ST. JOHN PROVIDENCE

2015 Annual Research Report

ST JOHN PROVIDENCE

Believe in better

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Annual Research Report

SJOHN PROVIDENCE
Believe in better

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Letter from the President and CEO

Greetings and welcome to the St. John Providence Annual Research Report. As leaders in the SJP ministry, we recognize the importance that medical research plays in the advancement of medicine and in providing treatment options and hope for our patients. Some of these treatment options may only be found within our healthcare system and thus represent an important access point for our patients. We are proud to support the many clinical research programs throughout SJP and we are dedicated to the development of an integrated research program that will optimize access to clinical studies by our physician investigators and patients, unify business and recruitment practices and leverage both our size and patient demographic diversity. The articles contained within this Annual Research Report speak to the dedication of our many physicians, nurses and associates who make medical research possible within SJP.

Best Wishes,

Jean Meyer

Jean Meyer
President and Chief Executive Officer
St. John Providence

Letter from the Vice President of Research

Welcome to the inaugural edition of the St. John Providence Annual Research Report. I am very happy to share with you this collection of clinically important research studies currently being conducted within our healthcare system. St. John Providence (SJP) is a leader in clinical research both locally and within Ascension Health. Medical research at SJP is a $3.58 million enterprise and spans a wide range of clinical specialties including Oncology, Internal Medicine, Cardiology, Surgery, Emergency Medicine, Obstetrics and Gynecology, Infectious Disease and Pulmonology, among others. Central to our values as a healthcare ministry, medical research at SJP advances medical knowledge, improves clinical practice and provides novel drugs, better treatment modalities and innovative medical devices to our patients. When standard medical treatment has failed or when no other treatment exists, medical research provides hope. Studies have demonstrated that healthcare organizations with an active clinical research program are safer, provide better care to their patients and as a result, patients have better clinical outcomes. Medical research also supports our many Centers of Excellence and our graduate medical education programs.

The promise of future medical innovation rests with the tireless efforts of our clinical investigators, clinical research nurses, research staff and our patients.

Sincerely,

David M. Svinarich

David M. Svinarich, PhD
Vice President of Research
St. John Providence

Cardiology

Miniature device signals the future of pacemaker technology

Sohail Hassan, MD
Cardiology/ Cardiovascular Disease/ Clinical Cardiac Electrophysiology

The future of pacemaker technology in Southeast Michigan took a giant leap forward in August 2014, when the Electrophysiology Team at St. John Hospital & Medical Center became the first in the area to implant the Nanostim, a wireless, non-surgical cardiac pacemaker placed directly into the right ventricle of the heart. The first patient to receive the device in Southeast Michigan was an 84-year-old man from Clinton Township.

"Nanostim is one of the most exciting advances yet in pacing technology," says Sohail Hassan, MD, director of Electrophysiology, St. John Hospital & Medical Center. "It has the potential to transform how heart rhythm patients are treated. Within seven months of the first Nanostim implant in the US, we were able to bring it to patients locally."

Currently, Nanostim is only available in the US through the LEADLESS II trial, an international clinical study to evaluate the safety and effectiveness of the pacemaker.

St. John Providence is one of 50 participating centers nationwide. The study is expected to enroll

approximately 670 patients total and is a key step toward FDA approval.

Every year in the US, more than 700,000 pacemakers are implanted to regulate the heart's rhythm. Traditional pacemakers have a pulse generator that houses a battery and small computer, and one to three leads, or wires. The surgeon implants the pulse generator through an incision in the upper chest and inserts the leads through one or more of the veins in the heart. The leads tell the pulse generator when to send an electrical signal to the heart, which regulates the heartbeat.

In contrast, Nanostim has no leads, doesn't require surgery, and is placed directly into the right ventricle of the heart through the femoral vein in the groin.

"Nanostim works much like a traditional pacemaker, but it has no leads," says Dr. Hassan.

"We implant it without making an incision in the chest or leaving a scar or permanent lump under the skin. The device is smaller than a AAA battery and less than 10 percent the size of a conventional pacemaker."

The device is smaller than a AAA battery and less than 10 percent the size of a conventional pacemaker.

Dr. Hassan and his team typically implant Nanostim in less than 30 minutes, compared to two to three hours for a traditional pacemaker. The risk of infection of the chest incision is eliminated, and the leads, which become dislodged in about two to three percent of cases nationally, are no longer a concern.

"Nanostim is the least invasive pacing technology available today, and by participating in the trial, we can bring it to our patients as soon as possible," explains Dr. Hassan. "We find patients are more comfortable following Nanostim implantation, and many of the restrictions that were necessary to prevent the leads from moving out of place or becoming damaged are no longer necessary. This enriches quality of life for our patients."

Nanostim leadless pacemaker

- Traditional pacemakers use leads and require surgical implant through an incision in the chest, which can cause complications.
- The St. John Hospital & Medical Center Electrophysiology Team, led by Sohail Hassan, MD, is bringing the most advanced pacemaker technology to patients through the LEADLESS II clinical trial.
- The tiny Nanostim pacemaker has no leads, does not require surgery or an incision, and leaves no bump under the skin.

