' awaiting any of department reviews such as Department Chair review, Contracts or Budgets review, COI review, etc. or in one of the IRB review states (such as 'IRB Staff Review', 'In Expedited Review' or 'Assigned to IRB Meeting').
o "Pre Review Status" tab lists all Department Reviews, indicating which ones have cleared and which are pending as well as indicates which departments/offices have been assigned those reviews.

How to request Reliance on another IRB:
o Sometimes researchers seek IRB review by an external IRB (rather than using HMH IRB). This may happen when a sponsor chooses to use a commercial IRB (such as Western IRB or Advarra IRB) or when HMH is part of a multi-site research protocol and the lead site is using their institution's IRB. But did you know that to rely on another IRB, a submission in eResearch is still required?
o To use another IRB, the following steps are needed:
▫ Submit an application in HMH's eResearch system (starting as you normally would to obtain HMH IRB approval). But once the submission asks which 'Reviewing IRB', select 'WIRB' (if using Western IRB), 'CIRB' if using the National Cancer Institute's Central IRB, or 'Other' specifying which external IRB will be used. This will abbreviate the submission to only a limited amount of pages/information needed to rely on another IRB. The submission does not go through IRB review (since the IRB component is being ceded elsewhere), but instead goes through the administrative reviews which remain HMH's responsibility even if another IRB is reviewing. For example, clearances by the Principal Investigator's Department Chair, Contracts and Budgets reviews, COI disclosure reviews, CITI training checks, etc. are all still conducted locally when HMH relies on another IRB. In addition, our Research Integrity Office (which serves as the administrative office to HMH's IRB) must ensure the protocol matches applicable institutional policies and state laws even though the IRB review is occurring externally.
▫ Once the administrative (non-IRB) reviews clear in eResearch, you'll receive documentation which will allow you to move forward and submit to the external IRB.
Questions about the reliance process? Contact HMH's IRB Reliance Analyst Dawn DeCicco at dawn.decicco@hmhn.org

Short Form Use Update:
The policy regarding Short Form use for non-English speakers has been revised. Specifically, the use of the short form process is limited to situations when both are true:
• A full-length version of the consent form in a language understandable to the subject is not available, and
• It is in the subject's best medical interest to be enrolled in the research before a translated consent form can be obtained.
For more information, please review the announcement that was sent out via eResearch this past November here.

From the Investigator Initiated Research Program

ProtocolBuilder is no longer available in HMH. Moving forward, all investigators are strongly encouraged to use one of the new protocol templates when preparing their IRB submission. Protocol templates are available

in eResearch (eResearch Home > Protocol Development Resources & Templates) and in the Office of Research Administration website (Research | Office of Research Administration | Researcher Resources | Protocol Development

From Biostatistics Core

Need support in Biostatistics for your new research project? When planning your project, please submit your request through our Biostatistics Project Request Form (https://redcap.hackensackumc.net/Redcap/surveys/?s=CKAAJLNTFT) to get an early start.

From Compliance/Conflict of Interest Management

Three new policies went into effect this summer that govern the conduct of research to ensure the highest quality of research integrity.
The policies can be found on PolicyStat. If you have any questions or concerns, please contact Michelle Benson, PhD (michelle.benson@hmhn.org). Virtual trainings on these policies and how they impact research at HMH can also be scheduled for your research group or department.

Individual Conflict of Interest and Research Policy - https://hmh.policystat.com/policy/8263167/latest/
Institutional Conflict of Interest and Research Policy - https://hmh.policystat.com/policy/8263276/latest/
Research Misconduct Policy - https://hmh.policystat.com/policy/8263298/latest/

As of August 1st, IRB Manager is no longer being used to collect COI disclosures for research.
An interim REDCap survey is being used while HMH research systems are being upgraded. The REDCap survey does not require a user name and password and can be accessed via this link: https://redcap.link/COI_Research.

