



Making good on a promise

2016-2017 Annual Report



Feinstein Institute for Medical Research
Northwell HealthSM

▾ Promises delivered



Saving lives from sepsis

In May 1985, Kevin J. Tracey, MD, was working as a neurosurgery resident when he met Janice. At 11 months old, she had crawled on the kitchen floor under her grandmother's legs, causing her to trip and accidentally spill a pot of boiling pasta water onto her granddaughter.



1 million Americans are diagnosed with sepsis annually — 50 percent of cases are fatal.

We aim to know the early signs of sepsis.

Severely scalded over most of her body, Janice was Dr. Tracey's patient for a month. In the end, she went into shock and died in his arms. She had no evidence of infection.

"Her shock was unexplainable, and I was haunted by her case. She was so innocent, yet I was at a complete loss to understand the mechanism for her death," said Dr. Tracey. "I went into the laboratory in July and began to study the molecular basis of shock and inflammation. I promised myself I would find out what happened to Janice and make sure there were less cases like this. I have been studying it ever since."

Today, we know much more than we did in 1985. We know that what Janice faced was sepsis — the body's overreaction to infection that leads to organ deterioration and ultimately loss of life. Sepsis affects more than one million Americans each year, and 50 percent of those affected die. Dr. Tracey's lab continues to study sepsis. The Northwell Health Sepsis Task Force, headed by Martin Doerfler, MD, is taking Dr. Tracey's work and bringing it into clinical

practice. Knowing that early detection and a shortened diagnosis time are key to preventing loss of life to sepsis, Drs. Doerfler and Tracey identified a protocol based upon rapid assessment of signs of organ injury, which includes administering fluids and antibiotics immediately upon diagnosis. This protocol was implemented across Northwell Health's hospitals in 2008.

Ryan Barnett is one of thousands of lives saved because of this work.

"My son's pediatrician told me that he had a stomach virus, but mother's intuition told me otherwise. And when Ryan got worse, the ambulance took us to Northwell Health where immediately they recognized he had sepsis," said Kathleen Theune, Ryan's mother. "Ryan is alive today, playing lacrosse and acting like a normal teenager, because of Northwell Health knowing better. I couldn't be more thankful for the research and protocols in place so that I still have my son with me."

To view a video about our efforts in sepsis, visit bit.ly/2p1CO8b or scan the QR Code at the right.





Intervening schizophrenia

John M. Kane, MD, Feinstein Institute professor and senior vice president, Behavioral Health Services, Northwell Health, has worked at Zucker Hillside Hospital for more than 30 years. Over that tenure, he became a champion for those suffering from schizophrenia, dedicating much of his professional medical career to research on the condition.

3.5 million Americans are living with schizophrenia.
We're working to make sure they receive the care they need sooner.

“One of the first patients I treated with schizophrenia in medical school was a young man around my age who was bright, very well educated, but he had these fixed false beliefs called delusions,” Dr. Kane said. “It was hard for me to understand how anyone, especially someone that was at a similar stage in life as me, could believe the things that he believed. The patient had been hospitalized more than once before he came under my care and was not doing as well as hoped. It was this man who inspired my research into schizophrenia — I wanted to solve this puzzle and help patients maintain a normal course of life.”

Dr. Kane’s initial research explored the effects of medication to treat schizophrenia and was integral to the research that led to the first US Food and Drug Administration (FDA)-approved medication for treatment-resistant schizophrenia.

Dr. Kane’s line of study most recently has focused on the early intervention programs for mental illness. “Early identification and engagement in treatment is an important component to improved mental health because we were seeing that the duration of untreated illness was remarkably long and recovery rates from a first episode of schizophrenia were not great,” Dr. Kane said. “We also found that the duration of illness before someone receives any treatment was a predictor of outcome.” He and his colleagues set out to develop and implement a coordinated specialty

care model to improve the trajectory of early phase schizophrenia called the RAISE Early Treatment Program. They conducted a study involving 34 community care clinics in 21 states across the US. The RAISE program looks to act early on identifying and treating patients with schizophrenia. Clinicians using the RAISE program found that those patients who received coordinated specialty care, intended to optimize medication management and provide individual as well as family therapy and psychoeducation along with supported employment or education, made greater strides in improvement and return to work or school over the first two years of treatment than patients who received usual care.

Based on the findings of this study, Dr. Kane is now a public advocate for early intervention programs, and has spoken before congressmen about their benefits. His testimony likely influenced the 21st Century Cures Act, a 2016 law which includes a provision requiring states to use at least 10 percent of their mental health block grants on early intervention for psychosis. This important piece of mental health legislation inspired by Dr. Kane’s work will help to fund early intervention, and ultimately improve outcomes for this population that he has dedicated his life to help.



Pursuing science and advancing women

The curriculum of the all-girls high school that Betty Diamond, MD, attended emphasized history and literature, so she pursued art history in college until senior year when she thought to herself: “What am I going to do with an art history degree? I don’t want to teach.” When she realized that science was more interesting to her, she attended a summer science program.



46% of those working in life, physical and social science occupations are women.

We are looking to empower women to continue to grow within the scientific arena.

At the end of the program, during an evaluation of her scientific potential, she was told that she would have to choose between an interest in science and an interest in men. She decided to go to medical school. From the moment Dr. Diamond learned about lupus in medical school, she knew she wanted to study it and make a difference in the lives of patients suffering from autoimmune diseases.

Today, Dr. Diamond is the head of the Center for Autoimmune and Musculoskeletal Disease. She leads a laboratory and center of scientists and doctors dedicated to researching and treating major types of autoimmune disease, including arthritis, lupus, hearing disorders, multiple sclerosis, spinal cord injury and disc degeneration. Dr. Diamond is consistently one of the top recipients of NIH funding in the New York metropolitan area.

Throughout her scientific career, Dr. Diamond has remembered how she was told during high school that she would have to choose between science or men. She faced other gender biases and inequalities, and while she recognized these as unfortunate incidents that often arise from habit, misplaced energy or inattention, rather than from malice, she was motivated to ensure a supportive environment for women at the Feinstein Institute.

“The facts are that female scientists have lower salaries than their male counterparts, need to have more publications to be

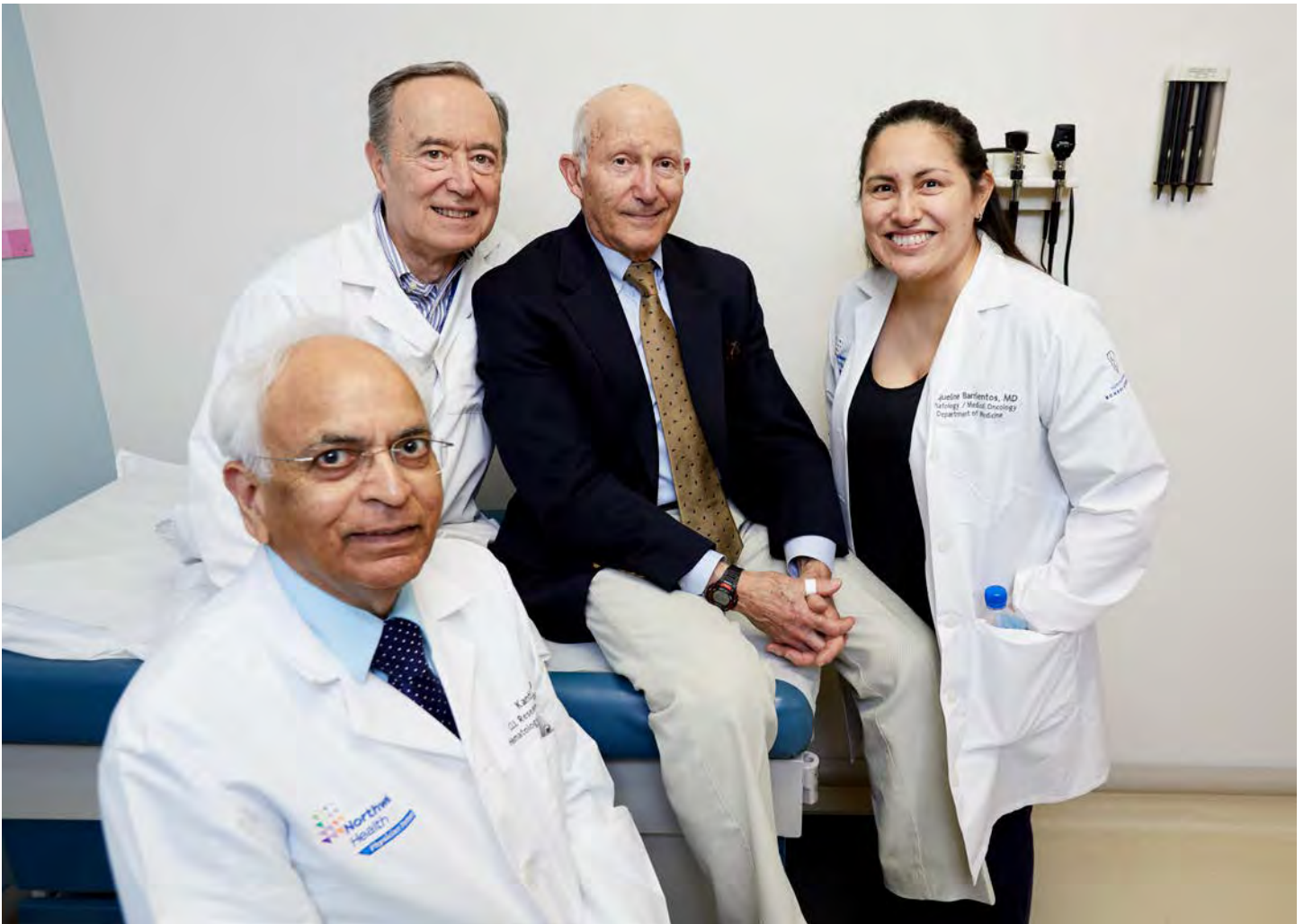
considered for promotion, and only a very few are chosen to write reviews and speak at national meetings,” said Dr. Diamond. “Furthermore, what may be surprising is that we have learned that women, themselves, contribute to the lack of advancement of women scientists — they can be competitive more than collaborative and too insecure to be supportive. If we look at successful women, we see that what they have in common is someone providing encouragement and advocating for them in professional fora. What we need instead of more anger, more self-pity or more amassing of data is self-confidence, empowerment and mutual support.”

With this in mind, and with a community of interested women, Dr. Diamond and several others started an organization of female scientists call AWSM (pronounced “awesome”), which stands for Advancing Women in Science and Medicine. AWSM aims to empower women and provide them with financial support, positive reinforcement, scientific critiques and assistance, recommendations for advancement and professional opportunity within the institution and at national and international organizations. The group also reaches young women in high school, college and thereafter who are interested in science. Their main goals are at least two-fold: 1) to aid scientists during a time when support from many private and government sources is low, and 2) to re-educate female and male colleagues through performance,

ability to nurture and support, self confidence, willingness to engage, and intelligence. AWSM has made great strides since its beginnings in 2010. They have raised \$605,000 in donor support. Most importantly, women scientists at the Feinstein Institute are more successful and are finding more satisfaction in their work.

“AWSM has achieved success in gaining recognition for women in science and showcasing their impressive achievements,” said Kevin J. Tracey, MD, president and CEO of the Feinstein Institute. “The initiative is important to the Feinstein Institute. We want to ensure that women in science feel supported and celebrated today and in the future.”

“We need to maintain our progress and continue to demonstrate that the diversity in the workplace contributes to a better work product and a better community,” said Dr. Diamond.



Battling leukemia for 60 years

Kanti R. Rai, MD, made a promise 60 years ago that has saved hundreds of lives. While still a resident in 1958 at North Shore University Hospital, Dr. Rai observed the case of a three-year-old girl named Lori who was diagnosed with acute childhood leukemia.

20,110 new Americans will be diagnosed with CLL. We're looking to extend the lives of each and every one.

While treatable — and even curable today — this condition was a death sentence at the time. Despite administering all available treatments, Lori passed away after six months. Devastated that Lori couldn't be saved, Dr. Rai promised that he would devote himself to saving others from leukemias and other cancers.

"After the death of Lori, my teacher and mentor Dr. Arthur Sawitsky suggested I go into research so I did," said Dr. Rai. "During the course of my research, in the clinic, I was seeing two patients with chronic lymphocytic leukemia (CLL). One had been suffering from CLL for 12 years and was still doing well and living a full life, while the other was diagnosed under a year ago and was close to death. I had to find out why there was such a disparity in prognosis."

In the 60s, after conducting 10 years of research with Dr. Eugene Cronkite as his mentor at the Brookhaven National Laboratory, Dr. Rai developed the Rai Staging System, which is still used today by medical professionals to help determine severity and course of treatment for CLL. CLL is a cancer of the blood and bone marrow and the most common type of leukemia in adults.

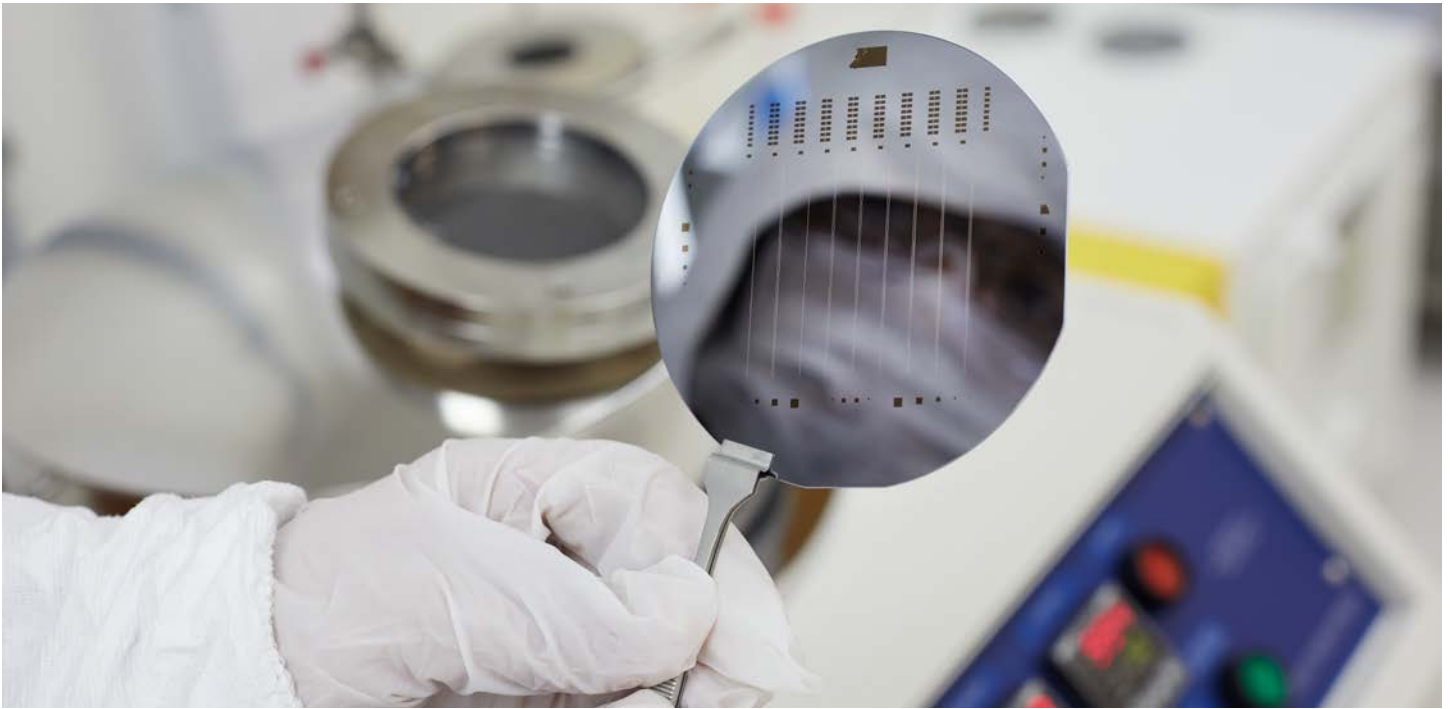
Since then, Dr. Rai has acted as an educator and mentor, helping to inspire the next generation of researchers who are studying CLL. He currently collaborates with Nicholas Chiorazzi, MD, and Jacqueline Claudia Barrientos, MD, who continue to make discoveries in the diagnosis and treatment of CLL.

