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Researchers identify potential nanotechnology therapy for chondrosarcoma

At Rhode Island Hospital, cancer physician collaborates with molecular researcher to study use of nanotechnology to deliver medicine inside cancer cells

PROVIDENCE – Researchers at Rhode Island Hospital have employed nanotechnology to identify a potentially groundbreaking treatment for chondrosarcoma, an aggressive bone cancer that is disappointingly unresponsive to existing cancer therapies.

In a paper published in the November Molecular Cancer Therapeutics, a journal of the American Association for Cancer Research, the researchers describe a new approach to treating the cancer, which typically afflicts adults and has poor survival rates. Their research, using a mouse model, suggests that deploying nanoparticles might prove to be an innovative and effective way to penetrate tumor cells. These “nanopieces,” as the research team call them, could then deliver nucleic acid therapeutics directly inside the cancer cells and slow tumor growth.

RICHARD TEREK, MD, chief of musculoskeletal oncology at Rhode Island Hospital, an orthopedic oncology surgeon with the Lifespan Cancer Institute, and a professor of orthopedic surgery at the Warren Alpert Medical School of Brown University, has long researched ways to fight chondrosarcoma. For this study, funded by the National Institutes of Health, he teamed up with molecular and nano-medicine researcher QIAN CHEN, PhD, director of the NIH-funded Center of Biomedical Research Excellence in Skeletal Health and Repair at Rhode Island Hospital and a professor of orthopedic research and medical science at Brown’s medical school.

“What is most novel about the work is that we have used a special type of nanoparticle which we call a ‘nanopiece delivery platform,’ developed by my collaborator Dr. Chen, for systemic delivery of anti-microRNA sequences (antago-mirs),” said Dr. Terek. “The work has been performed in cell culture and in a mouse model. We have been able to inhibit metastatic pathways and slow down the spread of cancer. This approach is in keeping with current strategies to turn cancer into a chronic disease. An advantage of the nanopiece platform is its safety and ability to penetrate into the tumor matrix and deliver the cargo to the tumor cells.”

Said Dr. Chen, “This has very strong translational value in developing treatment for chondrosarcoma, a lethal disease that currently does not have any effective treatment. Dr. Terek devoted his whole career in developing treatment for this disease, and this may be the most promising potential treatment so far. The nanopieces delivery platform, which we developed at Rhode Island Hospital and Brown University, is able to penetrate the tumor, reduce tumor growth and prolong survival period in the mice model.”

He added, “Based on these promising pre-clinical data, the next step is to develop biologic therapeutics specifically targeting human chondrosarcoma.”

They are seeking collaboration with industry and academia to advance development of the potential chondrosarcoma drug.

This study is supported by NIH funding (CA166089 and GM122732). It was previously published online.

$6.8M in NIH grants will enable Brown researchers, RI to evaluate, expand opioid interventions

PROVIDENCE [BROWN UNIVERSITY] – With opioid drug overdose deaths skyrocketing in recent decades, researchers at Brown University’s School of Public Health are confronting the epidemic in multiple ways. Two new five-year grants from the National Institutes of Health, totaling $6.8 million, will expand those efforts.

The first will launch a partnership with the State of Rhode Island that will result in neighborhood-based intervention strategies across the state’s cities and towns informed by a new predictive forecasting model. The second will enable researchers to evaluate the effectiveness of test strips used to detect fentanyl, a highly potent prescription opioid often used to lace other heroin or cocaine, but hard for drug users to detect.

“Both projects are trying to bring innovative technologies to help solve the overdose crisis,” said BRANDON MARSHALL, an associate professor of epidemiology at Brown and principal investigator for both projects. “That’s the long-term goal – to reduce the risk of overdose and to save lives.”

The first project – titled Preventing Overdose Using Information and Data from the Environment (PROVIDENT) – expands on several years of collaboration among Brown researchers and agencies across Rhode Island.

PROVIDENT will unite Brown scholars with colleagues from NYU School of Medicine [Magdalena Cerdá, associate professor of population health, is co-principal investigator] and the University of California, Berkeley, to develop a machine-learning forecasting model to predict which neighborhoods in Rhode Island are most at risk for outbreaks of opioid overdose.