Who needs to disclose?
Anyone who conducts research under the auspices of HMH
Designing or directing research
Enrolling research subjects (including obtaining informed consent)
Making decisions related to eligibility or risks of participating
Collecting, analyzing or reporting data
Contributing to manuscripts for publication
This can include trainees, residents, technicians and volunteers
When to disclose?
Upon hire and/or when initiating/engaging in research at HMH and updated annually thereafter
Update disclosure within 30 days of receiving a new financial interest and/or associational relationship

All personnel engaged in research HMH (as defined above) must have an up-to-date COI disclosure for research. Missing COI disclosures may result in study delays.

Questions regarding COI policies can be directed to Michelle Benson, PhD (michelle.benson@hmhn.org)

From the BioR (Network Biorepository)

The BioR offers an extensive and diverse selection of specimens linked to their associated patient medical information. These specimens have been collected in accordance with federal, state, and institutional regulations and may be provided for researchers with all identifiers removed.
Investigators may also request specimens from specific patient populations; the BioR is equipped to prospectively obtain consent and collect the specimens for possible future research. For more information about the BioR, please visit here.

Researchers submitting studies to the IRB for review which propose access to the BioR patient population, samples, data, or assistance with procurement and/or storage should select the “BioR option” in the IRB application in eResearch. This will alert the BioR staff to review your application and determine whether they can accommodate your need.

To access specimens for a non-human subjects study (in vitro or animal research utilizing de-identified samples and their associated medical information), please reach out to Ya’el Kramer (yael.kramer@hmhn.org), the BioR Manager, for the Biorepository Research Integrity Committee (BRIC) application. This application undergoes an expeditious peer review to approve the release of samples.

Ya’el is also available to answer any questions about the process or the services offered by the BioR and can be reached at the email address above.

HMH INITIATIVES, RESEARCH, PROGRESS & STATS

JANUARY 2021

Hackensack Meridian Health is Making its Mark in Research

As of the end of December 2020, our network has over 90 publications from a variety of HMH institutions. The vast majority of the publications are in peer-reviewed journals and several have been featured in high impact factor ones, such as the *New England Journal of Medicine, JAMA, Lancet,* and *BMJ*. Our publications are an excellent example of collaboration within HMH and between HMH and well recognized academic and research institutions and reflect on the high quality of the research taking place across our network.

JTCC Researchers Present more than 50 Abstracts at ASH

Clinical investigators from John Theurer Cancer Center (JTCC), presented updates on treatment advances in multiple myeloma (MM), mantle cell lymphoma (MCL), and other types of B-cell lymphoma (BCL), as well as leukemia, at the 62nd American Society of Hematology (ASH) Annual Meeting and Exposition, held virtually in December.

"Once again, and despite COVID, our team has a full presence at ASH 2020, being part of 52 abstracts. This shows our commitment to clinical science and collaboration with other leading institutions, from new studies on CAR-T cells, bispecific T cell engager antibodies, and other new small molecules in leukemia, lymphoma, and myeloma," said Andre Goy, MD, MS, Chairman and Director of John Theurer Cancer Center (JTCC) at Hackensack University Medical Center. "It is not just a requirement for our patients but a privilege to contribute to the phenomenal acceleration of cancer medicine."

READ THE FULL LIST HERE

CDI Partners with U-Mich on COVID-19 Antibody Assay

A more efficient and much faster method to assess high levels of neutralizing antibodies to COVID-19 could point the way to better understanding and treatment of the disease, according to new published findings by scientists from the Hackensack Meridian Center for Discovery and Innovation (CDI) and the University of Michigan (U-M).

A new portable "lab on a chip," developed by the U-M scientists and demonstrated with help of the CDI, can identify the presence of COVID-19 antibodies in blood donors with greater speed and efficiency than the current standard "enzyme-linked immunosorbent assay" or ELISA technology. The device can identify COVID-19 antibodies in human blood in 15 minutes – much shorter than the few days the process normally takes.

The work could have particular value for the validation of convalescent plasma as a treatment for COVID-19. A paper on the findings is published in Biosensors and Bioelectronics.