Drs. Rai, Chiorazzi and Barrientos' most recent research has focused on the activation and maturation of B-lymphocytes in CLL. CLL cells are responsive to signals, in particular those delivered by the B-cell antigen receptor (BCR), leading to leukemic cell growth or death. They have found that the type of BCR a patient has can influence the progression of their disease. These findings have led to further refinement of patient prognosis. The team is also conducting clinical trials of various drugs and chemo-immunotherapies.

The results of this lifetime dedication can be experienced in the stories of grateful patients. Abe Bernstein is one of them. Mr. Bernstein participated in a clinical trial led by Drs. Rai, Barrientos and Chiorazzi. Thirty days after being treated in the clinical trial, Mr. Bernstein, an avid runner for more than 50 years, participated in the Penn Relays, the oldest track and field event in the US. At age 75, while undergoing treatment, Mr. Bernstein was able to not only compete, but he also took third place in the 100 meter in the 75 to 79 age group. Now that his cancer is in remission, Mr. Bernstein continues to compete and is one of the top three US track competitors in his age bracket.

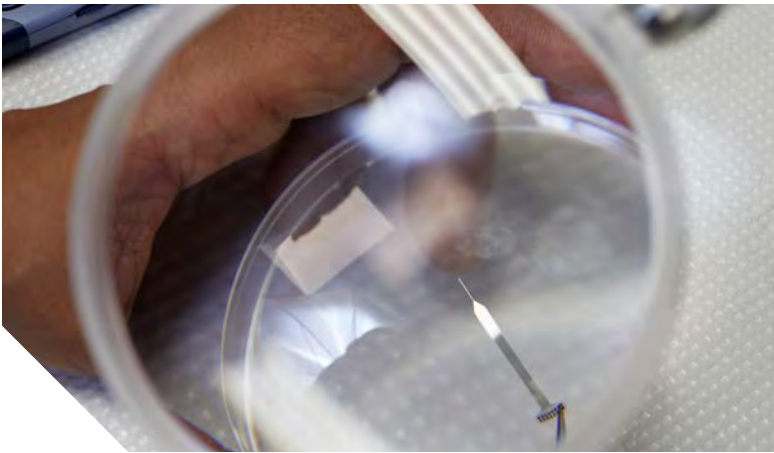
"Without Dr. Rai, Dr. Barrientos and Dr. Chiorazzi's research, I would be dead," Mr. Bernstein said. "Thanks to their discoveries, I have been able to maintain the active life I was living before being diagnosed with CLL. In fact, it seems I might be healthier today — the last time I ran in the Penn Relays back in 1960, I did not place. Now I was able to win third place!"

Future promises



Using nerves to treat disease

Imagine a day when microchips replace most drugs. This might sound like a science fiction novel, but with Feinstein Institute research, bioelectronic medicine could make this a reality, and sooner than you might think.



45 million patients are living with conditions — from paralysis to diabetes — that bioelectronic medicine could help improve.

We aim to harness the power of the nervous system to treat these conditions.

Through investment in cutting-edge resources, expert staff and strategic partnerships, the Feinstein Institute's Center for Bioelectronic Medicine (CBEM) is the engine driving this new area of medicine. Findings made in the center prove bioelectronic medicine is a promising treatment for a variety of conditions.

"Within the last year, we opened five new labs, including the only Class 100 clean room in Nassau County, Long Island," said Chad Bouton, director of the Center for Bioelectronic Medicine. "With these new labs, we are developing new bioelectronic medicine devices aimed to treat a variety of medical conditions. When we couple these new capabilities with our existing expertise, there is no doubt in my mind that we will innovate an entirely new class of treatment options for patients."

In a study published in the prestigious *Proceedings of the National Academy of Sciences*, researchers from the Feinstein Institute, Academic Medical Center/ University of Amsterdam and SetPoint Medical found that an implantable bioelectronic stimulation device could reduce the pain and inflammation in

patients suffering rheumatoid arthritis. The findings of this study show that instead of treating rheumatoid arthritis with pharmaceutical agents that are costly, often not effective and have numerous side effects, in the future it could be treated with a stimulation device, which is implanted once and does not produce harmful side effects.

Bleeding and hemorrhage is another area of focus for the Center. Even though there are more than half a million blood loss deaths each year, the treatment for bleeding (wrapping a rubber tourniquet around the wound) hasn't changed since their first use in ancient Greece more than two thousand years ago. The Feinstein Institute is developing the Neural Tourniquet — a medical device that uses electronic vagus nerve stimulation to reduce blood loss. We envision a day when the Neural Tourniquet could be used by first responders to car accidents to treat bleeding trauma victims and by fellow military personnel to treat the blood loss of wounded service men and women on the battlefield. In 2016, it was announced that the Feinstein Institute, the Global Good Fund, a collaboration between Intellectual Ventures and Bill Gates, and

Sanguistat Inc., are partnering on clinical trials of the Neural Tourniquet to evaluate its efficacy in treating blood loss associated with postpartum hemorrhage, the leading cause of maternal deaths worldwide, killing close to 80,000 women in Africa and Asia, and approximately 6,000 in the US each year.

Beyond rheumatoid arthritis and bleeding/hemorrhage, Feinstein Institute researchers are finding new ways to understand the language of the nervous system to perform advanced diagnostics with immediate plans to look into devices to treat paralysis. They are developing bioelectronic technologies to decode and re-route signals around devastating spinal cord injuries to restore movement in paralyzed patients and intend to start tackling restoring the sense of touch. This research may be applied to treating stroke and brain injuries in new ways as well as provide a foundation for advanced neural signal detection, which may be used to diagnose and treat disease earlier in its progression. Other conditions the CBEM team will study as candidates for bioelectronic medicine include diabetes, lupus, hypertension, post-transplant tolerance induction and potentially cancer.

To view a video of our work in bioelectronic medicine, visit bit.ly/2p1wT3j or scan the QR Code at the right.





Using robots to regain movement

Like most patients who suffer from strokes, there was no warning that Kathleen Taravella would experience a blockage of blood to her brain. She went to bed, only to wake hours later with a feeling that something was not right.

Ms. Taravella roused her husband, Santo, who helped her reach the care she needed to survive and begin the process of recovering from her incident.

A stroke occurs when blood flow to the brain is interrupted, typically by a blockage in a blood vessel. Depending on the portion of the brain affected by the stroke and the extent of the damage, patients may experience a variety of post-incident side effects including muscle weakness, cognitive difficulties and vision and language problems.

“My child was very young at the time of the stroke, so I was worried that, with my limitations, I would not be capable of being a good mother,” Ms. Taravella said. “I was

given the opportunity to participate in a clinical study using robotics, and I went for it. Whatever I could do to be the mother I envisioned, I was going to do.”

Ms. Taravella began rehabilitation with Bruce T. Volpe, MD, and Johanna Z. Chang and their team in the Laboratory for Stroke Rehabilitation Research. Using technology developed in collaboration with investigators from Massachusetts Institute of Technology (MIT), the Feinstein Institute team mapped out a treatment plan that included the use of a series of robotic devices. Active assist devices are robots designed specifically to help patients similar to Ms. Taravella with limited mobility in their arms, hands and legs. During a typical therapy session, patients’

6.3 million adults in the US have a stroke each year.

We aim to restore their ability to move.

arms are connected to a robotic arm with a joystick-like handle. In front of the patient, a monitor displays a target. Patients must move their limbs to match up with different points around the target. These points move, and the patient must speed up to reach the target and make movements with more precision.

Under the watchful eye of Ms. Chang and her support staff, patients complete the series of movements to the best of their abilities. When they are not successful, the robot steps in, putting their limbs through the completed motion. Feinstein Institute researchers hope these devices will help train the impaired limb to repeat motions on its own over time and that the challenge will help maintain patients' motivation and attention.

"Using the Feinstein Institute's robot program is like playing a video game, and it helps me push myself harder," Ms. Taravella said. "After my session is finished, even though it is challenging, I want to do more so that I can regain use of my arms and legs."

Under Ms. Chang's guidance, Ms. Taravella's therapy was expanded to include bioelectronic stimulation, another advanced treatment protocol being explored by researchers at the Feinstein Institute. In these trials, stroke therapy with robotics is combined with external stimulation. Patients who have had a stroke experience increased activation of their spinal cord signals, which causes muscles to tighten. This can present as hands being permanently clenched, making fine motor skills difficult.

Ms. Chang believes that stimulation can help quiet the noisy signals of the spinal cord so the body's motor system can take over. She and her team are conducting two studies into the use of nerve stimulation in stroke patients and plan to publish study results within the next year.

"The latest studies we are conducting are noticeably improving patient's mobility not only during an on-site session, but also after a session while at home," said Ms. Chang. "This is why I love my job and working with my team — it is clear that our research and technology are helping those recovering from stroke live the lives they lived before stroke, and you can tell they are so thrilled and appreciative of that."

"After rehabilitation with the robots and receiving stimulation, I can move my arms and legs better," Ms. Taravella said. "I no longer worry about not being a good mother. With Johanna's help, I am able to do what I need to do to be the mother I want to be."

"This is why I love my job and working with my team — it is clear that our research and technology are helping those recovering from stroke live the lives they lived before stroke, and you can tell they are so thrilled and appreciative of that."

-Johanna Z. Chang

To view a video of our stroke robots, visit bit.ly/2oIXbEI or scan the QR Code at the right.





Creating digital solutions for patients

Mobile devices have become a part of our daily routine and very soon could play an active role in health care and medical decision-making.

Over the past years, mobile health solutions have been developed to address serious issues in behavioral health. Much like mobile devices have changed how we conduct business and interact with friends and loved ones, they have also begun to impact health care by offering support for patients with chronic conditions and guidance in decision-making. Feinstein Institute researchers harness mobile technology's potential to impact patient care by developing digital solutions to help with everything from reducing problem drinking to providing personalized health decision support.

For those who face excessive social or binge drinking, finding a successful treatment plan is often challenging. Like many behavioral health issues, treatment for problem drinking requires multiple support systems like one-on-one therapy and mutual support groups. Frederick Muench, PhD, Feinstein Institute researcher and director of Northwell Health's Digital Health Interventions in Psychiatry, theorized that text messaging might help reduce problem drinking for patients. His studies confirm that when people affected by problem drinking receive texts tailored to their current situation and past drinking



15.1 million adults in the US have an alcohol use disorder.

We're designing tools to reduce that number.

behaviors, they reduced their drinking just as much as others who received in-person treatments. The availability of mobile systems, like Dr. Muench's, could provide instantaneous support for patients facing real-world challenges and offer access to treatment in remote areas, where attending therapy may not be convenient.

In addition to problem drinking, Dr. Muench studies other areas of behavioral health, including impulsivity control issues. Recently he has partnered with Cornell Tech and Sage Bionetworks to design smartphone-based tools to support patient efforts to change impulsive behaviors and improve resistance to unhealthy temptations.

A second area of active behavioral research at the Feinstein Institute involves support for patients making treatment decisions after a cancer diagnosis. In particular, newly diagnosed prostate cancer patients not only have to cope with a cancer diagnosis but also need to consider different treatment recommendations that can affect very personal aspects of life, such as incontinence and impotence. To help guide their decision, Michael A. Diefenbach, PhD, Feinstein Institute researcher and director of Northwell Health's Behavioral Research, has developed a web-based decision-making tool that allows patients to reconcile their personal values and lifestyles with a treatment recommendation.

The software prompts patients to consider a series of statements regarding different treatment implications that helps them evaluate each treatment option. The results from this brief evaluation can then be used to more thoroughly discuss their preferred treatment with their health care provider.

"We like to treat each patient as an individual and offer solutions that can be implemented into their lives and daily routine," said Thomas McGinn, MD, MPH, senior vice president, Physician Network Operations, and deputy physician-in-chief, Northwell Health, chair of medicine, Hofstra Northwell School of Medicine. "Those who suffer from addiction or cancer often want privacy and the ability to make treatment decisions based on their own preferences. The applications being developed by Dr. Diefenbach and Dr. Muench empower patients to do that by offering resources on their personal mobile devices."



Personalizing treatment through a living biobank

Over the last decade, physicians and scientists have become increasingly aware that genetic factors dictate our physical and mental characteristics, and can be used to detect and manage a wide range of health problems.

Feinstein Institute researchers are diving deeper and examining the genetics of those that are sick and those that are well to find a genetic definition of “what is well.” Defining “what is well” can help medical professionals see, depending on that person’s particular genetics, what is required to bring a patient to health. Through research using the biobank, Northwell Health researchers and doctors hope to soon use a patient’s own DNA to develop a personalized treatment plan.

The Northwell Health biobank, overseen and maintained by Peter K. Gregersen, MD, and James M. Crawford, MD, PhD, is one of the largest and most diverse collections of blood and tissue in the New York metropolitan area. Samples for the

biobank come from Northwell Health’s 21 hospitals, which serve the most culturally diverse population in the US. Having such a diverse pool to study is advantageous to research because it allows examination of how different factors such as age, race and medical histories play into different diseases and conditions. Through strategic affiliations, we also provide the samples from our biobank to researchers outside of Northwell Health, giving them access to samples they wouldn’t have access to otherwise.

“With the biobank, we are aiming not only to advance research and discovery but to establish new standards of care for patients,” said James M. Crawford, MD, PhD, executive director and senior vice president



1.6 million Americans will be diagnosed with cancer this year.

We aim to use genetics to develop a targeted diagnosis and treatment plan.

of laboratory services for Northwell Health, who has been integral in growing Northwell's biobank. "The system we have established with the biobank can be seen as a circle — Northwell Health provides patient care and obtains tissue or blood that can be used for research; the discoveries can then be brought back from partners like Cold Spring Harbor Laboratory, the Feinstein Institute and others to Northwell Health patients for first-to-human clinical trials and therapy."

The biobank is a critical component of a successful strategic partnership in cancer with Cold Spring Harbor Laboratory (CSHL), a leader in molecular biology and genetics research. One of the reasons why cancer is so difficult to treat is because the cells in a tumor do not necessarily share features with their tissue-of-origin — they can exhibit the genetic characteristics of a different type of cancer. For example, a patient could have colon cancer that exhibits the same genetic characteristics typically found in lung cancer. This is where the biobank can be an asset to treatment. A patient's tissue is taken during a procedure and brought to the lab to grow a copy of the patient's tumor and then test that tumor's genetic and functional characteristics. Once these characteristics are determined, the team can best identify an effective treatment for that patient. Going back to the example, it may be best to treat a patient's colon cancer tumor with a treatment for lung cancer based on those genetic and functional characteristics.

A new member to the Feinstein Institute, investigator Kenan Onel, MD, PhD, is helping to spearhead the Institute's genomics initiatives and is using this research to find treatments for pediatric cancer. Dr. Onel sees children as a potential barometer for

the genetic causes of both pediatric and adult cancers because their bodies have not been exposed to as many environment or lifestyle factors as their adult counterparts. One of his studies is GREAT Kids (Genomics for Risk Evaluation and Anti-cancer Therapy in Kids), which is examining the genetics of children with cancer and their family members to look for early indicators of the disease. The hopes of this study are to help prevent the patients' other family members from getting cancer and translate genetic markers found into cancer identifiers for other patients. Dr. Onel's research focus then goes beyond cancer, through his LIFE (Long Island Family Empowerment) Project, which will follow 20,000 children treated by Northwell Health and their parents for their entire lives to examine the genetic and environmental factors which contribute to different health conditions. By understanding what contributes to disease and wellness, Dr. Onel and his team hope to develop preventative diagnostics and more targeted treatment.

