Clinical Research Trial

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**New Treatment Using the Immune System to Fight Pancreatic Cancer**

Identifying cancerous tissue so that it can be eliminated from the body

Dhimant Patel, MD, is studying HyperAcute®-Pancreas Immunotherapy, a new vaccine for pancreatic cancer developed by NewLink Genetics that uses the immune system to fight off foreign tissue.

Despite the best clinical efforts and breakthroughs in biotechnology, most patients diagnosed with pancreatic cancer continue to die from the rapid progression of the disease. The new treatment targets the immune system – an important part of the body – as a therapy against the disease. Pancreatic tumor cells produce abnormalities that can cause an immune response similar to that stimulated by infected tissue. In progressive cancers, for reasons not yet fully understood, the immune system fails to identify, respond and destroy the cancer cells.

The HyperAcute®-Pancreas Immunotherapy clinical trial proposes a new way to stimulate the immune system to recognize the abnormal components and start an immune response that destroys or blocks the growth of the cancer. In this experimental therapy, patients are given injections of an immunotherapy drug consisting of two types of pancreatic cancer cells modified to make them more easily recognized and attacked by the immune system.

**HyperAcute®-Pancreas Immunotherapy helps the immune system identify and eliminate cancerous pancreatic tissue from the body in much the same way a transplanted organ of another animal may be hyperacutely rejected in a human.**

Dr. Patel and his research team will test the treatment in patients with pancreatic cancer who have undergone tumor removal surgery but remain at extremely high risk of disease progression. The goal is to demonstrate that the immunotherapy vaccine increases the time until tumor recurrence or increases overall survival when given in combination with the current standard of care therapy for pancreatic cancer. Specializing in the areas of internal medicine and medical oncology, Dr. Patel serves as the Aurora principal investigator on this trial and is on the staff at the Vince Lombardi Cancer Care Clinic in Green Bay, Wisconsin.
Leading Edge Biomedical Research

Surprising new information regarding the treatment of acute hypoxia in infants

Hershel Raff, PhD, is leading a team of Aurora Health Care investigators studying the treatment of acute hypoxia in infants. The director of Aurora St. Luke’s Medical Center Endocrine Research Laboratory and professor of medicine at the Medical College of Wisconsin, Dr. Raff is working with assistance from Aurora scientists Eric D. Bruder and Mitchell A. Guenther. Their leading edge biomedical research has given way to surprising new information regarding the treatment of acute hypoxia in infants and a connection with body cooling.

Acute hypoxia is a condition in which tissues do not receive enough oxygen, resulting in brain damage. It is known that the lungs of the human fetus are among the last organs to mature. Therefore, when a baby is born prematurely, the lungs have not developed into the full capacity required to intake enough oxygen and the baby is susceptible to acute hypoxia.

Doctors have traditionally placed hypoxic newborns in incubators or under warmers. However, by studying acute hypoxia conditions in baby rats, Aurora researchers have concluded that this practice is more harmful than helpful; warmer temperatures exacerbate rather than abate hypoxia. When the animals were exposed to low levels of oxygen for up to three hours, accompanied by maintenance of body temperature with warming pads, the research team noted marked changes in insulin and glucose regulation that could lead to hypoglycemia. Hypoglycemia, when coupled with the effects of hypoxia, increases the risk of brain damage in the infant.

New observations, new hope

During the course of their research, investigators made a specific observation in regard to body temperature in the case of neonatal rats. It was observed that when the animals were allowed to cool spontaneously, their glucose and insulin levels stabilized. This observation was then considered along with the knowledge that the natural response to oxygen-deprivation is spontaneous cooling. Based on the study’s findings, the researchers concluded that infants who experience oxygen deprivation should undergo cooling rather than maintaining a constant body temperature with heat in order to avoid potential brain damage. Notably, the researchers claim, that to their knowledge, there are no specific guidelines for body temperature management for premature babies with hypoxia. According to Dr. Raff, the team hopes that their “studies in the neonatal rat will translate to appropriate studies and guidelines for the control of body temperature in the hypoxic newborn.”

Designed to Save Lives

A new cooling blanket has the potential to improve the treatment of patients with sudden onset of life-threatening conditions

Because brain damage begins within three to five minutes after oxygen or blood flow ceases, timing is critical in order to preserve brain function in a life-threatening situation. However, studies show that brain function can be preserved when the body temperature is reduced to between 32 and 34 degrees Celsius.

For clinical events such as cardiac arrest, stroke, shock and asphyxia that limit blood circulation and oxygen to the brain, hospitals currently use hypothermic therapy to artificially lower body temperature and reduce metabolism, cell death, seizures and inflammation.

In hospital settings, hypothermic therapy involves cold saline infusions, ice packs, air or water mats, cold water baths and intravascular cooling. This allows for close temperature monitoring, but includes a lag time from condition onset to therapy implementation. Additionally, some therapies are expensive, invasive or can cause thermal injury. The good news is there is an alternative being developed that can address these challenges.