Next, the Brown team will work with the Rhode Island Department of Health [RIDOH] to test whether the
model’s predictions can help deliver interventions – peer recovery coaching, opioid agonist therapy or naloxone distribution – specifically to neighborhoods that would benefit most. In a randomized trial, half of the state’s 39 cities and towns will be assigned PROVIDENT model predictions that will guide RIDOH’s distribution of resources, while the other half will receive interventions without the targeting of particular neighborhoods.

“We hope that in towns where we develop the predictions, we’ll see a 40% reduction in all overdoses, fatal and nonfatal,” Marshall said. “That’s an ambitious target. But we think we can get there by working collaboratively across the state and with organizations that deliver services.”

**DR. NICOLE ALEXANDER-SCOTT**, RIDOH director and an associate professor at Brown, said the state/university partnership is illustrative of the collaborative approach that often leads to the most innovative solutions to public health challenges.

“This research partnership between the talented public health professionals throughout RIDOH who are responding to the overdose epidemic and the Brown University School of Public Health, with support from the RIDOH Academic Institute, represents a cutting-edge intervention to get tools and resources related to substance-use disorder into the communities where they are needed most,” Alexander said. “By synchronizing existing statewide overdose surveillance systems with powerful predictive analytics and data forecast tools, we will be leveraging data in powerful new ways to prevent overdoses and safe lives. Saving lives remains our absolute priority in this crisis.”

Marshall, an expert adviser to Rhode Island Gov. Gina Raimondo’s Overdose Prevention and Intervention Task Force, said that if the trial proves successful, the research team’s long-term goal is to ultimately expand the use of the model beyond the Ocean State.

“Rhode Island is a perfect laboratory for this particular project, to see whether we can successfully predict overdoses at a neighborhood level,” Marshall said. “If we can, then the next steps would be disseminating the forecasting tool to other states and evaluating whether it’s useful in other contexts.”

The second NIH grant, which will fund a project titled Rhode Island Prescription and Illicit Drug Study (RAPIDS), will address a very different facet of the opioid crisis – fentanyl. The highly potent synthetic opioid can be deadly even in trace amounts and is a major factor in the rise in fatal overdoses.

“Fentanyl is about 50 to 100 times more powerful than heroin or morphine, and it has cut into the illicit drug supply,” Marshall said. “Essentially, people can’t find pure heroin on the East Coast – nowadays, it’s all adulterated with fentanyl. In the last couple of years, we’ve seen evidence that it may be appearing in other types of illicit drugs as well.”

About five years ago, fentanyl test strips became available. Originally developed for urine drug screens, the rapid-acting strips have increasingly been used to detect the presence of fentanyl in illicit drugs. They work essentially like over-the-counter pregnancy tests. Each single-use strip is dipped into water containing a bit of drug residue, and after a minute, either one or two red lines appear – one line means the liquid contains fentanyl, and two lines means the test did not detect the drug.

The RAPIDS project will consist of a randomized trial that includes individuals who use drugs and are at risk for fentanyl overdoses. The project will test whether informing people about the dangers of fentanyl and teaching them to use the strips reduces risk of overdose. Marshall said he expects the trial to launch in December 2019, and the research team hypothesizes that the test-strips will lower overdose rates.

“The hope is that people at risk for fentanyl overdose will use these strips, like them and take actions that meaningfully reduce their risk,” Marshall said. “I’m optimistic that we will see those reductions.”

The project will expand significantly on the results of a 2018 pilot study led by Marshall. The study provided test strips to 93 young adults who reported injecting opioids or using heroin, cocaine or prescription pills bought off the streets. The preliminary results were promising.

If the expanded trial indicates that strips can decrease overdose rates, Marshall and his colleagues will next evaluate the extent to which they’re disseminated, and how. Participant safety is a top concern, he added.

“There are other adulterants out there that increase the risk of overdose that the strips don’t detect, including some fentanyl analogs,” he said. “So the strips aren’t perfect, and we’re focusing on how to communicate that to participants – to let them know that they should take universal precautions whenever they use an illicit substance, like not using alone and having someone there who could call 911 in the event of an overdose.”