Feinstein Institute Professor Peter K. Gregersen, MD, an expert in genetics, has established a unique biobanking program called the Genotype and Phenotype (GaP) registry. The GaP is essentially a "living biobank" of volunteer subjects who agree to be recalled for specific research studies based on their genetic makeup. Over 7,000 volunteers have signed up for the GaP over the last decade, and over 80 research studies have been carried out using this resource, including by investigators from leading research institutions nationwide. An expansion of the GaP to 50,000 volunteers is planned in order to accommodate interest from researchers around the world.

One such study is directed to developing new diagnostic and treatment approaches

for endometriosis. Endometriosis, which affects approximately 176 million women globally, is a condition in which tissue from the uterus grows outside the uterus, causing significant pain and discomfort — it may even lead to infertility. It often takes more than 10 years to diagnose as it can be mistaken for other conditions, and to confirm that it is endometriosis, patients have to undergo surgery. Dr. Gregersen's team is developing a novel test that may allow for early diagnosis of the disease so that patients may be treated early and not have to undergo surgical treatments.

Drs. Crawford and Gregersen and George Raptis, MD, senior vice president, Cancer Service Line, acting executive director, Northwell Health Cancer Institute, are working to expand the scope of the benefits of the biobank to help all patients who enter Northwell Health hospitals. Following patient consent, Northwell Health hospitals will be able to test patients' blood with a DNA "chip" called the Global Screening Array (GSA), which can quickly characterize a person's DNA and identify particular genetic markers of disease. The information from this test can help medical professionals more rapidly diagnose conditions and develop a personalized treatment plan. Patients will also have the option to have these samples included in the Northwell Health biobank to help move research forward with the goal of providing personalized treatment based on genetics.

"Northwell Health is one of the first health organizations to incorporate a GSA into its standard diagnostic protocols," said Dr. Gregersen. "This cutting-edge technology will help to accelerate diagnosis and identify effective treatment while also providing data to help researchers develop the next generation of targeted therapies."

Empowering imagination. Pioneering discovery.

Science + Discovery

Volume 2, 2018

Data drives new
perspectives on
health care



**Feinstein Institute
for Medical Research**
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and Outcomes Research**

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Listening to the body to cure disease

Researchers identify best recording methods for vagus nerve to expand knowledge in bioelectronic medicine.



The vagus nerve is a nerve in our neck that connects to every major organ and communicates changes in our bodies to our brainstem, including infection and inflammation which are a part of diseases like sepsis, hypertension, Crohn's disease and rheumatoid arthritis. Mapping the signals transmitted in the vagus nerve will help identify neural pathways, and develop bioelectronic medicine

technologies that target these neural pathways to treat various diseases.

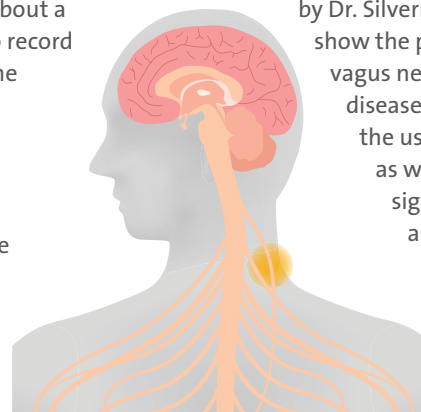
Bioelectronic medicine is an emerging field of medicine that combines neuroscience, molecular biology and bioengineering to tap into the nervous system to treat disease and injury without pharmaceuticals. Scientists Harold A. Silverman, PhD, and Sangeeta S. Chavan, PhD, recently published their novel findings in the medical journal *Bioelectronic Medicine* about a standardized method to record signals transmitted in the vagus nerve.

"We can use this new understanding to develop devices that simultaneously diagnose and treat disease" says Dr. Silverman.

"By catching certain symptoms early,

we may be able to better treat or even prevent the major symptoms associated with diseases," says Dr. Chavan

Researchers like Dr. Silverman and Dr. Chavan in the Centers for Biomedical Science and Bioelectronic Medicine are mapping the signals of the nervous system so that we can listen for signs of disease or injury. Using bioelectronic devices and methodology to record signals in the vagus nerve, such as used by Dr. Silverman and Dr. Chavan, show the potential to harness vagus nerve activity to treat disease and injury without the use of pharmaceuticals as well as reducing significant side effects associated with drugs.



The next generation of top scientists

A summer intern at Northwell Health's Feinstein Institute for Medical Research was named a finalist in the prestigious Regeneron Science Talent Search.

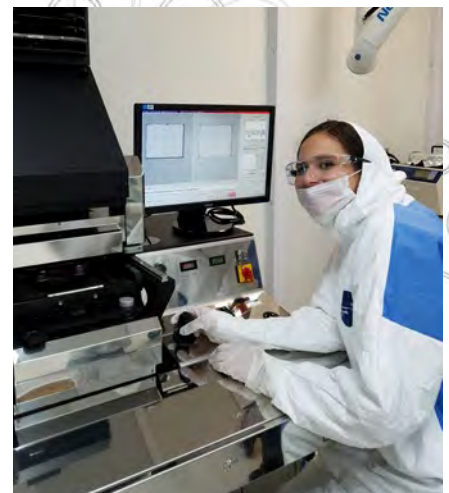
Caroline Smolensky, a senior from Woodbury who attends St. Anthony's High School in South Huntington, is a finalist in the 2018 Regeneron Science Talent Search. Under the mentorship of the Feinstein Institute's Chunyan Li, PhD, and Raj Narayan, MD, she designed, built and tested a brain implant device that detects secondary injuries after a traumatic brain injury (TBI).

"I have a responsibility to encourage young scientists, but I also get a lot out of it personally," said Dr. Li. "They are so creative and their ideas are so original, I find myself inspired by them."

The Feinstein Institute Summer Student Intern program is a competitive program for high school, college and graduate students. Leading Feinstein Institute researchers select promising students to join their labs and complete original projects over the course of eight weeks.

"We worked with Caroline to develop and execute her project, which was not easy to accomplish in such a short period of time, because it was a complex idea," said Dr. Li, an assistant professor.

The 2018 Summer Student Intern Program is now closed, but to find out more information about applying for the 2019 program, please visit bit.ly/research-intern.





Developing opioid-free pain control for breast reconstruction surgery after cancer

New treatment shortens hospital stay and reduces risk of addiction.

Two million Americans suffer from opioid use disorder involving prescription medications, while more than 20,000 deaths annually are attributed to opioids.

Furthermore, the use of opioids can extend the length of a patient's hospital stay. Considering these facts, Mark L. Smith, MD, member of the Feinstein Institute and vice-chair of the Department of Surgery at Northwell Health, was driven to find an alternative to intravenous and oral opioids, which are the mainstay of postoperative pain control for his microsurgical breast reconstruction patients.

“By substituting non-steroidal, anti-inflammatory medication for opioids and using long-acting nerve blocks that work locally to minimize pain at the surgical site, our microsurgical breast reconstruction patients not only had less pain, they also avoided the effects of opioids, like grogginess and nausea. This allowed them to get up and walk sooner and leave the hospital on their second day instead of the national average of four to five days,” said Dr. Smith. “Our patients are pleased to be back to their lives more quickly and relieved not to deal with opioid side effects or risk of dependence.”

Dr. Smith and his team found they could effectively block post-operative pain for microsurgical breast reconstruction procedures by using a combination of anesthetic injections, including a technique called “transversus abdominis plane block,” or “TAP block.” The drug they used for the injections, liposomal bupivacaine, can provide local pain relief for two to three days, when pain is typically greatest.

Dr. Smith's findings were published in *Plastic and Reconstructive Surgery*, and the team is encouraging other doctors to adopt the regimen. Hospitals that are trying the new pain regimen and seeing benefits for their patients include Long Island Jewish Medical Center in New Hyde Park, Southside Hospital in Bay Shore, Huntington Hospital, North Shore University Hospital in Manhasset, Peconic Bay Medical Center and Staten Island University Hospital. Patients like Lynn Bertsch, of Plainview, NY are seeing the benefits.

“After facing breast cancer and a double mastectomy, I didn't want to also confront the side effects of opioids or the potential of being dependent on opioids. I thought it was important to my recovery to not be in a fog. I wanted to drive, and I wanted my body to feel healthy and clean,” said Bertsch. “My recovery exceeded my expectations. My pain was completely manageable and, by the time I was wanting to get home, I was there sitting up in my favorite chair and even walking around.”

“Targeted injections can reduce the need for opioids after breast surgery”





Data drives new perspectives in health care



New center puts cutting-edge technology and big data to work for patients.

“Our research saves lives today — our findings have an immediate impact on patient care.”

— Thomas McGinn, MD, MPH
Center Head

The Center for Health Innovations and Outcomes Research (CHIOR), a new 20,000-square-foot facility, is home to a team of internationally-renowned researchers who use technology, big data and creative new ways of thinking about health care outcomes to measure and improve health care delivery.

CHIOR’s researchers work mostly outside of a traditional lab — they are more often found crunching data or analyzing patient and physician behavior to gain a different perspective on health care: that of the patient or community. The solutions crafted at CHIOR range from new types of health care technology to behavioral interventions. They all have the same goal: to keep patients well, starting now.

“Our research saves lives today — our findings have an immediate impact on patient care,” said Thomas McGinn, MD, MPH, head of the Center for Health Innovations and Outcomes Research. “Leveraging the unique diversity and size of Northwell Health’s patient population, we are able to learn about the struggles and challenges faced by both patients and health care professionals and identify ways to improve care.”



Some of the research projects underway at the Center for Health Innovations and Outcomes Research include:



Negin Hajizadeh, MD, MPH, associate professor is examining how exercise and remote monitoring can improve quality of life

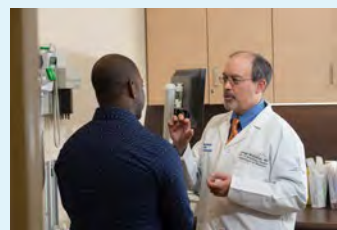
for African-American and Hispanic patients with COPD.



Professor Michael Diefenbach, PhD, and his team have developed a decision support application, Healium, to help each patient decide which prostate cancer treatment best suits his needs.



Assistant Investigator, Catherine Benedict, PhD, is leading an initiative to develop a long-term digital planning tool that will help cancer survivors consider important fertility decisions.



Professor Joseph McGowan, MD, and his team have implemented mobile apps and videochat to encourage HIV-positive patients to take their

medications. The team has also identified which metro New York areas have the highest incidence of HIV and other sexually transmitted diseases.

CHIOR's more than 100 researchers include physicians, nurses, psychologists, economists, IT programmers, biostatisticians and public health professionals.

"It's an eclectic mix of individuals and specialists that crosses disciplines and integrates areas that many might think would not normally go together," said Dr. McGinn. "But these cross-disciplinary collaborations allow us to deliver innovative solutions that can be rapidly implemented to influence the practice of care."

Scientists in CHIOR leverage widely-available technology to identify and address areas of patient need and quickly craft solutions. For example, scientists working in CHIOR and Northwell's Center for AIDS Research and Treatment aggregated data to identify the areas in the New York metropolitan areas with the highest rates of human immunodeficiency virus (HIV) and sexually transmitted infection. With these identified, researchers are working with community leaders to create ways to address care, prevention, and testing in those communities. Additionally, the same team has developed a mobile app that helps patients with HIV manage their medication regimens.

Another CHIOR project developed in Northwell's Departments of Medicine and Urology is a software program called Healium that helps prostate cancer patients think about and prioritize their decisions regarding treatment. The program is an example of how CHIOR's work hits the ground quickly to impact patients: total development time for the software was 10 months after researchers collected data from patients and caregivers about what was important to them.

First-ever treatment for a common problem

Skin irritation caused by adult incontinence — known as incontinence-associated dermatitis or “adult diaper rash” — is common in hospitals. Nurses at North Shore University Hospital orchestrated a clinical trial that launched a promising new treatment for this problem.



Photo Caption: Pictured from left to right: Marie Agrell-Kann, RN, Magdalena Litwinczuk, RN, Assistant Director of Wound and Ostomy Care at North Shore University Hospital Mary Brennan, RN, Renee Gilchrist, RN, and Kelly McSherry-Ng, RN, were part of a multi-center clinical trial which tested a new treatment for incontinence-associated dermatitis.

Skin is the first line of defense against many threats, including bacteria, viruses, irritants and dehydration. When the skin is damaged, people can experience inflammation, pain and infection.

Nurses are all too familiar with skin problems. One of the most common conditions they deal with is called incontinence-associated dermatitis (IAD), skin damage that results from incontinence in adults. Incontinence damages skin with exposure to excessive moisture, high pH, fecal enzymes and bacteria. IAD affects up to 95 percent of patients with incontinence and can lead to total breakdown of the skin and intense pain.

For a long time, nurses were limited in what they could do to prevent and treat IAD. “Protecting the skin is critical for preventing skin damage and breakdown,” said Mary Brennan,

RN, MBA, assistant director of wound and ostomy care at North Shore University Hospital. “Unfortunately, the protective treatments we had to prevent IAD were made for babies with diaper rash and weren’t effective for adult skin issues.”

Thanks in part to the efforts of Brennan and other nurses at North Shore University Hospital, there is a new option for preventing this skin damage. The nurses were chosen by 3M to join a multi-center clinical trial of a product developed specifically for IAD. In all, 12 North Shore University Hospital patients were enrolled in the trial. Nurses came in on their days off to conduct the study, which involved applying a thin liquid polymer film to the affected skin of patients twice a week for three weeks.

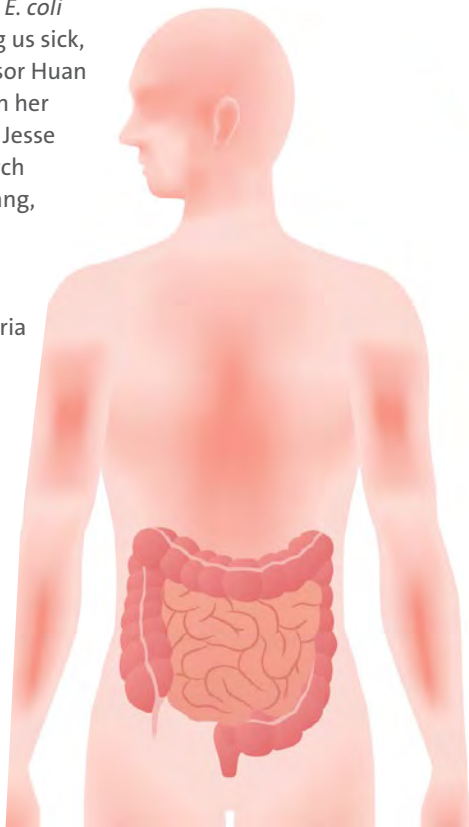


The new treatment proved very effective in patients — the vast majority saw improvement in their IAD and reported significantly reduced pain. As a result of the study, it was approved by the Food and Drug Administration (FDA) and is now on the market under the brand name 3M Cavilon™ Advanced Skin Protectant.

“We are so pleased and proud to have been part of this study,” said Brennan. “Incontinence-related skin damage is a terrible problem for patients. As nurses, we want to be able to help our patients, so it’s a relief to be able to finally offer these patients a treatment that works.”