Impact

Nanostim may eliminate the need for pacemakers with leads and the complications associated with traditional pacemakers, enabling patients to live more comfortable, restriction-free lives after a simpler, easier implant procedure.

Infectious Disease

Flu studies involve local patients for worldwide impact

Rodger MacArthur, MD
Infectious Disease/ Internal Medicne

Every year, between five and 20 percent of the US population gets the flu, or influenza virus. If you've ever had influenza, it's memorable: Fever, body aches, exhaustion, cough, sore throat and a symphony of other symptoms cause seven to 10 days of misery. Influenza can lead to serious complications, including pneumonia.

This flu season, St. John Providence researchers are participating in FLU PLUS 002, a worldwide study funded by a division of the National Institutes of Health (NIH) to find out more about influenza.

"This is an observational study, so participants can use any treatment they wish for their symptoms. We are simply collecting information," says Rodger MacArthur, MD, St. John Providence infectious disease and internal medicine specialist. "With these data, we'll learn about various strains of the influenza virus that circulate in different parts of the world and correlate the information with individual health histories. We'll find out about virulence, or severity of certain strains, discover which strains are geographically limited, and identify specific strains of the virus that are associated with poor clinical outcomes."

The study began this season in November 2014 and continued through mid-March 2015. The NIH expects to continue the study for two to three more flu seasons. The St. John Providence research team finds interested participants primarily through local physician offices.

"To take part in the study, a person doesn't need to have confirmed flu. If someone thinks they have the flu, they can participate," says Dr. MacArthur. "The only criteria are a temperature of 100.4 or higher or feeling feverish, and a cough and/or sore throat."

Participants, which may include patients, staff, visitors, or others, meet with a researcher and provide a history of their symptoms, other health problems and medications, and give a blood sample, which will be used for influenza testing. Researchers also take throat and nasal swabs to confirm flu and identify the strain. Over the next 14 days, participants keep a "flu diary," checking off the symptoms they experience.

At their second visit, participants bring their flu diaries with them. Researchers collect a blood sample and information about any hospitalizations, complications or new health problems that arose because of their flu symptoms. To compensate them for their time, participants receive $50 for completing both visits.

As part of the FLU PLUS 002 study, Dr. MacArthur and his team are also conducting two important sub-studies. "The first is a flu genomics study, which involves genetic testing on an extra blood sample from participants who agree to participate. We'll be looking at patient DNA and correlating it with patient health information and flu strain. The intent is to learn more about whether certain genetic factors make people more or less susceptible to flu and secondary health problems caused by the virus," says Dr. MacArthur.

With results of the genomic data, researchers could identify genetic markers that reveal who is more likely to get influenza. Care and vaccinations could strategically target people with those genetic markers, making flu prevention highly specific and effective.

The second is the FLU-PRO study. Participants fill out an online flu symptom questionnaire or speak daily on the phone with a member of the research team for 14 days. "The goal is to develop an online symptom questionnaire that provides more valuable data than the symptom diary," explains Dr. MacArthur. "The data could be used to design an improved data-collection instrument for future flu studies and clinical care."

Participants who complete the sub-studies receive additional payments. "Many people enjoy being part of a research study because they become part of the answer rather than the question. Research studies like this are invaluable as we strive to provide better care for influenza patients in the future," says Dr. MacArthur.

The FLU PLUS 002 study

- A worldwide study sponsored by the National Institutes of Health (NIH) and run locally by a team of researchers at St. John Providence.
- Participants who have flu-like symptoms are observed and researchers collect blood samples, symptom diaries, and health histories.
- A sub-study could identify genetic markers that indicate who is more susceptible to the influenza virus and complications; another sub-study aims to improve methods for collecting information on the course of influenza illness.

Impact

The NIH will gather valuable information from St. John Providence researchers about the influenza virus and the strains that are found in different parts of the world. The goal is to improve prevention and treatment and discover which strains of the virus are more likely to cause serious health complications.

Oncology

Strategic chemotherapy regimen offers new hope for pancreatic cancer patients

Susan Lyons, MD, PhD
Hematology and Medical Oncology

Providence-Providence Park Hospital, Southfield Oncologist Susan Lyons, MD, PhD, together with a team of physicians from the hospital's Hepato-pancreatobiliary Surgery, Radiation Oncology, Gastroenterology, Pathology, Radiology, and Medical Oncology departments, are investigating whether a new chemotherapy treatment plan could enable more pancreatic cancer patients to benefit from surgery.

...patients who originally had cancer that could not be removed, now become surgical candidates.

"Pancreatic cancer is particularly difficult to treat, in part because it's often diagnosed at later stages," says Dr. Lyons. "Patients often cannot have surgery because the tumor is too large or because the cancer is impinging on blood vessels and other structures. Only 10 to 20 percent of patients are candidates for surgery to remove the cancer, which offers the best chance for survival."

In the last few years, a new chemotherapy regimen has been shown to improve survival for patients with advanced disease. The chemotherapy regimen, called FOLFIRINOX,is a cocktail of three chemotherapy drugs, and shows promise as a neoadjuvant therapy – a first step before the main, surgical treatment.