National Institutes of Health funding for PROVIDENT (No. R01DA046620) is expected to total $3.3 million over five years. NIH funding for RAPIDS (No. R01DA047975) is expected to total $3.5 million over five years.
RI MomsPRN, new statewide initiative, addresses maternal depression and related behavioral health needs

To help perinatal-care providers meet the behavioral healthcare needs of pregnant and postpartum women in Rhode Island, the Rhode Island Department of Health (RIDOH) and the Center for Women’s Behavioral Health (CWBH) at Women & Infants Hospital have partnered to create the Rhode Island Maternal Psychiatry Resource Network (RI MomsPRN).

This new statewide program provides real-time psychiatric teleconsultation services for healthcare providers, who can call 401-430-2800, Monday through Friday, 8am to 4pm. The telephone service is staffed by a team of perinatal behavioral health experts from CWBH, including a resource and referral specialist, perinatal psychiatrist, and perinatal psychologist. They are available to help with diagnosis, treatment planning, and medication management for pregnant and post-partum patients.

“We want to make sure that all babies, moms, and families in every ZIP code in Rhode Island have an equal opportunity to be healthy,” said Director of Health NICOLE ALEXANDER-SCOTT, MD, MPH. “The most common medical complication of childbirth is depression. It is crucial that we equip healthcare providers in Rhode Island with the tools and resources they need to support women during this critical phase. Connection is everything.”

An estimated 20% of Rhode Island women experience depression before, during, or after pregnancy. Depression symptoms in the perinatal period can range from a sad mood and loss of interest in activities to feelings of worthlessness, problems in concentrating or making decisions, and changes in eating or sleep. There is also growing evidence that perinatal substance use is increasing. Routine screening for maternal depression and related behavioral health needs throughout the perinatal period is a recommended best practice and results in better outcomes for mother and child.

“Perinatal mood and substance use disorders are highly treatable,” said Director of CWBH MARGARET HOWARD, PhD. “Rhode Island is fortunate to have a robust community of perinatal mental health experts, unique programming at CWBH, and services at the Day Hospital at Women & Infants. However, there is still a need for more specialized providers. RI MomsPRN is designed to build provider capacity in treating mild to moderate cases of perinatal mood complications and to prioritize specialty resources for high-risk women with more complex conditions.”

The RI MomsPRN team can also help identify community-based resources, such as mental health care, recovery services, support groups, and other case-dependent resources for pregnant and postpartum patients.

This program is funded by a five-year grant from the US Health Resources and Services Administration and draws on the successful outcomes of Rhode Island’s PediPRN Program at the Emma Pendleton Bradley Hospital that helps pediatricians manage children’s psychiatric needs.

To learn more about RI MomsPRN phone consultation service for healthcare providers, visit http://www.womenandinfants.org/services/behavioral-health/ri-momsprn.cfm

This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $650,000 with 1% financed with non-governmental sources. The contents included in this news release were prepared by RIDOH and the CWBH and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government.

Groundbreaking for Providence VAMC’s Research Service

From left to right, U.S. Sen. Sheldon Whitehouse; U.S. Sen. Jack Reed; Dr. Susan MacKenzie, director of the Providence VA Medical Center; Jessica Ramos-Tinney, project manager from Ironclad Services of Springfield, Mass.; and Erin Clare Sears, associate director for operations at the Providence VAMC, officially broke ground on Nov. 8th on the project to renovate the former Harwood U.S. Army Reserve Center in Providence for use by the Providence VAMC’s Research Service. The $12 million project is scheduled for completion next year.

[PROVIDENCE VA MEDICAL CENTER PHOTO BY WINFIELD DANIELSON]
Dr. Elizabeth Goldberg awarded $1.1M in NIH funding to study fall prevention

*Named recipient of the Paul B. Beeson Career Development Award*

PROVIDENCE – ELIZABETH GOLDBERG, MD, ScM, an emergency medicine doctor with Brown Physicians, Inc. and an attending physician at The Miriam and Rhode Island Hospitals, was named the recipient of the Paul B. Beeson Career Development Award. Dr. Goldberg will lead a five-year, $1.1 million research project funded by the National Institute of Health, titled “the Geriatric Acute and Post-Acute Fall Prevention Intervention II” project (GAPcare II).