E. coli could be the key to calming intestinal inflammation

We usually associate *E. coli* bacteria with making us sick, but associate professor Huan Yang, PhD, along with her colleagues professor Jesse Roth, MD, and research scientist Xiaoling Qiang, MD, PhD found that *E. coli* can be helpful in our bodies. They found that the bacteria in our intestines are communicating with the cells of our body to reduce inflammation. Dr. Yang is hopeful that this finding could lead to new therapies for treating conditions associated with excessive inflammation such as sepsis and colitis.



“We found that one of the intestinal bacteria, *E. coli*, actively release hormone-like peptides or amino acids that are anti-inflammatory, calming the body’s white cells and other defenders,” said Dr. Yang. “By further understanding the interactions between microbes like *E. coli* and the body’s hormones, we may be able to identify therapies that use our body’s own bacteria to treat this inflammation.”

Dr. Yang suspects that some subset of patients who suffer from inflammatory diseases of the intestine could be helped by recolonizing their intestines with harmonious bacteria that can calm the inflammatory processes. These findings were published in *npj Biofilms and Microbiomes*.

NOTABLE EVENTS

Bioelectronic medicine symposium

Bioelectronic Medicine: Technology Targeting Molecular Mechanisms

The Feinstein Institute, which continues to drive the scientific conversation in the field of bioelectronic medicine, co-sponsored the Bioelectronic Medicine: Technology Targeting Molecular Mechanisms symposium. The event, which took place on June 12-14, 2018 in Saltsjöbaden, Stockholm, Sweden was presented with the Karolinska Institutet, and their *Journal of Internal Medicine* (JIM). The three-day symposium brought together leaders in bioelectronic medicine who explored, defined and advanced this emerging field. Speakers included:

- Isaac Chiu, PhD, Harvard Medical School — neural regulation of bacterial infection and host defense
- Paul-Peter Tak, MD, PhD, GlaxoSmithKline — clinical updates
- Charles N. Serhan, PhD, DSc, Harvard University — novel mediators and mechanisms in the resolution of inflammation
- Colin Duncan, MD, University of Edinburg — the role of the autonomic nervous system in polycystic ovary syndrome
- Goran Hansson, MD, PhD, Karolinska Institutet — inflammation in atherosclerosis — from mechanisms to therapy
- Chad Bouton, Feinstein Institute for Medical Research — neural decoding and restoring hand function in tetraplegia.

This was the latest in a series of symposiums that the Institute hosted on the topic. Topics discussed at this symposium included defining circuits, molecular targets, neural interfaces, signal processing, disruptive tools and technology, clinical updates and accelerating clinical translation.

For more information about the event, please visit: bit.ly/bioelectronic-stockholm.

Science + Discovery

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Clinical Study: MapYourHealth

Where patient diversity drives discovery.

Have you ever wished that you could contribute to groundbreaking medical research? Northwell Health is offering patients an opportunity to do just that, and all it takes is a blood sample. The MapYourHealth program is designed to advance the field of precision medicine with the help of patients.

Precision medicine is a new approach to medical care that takes individual variations in genetics, environment and lifestyle into account when developing treatments. The goal is that every patient gets exactly the right treatments for diseases and conditions, tailored to his or her genetic makeup.

In order to create these treatments, physicians and researchers need an understanding of the diversity of differences between individuals, and which of these can be targeted for treatment. That's where you come in.

You can help by allowing us to collect a small sample of blood during your next scheduled doctors appointment. All data will remain secure and confidential. As thanks for your participation, you may choose to receive genetic results that explain your ancestry, free of charge.

All Northwell Health patients are welcome to participate. The more data we collect, the more information we will have to shape the future of health care.

Interested in participating? Want to learn more? Contact us:

MapYourHealth Program
(516) 562-GENE (562-4363) • bit.ly/mapyourhealth
MapYourHealth@northwell.edu

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- LIJ Valley Stream
- Mather Hospital
- North Shore University Hospital
- Northern Westchester Hospital
- Peconic Bay Medical Center
- Phelps Hospital

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Volume 1,
2018

Discovery will
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hearing aids
closer to reality

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**Food as
medicine:**
using a plant-based
diet to treat reflux

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Existing Alzheimer’s medication slashes inflammation related to metabolic syndrome

Researchers at Northwell Health’s Feinstein Institute for Medical Research may have found a way to treat more than just the symptoms of metabolic syndrome.

“**Inflammation and insulin** resistance underlie metabolic syndrome, which is a precursor to Type 2 diabetes, so the traditional approach of using medications to manage hypertension and high triglycerides doesn’t address the condition itself,” said Valentin A. Pavlov, PhD, associate professor in the Center for Biomedical Science and the Center for Bioelectronic Medicine. “Previously, we found the Alzheimer’s disease drug galantamine reduced both inflammation and insulin resistance in an animal model, and we wanted to see if it could do the same in humans.”

Working with a team from the University of São Paulo, Brazil, Dr. Pavlov and his colleagues from the Feinstein Institute gave galantamine for 12 weeks to 30 patients living with metabolic syndrome. Another group of 30 patients received a placebo. When the treatment regimen ended, the galantamine group had lower levels of two pro-inflammatory molecules and higher levels of two anti-inflammatory molecules, as well as lower insulin resistance. The patients experienced those results while taking less than the highest daily dose of galantamine approved for Alzheimer’s disease patients. Further research is required to confirm the drug’s benefit for treating metabolic syndrome. The researchers’ study recently appeared in *JCI Insight*.

A million-dollar donation to target diabetes with bioelectronic medicine

The Knapp Family Foundation gives the Feinstein Institute \$1 million to fund a four-year bioelectronic medicine-based research program.

Nearly 10 percent of Americans have diabetes, and almost 25 percent of those who have diabetes are undiagnosed and unaware. To improve their lives, the Feinstein Institute is studying how to use bioelectronic medicine to treat the condition. The Knapp Family Foundation made a significant donation to support this pioneering work.

“Diabetes affects our family as it impacts millions of other

families around the world,” said Charles Knapp, president of the Knapp Family Foundation. “We are passionate in our support of the Feinstein Institute’s innovative and scientific efforts in combating this debilitating condition.”

Chad Bouton, director of the Feinstein Institute’s Center for Bioelectronic Medicine and vice president of advanced engineering for Northwell Health, leads the research team. They hope to

develop an implantable device that will work as an electronic pancreas to regulate glucose metabolism without insulin.

“Patients living with diabetes currently have to pay a lot of money for and face damaging side effects of their treatment,” Mr. Bouton said. “I’m excited about starting this deeper research into developing devices that help the body heal itself instead of relying on drugs.”

Discovery will bring cognitive hearing aids closer to reality

Picture yourself in a crowded restaurant with your closest friends, catching up and sharing the latest news. For most people, this sounds like an idyllic evening, but for those with a hearing impairment this setting can be stressful.

Current hearing aid technology can only suppress background noise — not select a voice out of the crowd — making it difficult to hear a particular speaker. Associate Professor Ashesh Mehta, MD, PhD, identified the neural signals that help us home in on certain speakers to translate this brain function into device technology.

Cognitive hearing aids incorporate technology that not only picks up sound and amplifies it, but is also able to identify what the patient is trying to listen to and amplify that particular sound. To develop this technology, Nima Mesgarani, lead researcher, and his team at Columbia Engineering need to understand how the brain processes what we hear and how it tells the ears to focus on different sounds. This is where Dr. Mehta's expertise comes into play. He is a part of The Laboratory for Human Brain Mapping at the Feinstein Institute, which uses the

latest methods for measuring brain structure and function to advance our understanding of how the human brain works. For this study, Dr. Mehta and his team performed brain recordings while patients were undergoing epilepsy surgery to identify the portion of the brain that determines who is speaking and then map those neural signals.

“In our neural recordings, you could see the shift in focus from one person to another during the course of a conversation, and this could be identified solely on the basis of the brain recordings within seconds of the attention shift,” Dr. Mehta said. “The Columbia Engineering team was able to use these recordings to develop their technology and prove that it mirrored the functionality found in the human brain.”

The Columbia Engineering team developed auditory attention

decoding (AAD) methods, which receive one audio channel with multiple speakers being heard by a listener along with the listener's neural signals. It then automatically separates the individual speakers from the mix, determines which speaker is being listened to, and amplifies the attended speaker's voice to assist the listener — all in seconds.

“This study shows we have the technological capability to automatically and rapidly separate an attended speaker from a mixture of multiple sources,” said Nima Mesgarani, associate professor of electrical engineering at Columbia University. “We hope to continue developing this technology and work with a developer of hearing devices to take it into clinical trial.”

This discovery was recently published in *Journal of Neural Engineering*.





Food as medicine: using a plant-based diet to treat reflux

The old proverb “an apple a day keeps the doctor away” could prove true for patients suffering from laryngopharyngeal reflux.

A plant-based, Mediterranean-style diet with alkaline water has been shown to provide the same medical benefits for treating laryngopharyngeal reflux as popular reflux medications, according to a recent study by investigator Craig H. Zalvan, MD, FACS, published in *JAMA Otolaryngology Head Neck Surgery*.

In addition to being a researcher, Dr. Zalvan is chief of otolaryngology and medical director of The Institute for Voice and Swallowing Disorders at Northwell Health’s Phelps Hospital. He identifies himself as formerly one of the region’s largest prescribers of proton pump inhibitors (PPI) — the most popular type of medication for reflux. Recognizing that there should be a better approach to treating chronic conditions like laryngopharyngeal reflux, Dr. Zalvan decided to look into alternatives.

“Although effective in some patients, I felt medication couldn’t be the only method to treat reflux, and recent studies reporting increased rates of kidney damage, dementia, stroke and heart attack from prolonged PPI use made me more certain,” Dr. Zalvan said. “I did research and saw a lot of studies using plant-based diets to treat patients for many other chronic diseases, so I decided to develop a diet regimen to treat my laryngopharyngeal

reflux patients. Our results show we are heading in the right direction for treating reflux without medication.”

Cora is one of Dr. Zalvan’s patients benefiting from this new treatment regimen. Starting early last year, Cora, 38, a resident of Northern Westchester, began experiencing hoarseness, a lump in the throat, as well as periodic voice loss. As a speech therapist and vocalist/songwriter, losing her voice made it nearly impossible to demonstrate proper speech sounds to her patients and perform her best with her band. After finding no improvement with two medical professionals who prescribed PPIs, Cora saw Dr. Zalvan, who diagnosed Cora with laryngopharyngeal reflux and tried to find a treatment plan that didn’t include prescription drugs.

“After hearing on the news all the potential side effects associated with PPIs,” Cora said, “I wanted to find an alternative, which brought me to Dr. Zalvan.”

Evaluating diet vs. medication

The diet suggested by Dr. Zalvan consists of mostly fruits, vegetables, grains and nuts with near-complete cessation of dairy and meats, including beef, chicken, fish, eggs and pork. This is in addition to standard reflux dietary




A snapshot of Dr. Zalvan's reflux diet

A 90 to 95 percent plant-based diet means having three meals per week that include meat and dairy. Dr. Zalvan encourages his patients to get creative and make this diet their own.

"Mostly I suggest patients do their own research," he said. "Read about diet choices and learn to cook and enjoy a healthy, plant-based lifestyle."

If you don't have the time to shop and plan, he also recommends checking out online vegan-based food-delivery services.

Below are some suggested meals he said patients could easily build upon.

Breakfast	Lunch	Dinner
<ul style="list-style-type: none"> Whole-grain cereals with plant-based milk (like almond or soy) Fruit bowls with plant-based yogurt  <ul style="list-style-type: none"> Smoothies made of plant-based milks, fruits, soft tofu, avocado, chia and flaxseed Avocado toast 	<ul style="list-style-type: none"> Salads with whole grains, chickpeas, nuts and fruit Whole-wheat veggie wraps  <ul style="list-style-type: none"> Wraps containing veggie burgers mixed with multiple grilled vegetables (prepared without grease) Veggie takeout choices, such as broccoli with garlic sauce 	<ul style="list-style-type: none"> Grilled vegetables and tofu Lentil dishes, including those prepared with Indian-style spices  <ul style="list-style-type: none"> Plant-based soups made without meat-based broths

precautions, such as avoiding coffee, tea, chocolate, soda, alcohol, and foods that are greasy, fatty, fried or spicy.

Working with researchers at New York Medical College, Dr. Zalvan and his team reviewed the charts of patients he treated with PPIs (prior to developing the diet) and then those treated with the plant-based diet he designed. When compared with patients who took PPIs, those patients who consumed a 90 to 95 percent whole-food, plant-based, Mediterranean-style diet paired with alkaline water had the same if not better reduction in reflux symptoms. Although it took some adjusting (and some convincing of her boyfriend, who she regularly cooks for), Cora moved to a plant-based diet and is seeing a drastic improvement in her reflux symptoms.

"I still have a little hoarseness, but as long as I stick to the diet, my symptoms have become greatly reduced," Cora said. "In fact, I'm able to expand my songwriting outside of the key of A again. Before finding this diet, my voice was so damaged I could only sing in one key."

Although this research focused only on those diagnosed with laryngopharyngeal reflux, the same diet regimen could also help patients with gastroesophageal reflux disease (also known as GERD).

Dr. Zalvan also noted that many of his patients who were treated with a plant-based diet also experienced some weight loss and a reduction of symptoms and use of medications for other medical conditions such as high blood pressure and high cholesterol.

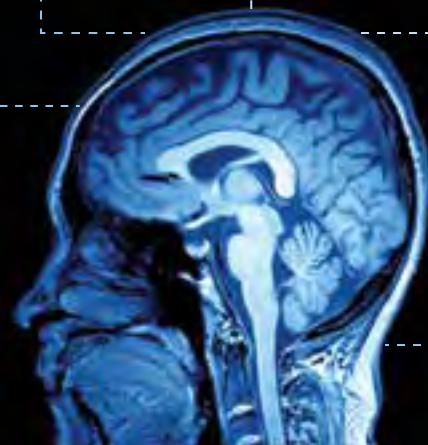
While this study is a major breakthrough in how reflux is treated, Dr. Zalvan does not recommend that patients suddenly abandon the medications they were prescribed.

"Patients will need to discuss with their medical providers whether this option is personally appropriate," Dr. Zalvan said. "I recommend that a plant-based diet approach with alkaline water and standard reflux precautions should either be attempted prior to the use of medication or with the short-term use of medication for more severe needs."

To learn more about Dr. Zalvan and The Institute for Voice and Swallowing Disorders at Northwell Health's Phelps Hospital, visit 4healthier.me/NWSD-diet.

A new way to combat brain tumors

Scientists at the Feinstein Institute are investigating an alternative use for a popular antiparasitic drug — as a brain tumor treatment.



For years, **low-grade glioma** — a tumor that originates from cells that support and protect the brain's nervous system — has been treated through a combination of surgery, radiotherapy and chemotherapy. The chemotherapy aspect of treating brain tumors has always been challenging due to one major obstacle.

“The critical problem we face is that most anti-cancer drugs have trouble penetrating the blood-brain barrier,” said Marc Symons, PhD, professor in the Karches Center for Oncology Research. “This natural defense mechanism protects the brain from substances in the bloodstream, but it can also keep medications and chemotherapy drugs from reaching their intended targets, namely tumors within the brain.”

Conventional treatment

Vincristine, a drug commonly used in combination with other chemotherapy medications to treat brain tumors, is rather toxic and poorly crosses the blood-brain barrier.

“When we used vincristine in animal models, we were shocked to discover that it simply didn't work,” Dr. Symons said. “Although it is in use for many types of brain tumors, this study showed it to be ineffective.”

Dr. Symons explained the inaccurate assumption about vincristine's effectiveness may be due to its having been used in combination with other treatments — rather than being tested in isolation.

Fortunately, Dr. Symons and his colleagues examined another drug that fared much better at treating brain tumors: mebendazole.