A course of therapy with FOLFIRINOX may shrink the tumor enough so that patients who originally had cancer that could not be removed, now become surgical candidates. Many hospitals and researchers around the country are conducting research with FOLFIRINOX for their patients, and the researchers at Providence-Providence Park Hospital, Southfield are included in that forward-thinking group.

"FOLFIRINOX improves survival for patients with advanced disease to a degree we have never seen before," says Dr. Lyons. "Our team reviewed multiple research protocols being conducted throughout the country and we developed what we believe is the best approach for care."

The team will treat non-surgical candidates with FOLFIRINOX , monitoring them closely with CT scans for changes in the mass. When the tumor has responded adequately, the patient can be scheduled for surgery. Their hope is to create a new subset of surgical candidates who will gain a significant "leg up" on beating their cancers. Following surgery, patients receive follow-up treatment with chemotherapy and radiation.

Dr. Lyons has recently embarked on the study and expects it to continue for at least two years. The goal is to enroll 25 to 40 patients.

"Our entire team is very excited about the possibilities this treatment may hold, and in our ability to bring treatment to patients locally," says Dr. Lyons.

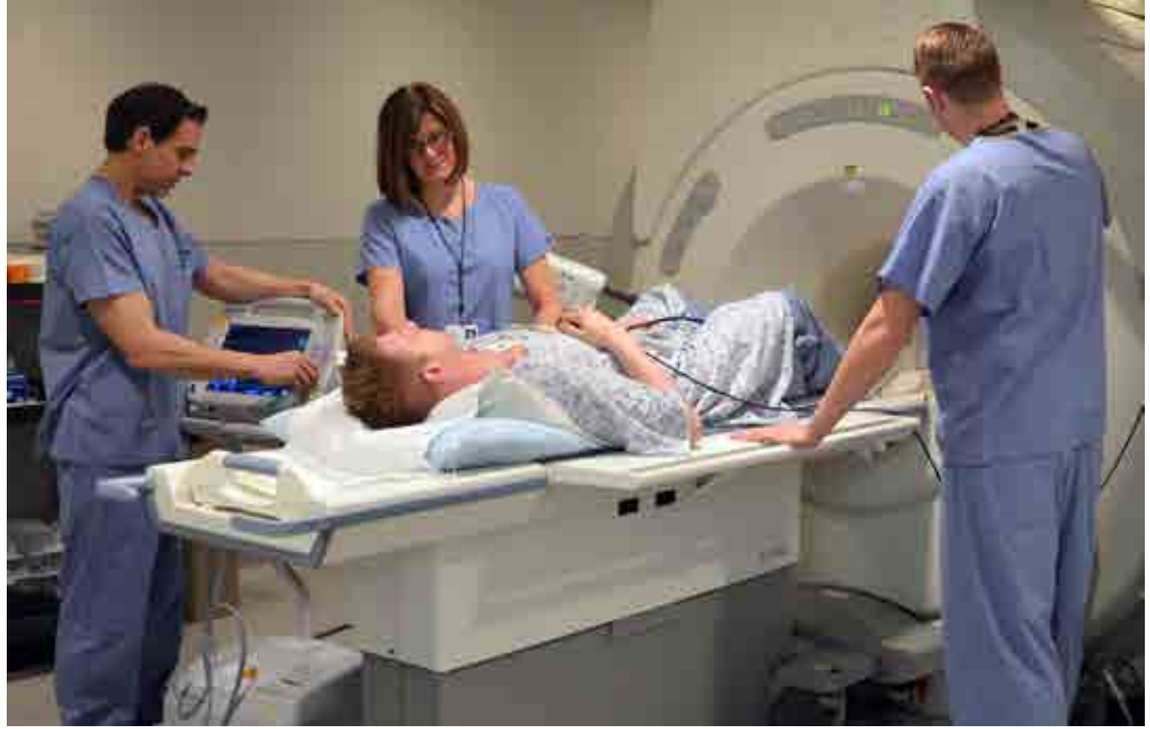
For more information, contact the Assarian Cancer Center, (248) 552-0620, or email slyons@newlandmedical.com

Neoadjuvant FOLFIRINOX therapy for pancreatic cancer

- Only 10 to 20 percent of patients diagnosed with pancreatic cancer are candidates for surgery to remove their tumors.
- A multidisciplinary team of Providence-Providence Park Hospital, Southfield physicians is conducting a study with the chemotherapy regimen, FOLFIRINOX .
- The regimen will be given to patients who are not surgical candidates to shrink their tumor enough to make surgery possible.

Impact

A FOLFIRINOX treatment regimen may enable a greater percentage of patients with pancreatic cancer to have surgery to remove their tumors.



Cardiology

Making MRI possible for patients with pacemakers and defibrillators

Christian Machado, MD
Cardiology/ Cardiovascular Disease/ Clinical Cardiac Electrophysiology Cardiologist

Pacemakers and defibrillators, implanted in the chest or abdomen to regulate abnormal or irregular heart rhythms, are essential for many individuals. In fact, more than three million people worldwide have pacemakers and almost 600,000 have defibrillators.

But until recently, having one of these devices meant being ineligible for an important diagnostic test – an MRI (magnetic resonance imaging). It was thought that the powerful magnetic and radio frequency fields generated during imaging would damage or inhibit the device and cause discomfort or even harm to the patient. Researchers at Providence-Providence Park Hospital, Southfield are leading the way to show that MRI is safe for patients with pacemakers and defibrillators and that they too, can benefit from this advanced diagnostic tool.