The Beeson Award is given annually to a handful of physician-researchers across the country who have demonstrated leadership potential in the field of geriatrics research, and are at the early stage of their career.

The project, currently underway, is examining the effectiveness of multi-disciplinary approaches when caring for older adults who have been admitted to the ED after a fall.

The study of falls among older adults should be prioritized, Dr. Goldberg says, given the prevalence of this type of injury. One in three adults over the age of 65 fall each year and many falls are preventable. Statistics indicate that falls remain one of the most common causes of ED visits among older adults, and people who seek emergency care after falls are 30 percent more likely to experience another fall within six months.

One reason older adults return to the ED is because the cause of their fall was never determined, according to Dr. Goldberg. “We are doing a pretty good job at injury assessments, but doctors are at a standstill when it comes to removing obstacles that led to a fall in the first place,” Dr. Goldberg added.

Dr. Goldberg says falls often go unreported since older patients might have cognitive impairments such as dementia. Alternatively, she says some people avoid care due to the stigma associated with falls and old age.

As part of her effort to pinpoint causes of falls and help connect older individuals with specialists that can help them prevent future falls, Dr. Goldberg will be equipping patients with Apple Watches to help detect when a fall occurs. Participants who experienced a fall would be connected with physical therapists and pharmacists as part of an effort to reduce the likelihood of another fall.

A separate clinical study found that this coordination of care is effective in preventing falls. Dr. Goldberg is hopeful that the results of her research project could provide the sufficient evidence needed to roll out similar programs across the country.

The first two years of the project will involve assessing participants’ ability to use an Apple Watch effectively and suggesting revisions to improve the usability of the wrist watch.
RI researchers, policymakers outline new framework for opioid use disorder treatment

PROVIDENCE [BROWN UNIVERSITY] – Every day, more than 100 Americans lose their lives to the opioid crisis, and researchers from across the nation are racing to find solutions. One of the latest strategies—a cascade of care model for the State of Rhode Island—was developed collaboratively by a diverse group of stakeholders, including experts from Brown University, state agency leaders and community advocates.

The research team detailed the model in a paper published in the journal *PLOS Medicine* in November.

“We hope we’ve created a tool that policymakers and state agencies can use to make data-driven decisions that improve care in our state,” said JESSE YEDINAK, the study’s lead author and a project director at the Centers for Epidemiology and Environmental Health at the Brown University School of Public Health.

To create the model, the team revised an existing framework to define five stages of care for people with opioid use disorder (OUD):

- Stage 0: at risk for OUD
- Stage 1: diagnosed with OUD
- Stage 2: initiated a medication-based treatment plan
- Stage 3: continuously engaged with this treatment plan
- Stage 4: recovery

Next, the team consulted national surveys and statewide insurance claims databases to estimate the number of Rhode Islanders in each stage. These estimates help to identify gaps in care, the researchers said.

For instance, 47,000 Rhode Islanders were estimated to be at risk for OUD in 2016, meaning that they reported using heroin or taking other opioids for non-medical purposes. However, only about 26,000 of those individuals—55 percent—had received an OUD diagnosis.

“This first gap suggests that we need a lot more screening to identify people who have active opioid use disorder or are significantly high risk of overdose,” said BRANDON MARSHALL, an associate professor of epidemiology at Brown and senior author of the paper.

The model also highlights a significant gap between diagnosis and linkage to treatment: Of those estimated 26,000 individuals who had been diagnosed, less than half had initiated medication-based treatment. As a follow-up to this finding, further research is being done to evaluate the factors that make people more likely to seek treatment after an OUD diagnosis.

Stage 3, which contained an estimated 8,300 Rhode Islanders, consisted of individuals who stayed in medication-based treatment for more than 180 days. Stage 4—recovery—contained about 4,200 and was a unique feature of this model.

“In many of the other opioid use disorder care continuums, the final stage is remission, which is clinically defined as the absence of opioid-related problems,” Marshall said. “The committee did not feel this was very inspiring or patient-centered, so they strongly encouraged us to define the final stage as recovery—which is more positive and moves beyond the absence of OUD-related problems to look at the person as a whole.”