READ MORE

New Breath: Center for Paralysis and Reconstructive Nerve Surgery Celebrates its 500th Phrenic Nerve Patient

Matthew Kaufman, M.D., FACS, is a plastic/reconstructive and head and neck surgeon at Jersey Shore University Medical Center. More than a decade ago, his expertise expanded to the understanding how to reconstruct and fix facial nerves and peripheral nerve injuries.

He's since become the most experienced surgeon in reconstructing damaged phrenic nerves – literally giving people back the gift of breath.

Kaufman and his team at Hackensack Meridian Jersey Shore University Medical Center's **Center for Paralysis and Reconstructive Nerve Surgery** have just passed a remarkable milestone – their 500th patient treated. This makes it be far the largest surgical program of its kind in the world.

READ MORE

Immunotherapy Combo Halts Rare, Stage 4 Sarcoma in Teen

A patient with end-stage and rapidly progressing soft-tissue cancer whose tumor did not respond to standard treatment, had a "rapid and complete response" to a novel combination of immunotherapy, according to new research published by a team of scientists from John Theurer Cancer Center at Hackensack University Medical Center and the Georgetown Lombardi Comprehensive Cancer Center, both of whom are part of the Georgetown Lombardi Comprehensive Cancer Center Consortium.

The single case was reported in the Journal of Immunotherapy (with the patient's consent).

The patient was first diagnosed with the soft-tissue sarcoma along the spine in 2017, as a 17 year old. Chemotherapy, radiation and standard of care drugs, were administered, and surgery was performed to achieve partial response. The patient was admitted to the hospital in April 2019 in severe pain and his cancer had progressed to stage 4. The doctors at John Theurer Cancer Center, working as a team with Georgetown's experts, obtained a compassionate use authorization to try two checkpoint inhibitors, ipilimumab (anti-CTLA4) and nivolumab (anti-PD1) in May 2019.

By October, the patient was in complete remission. As of his last visit in June 2020, he has resumed normal activities and normal physical examination and is essentially asymptomatic.

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FEATURED RESEARCHERS

JANUARY 2021

Edward Liu, M.D., *Infectious Disease Physician, Jersey Shore University Medical Center*

Dr. Liu always knew a pandemic was on its way. As an infectious disease specialist, he and his colleagues were taught to anticipate one and to be prepared. What really threw him for a loop was the length of time that it has dragged on and the extent of the effect on everyone's lives outside of the medical world. COVID-19 has impacted people's jobs and lifestyles in ways that few, even in the medical community, could have imagined.

At the forefront of the fight against COVID-19, Dr. Liu's work towards the cause has been on both the clinical and research fronts – though the two have been intermingled lately in an almost unprecedented manner. He has worked hard to offer his patients the best care for a previously unknown but potentially deadly disease. Research has played a large part in this for him; he has led study teams in clinical trials and has paid close attention to scientific findings that have emerged.

Dr. Liu shared his experience with the COVID-19 pandemic:

What was your early experience with COVID-19 and how does it compare to the current situation (i.e. the "second wave")?

When COVID hit, it was really jarring. We were confronted with a disease for which we didn't have any treatments, and the only options we had were very limited. So many people were getting sick, and the only real treatments were supportive – oxygen and respiratory support.

Currently, we have more of a protocol and have learned strategies for managing the patients' conditions more efficiently. What we tended to do in the beginning was to try to focus on the sickest – that is the natural tendency of most doctors. Now we know to put as much effort as possible in getting patients treated as quickly as possible early on, because once someone ends up in the ICU with multiple pressors and on the ventilator, there are not as many things that can help them.

What has been most challenging during the pandemic?

The sheer volume – at one point, ¾ of the hospital was filled with COVID patients. I've never seen one disease take over a hospital. We quadrupled the ICU capacity and had 80-100 ventilators going at once.

What kind of research did you conduct before the pandemic, and in what ways have you been involved in research during the pandemic?