"In 2009, we performed a study at Providence-Providence Park Hospital, Southfield to show that MRI can be done safely for patients with pacemakers and defibrillators," says Christian Machado, MD, director of Electrophysiology Services at Providence-Providence Park Hospital and medical director of the Defibrillator and Pacemaker Clinic/Arrhythmia Device Clinic at Providence and Providence-Providence Park Hospital, Southfield. "We wanted to show that patients don't have to be denied the many benefits of a diagnostic MRI because they have these devices."

The study was published in the *Journal of Interventional Cardiac Electrophysiology* in December 2009, and together with similar studies, got the attention of the National Institutes of Health. The result was a national, multi-center trial, and Providence-Providence Park Hospital, Southfield was recruited to take part

The goal of the new study – the MagnaSafe Registry – is to examine the safety of MRI for patients with pacemakers and defibrillators on a large scale.

"We are the number one recruiting center for the MagnaSafe trial," says Dr. Machado. "There are 60 centers nationwide recruiting, and more than 1,500 patients have enrolled. We have 400 of those – more than one-quarter of the total. The study goal is to enroll 2,500 patients."

In the study, physicians only perform MRIs if there are highly compelling circumstances and when the benefits clearly outweigh the risks. The patient's cardiac device is examined before and after the MRI by a cardiologist, and physicians monitor patients during the MRI.

Preliminary results are positive. "There have been no deaths, device failures, generator or lead replacements, ventricular arrhythmias, or losses of capture during non-thoracic MRI," says Dr. Machado.

The results could change the published guidelines for performing MRI in patients with pacemakers and defibrillators, and provide patients and physicians with the risk-assessment data needed to assess the use of MRI as a diagnostic tool when no alternative diagnostic imaging technology is appropriate.

The MagnaSafe Registry

- Patients who were not candidates to receive MRI may soon be able to have the procedure safely.
- A Providence-Providence Park Hospital, Southfield study led to a nation-wide study headed up by the National Institutes of Health.
- Providence-Providence Park Hospital, Southfield is the lead recruiter in the national study, the MagnaSafe Registry.

Impact

Early results reveal that patients with pacemakers and defibrillators can safely benefit from MRI.

Every year, 225,000 people in the United States are diagnosed with non-small cell lung cancer. Half will have metastatic disease, in which the cancer has spread to another organ, also referred to as stage IV disease. The median survival time for cancer of this type is about 10 months.

Oncology

Immunotherapy research offers new hope for lung cancer treatment

Michael Kraut, MD
Medical Oncology

Patients with stage IV lung cancer have few treatment options. Surgery is not possible, radiation is not typically effective, and chemotherapy often fails after some time. For most patients, living about one year with their cancer is realistic. However, a national research trial exploring the effects of Nivolumab – a different type of drug – on non small cell lung cancer offers patients new hope.

"Nivolumab is the biggest advance in lung cancer treatment in at least 10 years," says Michael Kraut, MD, director, Providence Cancer Center. "In non-small cell lung cancer, it's rare for a patient to mount an effective immune response. The body doesn't recognize the cancer, and the molecules from tumor itself actually turn off an immune response. Nivolumab blocks the mechanism for turning off the immune system and allows the patient's own natural defenses to fight the cancer."

Earlier Nivolumab research involved patients with several different types of cancer. An unexpected result was that it also worked against non-small cell lung cancer.

"Researchers observed that if we can turn the patient's immune system back on, we get a brisk response to lung cancer and can treat the tumor for several months or longer," says Dr. Kraut.

Every patient enrolled in the study receives Nivolumab and can continue treatment as long as it is working. This research is considered a compassionate use trial, which means it is designed specifically to allow patients who need another treatment option the chance to try it before the drug has received FDA approval.

Dr. Kraut expects to enroll between five and 10 patients during the first year, but says it is possible demand for the drug will be so great that enrollment will exceed expectations. The only other research site in the area is located in Ann Arbor.

Like other autoimmune drugs, Nivolumab does have some side effects that come from "stirring up" the immune system. However, they tend to be mild and manageable, and don't interfere with quality of life.

"The goal for our lung cancer patients, and in all cancer care, is to offer the best available treatment and extend life with quality. Every oncologist wants the best treatment possible for their patients. Frequently, the best treatment comes in the form of a clinical trial," says Dr. Kraut. "We offer patients the best – or better than the best – treatment available."

Nivolumab was recently FDA approved for treatment of non-small cell lung cancer, clinical trials like this one that are an essential step toward obtaining FDA approval for any drug. It's important to note that researchers will not offer a clinical trial if any part of the study has been shown to provide clinically inferior treatment. The study will only give patients better or equal results than standard therapies.

Down the road, it's possible that a drug like Nivolumab could be combined with other treatments, such as chemotherapy.

"When standard treatment options have been tried and failed, we need to try something new," says Dr. Kraut. "There is a great need in the community for this clinical trial. We can offer patients access to a promising drug that is otherwise unavailable and potentially extend life and improve the quality of life. We are very excited to be able to offer Nivolumab to patients."