An exciting new option

Mebendazole is a medication typically used to treat parasitic pinworms. Dr. Symons' research found that mebendazole works similarly to vincristine in the way it kills cancer cells. However, in contrast to vincristine, it

The benefits of repurposing

One of the most expensive aspects of creating a new drug is the development stage. Creating a new medication from scratch is a complex process involving both preclinical and clinical studies that can take years. That's why drug repurposing has become so popular. Medications that have already been tested for safety and efficacy for one purpose can be brought to patients sooner.

“There's a premium on trying to find drugs that were created to treat other diseases but can be repurposed to fight cancer,” Dr. Symons said. “This skips the expensive drug development stage and can readily be tested in patients.”

While mebendazole may soon become the poster child of repurposing success, researchers all over the nation are excited about what other possibilities are out there.

effectively crosses the blood-brain barrier and slows down brain tumor growth.

“Our results showed that blood-brain barrier permeability really matters for the therapeutic effects of brain tumor drugs,” Dr. Symons said. “In addition, the side effects associated with mebendazole appear to be milder than those associated with vincristine.”

Humans have used mebendazole with minimal problems for decades as an antiparasitic. In addition, the medication is extremely affordable compared with the cost of other cancer-fighting medications.

“These findings are exciting, and it is obvious that mebendazole is a very good candidate to replace vincristine for the treatment of whatever brain tumor it's currently being used for,” Dr. Symons said. “When comparing the two drugs, it's clear which option will benefit cancer patients the most.”

Visit FeinsteinInstitute.org/programs-researchers/cancer to learn about our work identifying causes of and discovering treatments for brain tumors.

A breakthrough in the management of postpartum depression

Medication personalized to the underlying cause of the condition could revolutionize treatment.

Even though physicians suspect postpartum depression may be caused by fluctuations in estrogen and progesterone, the most common medication used for the condition treats depression, which is biologically different. Developing a therapy specifically for postpartum depression may enhance treatment results. That's the goal of researchers from Feinstein Institute and study sponsor Sage Therapeutics Inc., who recently examined the efficacy of using brexanolone iv (USAN; formerly SAGE-547 injection) in treating severe postpartum depression.

Women's bodies naturally create allopregnanolone, a metabolite of the hormone progesterone that has a calming effect. Previous research found a potential link between low levels of allopregnanolone during the second trimester of pregnancy and postpartum depression in at-risk women.

Hastening the path to symptom reduction

In the current study, published in *The Lancet*, the research team administered a 60-hour IV infusion of brexanolone to 10 women with postpartum depression who scored 26 or above on the Hamilton Rating Scale for Depression (HRSD), which defined severe disease in this study. Eleven women with similar HRSD scores received a placebo infusion.

Researchers monitored the two groups for 30 days. At the end of that period, they observed an average 21-point reduction in depressive symptoms in the women who received brexanolone, compared to an eight-point reduction in the placebo group.

Did you know?

Fifteen out of 100 women in the United States will get depressed in the first three months after giving birth. About half of these women (eight out of 100) will have mild to moderate depression, and around seven out of 100 will suffer from severe depression.

"How much the depression resolved and how quickly it resolved were the standout results in this study," said Kristina Deligiannidis, MD, co-author of *The Lancet* study, associate professor in the Center for Psychiatric Neuroscience at the Feinstein Institute and director of women's behavioral health at The Zucker Hillside Hospital. "Currently, FDA-approved antidepressants can take weeks to fully resolve postpartum depression."

As a continuation of this study, Sage Therapeutics is conducting larger phase 3 clinical trials of brexanolone in women with moderate and severe postpartum depression at several major US academic medical centers, including Northwell Health's Zucker Hillside Hospital. Positive initial results from the phase 3 trial were recently announced.

"This investigational medicine may target the specific underlying causes of postpartum depression," Dr. Deligiannidis said. "If we replicate the findings that we observed in the small sample size of 21 women during the phase 3 trial, we'll have a new way of thinking about and treating the larger population of women who experience postpartum depression."

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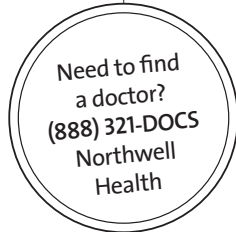
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Could a more culturally sensitive approach improve asthma management among Hispanics?

Asthma is common in and detrimental to the Hispanic community. Two Feinstein Institute researchers seek to help by changing the approach to educating people about the condition and ways to manage it.

Language and cultural differences can create obstacles to asthma care in the Hispanic community, according to Negin Hajizadeh, MD, associate professor of medicine in the Feinstein Institute Center for Health Innovation and Outcomes Research and the Department of Medicine at Northwell Health. Instructions do not always translate well and misconceptions persist, such as the notion that it is better to use herbal teas and ointments because inhalers may become addictive.

Focusing on what matters to patients

In a first-phase project, Dr. Hajizadeh and Research Coordinator Sonia Jacome, MSCH, partnered with Queens-based community organization El Poder de Decidir to meet with the local Hispanic community and learn about the

asthma education barriers they face. Three priority areas for further investigation emerged: asthma education, patient/caregiver communication and conventional treatment vs. natural therapies.

With support from the Patient-Centered Outcomes Research Institute (PCORI), Dr. Hajizadeh and Ms. Jacome began a one-year, second-phase project in September to determine which of the three topics the Hispanic community believes will be most beneficial.

“The purpose of our project is to generate a research question, such as, ‘Would culturally sensitive tools be better than those now available, many of which are just translations from English to Spanish,’” Dr. Hajizadeh said. “The Hispanic community is quite diverse.

Would it be better to have culturally attuned translators present who, rather than translate verbatim, can help a physician ask more relevant questions?”

Once the Hispanic community identifies a single area of focus, the researchers will apply for additional support from PCORI to conduct a third phase project.

“The questions we’re exploring come from the community,” Dr. Hajizadeh said. “That makes a potential clinical study more likely to produce relevant, helpful results.”

For more information about upcoming meetings or workshops, please contact Research Coordinator Sonia Jacome, MSCH, at (516) 600-1487.

THE

Ultimate Guide to
Everything

Chocolate

Everything to
take you from
Chocolate *Enthusiast* to
Chocolate *Expert*

NASSAU CANDY

Specialty Confections & Fine Foods



Consumers crave more than the latest flavors and finest ingredients—they want to take a trip beyond the taste and learn the story behind chocolate.

As a leading chocolate and confectionery manufacturer and distributor, we believe “if you sell it, you should have a deep understanding of it.” Customers routinely ask us questions about chocolate, so we’re sharing our rich knowledge, unwrapping what we’ve learned over 80+ years in the business.

What you'll learn...

- 3 From Bean to Bar - How Chocolate is Made
- 5 Chocolate Types - Know the Difference
- 9 Chocolate Tasting
- 11 Top Terms in Chocolate Making
- 14 Chocolate Merchandising
- 21 Chocolate Storage & Transport

If you sell it,
you should have a
deep understanding
of it.

Les Stier

Founder & CEO, Nassau Candy



From Bean to Bar

How Chocolate is Made

Before diving into the various types of chocolate, how to make it, and how to sell it, you need to understand the ingredients and how they are processed.

Regardless of the type,
all chocolate begins with
the cocoa bean.

Indigenous to South America, where they are still primarily sourced, cocoa beans are also grown in parts of South Asia and Africa. As with coffee and wine, the type of bean (there are three major classes) and where it's grown all impact taste. For example, cocoa from Ghana has a slightly bitter and toasted nutty taste, while cocoa beans from Venezuela boast fruity and caramel notes. The majority of manufacturers use a blend of cocoa beans for flavor consistency, but 'single source' cocoa confections are quickly emerging as a premium item for those desiring an exceptional sensory experience from their chocolate.

At Nassau Candy, we source our chocolate from a variety of growers around the world and use an assortment of blended and single-source cocoa, depending on the confection we're crafting.

Did you know...

if you picked a cocoa bean in the wild, it would not taste like chocolate? The bean must be processed to coax out the chocolate flavors we have come to know and love. After cocoa beans are harvested and still in the pod, they are fermented to help to develop the flavor and character.



5 Million Pounds
of chocolate is used
every year by Nassau Candy's
Chocolate Experts for
our divinely delicious
chocolate creations

Next is the roasting process



Roasting eliminates the harsh, acidic vinegar-like taste that emerges during the fermentation process, creating nutty, brown chocolate notes. Roasting also helps separate the bean from the outer husk. The beans must be cracked and winnowed (removing the outer husk) before they can reach the last step — conching.

The Last Step is Conching This is the process of evenly distributing the cocoa butter. It rounds out the flavor profile and creates the final chocolate ready to be molded, or incorporated with other ingredients to create the various chocolate types. Conching gives each brand of chocolate its distinct flavor and character.

In fact, many chocolate manufacturers keep their conching process a deeply guarded secret.



At the completion of the bean prep, there are two end products:

COCOA SOLIDS and COCOA BUTTER.

It's at this point in the bean-to-bar process when things really start to get lusciously delicious.

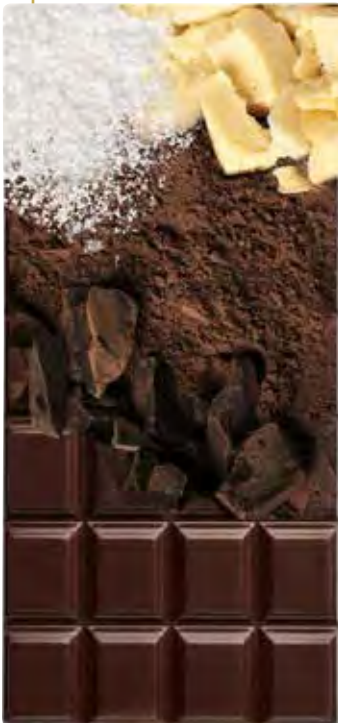
Chocolate Types **Know the Difference**

Cocoa solids and cocoa butter are produced at the end of cocoa bean processing. Cocoa solids and cocoa butter are the base for all chocolate types.

Chocolate types are determined by the ratio of cocoa solids to cocoa butter, and also the addition or omission of other ingredients. Knowing the chocolate type helps customers anticipate the product's taste without even having to open the wrapper. Let's dive into what makes each chocolate type a unique experience.

Anatomy of Chocolate

CHOCOLATE TYPES DEFINED



Dark **Chocolate**

cocoa solids,
cocoa butter, sugar



Milk **Chocolate**

cocoa solids, cocoa butter,
sugar, milk



Ruby **Chocolate**

red cocoa bean solids,
cocoa butter, sugar, milk

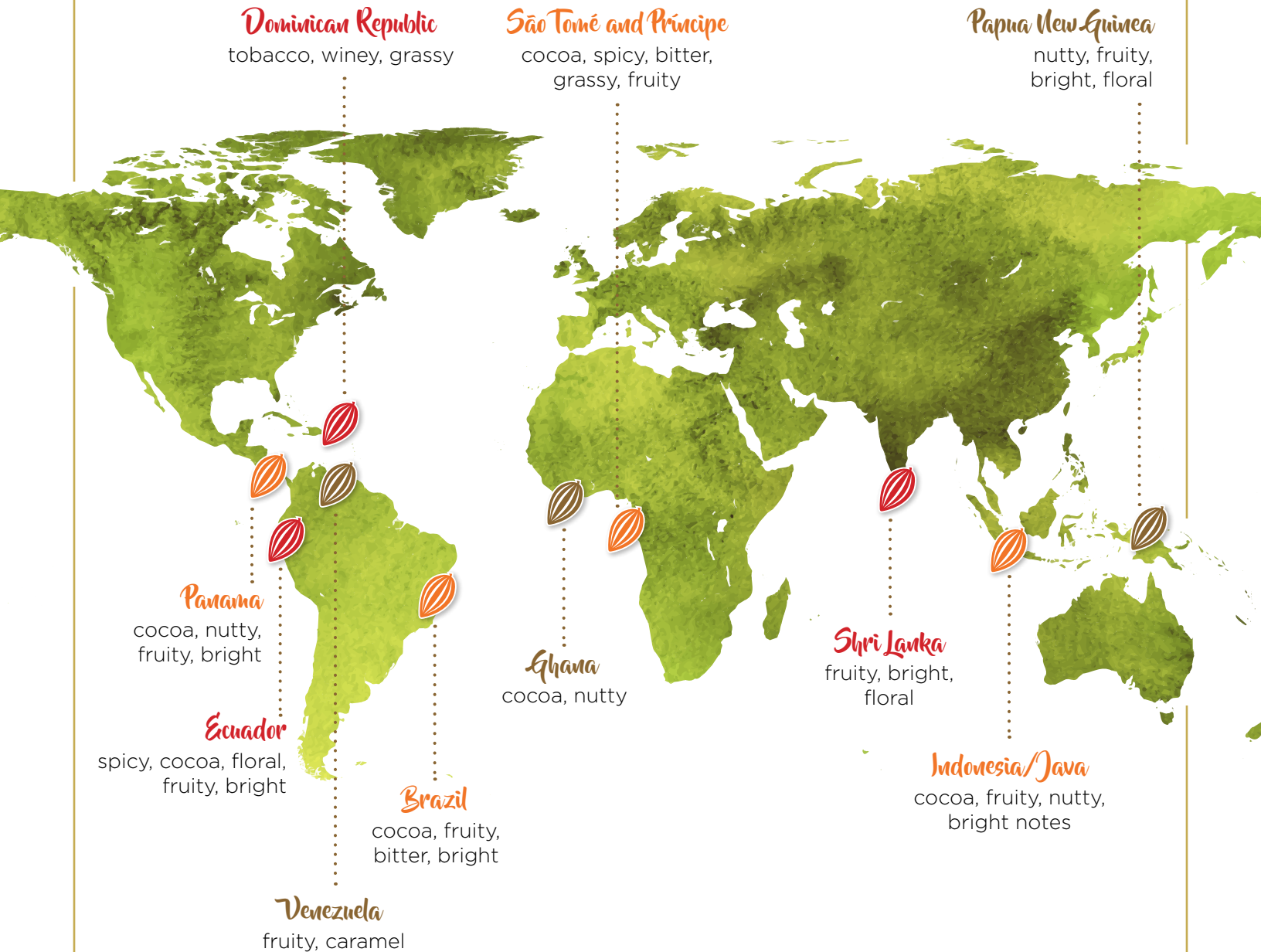


White **Chocolate**

cocoa butter, sugar, milk

SOURCE MATTERS

Like wine, a cocoa bean's origin can impact *flavor*



Chocolate Types *Know the difference*

Dark chocolate

is the chocolate variety that comes closest to resembling the flavor of the processed cocoa bean. Dark Chocolate contains only **cocoa solids**, **cocoa butter** and **sugar**.

Expect a tart, bitter flavor and a deep, dark brown color. Since dark chocolate bars are perceived to be chocolate in its purest form, manufacturers will often tout the cocoa percentage on their packaging. That's with good reason —

the higher the cocoa percentage, the more cocoa solids. This means a truer chocolate taste.



What THAT % REALLY MEANS

The higher the % the more cocoa solids included = the purer the chocolate



White chocolate

is probably the most hotly debated of the chocolate varieties. Until 2002, white chocolate wasn't considered 'chocolate' under U.S. law because it contains no cocoa solids, only **cocoa butter**. However, cocoa butter is a highly prized material and high-quality white chocolate actually contains more of it than other types of chocolates. Additional ingredients necessary to yield white chocolate are **sugar**, **milk**, and **vanilla**. Variations on white chocolate include blonde or golden chocolate, which are white chocolate varieties caramelized for a toastier flavor and a distinctive golden, tan color.



A FAMILY Recipe

The secret behind our milk chocolate's signature taste - vanilla!