Before COVID, I had been involved primarily in general infectious disease trials and in HIV trials. The HIV research slowed down at sites like ours as research became more centralized, but I have continued working on infectious disease research. I also serve as the vice-chair of the Institutional Review Board.

Once COVID hit, it changed a lot of things. Research was the only way to address a huge unmet need for so many people. Early on, we gained access to remdesivir

through Emergency Use Authorization, but at JSUMC, we were not involved in the clinical trial.

One of our first research efforts was involvement in the plasma study based out of the Mayo Clinic. It was an open label protocol that arranged for multiple blood banks to draw blood from recovered COVID patients, extract the plasma, and offer it to physicians who could order it like a blood transfusion. I was impressed with the Lakewood community's commitment to donating blood for this study.

We also conducted a study on sarilumab, an Il-6 inhibitor. Additionally, we are studying JAK-inhibitors, which have anti-inflammatory properties. Neither has shown definite benefits in the sickest patients, but that's the nature of research.

At this point, we are focused primarily on remdesivir and steroids because the data are strongest for those treatments.

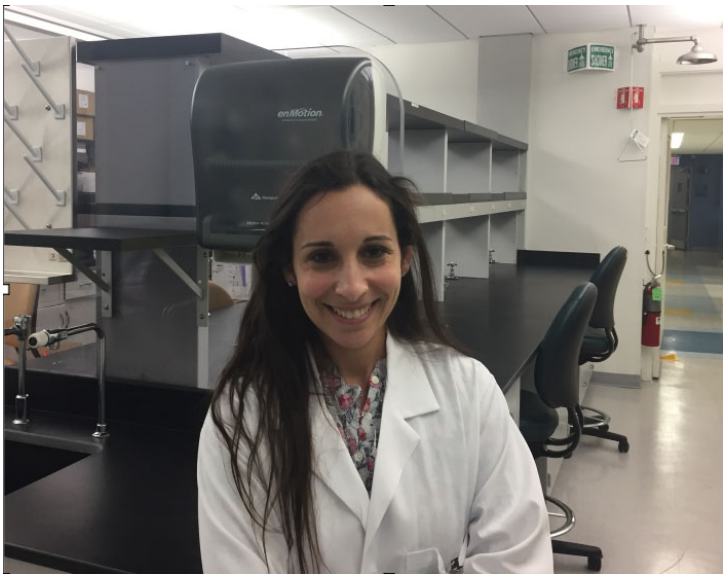
The tremendous support from the Office of Clinical Research has been invaluable. They have managed consenting, data tracking, and they worked 7 days a week for months.

Has the pandemic changed your perspective on research?

It has made research even more important because previously you had some therapeutics for most diseases, but when you have absolutely none, there is a much greater urgency. This type of scenario emphasizes the importance of research because you don't have a standard of care. In the last 9 months, there has been so much speculation about what the best treatments are, but when it comes down to it, you need a rigorous clinical trial to really be able to ensure that there is benefit with acceptable side-effects.

What are your thoughts on the vaccine? Do you think that this is the beginning of the end?

This is the biggest step in moving ahead. I got my vaccine last week.



Rachel Rosenstein, M.D., Ph.D., *Assistant Professor, Dermatology Division, Hackensack Meridian Health Center for Discovery and Innovation*

Dr. Rosenstein, M.D., Ph.D., worked for two years at the National Institutes of Health in Maryland. There, the dermatologist saw some of the most challenging complications for cancer patients. Her niche seems highly specific, but it is a crucial one: diseases of the skin that develop in cancer patients (oncodermatology) – and not specifically skin cancer. She arrived in the fall at Hackensack Meridian *Health* and splits her time between the Center for Discovery and Innovation (CDI) and Hackensack University Medical Center. Here, the physician-scientist aims to make more of a clinical impact with her science than ever before.

Q: Tell us a bit about your time at NIH and your goals for your research here.

Patients come to the NIH oftentimes as a last resort – their home institutions had already been working very hard to treat them. We would often see patients in late stages of disease processes. My goal now is to study disease earlier in the process.