For more information about the Nivolumab clinical trial, call (248) 849-3188 or email Kathy.Honsowetz@stjohn.org.

The Nivolumab clinical trial

- Patients with non-small cell lung cancer often have few treatment options, especially when chemotherapy has failed.
- A national clinical trial, offered locally at Providence-Providence Park Hospital, Southfield and Novi, is examining the effectiveness of an immunotherapy drug, Nivolumab, against the disease.
- Nivolumab helps the body's own immune system mount an immune response against the cancer.

Impact

This drug could extend life and improve quality of life for patients with non-small cell lung cancer when chemotherapy has failed.

Oncology
Novel treatment disables lymphoma gene

Ayad Al-Katib, MD
Hematology and Medical Oncology

Beating lymphoma, or cancer of the lymph nodes, is a tough fight. Typically patients undergo chemotherapy, which causes debilitating side effects. However, the future of lymphoma care is looking brighter due to the combined ingenuity of several researchers and organizations in southeast Michigan.

Working in the laboratory in combination with Wayne State University, Ayad Al-Katib, MD, medical director of East Region Oncology and section chief of Hematology at St. John Hospital & Medical Center, and medical director of the Van Elslander Cancer Center, used a stretch of 24 DNA bases called oligonucleotides that bind with the gene that causes B-cell lymphoma, BCL2, and disables it. "It was exciting and proved that lymphoma cells depend on BCL2 for survival," says Dr. Al-Katib. "When we inhibited BCL2, the cancer cells died. This was proof of principle, but now we had a new challenge: How do we make this into a medicine that can be used to treat people with lymphoma?"

It's not possible to simply inject DNA into a person and let it go to work on "enemy" cells. The body's own enzymes defend against this kind of invasion.

"Our challenge was to package it in a way that would protect the oligonucleotides so they can reach their destination," says Dr. Al-Katib. "We turned to liposomes – tiny lipid pockets. These are created in the lab from the same material as cell membranes and can be filled with the oligonucleotides."

These lipid pockets measure just one billionth of a meter, and each one can hold and protect up to 300 oligonucleotides. This delivery system was developed in concert with ProNAi Therapeutics, Inc., a Michigan company located in Plymouth.

After extensive lab research that showed BCL2 was effective against lymphoma when injected into the body, the team was ready to conduct the first clinical trial with patients.

"In early research trials like this, we do not give a new medicine that is not proven as a first line of treatment," explains Dr. Al-Katib. "Our trial involved patients who had failed previous standard treatment. For 11 of the 13 patients, the new treatment was beneficial."

The success of the first clinical trial led to more funding, in particular, a grant from the National Institutes of Health to expand the study and make it available to additional patients. The novel treatment has been coined "DNAi," or DNA inhibition. It is the very first of its kind to be used in a clinical trial of this magnitude.

The clinical trial is another notch in the belt for medical research in southeast Michigan. Many individuals and organizations, including Dr. Al-Katib, St. John Providence, the Van Elslander Cancer Center, ProNAi, and Wayne State University were essential in discovering and developing the technology and bringing it to patient care through clinical trials.

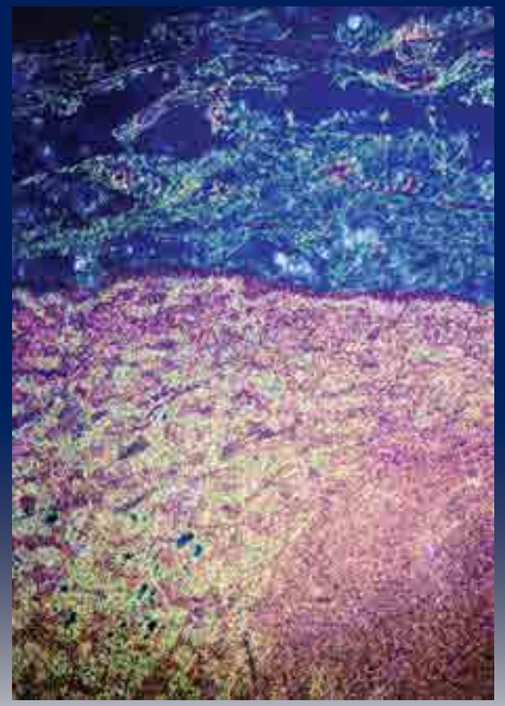
"This is the future of lymphoma care I've always dreamed about," says Dr. Al-Katib. "Genetic technology has the potential to be applied to inhibit any disease-causing gene. There is a long road ahead to continue developing this knowledge into treatment, but finally, we are getting to the genetic root of disease and attacking it there."

Treatment disables lymphoma-causing gene BCL2

- Southeast Michigan researchers, including St. John Providence Oncologist/Hematologist Ayad Al-Katib, MD, have developed a method to disable BCL2, the gene that causes lymphoma.
- Working together, St. John Providence, Michigan-based ProNAi and Wayne State University researchers have pioneered a method to package the disease-blocking DNA so it can be introduced into the human body and reach the BCL2 gene.
- Early research led to a grant from the National Institutes of Health to expand the clinical trial for patients with lymphoma.