Aurora Health Care prenatal and perinatal medicine practitioner, Charles Potter, MD, and Medical Thermodynamics, LLC (MTD) of Milwaukee are developing a Thermochromic Cooling Blanket. The blanket is designed to be flexible enough for a caregiver to wrap around a patient, the blanket can provide immediate and controlled cooling in cases of the sudden onset of life-threatening conditions. The blanket is also insulated and made of multiple cells that can be selectively activated to control temperature reduction. Each cell contains two solutions separated by a membrane. An endothermic reaction takes place that absorbs heat when the membrane in the cell is broken. Thermochromic ink sensors allow caregivers to monitor temperature.

The flexibility of MTD’s technology is extremely effective at reducing shock and neurological injury in patients who are treated by emergency medical services and in outpatient and hospital settings.

"Ultimately, this Thermochromic Cooling Blanket holds the possibility to improve survival rates and decrease morbidity, as well as create long-term cost savings," said Dr. Potter. “Aurora’s continued research into the blanket and its many uses could potentially change the treatment of patients with sudden onset of life-threatening conditions that limit blood circulation and oxygen to the brain.”
Clinical Research Trial Impacts Lives

Courage and hope help a couple living and coping with multiple sclerosis

In 2009, Mary Henning of Sheboygan Falls was experiencing ear infections, perpetual dizziness and debilitating headaches that did not cease, even after three weeks. Mary and her husband Jeff met with brain specialists who performed neurology tests, a spinal tap and a magnetic resonance imaging scan (MRI). The couple has nurtured an indelible bond as they together faced this major health scare and, over the next three years, months of uncertainty and an initial misdiagnosis of Lyme disease.

Finally in January 2011, they had an answer. Mary was diagnosed with multiple sclerosis (MS). MS is a disease in which the immune system’s T-cells attack the body’s central nervous system, which consists of the brain and spinal cord. Normally, T-cells are a part of the immune system and help fight infections in the body. However, in patients with MS, the T-cells attack and damage the central nervous system.

As soon as Mary received her diagnosis, Jeff began researching clinical research trials and came across DECIDE*, a study investigating a new treatment for patients with MS, the T-cells attack and damage the central nervous system.

The Hennings entered the study knowing the potential effects both on Mary’s struggle as well as the struggle of others with MS. “We understand the importance of this (DECIDE) trial not only for our family but for other MS patients. We wanted to participate in the trial. It’s good for Mary and mankind,” says Jeff.

From the start, the Hennings knew they had made the right decision. Mary has high praise for the staff at the Center for Neurological Disorders at Aurora St. Luke’s Medical Center based on the positive experiences of several family members, some of whom work at Aurora, and the facility’s proximity to their home.

Led by neurologist and principal investigator Bhupendra Khatri, MD, DECIDE is a “double-blind, randomized clinical research trial. All participants are randomized by a computer program into one of two study groups—a process similar to flipping a coin. Double-blind refers to the fact that neither the principal investigator nor any of the participants know into which group any participant is placed or the drug any specific person is being given. As these details of the trial must remain anonymous to ensure the validity of the data, neither Dr. Khatri nor Mary have access to this information.

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What Is MS Disease?

Multiple sclerosis is a progressive disease, meaning nerve damage gets worse over time. How quickly it worsens varies from person to person. Damage to the nerve covering is caused by inflammation that occurs when a person’s own body’s immune cells attack the nervous system. MS seems to direct its attacks in the brain areas and spinal cord. We’re still not sure what triggers the inflammation. The most common theories point to a virus or genetic defect, or a combination of both.

What do we do know is that MS affects women more than men. And the disease most commonly begins between ages 20 and 40, but can be seen at any stage of life.
Drug Combination Therapy Holds New Hope for Breast Cancer Patients

It is a difficult prognosis for patients to hear. Diagnosed with triple-negative breast cancer (TNBC) or metastatic cancer (i.e., breast cancer that has spread via the lymph system to other parts of the body), patients often hear that their cancers come with a very poor overall survival rate because they are generally resistant to first-line conventional therapy,” said Aurora Health Care’s neuro-oncologist George Bobustuc, MD. “Developing effective treatment options for these aggressive cancers is a real need.”

Researchers have found that a combination of two drugs, Xeloda™ with Temodar™ — referred to as XT — works synergistically to slow tumor growth and may be very effective in treating some breast cancer patients such as those with TNBC.

With metastatic cancer, drug combination therapy can also be used by introducing a third drug into the treatment plans of breast cancer patients whose disease has metastasized in the brain. Dr. Bobustuc has successfully incorporated Xeloda™, Temodar™ and a third drug called Tykerb™ — referred to as XT(T) — into the treatment plan of breast cancer patients with extensive metastatic disease. Drug combination therapy offers hope and improved outcomes over conventional treatments such as chemotherapy and radiotherapy.

Knowing that conventional treatments, such as chemotherapy and radiotherapy, are not effective against these subtypes of breast cancer, Dr. Bobustuc and a team of multidisciplinary researchers have turned their attention to new, unexplored treatments. In an Aurora study that began in August 2012 and will conclude in December 2013, the team is pursuing a new treatment in which two to three drugs are used in combination, referred to as drug combination therapy.