One of your specialties is sclerotic chronic graft-versus-host disease (GVHD, an affliction for those who undergo bone marrow transplantation. Can you tell us a bit more about its effects?

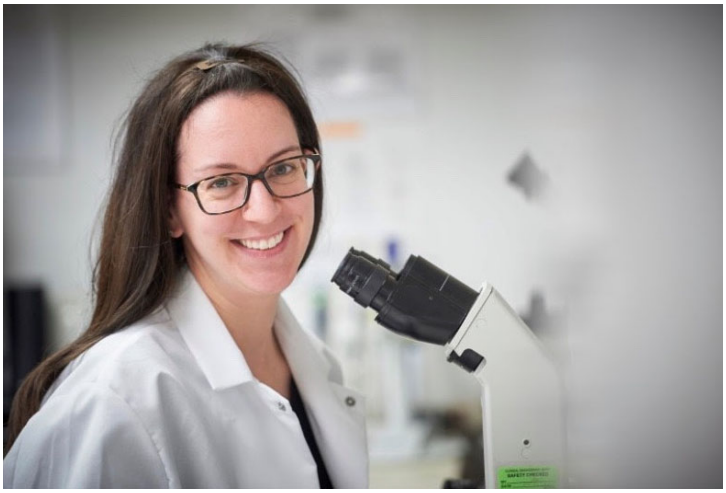
GVHD is a multi-systemic disease. It can affect the eyes, mouth, skin, gastrointestinal tract, lungs, joints, among other organs. And the effects in these organs can be quite heterogeneous. It's thought to occur because transplanted T cells attack the host. But the progression from inflammation and T cell infiltration into different tissues to fibrosis is still really being defined.

What is a fundamental challenge at this point in GVHD research?

There are now multiple treatment options for chronic GVHD, which have proven to work for some patients, and not for others, but understanding which patients will respond to which drugs and at which stage of their disease is difficult to tease out. One objective at the CDI is to take lab discoveries to the clinic, and vice-versa – and that's always been an important goal for my research. Being somewhere that can easily broach the divide between research and clinical care is a great opportunity.

FEATURED RESEARCH ADMINISTRATOR

JANUARY 2021



Ya'el Kramer, M.S., Manager, *Hackensack Meridian Health Network Biorepository*

As the pandemic descended upon us this past March, Ya'el and her team shifted into high gear. They knew that COVID-19 specimens would be invaluable in helping researchers learn more about the enigmatic virus, and time was of the essence. Working closely with Dr. Chow, Director of the biorepository (BioR), Ya'el and her team have so far managed to consent over 1,600 patients from the COVID population throughout the network and to bank over 43,000 aliquots of diverse specimens. These specimens have been distributed to HM*H* researchers and their collaborators and have been instrumental in many research efforts.

Starting even before the pandemic, the BioR has been transformed since Ya'el's arrival at HMH over two years ago. Dr. Chow, Ya'el, and her team hold an IRB-approved protocol that enables them to consent patients more seamlessly and to collect more diverse samples more widely throughout the network than before. Currently, they have stored specimens from an array of pathologies and also collect specimens prospectively to accommodate future potential research needs.

Ya'el shared with us a little more about herself and how she views her role within the BioR:

Were you always interested in scientific research?

I became interested in science when I was about 6 years old. My father was a research physicist. It was he who initially piqued my interest in science, and he later encouraged my pursuit of it.

How have your earlier experiences informed your work at HMH?

My 11 years at the NYU Fertility Center [directly before this] made a tremendous difference in the kind of work I do today. From there, I learned the importance of rigorous attention to detail, mindfulness of ethical considerations, and strict adherence to all regulations in both the clinical and research arenas. This was really underscored at the NYU Fertility Center, where each sample was a potential for new life.

What is most gratifying about your work as the BioR Manager?

I really enjoy helping others and enabling promising research to progress. I view my role as supporting the researchers, so they can make the discoveries.

What do you like to do when you're not overseeing the HMH BioR?

I enjoy spending time with my four kids and husband. I also love to garden.