Impact

Lymphoma patients who failed standard treatment now have an option in their fight against cancer. At the same time, this genetic technology could be applied to other disease-causing genes, creating an entirely new way to fight cancer and other diseases.



Cardiology

Lifesaving procedure could change aortic stenosis treatment

Thomas Davis, MD
Cardiology/ Cardiovascular Disease/ Interventional Cardiology

Patients with aortic stenosis typically require surgery to relieve the symptoms caused by the narrowing of their heart's aortic valve. They suffer from fatigue, faintness and dizziness, chest pain or tightness, and shortness of breath. While these symptoms make life challenging, when patients with aortic stenosis also develop heart failure, their average life expectancy falls to just two years or less.

Tom Davis, MD, director, Cardiac Catheterization Lab, Peripheral Vascular Intervention and Cardiac Research and co-principal investigator of the Medtronic CoreValve® System Trial at St. John Hospital & Medical Center, is conducting research that could change how patients with aortic stenosis and heart failure are treated. Sanjay Batra, MD, chief of Cardiac Surgery, St. John Hospital & Medical Center, is co-principal investigator of the trial.

"We are performing a non-surgical treatment for aortic stenosis that could eliminate the need for patients to undergo surgery for an aortic valve implant, which until recently was their only option," explains Dr. Davis. "Through a series of different studies with the Medtronic CoreValve® System, we have shown that the transcatheter procedure – which does not require open surgery – is safer and offers better outcomes for high-risk patients and patients who cannot tolerate surgery."

The outcomes are truly life changing. A patient in his mid-80s who has aortic stenosis but is relatively healthy otherwise may live to age 93 or longer following a successful procedure, and with a much higher quality of life. "For patients in otherwise good health, the procedure returns life expectancy to normal. They no longer have heart failure," says Dr. Davis. "Many patients are older, but there is no reason they cannot live many more years and enjoy them without the symptoms of aortic stenosis."

The Medtronic CoreValve® System replaces the patient's narrowed aortic valve through a minimally invasive, non-surgical approach. "Guided by a catheter inserted in the groin, we attach the artificial aortic heart valve to a wire frame. Once in the proper position in the heart, the wire frame expands, allowing the new valve to open and function. We do not open the chest and most patients recover with no visible surgical incisions," says Dr. Davis.

The procedure takes about one hour to complete, and patients can usually sit up in a chair later the same day or the next morning. After a hospital stay of five days or less, patients go home and usually return to normal activities within a week. Open surgery requires surgeons to break the patient's chest bone, which means a much longer recovery of one to three months following hospital discharge.

After a hospital stay of five days or less, patients go home and usually return to normal activities within a week.

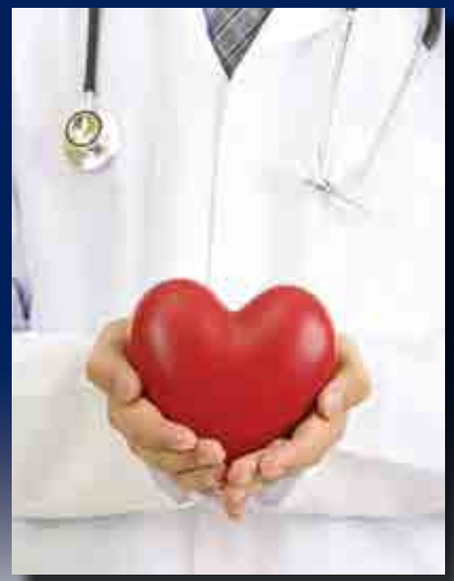
Studies have expanded to include patients at lower risk. With multiple study sites throughout the United States, Medtronic's goal is to achieve FDA approval when the clinical trials are complete. If that is accomplished, all appropriate patients with aortic stenosis will have access to the transcatheter procedure.

Any St. John Providence physician can refer a patient for the clinical trial, and patients outside the health system can self-refer. Simply call the St. John Providence Valve Clinic, (855) 98-valve (8-2583) or contact Renee Bess, BS, CCRP, study coordinator, at renee.bess@stjohn.org.

Accepted patients are randomized into one of two study groups. One group receives treatment with the Medtronic CoreValve® System, and the other group receives traditional open surgery. Patients are followed for five years. Costs not covered by insurance are generally covered by the study.

Dr. Davis reports that patients who have had the procedure are "gratified." One recent patient was up and walking around the hospital the next day. Prior to the valve replacement, he became short of breath just walking from his bedroom to the bathroom.

"Many high-risk patients would not even have been candidates for treatment because the risks of surgery were just too high," says Dr. Davis. "What it comes down to is, transcatheter valve replacement is a lifesaving procedure that may become the way we treat aortic stenosis in the future."



Non-surgical aortic stenosis treatment

- Patients with aortic stenosis have debilitating symptoms, and those with heart failure generally have a life expectancy of two years or less.
- St. John Providence cardiologists Tom Davis, MD, and Sanjay Batra, MD, are participating in the Medtronic CoreValve® System Trial to investigate the use of this non-surgical treatment.
- Instead of open surgery, which involves breaking the chest bone, surgeons insert the valve replacement through the groin in an hour-long procedure.
- Outcomes are the same or better than open surgery, and recovery is far quicker.