Milk chocolate

builds on the ingredients of dark chocolate, incorporating solids and **cocoa butter** with **sugar** and — you guessed it — **milk!** It's the addition of smooth milk that gives this chocolate variety all of its character, creating caramel dairy notes from browning reactions in the final chocolate processing. Milk also impacts the chocolate's texture, creating a creamier, softer chocolate with a sweet, velvety finish. Each chocolate producer generally applies a different process for milk chocolate, using various cooking temperatures, times, and moisture levels, which all result in a delightfully diverse array of flavor profiles and textures.



The newest type of chocolate to hit the market is *Ruby Chocolate*. Just like the name implies, ruby chocolate has a pink hue that sets it apart from all the rest. Discovered by cocoa product manufacturer Barry Callebaut, ruby chocolate gets its unique character from a combination of specific cocoa beans and the signature fermenting and processing method. Ruby chocolate is made from



'red' cocoa beans that originate in Ecuador, Brazil, and the Ivory Coast. A blend of **red cocoa bean solids, cocoa butter, sugar, and milk**, ruby chocolate stands out for its pale pink color and its singular fruity flavor. Ruby is gaining popularity around the globe, but since the process is patented, don't expect to see other manufacturers producing ruby chocolate confections any time soon.



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Chocolate is Going *Vegan*

Vegan chocolate is an emerging trend that could change how we designate chocolate types. It swaps out milk for a plant-based milk replacement, such as soymilk powder, coconut milk powder, cashew flour, hemp seed powder, or even oat flour. Due to the change in fat content, using plant-based ingredients as a dairy replacement can affect the tempering process. This makes crafting the ideal recipe a complicated process. For existing manufacturers to move into the vegan 'milk' chocolate arena, it would require a major investment in space, resources, and equipment. To boast a 'vegan certified' logo and achieve true vegan status, manufacturers have to comply with rules set forth by a global certification group. Until there is substantial demand from a major national retailer, or investment in the space by several major international manufacturers, vegan chocolate will more than likely remain a specialty product.



Chocolate Tasting

Like coffee and wine, chocolate is a premium food product with subtle nuances in flavor, texture, and appearance

Tasting chocolate should be an *unforgettable* high-end experience

But don't take out the white linens and fine china just yet. You don't need much to create this premium encounter. Just bring your taste buds and your other senses. Chocolate tasting education is a great opportunity to differentiate yourself from the competition while deepening your customers' appreciation of chocolate, all with minimal investment.

Everything you need to know about Chocolate Tasting

Tips & Tricks



Go up in % Start with lower cocoa % first and work your way up



Look at the chocolate's texture, sheen, and color



Smell the chocolate, picking up the different flavor notes



Touch not with your hands but by letting the chocolate melt on your tongue



Taste take in the different flavor notes by breathing in while the chocolate is still on your tongue

Skip the chips

Chocolate chips, though delightful in baked goods, have different ingredients and are not preferable for a chocolate tasting menu

Top Terms in Chocolate Making

Prepping cocoa beans to form the different chocolate types isn't where chocolate manufacturing ends, but where the whole process begins

As a chocolate expert, it's important to know the major terms in chocolate making as they provide a better understanding of the chocolate products you purchase and can help you to better direct customers to their chocolate favorites and give them reason to try new varieties.

- Bean to Bar
- Bittersweet
- Blend chocolate
- Bloom
- Cocoa Powder
- Conching
- Dutched/Dutch cocoa
- Enrobed
- Filled chocolate
- Ganache
- Hand-Dipped
- Molded
- Nibs
- One Shot Molding
- Panning
- Semi-sweet
- Shell Molding
- Single Origin Chocolate
- Tempering



Top Terms in *Chocolate Making*



A BEAN TO BAR

A term used by craft chocolate makers to indicate that they process the cocoa beans used to create their chocolate.

BITTERSWEET

Dark chocolate used in chocolate making and baking that has less than 50% sugar added.

BLEND CHOCOLATE

Chocolate made with a blend of cocoa beans from various countries and/or regions.

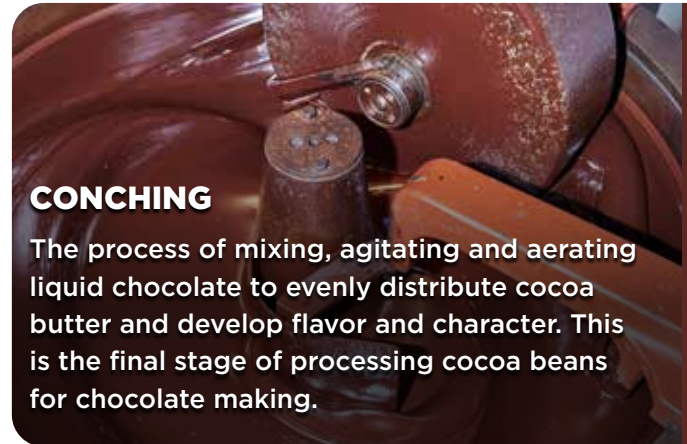


BLOOM

The white film that appears on chocolate when it is kept at too cold of a temperature, causing its fat to come to the surface.

COCOA POWDER

The leftover dried cocoa solids produced when all the cocoa butter is removed from cocoa beans. Cocoa powder is used in baking to create chocolate flavor.



CONCHING

The process of mixing, agitating and aerating liquid chocolate to evenly distribute cocoa butter and develop flavor and character. This is the final stage of processing cocoa beans for chocolate making.

DUTCHED OR DUTCH (ALKALIZED) COCOA

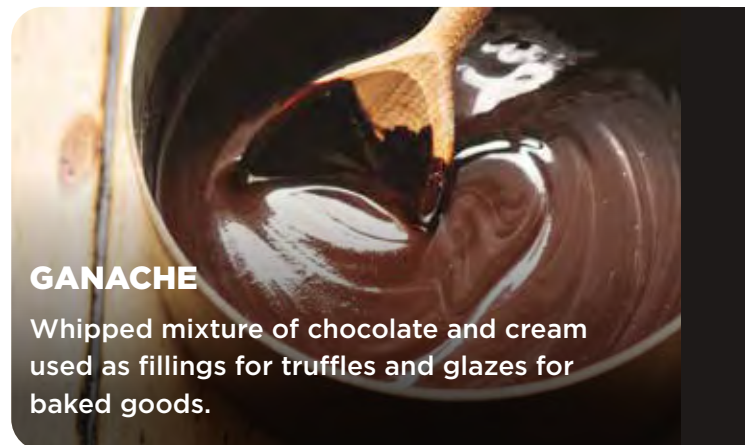
Cocoa powder made from ground cocoa beans that have been washed with a potassium solution to bring the pH up to 7, which produces a milder chocolate flavor when used in baking.

ENROBED

The process where the center of a chocolate candy (like caramel) is made first and then put through a machine called an enrober to evenly coat the piece in a crisp chocolate coating.

FILLED CHOCOLATE

Any piece of chocolate with a center filling.



GANACHE

Whipped mixture of chocolate and cream used as fillings for truffles and glazes for baked goods.

Top Terms in Chocolate Making

HAND-DIPPED

The same process as enrobing, where the center of a chocolate candy is made first and then coated by hand in a thin, crisp chocolate coating. Also used for chocolate cherries, and fruit (candied, dried, or fresh).

MOLDED

The process of pouring liquid chocolate into a mold (plastic, metal, or silicone) to create a shaped chocolate.



SEMI-SWEET

A dark chocolate used in chocolate making and baking that contains more sugar than bittersweet chocolate contains, as well as added cocoa butter.

SHELL MOLDING

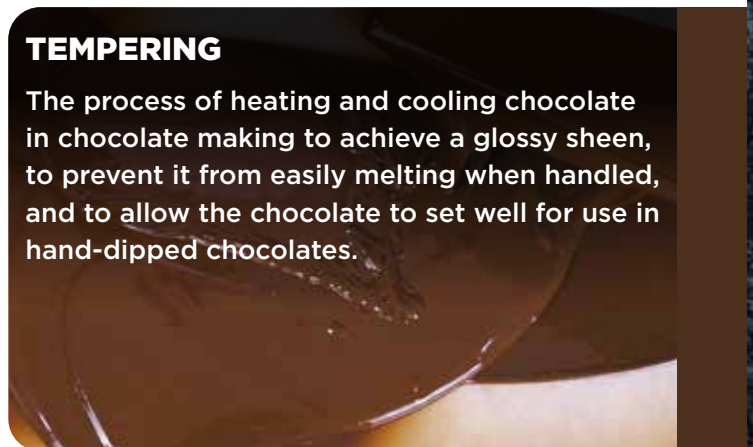
A process to make a filled chocolate bar, piece, or peanut butter cup where a thin layer of chocolate is poured into a mold to create an outer shell, then the filling is added and topped off with additional chocolate.

SINGLE ORIGIN CHOCOLATE

Chocolate with cocoa beans sourced from one single region.

TEMPERING

The process of heating and cooling chocolate in chocolate making to achieve a glossy sheen, to prevent it from easily melting when handled, and to allow the chocolate to set well for use in hand-dipped chocolates.



NIBS

Crumbled bits of dried cacao beans used to add intense chocolate flavor to sweet and savory dishes.

ONE SHOT MOLDING

A manufacturing process for filled chocolate bars or pieces where the filling is injected directly into the center of the piece while the chocolate shell is poured at the same time.

PANNING

The process of coating nuts, dried fruit, or other centers in chocolate. Melted chocolate is tumbled around a pan that looks like a large kettle, constantly moving the centers to evenly coat each piece. Sometimes confectioners glaze is added to give the finished product a lustrous shine.

10 Million Pounds

of chocolate product is manufactured by Nassau Candy every year



Chocolate Merchandising

Even a confectionery superstar like chocolate can use a boost from proper merchandising.

You don't need a design or marketing degree to create a stellar merchandising program

Here are a few easy ways to leverage the star power of chocolate into sales.

Upscale Presentation Translates to Higher Retail Prices

1 Creating Perceived Value

Perceived value is a general marketing term meaning what a consumer is willing to pay for a particular product.

That willingness to open their wallet can be influenced by your decision of where to place chocolate products in your store. For example, placing your chocolate products in elegant packaging, a refrigerated glass case, glass jars, or trays only accessible by store staff translates to 'premium product' in the eye of the consumer.

Its inaccessibility means consumers perceive the product as high-end, meaning they are willing to purchase it at a higher price.

2 Color is Key

When it comes to pre-packaged chocolate, color groupings can help increase sales — particularly in the impulse section.

Include a few products with vividly colored packaging that appeals to adults and children.



For little ones, chocolates in bright orange or bright yellow packaging will delight their eyes. Adults are drawn to high-contrast packaging, and/or packaging with trending colors, such as bright blue and pink.

A good rule of thumb: Do not place packages or items of the same color next to each other— they won't stand out! For example, in bulk displays, chocolate-covered items can start to look similar, so alternate unwrapped chocolate confections with foil-wrapped chocolates to inject color.

Don't forget the time of year when arranging impulse packaged chocolate, chocolate in a showcase, or bulk displays. Typically, during the fall and winter months, customers are attracted to darker colors because they have a comforting, warm appeal. While in the spring and summer, consumers prefer lighter and brighter colors.

3 Bulk up Bulk Sales with Unique Containers

Self-serve bulk chocolate items are always appealing. Customers love the power and fun of selecting a personalized sampling of their favorite chocolate items.

Amp up the opportunity by offering colorful containers. You can't go wrong with seasonal themes or event-focused containers such as Mother's Day, baby showers or birthdays. Customers are often willing to purchase special containers at an additional cost for use with your bulk candy selection. This creates a very personalized gift customers will love to share. For added fun, pick trending containers that can be re-used like insulated tumblers, coffee mugs with humorous sayings, floral vases, and colorful takeout containers. Stick a label on the package or tuck a business card in between the package and the wrapping so recipients know where to purchase when it is their turn to gift.



4 Gift Sets are Always in Season

Chocolate gift sets have year-round appeal, even in the warmer months.

Standard year-round gift set options that feature your own themed packaging are a must for regular customers, like real estate agents, who purchase gifts on a consistent basis.

When it comes to seasonal gifts, save some time by pairing your own seasonal chocolate creations with everyday best sellers. Don't be afraid to use high-end chocolate brands in your gift baskets, mugs, and other containers.

It's a real time-saver. Or, you can mix in seasonal items from top manufacturers with your own year-round confections for a stunning presentation with minimal time investment.

If you don't have the manpower to package your own gift sets, there are other ways to capitalize on gift sets. Chocolate items packaged in acetate tubs are a timesaving (and cost saving) solution. On their own, clear tubs are ideal as grab & go items, and when stacked, 3 or more, tubs can be tied with colorful ribbon and a gift tag, to create an instant gift opportunity.



5

Readymade Chocolate Occasion Kits

Don't wait for a holiday or special occasion to inspire customers to purchase chocolate. Transform any day into a special event with chocolate occasion kits.



Tasty Fun: Readymade S'mores Kits are a hit with customers any time of year. Curate your own collection of premium chocolate bars, fluffy marshmallows, and graham crackers. For a gift-worthy version, swap graham crackers with imported biscuits like shortbread or speculoos. Slip the ingredients into your own branded packaging and watch sales heat up.

DIY Gourmet: In the age of Pinterest and amateur cooking competitions, everyone wants to get in on the DIY craze. Make it easy for customers to make their own chocolate creations at home with a Hand-Dipped Chocolate Kit. Offer melting chocolate along with popular dip-ins like pretzels, sandwich cookies, and marshmallows. Wrap up some sprinkles, mini chocolate chips, peanut butter chips, and nuts for use as colorful garnishes. Offer the option to purchase fresh strawberries or premium dried fruit slices for an additional add-on price.

Elegant Entertaining: Customers are looking for ways to up their entertaining game. Help them transform a get together into an event with a Chocolate-Tasting Party Kit. Customers will appreciate premium chocolates displayed on a pretty platter or cheese board. Include branded printed handouts with instructions for tasting chocolate (see section #2 chocolate tasting) and suggestions of different food and beverage pairings. If your business is specialty food, craft different size kits with all the trimmings: cheese, beverages, and alcohol that pair with each type of chocolate. You can dedicate a kit to pairings for one chocolate type, while also offering a premium kit with all represented.

Read on for some of our favorite
chocolate pairings

Chocolate Pairings by type

Dark CHOCOLATE



Milk CHOCOLATE



White CHOCOLATE



Ruby CHOCOLATE



Chocolate Storage & Transport

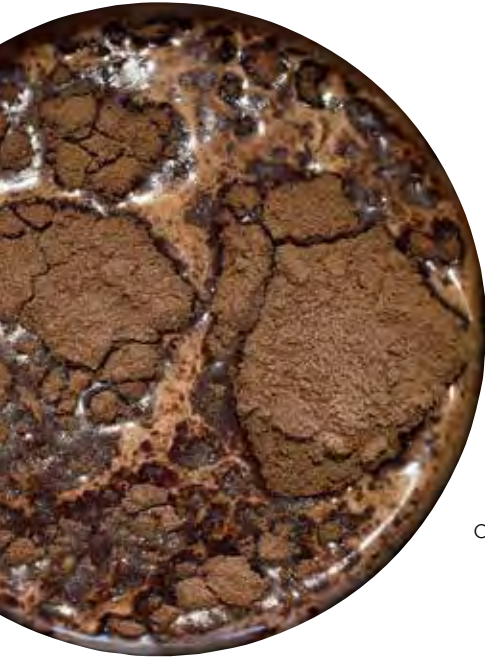
You could carry the most expensive chocolate, but if it has a white haze, that will ruin the experience – and your bottom line. To best understand how to store chocolate, you need to know the chemical reactions that can impact chocolate's quality.