During the development process, the team was also conscious of the broader impact the model could have. To that end, they tried to make it adaptable for implementation in other states. The paper includes a specific glossary, for example, and the data sources that the model drew from should be available throughout the nation.

Marshall and Yedinak added that they hope to update the model at least once a year, and they have several long-term goals in mind.

One goal is to use the model’s data to aid in the prevention of OUD by reducing the number of people who are classified as at risk. As a longer-term implication, they also hope to start generating population health targets. For example, the United Nations AIDS organization, UNAIDS, set a 90-90-90 target for HIV. By 2020, they aim for 90 percent of all people living with HIV to have received a diagnosis. Of those, 90 percent will receive treatment. And of the 90 percent receiving treatment, 90 percent will have achieved viral suppression.

“We don’t have a target like that for opioid use disorder yet,” Marshall said. “But now that we have the estimates, we can start thinking: What should we reach toward, given our current resources—and given more resources, what would be realistic to achieve?”

In addition to Yedinak and Marshall, WILLIAM C. GOEDEL, MAXWELL S. KRIEGER and JOSIAH D. RICH were other Brown University authors on the study. Additional contributors include KIMBERLY PAULL, REBECCA LEBEAU and CHEYENNE THOMPSON from the RI Executive Office of Health and Human Services, ASHLEY L. BUCHANAN from the University of Rhode Island’s College of Pharmacy, TOM CODERRE from the State of Rhode Island’s Office of the Governor, and Rebecca Boss from the R.I. Department of Behavioral Healthcare, Developmental Disabilities and Hospitals.

The study was funded by the COBRE on Opioids and Overdose, supported by the National Institute of General Medical Sciences of the National Institutes of Health [P20GM125507]. ☀
Dedication ceremony celebrates revitalization of industrial site for Lifespan

Ambulatory Care Center to include Men’s Health Center, Infectious Diseases and Immunology Center, pharmacy and laboratory

PROVIDENCE – An old industrial site on Corliss Street has gained a new lease on life after its owner and Lifespan collaborated on transforming the underutilized property into a modern healthcare facility. The redevelopment enhances a growing medical hub for Lifespan and The Miriam Hospital in the Mount Hope section of Providence.

The new building at 180 Corliss St. is about to become the Lifespan Ambulatory Care Center. It will be home to The Men’s Health Center and The Infectious Diseases and Immunology Center – both relocated from The Miriam – as well as a Lifespan Pharmacy and a Lifespan Laboratory. Another key tenant is Lifespan-affiliated Anchor Medical Associates. The building will be leased to The Miriam Hospital.

During a November 18 ribbon-cutting ceremony, the medical center was dedicated to the late Everett A. Amaral, who as president of Amaral Revite, oversaw the project until his death in 2018. His wife, Sheryl Amaral, who assumed the presidency of the company and saw the project through to completion, participated in the ribbon-cutting and called attention to a plaque dedicating the building in her husband’s memory.

The three-story, 57,000-square-foot building was built on the former site of Clifford Metal and was most recently being used for vehicle storage. Virtually all the original structure had to be razed during the 13-month construction project, which employed close to 150. Several hundred will be employed at the facility when it opens.

Services at 180 Corliss Street will include:

- **The Men’s Health Center**
  Formerly located in the Fain Building on Summit Avenue, the center offers a variety of specialized services related to male sexual health and experts in family practice, internal medicine, urology, psychology and physical therapy.

- **The Infectious Diseases and Immunology Center**
  Formerly located on North Main Street, the center includes clinics for HIV/AIDS screening and treatment, viral hepatitis, Lyme and tick-borne diseases, and other communicable diseases.

- **Anchor Medical Associates**
  Formerly located 1 Hoppin St., Providence, this relocated Anchor practice offers primary care services provided by a staff of six physicians and three physician assistants, and a support staff of about 20.

- **Lifespan Laboratory**
  These conveniently located labs perform a variety of tests for patients and deliver faster results thanks to a centralized, automated system.

- **Lifespan Pharmacy**
  This will be the third Lifespan Pharmacy, adding to existing locations at the The Miriam and Rhode Island hospitals. It will offer a full range of services, including free home delivery, courtesy refills, and both scheduled and walk-in vaccinations.