Impact

Transcatheter aortic valve replacement research could change the way aortic stenosis is treated, extend patients' life spans, improve their quality of life, and enable individuals who are not surgical candidates to receive treatment.

Orthopedics

Using an old antibiotic to strengthen joint replacements

David Markel, MD
Orthopedic Surgery

Weiping Ren, MD, PhD
Orthopedic Research

St. John Providence orthopedic surgeon David Markel, MD, in collaboration with Weiping Ren, MD, PhD, bone scientist, set out to find a solution to a common problem with joint replacements: Over time, friction between the mechanical parts of the implant produces tiny particles.

Joint Replacements in the US

- Over one million hip and knee replacements are performed in the US every year.
- Implants typically last 15 to 20 years.
- Approximately 10 percent require revision, but because people are living longer, this number is rising.

For some patients, the body's reaction to these foreign particles is an immune response – to dispatch macrophage cells to destroy the particles. Doing their work, the macrophage cells also destroy some of the bone around the joint replacement, resulting in bone erosion. This resorption of the bone causes joint replacements to become loose, and after 15 to 20 years, patients often need implant revision surgery. Several years ago, Drs. Ren and Markel asked the question: What can we do to strengthen the bone around the implant and make implants last longer?

"We have better and better joint replacement technology," said Dr. Markel. "People are receiving joint replacements at a younger age and living longer, and while technology has advanced so that the implant itself lasts many years, we haven't yet discovered how to keep the bone strong and solid enough to support the implant for the rest of the patient's life.

Typically, only 10 to 35 percent of bone attaches to the implant, but this provides enough strength to be very long lasting and strong. We want to make it possible for joint replacements to last as long as people are living with their new joints – as long as 30 to 40 years."

A possible solution comes from a familiar source: erythromycin. This common antibiotic was introduced in the 1950s and is effective against many bacterial infections, especially respiratory tract and skin infections. But discoveries show it may have other benefits.

According to Dr. Ren, "Over the past 10 years, researchers have confirmed that erythromycin is also effective in inhibiting particle-induced chronic inflammation in orthopedic settings. This is the same kind of wear we see in joint replacements. We wanted to know if the inflammation-fighting properties would affect bones. In the lab, we started with some pre-osteoblastic cells – cells that could become bone cells. We grew them in the presence of erythromycin, and discovered that erythromycin promotes bone cell growth."

Drs. Ren and Markel conducted further research, and showed that when a bone is connected with a metal pin and plastic particles are present in the joint resulting in bone loss (also known as osteolysis), oral erythromycin made the bone respond better and the joint became more stable.

"Now, we have resources at Providence-Providence Park Hospital, Southfield that allow us to continue our research on site," says Dr. Markel. "With these resources, we can speed our timeline and can bring research from bench to patients in a shorter time."

The next step in Dr. Ren and Dr. Markel's research is to examine the effect of oral erythromycin for patients undergoing hip or knee joint replacement revision surgery. After giving patients erythromycin before surgery, they'll examine any changes in the tissues at the time of surgery.

"We'll be looking for a positive biologic response and markers in the blood," says Dr. Ren.

But their work has a far more innovative end goal. They are working to innovate a delivery system that would bring the erythromycin directly to the implant and the bone using nanofibers.

These very thin fibers can be "infused" with erythromycin and potentially spun around the joint replacement. Once in place, the "coated" parts would deliver erythromycin slowly, strengthening bone over time, encouraging greater attachment between the bone and implant, and delaying or even eliminating bone wear.

"If we can find a way to deliver erythromycin to the bone that prevents the joint replacement from becoming loose over time, and enabling the bone to attach to it with greater strength and stability, we could be on the way to a groundbreaking development in joint replacement technology. It could change lives, making joint replacements a permanent solution for many people throughout the world," says Dr. Markel.

Joint replacement research

- Bone wear causes joint replacements to become loose, necessitating joint replacement revision surgery.
- St. John Providence orthopedic surgeon David Markel, MD and bone scientist Weiping Ren, MD, PhD, are examining the use of erythromycin on bone inflammation.
- Oral erythromycin may have a positive impact on tissues after joint replacement surgery.
- By innovating erythromycin-coated joint replacement technology, Drs. Ren and Markel could create a new delivery system, bringing erythromycin directly to the bone.

Impact

This research could eliminate loosening of joint replacements over time by strengthening bone, encouraging greater attachment between the bone and implant, and delaying or even eliminating the bone wear that causes joint replacements to become loose.

Neurology

SOCRATES trial is first of its kind for acute stroke treatment

Paul A. Cullis, MD
Neurology/Psychiatry & Neurology-Vascular Neurology

Bruce Silverman, DO
Neurology

After a patient has a stroke or transient ischemic attack (TIA), the risk of another stroke or TIA is high. A regimen of aspirin reduces risk by about one-third, but finding an equally or more effective alternative would reduce risk even more, especially for patients who can't take aspirin.

"Studies show that in the first three months following a stroke or TIA, more than 10 percent of patients will have another event," explains Paul Cullis, MD, section chief of Neurology and medical director of the Stroke Program at St. John Hospital & Medical Center.

"While aspirin is the most effective therapy available, some patients are allergic to aspirin. Aspirin can also cause upset stomach, and a number of patients cannot take aspirin due to a risk of bleeding."