As we previously covered, all chocolate types contain cocoa butter, while some contain cocoa solids and milk. The fat, contained in all chocolate, combined with light, temperature, and humidity, causes the majority of the storage issues you can encounter with chocolate.

Following are a few of the major chemical reactions that can ruin good chocolate. You don't have to memorize the science behind these reactions, but if you see any of these reactions happening in your chocolate selection, take that chocolate out of stock.

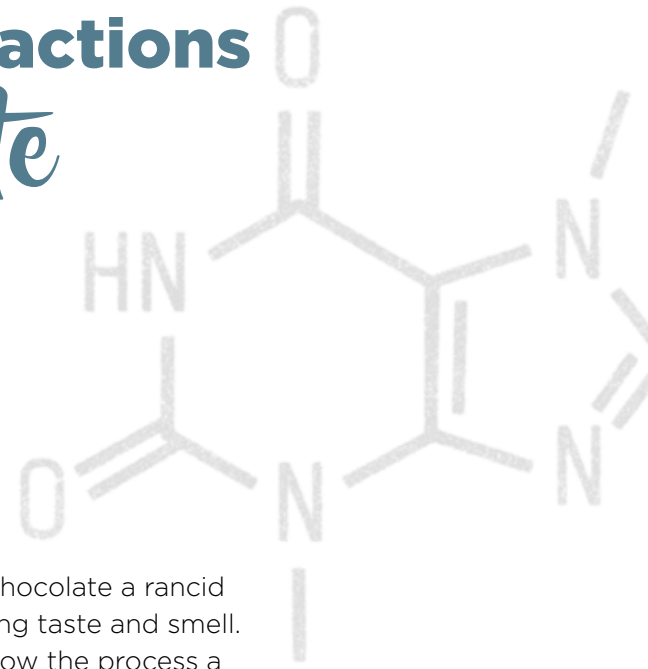


Major Chemical Reactions in Chocolate



Oxidation

Exposure to air and light can give chocolate a rancid taste. The fat disintegrates, impacting taste and smell. The antioxidants in cocoa help to slow the process a bit, making dark chocolate with a high cocoa content the least susceptible to oxidation, while milk chocolate is at medium risk. White chocolate, with its high fat content, is the most susceptible to oxidation.



Ostwald Ripening - fat bloom

Ostwald Ripening, commonly known as fat bloom, is the chemical reaction where you'll see the most change in chocolate. One of the causes of this issue is counterintuitive to what you might commonly think is important for storing food products — that cooler is better. When chocolate is stored at too low a temperature for too long a time, the fat seeps to the surface and causes fat crystals to appear. These crystals trigger the white film you might have noticed on some chocolates. Commonly referred to as chocolate bloom, this reaction makes the chocolate unappealing, as we eat with our eyes first. If a white film isn't unappealing enough, when chocolate with bloom is brought back to room temperature, it starts to 'sweat.' The entire surface of the chocolate becomes wet, which is really unappetizing.

Another reason you will experience fat bloom is also temperature related. When chocolate is kept at too warm a temperature, it melts (as you already know). When brought back to a cooler temperature, chocolate solidifies again. During the melting and solidification process, fat can rise to the surface and create that dreaded white film. This is most common during summer months or in areas of the country where it's warm year-round.

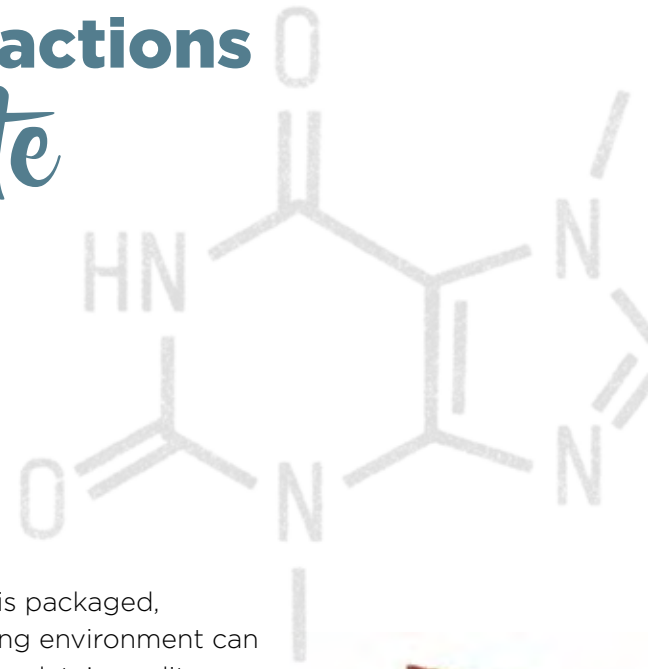


Major Chemical Reactions in Chocolate



Diffusion

Depending on how chocolate is packaged, substances from the surrounding environment can be absorbed and affect the chocolate's quality. If the chocolate is filled, water or alcohol that make up the filling can diffuse out of the chocolate, also sullyng quality and certainly degrading the appearance. (Think of jelly leaking out and crystalizing).



Scent & Taste Transfer

Much like butter, chocolate has a high fat content (from the “other” butter - cocoa butter), making chocolate vulnerable to absorbing scents - particularly nearby flavors from the environment, like a mint or berry filling. So, it's best to keep your stronger flavor filled chocolates away from other chocolate items. White chocolate is the most susceptible to taking on the flavor or scent of other foods because it has the highest fat content and lightest flavor. This not only goes for WHAT products are stored near your chocolate, but WHERE in your business the chocolate is stored. Grocery stores and specialty shops need to take into account a seafood or cheese department in proximity to chocolate displays. These smells also have the potential to seep into chocolate and impact flavor.

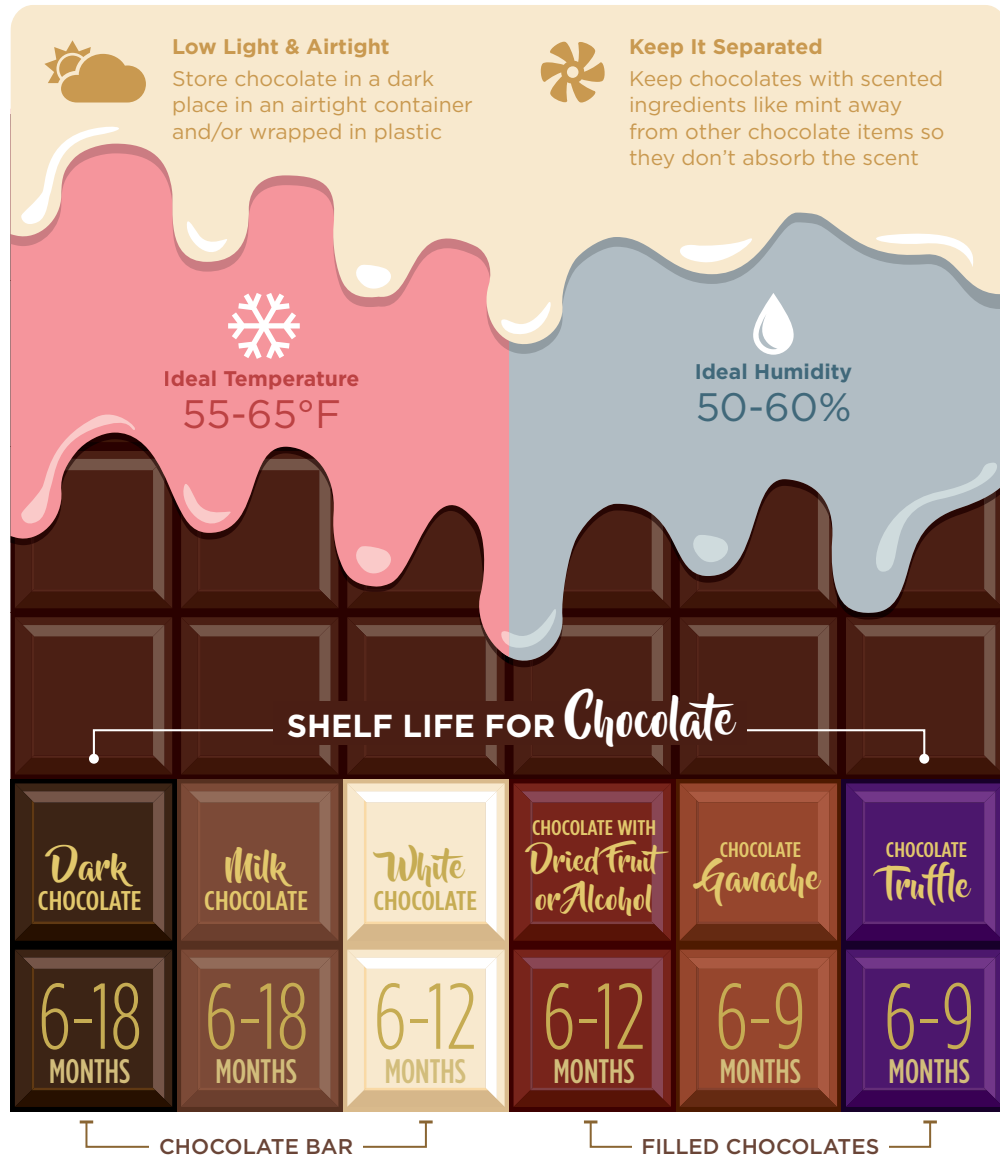


So now you've heard what could go wrong, but preventing that from happening isn't as difficult as you might think.

The following graphic outlines

The Ideal Chocolate Environment

Proper Chocolate Storage Environment



As much as temperature can impact chocolate quality, and cause melting, one of the factors that is hardest to detect and can be the biggest issue is humidity. High humidity, regardless of temperature, can cause chocolate products to sweat, impacting quality and detracting from appearance. In addition to having a thermometer measuring temperature, also have a hygrometer handy to keep a constant eye on relative humidity.

Storage of Chocolate

During Transport

The same environmental controls that apply to chocolate storage for your shop, apply to your supplier and their shipping methods as well. Is your supplier using refrigerated trucks to transport product? Is the product shipped in plastic and in a solid box to prevent oxidation and scent transmission?

This is also an instance where buying local is often better. The longer product is on the road, the higher the chance for issues to arise. A supplier like Nassau Candy with multiple local distribution centers across the country can be an asset.



We Keep it Cool

Our fleet of refrigerated trucks is kept at the ideal temperature, ensuring our confections taste factory fresh when they reach their destination.

Has all this *Chocolate* talk got you craving more for your assortment?

Nassau Candy's factory fresh creations will make your business the talk of the town.

Our comprehensive offerings of top national and international brands include everything you need to satisfy any chocolate craving.

Check us out at NassauCandy.com



About Nassau Candy

Nassau Candy is a family-owned business that has grown into one of the largest U.S. wholesale manufacturers of specialty chocolates and confections.

We create millions of pounds of chocolates and confections every year in our Hicksville, New York, factory, using prized family recipes and a combination of traditional and cutting-edge manufacturing techniques.

We are extraordinarily proud of all our confections, like our buttery smooth sea salt caramels, enrobed in rich chocolate and hand-sprinkled with sea salt. Our nonpareils are without peer — sporting our signature rounded edge, and decorated with sweet nonpareil sprinkles for a classic crunch. Nassau Candy's chocolate barks feature the colors and flavors of each season, wrapped up in colorful graphic gift tins.

Have something specific in mind? Our private label team and creative masterminds will work with you to develop delectable custom chocolate and candy creations.

With six distribution centers across the country and a fleet of refrigerated trucks, we proudly boast about our industry-leading on-time delivery.



NASSAU CANDY

Specialty Confections & Fine Foods



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Science + Discovery

SPRING 2017

Saving Lives
With the Neural
Tourniquet
PAGE 3

A Novel
Approach to
Treating Sepsis
PAGE 7



Integrated
Robotic
Therapy for

**STROKE
PATIENTS**

PAGE 4

 **Feinstein Institute
for Medical Research**
Northwell Health™

A Meeting OF THE Minds

Welcome to this edition of *Science + Discovery*, a publication celebrating the pioneering work of The Feinstein Institute for Medical Research. The pursuit of knowledge and its application are hallmarks of the work being done at the Feinstein Institute.

In these pages, we invite you to take a closer look at how our researchers are utilizing robotics, bioelectronic medicine and other innovative technologies to advance our understanding of how to heal human bodies. Join us on our journey to push the boundaries of medical discovery.


Researchers from around the world gathered to explore the application of bioelectronic medicine — a field that focuses on integrating electronics with nerves to treat disease and injury.

The Key Symposium 2016: Bioelectronic Medicine — Technology Targeting Molecular Mechanisms was hosted at the New York Academy of Sciences and organized with the assistance of the Feinstein Institute, the *Journal of Internal Medicine*, the Karolinska Institutet and the Royal Swedish Academy of Sciences.

Panels and sessions covered a variety of topics, including the application of bioelectronic medicine for fighting cancer and regaining limb control in paralyzed patients.

Led by PBS science correspondent Miles O'Brien, the closing panel, "What Life Will Be Like When We Can Fully Modulate the Nervous System: The Impact on Disease, Drugs, the Healthcare Industry, Personal Freedom and Privacy," expanded on the far-reaching benefits and consequences of bioelectronic medicine's rise in prominence and use.

To watch highlights from the Key Symposium 2016, visit 4healthier.me/NWSD-KeySymposium2016.



» The Center for Bioelectronic Medicine « Takes Shape

The Center contains three divisions with laboratories dedicated to study. In the Molecular Targets Division, biologists and chemists identify physiological triggers of illness. Within the Neurophysiology and Neuroscience Division, neuroscientists trace neural pathways to manipulate bodily responses. Engineers and computer scientists in the Neurotechnology and Analytics Division design devices to modulate disease pathways. Studies combine the expertise of each division. The result is an extensible research and development platform.

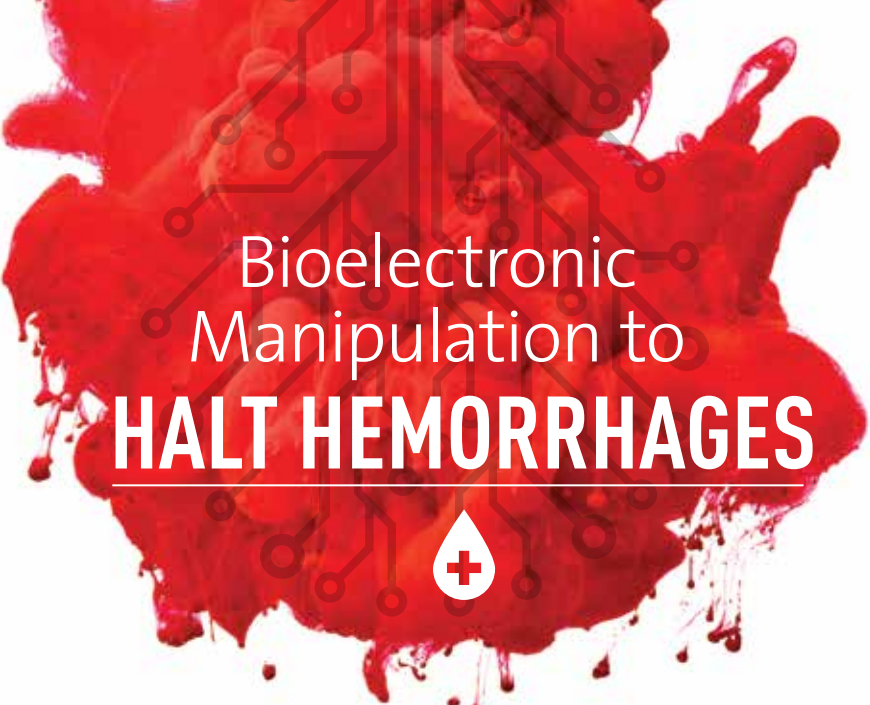
With the addition of new team members and formation of laboratory divisions, the Center for Bioelectronic Medicine at the Feinstein Institute is a hub for cutting-edge research.

A Growing Team

Top minds have been recruited to support the Center's diverse areas of study. Additions include research assistant Laura Goldman, MS, research assistant investigators Timir Datta-Chaudhuri, PhD, and Stavros Zanos, MD, PhD, assistant professors Harbaljit Sohal, PhD, and Theodoros Zanos, PhD, staff scientist Margo Straka, PhD, and electrical engineer Todd Levy, BS, MS. Chunyan Li, PhD, was appointed clean room laboratory director, and Yousef Al-Abed, PhD, now leads the Molecular Targets Division.

Visit 4healthier.me/NWSD-bioelectronicteam to meet the Center for Bioelectronic Medicine team.

The Center for Bioelectronic Medicine is hiring. Visit 4healthier.me/NWSD-bioelectronicpositions.



Bioelectronic Manipulation to HALT HEMORRHAGES

Pursuing a new solution to treat uncontrolled bleeding in postpartum patients, the Feinstein Institute partnered with Global Good and Sanguistat Inc. on a new bioelectronic treatment initiative.

Postpartum hemorrhage is the most frequent cause of maternal deaths worldwide. Close to 80,000 women in Africa and Asia lose their lives to it each year, as do around 6,000 women in the United States. Current treatment protocols include blood transfusions, surgical intervention with balloon catheters, anti-shock garments and uterine massage. However, no solution has proven to be sufficiently effective at saving the lives of women who have recently given birth and experience this complication.

“Blood loss is a major cause of maternal fatality, yet historically, there is little that can be done to treat this condition,” said Kevin J. Tracey, MD, president and CEO of the Feinstein Institute. “We are

pursuing the discovery of a new solution.”

Changing Outcomes

Together, the Feinstein Institute, Global Good (a collaboration between Bill Gates and Intellectual Ventures for inventing technology to improve life in developing countries) and medical device developer Sanguistat Inc. will initiate clinical trials to study the use of the Neural Tourniquet — a medical device that uses electronic stimulation of the vagus nerve to reduce blood flow and loss. The Neural Tourniquet was developed utilizing research from the Feinstein Institute, which found that vagus nerve stimulation supports prime platelets clotting.

The Feinstein Institute played a key role in initial research and clinical trials, and will remain involved in trials to test the efficacy of the device. Global Good will support feasibility trials, product development and the potential introduction into developing regions where women are at an increased risk of losing their lives to postpartum hemorrhage.

If successful, the Neural Tourniquet could have far-reaching positive implications not only for women giving birth, but also for soldiers wounded in battle, patients in emergency rooms and those with chronic bleeding diseases such as hemophilia.

“All postpartum hemorrhage deaths are tragic, and they are all too common in low-income countries, where many women suffer from anemia and lack access to obstetric care. When these mothers die, the tragedy also impacts their children’s health and education, perpetuating the cycle of poverty. This research could mean the difference between life and death for many mothers around the world.”

— DAVID BELL, DIRECTOR OF GLOBAL HEALTH TECHNOLOGIES SUPPORTING GLOBAL GOOD

Integrated ROBOTIC THERAPY

Helps Stroke Patients Regain Momentum, Their Lives

Robotic rehabilitation and stimulation therapy allow a new mother to be the mother she envisioned.

Like most patients who suffer from strokes, there was no warning that Kathleen Taravella would experience a blockage of blood to her brain. She went to bed, only to wake hours later with a feeling that something was not right. Kathleen roused her husband, Santo, who helped her reach the care she needed to survive and begin the process of recovering from her incident.

A stroke occurs when blood flow to the brain is interrupted, typically by a blockage in a blood vessel. Depending on the portion of the brain affected by the stroke and the extent of the damage, patients may experience a variety of post-incident side effects, including muscle weakness, cognitive difficulties and vision and language problems.

Road to Recovery

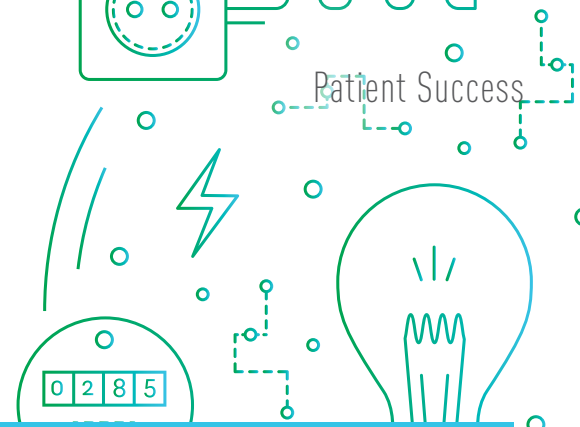
“My child was very young at the time of the stroke, so I was worried that, with my limitations, I would not be capable of being a good mother,” Kathleen said. “I was given the opportunity to participate in a clinical study using robotics, and I went for it. Whatever I could do to be the mother I envisioned, I was going to do.”

Kathleen began rehabilitation with Bruce T. Volpe, MD, a professor with the Center of Biomedical Science at the Feinstein Institute, and his team. Using technology developed in collaboration with investigators from Massachusetts Institute of Technology (MIT), Dr. Volpe mapped out a treatment plan that included the use of a series of robotic devices.

Active assist devices are robots designed specifically to help patients similar to Kathleen with limited mobility in their arms, hands and legs. During a typical therapy session, patients’ arms are connected to a robotic arm with a joystick-like handle. In front of the patient, a monitor displays a target. Patients must move their limbs to match up with different points around the target. These points move, and the patient must speed up to reach the target and make movements with more precision.

Under the watchful eye of support staff, patients complete the series of movements to the best of their abilities. When they are not successful, the robot steps in, putting their limbs through the completed motion.





Researchers hope these devices will help train the impaired limb to repeat motions on its own over time and that the challenge will help maintain patients' motivation and attention.

“Using Dr. Volpe’s robot program is like playing a video game, and it helps me push myself harder,” Kathleen said. “After my session is finished, even though it is challenging, I want to do more so that I can regain use of my arms and legs.”

Under Dr. Volpe’s guidance, Kathleen’s therapy was expanded to include bioelectronic stimulation, another advanced treatment protocol being explored by researchers at the Feinstein Institute.

“After rehabilitation with the robots and receiving stimulation, I can move my arms and legs better,” Kathleen said. “I no longer worry about not being a good mother. With Dr. Volpe’s help, I am able to do what I need to do to be the mother I want to be.”

To learn more about research being done to benefit stroke patients, visit 4healthier.me/NWSD-stroke.

Incorporating Bioelectronic Therapy

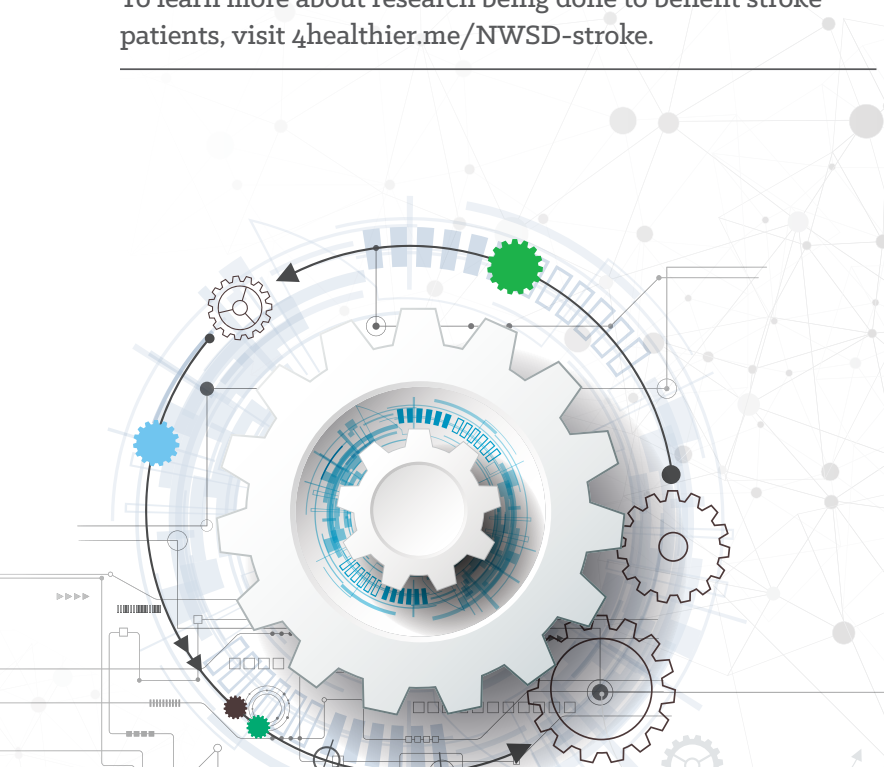
Expanding on the success of the robotics program, Bruce T. Volpe, MD, a professor with the Center of Biomedical Science at the Feinstein Institute, and his team have begun integrating noninvasive bioelectronic therapy with the treatment regimens of patients recovering from stroke.

In these latest trials, stroke therapy with robotics is combined with external stimulation. Patients who have had a stroke experience increased activation of their spinal cord signals, which causes muscles to tighten. This can present as hands being permanently clenched, making fine motor skills difficult.

Dr. Volpe believes that stimulation can help quiet the noisy signals of the spinal cord so the body’s motor system can take over.

His team is conducting two separate studies into the use of nerve stimulation in stroke patients. In one study, patients receive transcranial direct current stimulation — a noninvasive form of brain stimulation — as well as robotic therapy, three times a week for 12 weeks. Researchers hope to discover whether or not the combination of treatments will further improve arm mobility.

The second study examines the effect of stimulation on patients’ limb functionality when it is used alone. In this study, patients receive transspinal direct current stimulation, another form of noninvasive spinal stimulation, five times a week for two weeks, with the aim of reducing tightness of the wrist and hand.



Making decisions about cancer treatment and screenings is a complex process, particularly for patients with prostate cancer.



APP-GUIDED

Prostate Cancer Care

To assist in this process, Michael A. Diefenbach, PhD, a behavioral scientist with the Feinstein Institute, developed a software-based decision-making tool for prostate cancer currently in clinical trial.

The app helps design care plans for patients who suffer from this nuanced disease. Treatments range from immediate intervention with

surgery and radiation to a protracted period of careful observation called active surveillance. Patients and providers must also weigh the benefits of treatment against potential side effects, such as incontinence and impotence.

Prompts lead patients through the decision-making process. If they are interested in treatment, the

software then provides additional information related to requirements and outcomes, for which users rate their agreement or disagreement. Based on the patient's answers, the software's unique algorithm matches their preferences to a treatment option. Patients can then discuss treatment approaches with their physicians or email the results to start the conversation.

Bioelectronic Medicine IN CLINICAL PRACTICE

The pursuit of clinical applications drives the research and development being done at the Feinstein Institute's Center for Bioelectronic Medicine. The Center has achieved a variety of recent goals, including advances in treating:

Blood pressure — Scientists found that T-cells capable of producing the neurotransmitter acetylcholine can regulate blood pressure. T-cells contain choline acetyltransferase (ChAT), the enzyme responsible for the production of acetylcholine. With knowledge of ChAT cells' role and new data about the cells' response to vagus nerve stimulation, researchers are now exploring the use of bioelectronic medicine to treat blood pressure and hypertension.

Lupus — A new clinical trial will test the efficacy of bioelectronic medicine for treating pain associated with lupus, a potentially fatal chronic autoimmune disease that affects millions.

Bleeding — A preliminary clinical study is underway to see how vagus nerve stimulation affects bleeding time and clotting agent priming. Researchers estimate that stimulation could reduce blood loss by 50 percent. If proven correct, this could become a standard treatment for hemorrhages.



A STRATEGY Against Sepsis

The efforts of the Northwell Health Sepsis Task Force, combined with research conducted by the Feinstein Institute, have created an organization-wide system for sepsis prevention and saved thousands of lives.

Sepsis is a life-threatening, often body-wide immune system reaction to an infection, typified by symptoms such as fever, swelling, pain, fast heart rate, difficulty breathing, chills and disorientation. In advanced stages of sepsis — known as severe sepsis and septic shock — tissue is damaged and organs deteriorate. Organ failure and loss of life are possible if the condition is not swiftly diagnosed and treated.

Setting the Standard

One of the inherent issues with managing sepsis is that its symptoms are often incorrectly attributed to other conditions. Delayed treatment and the serious nature of sepsis contribute to the loss of 500,000 lives annually, according to the Centers for Disease Control and Prevention.

Feinstein Institute researchers have long examined sepsis and have identified some early signs of the condition. The Northwell Health Sepsis Task Force, led by Martin Doerfler, MD, has taken this work a step further and established a new approach for managing sepsis cases. Now, incidents are identified systematically, and medical professionals at Northwell Health follow a standardized sepsis treatment protocol based on rapid assessment of signs of organ injury. Rapid response, including administering fluids and antibiotics immediately upon diagnosis, opens a vital window of opportunity for providers to save lives before organs fail.

Current sepsis-related research being conducted at the Feinstein Institute is moving beyond diagnosis and early treatment protocols to focus on relieving sepsis symptoms. It is the team's hope that their work will help stem the tide of lives lost to sepsis and improve quality of life for survivors.

For more information about sepsis research, visit 4healthier.me/NWSD-sepsis.

Shifting Perceptions

Northwell Health channels resources and energy to raise national awareness for sepsis, presenting at national public forums, including the World Sepsis Congress, and crafting educational public service announcements with the help of the Rory Staunton Foundation for Sepsis Prevention.

Learn more about the active role the Feinstein Institute plays in sepsis advocacy and awareness. Visit 4healthier.me/NWSD-sepsisadvocates.

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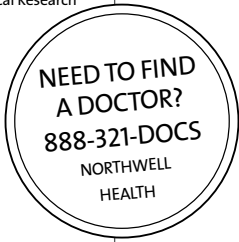
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SUPPORTING
THE FUTURE OF

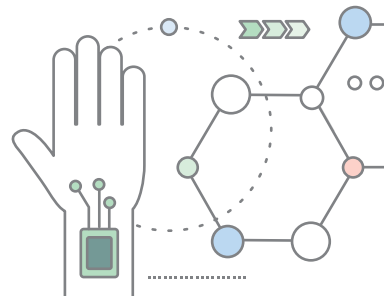
Medical Research

A \$25 million gift to the Feinstein Institute is the latest example of its namesakes' commitment to supporting cutting-edge medical research.

The donation from Bed Bath & Beyond Co-founder and Co-chair Leonard Feinstein and his wife, Susan, continues the tradition of research-focused philanthropy the couple began more than 30 years ago. In 2005, the Feinstein Institute was renamed in the Feinsteins' honor after they provided an initial \$25 million gift. Their recent gift helps fund the Feinstein Institute's efforts in areas including clinical trials, neuroscience, autoimmunity and bioelectronic medicine.

"The Feinstein Institute is pursuing many promising areas of research," Mr. Feinstein said, who also is a member of the Feinstein Institute's Board of Directors. "Within five to 10 years, we will see results and cures for some of the most confounding human diseases. Not many research initiatives show that kind of promise."

To join Mr. Feinstein in his support of research, visit healthier.me/NWSD-donate.



\$25 million
Initial gift from Leonard and Susan Feinstein

\$800 million
Total raised since then to support research, including:

- 21 research centers
- 7 partnerships with renowned research institutions
- 5 educational forums
- 3 schools for medical professionals

\$25 million
New donation from the Feinsteins

46 million
The number of patients living with conditions such as rheumatoid arthritis, paralysis/spinal cord injury and diabetes that research into bioelectronic medicine could help improve.

NORTHWELL HEALTH HOSPITALS:

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