Some alternatives to aspirin are available, but these drugs are not significantly more effective than aspirin and produce some side effects. To get closer to finding an alternative to aspirin that offers even greater benefit, Dr. Cullis and Bruce Silverman, DO, director of Neurosciences and the Stroke Initiative at Providence-Providence Park Hospital, Southfield and Novi, are participating in the worldwide SOCRATES Trial.

According to Dr. Silverman, "This very large, double-blind study is one of the first in history to examine acute prevention of recurrent stroke. The SOCRATES trial involves only a population at very high risk for a stroke. There is no evidence yet that any drug other than aspirin has significant benefit for stroke patients during this time frame. Perhaps ticagrelor will give better protection against recurrent stroke."

Participants are randomized into one of two study groups within 24 hours of having a stroke or TIA. One group receives the current approved treatment: aspirin therapy. The other group receives treatment with a drug called ticagrelor.

"Ticagrelor is a drug already on the market to prevent a heart problem called acute coronary syndrome, which is decreased blood flow to the heart," says Dr. Cullis, "but there is evidence that it could also be valuable in preventing stroke. The SOCRATES trial allows us, together with AstraZenica, the company that produces ticagrelor, to investigate if this medication could be more, less, or as effective as aspirin in preventing stroke or TIA in the first 90 days."

The physicians will follow patients closely for three to four months as outpatients through frequent phone calls and some follow-up visits. They expect to enroll

12 patients over the next year. If the study shows that ticagrelor is at least as effective as aspirin, it will provide an option for people who can't take aspirin. If results indicate it's even more effective than aspirin, it could change how patients are treated after a stroke or TIA, and potentially prevent future events.

"We will also continue working with patients to modify their risk factors for stroke. We want them to stop smoking, lose weight, exercise, limit alcohol use, and keep their blood pressure and cholesterol within normal ranges. But on top of that, medications like aspirin and now, potentially ticagrelor, play an important role," says Dr. Cullis.

The SOCRATES Trial

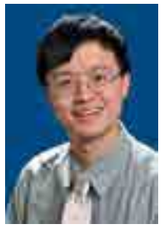
- Patients who have had a stroke or TIA have a 10 percent or higher chance of having another event in the first 90 days.
- Aspirin therapy is effective, but not all patients can take aspirin.
- The SOCRATES trial investigates the effectiveness of a different drug, ticagrelor, and is the first in history to examine acute prevention of recurrent stroke.

Impact

Ticagrelor could become an alternative or preferred therapy to aspirin for patients who have just suffered a stroke or TIA.

Otolaryngology

Study compares two hearing devices for single-sided deafness



Robert S. Hong, MD, PhD
Neurotology/ Otolaryngology

Providence-Providence Park, Novi was one of three centers that took part in a multicenter research study in 2014 examining the effectiveness of the Sonitus SoundBite, a non-surgical implant that transmits sound through the teeth, compared to the surgically implanted BAHA, Bone Anchored Hearing Aid, which transmits sound through bone. The BAHA has traditionally been used to improve hearing for individuals with single-sided deafness, but the SoundBite is now available as an option.

"Sonitus provided patients with the SoundBite at no cost, and many of our patients were interested in taking part in the study," says Robert Hong, MD, PhD, Otolaryngology/Head and Neck Surgery, Michigan Ear Institute at Providence-Providence Park Hospital, Novi. All study participants were already using the BAHA, and had the chance to try the SoundBite for a month.

"Through questionnaires and audiometric tests of speech and sound perception, the study offered a head-to-head comparison to determine if hearing through your teeth is comparable to the BAHA," says Dr. Hong.

Study participant George Kalso says, "I'm deaf in my left ear and always had trouble discerning where sounds originated when they were coming from behind me. The SoundBite provides better directional control and hearing, so I could tell where sounds were coming from.

"It also picks up different frequencies than the BAHA, so there were some voices I could hear better. It didn't pick up as much external sound, like nearby conversations, so with the SoundBite I didn't hear conversations I shouldn't have!"

Patients at the other study sites are in various stages of SoundBite testing. Data will be tabulated and released once the study is complete.

The Bone Anchored Hearing Aid (BAHA) is implanted in the temporal bone behind the ear and over several months, fuses with the bone of the skull. The implant converts sound waves into vibrations, which are carried via the skull to the bony portion of the inner ear, where they are converted into nerve impulses. Candidates must have hearing function in at least one inner ear to use the BAHA.

The Sonitus SoundBite is a non-surgical option available for patients who prefer not to use a hearing aid or have surgery. Similar to BAHA, this device transmits sound using bone conduction. However, patients wear a retainer in the mouth that conducts vibrations to the inner ear via the teeth. It is non-surgical and completely removable.

Sonitus SoundBite study

- Providence-Providence Park Hospital, Novi is participating in a study that enables patients already using the BAHA, an implanted device, to experience the SoundBite and compare effectiveness of the two devices.
- Individuals with single-sided deafness can experience hearing through the teeth using the Sonitus SoundBite.

Impact

This research will help patients and their physicians gain insight into which device will provide more benefit for their hearing and better fit their lifestyle.

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