Ultimately, if the approach proves more effective than traditional therapy, such as chemotherapy and radiotherapy, XT and XT(T) may become established components in breast cancer treatment. And this offers new hope for patients diagnosed with TNBC as well as patients diagnosed with breast cancer complicated by extensive metastatic disease.

This study is conducted under an Aurora Health Care Institutional Review Board (IRB), which is made up of a group of people (both scientists and lay persons) who review and approve research studies and ensure that clinical research follows clinical federal government regulations. The results of this study will be presented at cancer research meetings. The manuscript will be submitted for publication to clinical cancer research journals.

George Bobustuc, MD

Dr. Bobustuc is a board-certified neuro-oncologist and serves as medical director of Aurora’s neuro-oncology program. He brings more than 10 years of clinical and research experience in the field, serving most recently as neuro-oncology section chief at MD Anderson Cancer Center in Orlando, Florida. He is board-certified by the American Board of Psychiatry and Neurology.

Dr. Bobustuc’s special interests include primary brain tumors, metastatic brain cancer and leptomeningeal disease. He is an experienced provider of neuro-oncological treatment and is the author of numerous publications in peer-reviewed journals. Dr. Bobustuc’s research interest is the integration of new basic, translational and clinical knowledge into patient care in an individualized, safe, fashion, enabling patients to benefit in real time from the most recent advancements in the field of neuro-oncology.

Dr. Bobustuc is a member of the Brain Tumor Trials Collaborative (BTTC), whose members include professionals, entities and organizations dedicated to promoting brain tumor awareness and raising funds for research. Since 2004, this group has developed and performed hypothesis-based, state-of-the-art clinical trials focused on finding new treatments that will lead to improved outcomes for patients living with brain tumors.

Brain Tumor Trials Collaborative Participants

Aurora Cancer Care’s Neuro-Oncology Center

Baylor Health Care System

Cedars-Sinai Medical Center

Cleveland Clinic

Dana-Farber Cancer Institute

Henry Ford Health System

Huntsman Cancer Institute

Massachusetts General Hospital Cancer Center

Medical University of South Carolina

Memorial Sloan-Kettering Cancer Center

Methodist Hospital System

NewYork–Presbyterian/ Columbia University Medical Center

Northshore University HealthSystem

Northwestern University Feinberg School of Medicine

Texas A&M University of Texas: MD Anderson Cancer Center

The University of Texas: MD Anderson Cancer Center - Orlando

The University of Texas Southwestern Medical Center

University of North Carolina School of Medicine

University of Washington

US Oncology

Washington University School of Medicine in St. Louis

George Bobustuc, MD

In recognition of a researcher who has demonstrated exceptional dedication and success with his/her research projects and potential for growth in the research community.
Obstructive Sleep Apnea (OSA) and Cardiovascular Health

Evaluating new treatments for hypertensive patients with OSA

The number of individuals diagnosed with obstructive sleep apnea (OSA) has now grown to at least 18 million in the United States. As the number of individuals with OSA escalates due to increasing obesity and aging baby boomers, the need for innovative research to uncover new treatments also escalates.

Currently, the most common prescribed treatment is the use of a continuous positive airway pressure (CPAP) unit for patients diagnosed with OSA. Here’s how it works. OSA causes interrupted breathing while sleeping because the soft tissue in the back of the throat relaxes, blocking the airway. The CPAP unit helps clear the blocked airway by applying continuous pressure. Once the blocked airway is cleared, a patient does not experience pauses in his breathing, thereby alleviating the symptoms of OSA which are restless sleep, loud snoring and mood changes. While an effective treatment, up to 30 percent of patients do not experience pauses in their breathing and lower blood pressure — and of course, ultimately, reduce morbidity and mortality rates.

For those with OSA, blockage of the airway disrupts activity in the sympathetic nervous system, which maintains the body’s homeostasis. This correlates to hypertension, or high blood pressure.

One researcher looking for ways to treat cardiovascular disease in OSA is James Gapinski, MD, director of the sleep centers at Aurora BayCare Medical Center in Green Bay and Aurora Medical Center in Manitowoc County. Dr. Gapinski is part of a research team evaluating various OSA treatments for hypertensive patients. The team is studying responses to a drug called Allopurinol, used to reduce uric acid, and a second drug called Losartan, to control blood pressure. Taken together, these medications help block signals from the carotid body, which in turn may mediate the cardiovascular problems seen in sleep apnea.

As OSA and hypertension are a growing problem for Americans, researchers hope to normalize neurological and cardiovascular activity for those diagnosed with OSA. The use of Allopurinol and Losartan is one possible treatment. The goal of such interventions and the focus of Dr. Gapinski’s research are to reduce the severity of sleep-disordered breathing and lower blood pressure — and of course, ultimately, reduce morbidity and mortality rates.

A collaborative research effort across Wisconsin

Aurora BayCare Medical Center in Green Bay is one of four OSA study sites in Wisconsin. The others are Gundersen Lutheran (LaCrosse), Marshfield Clinic (Marshfield) and the University of Wisconsin — Madison. All are members of the Wisconsin Network for Health Research, which is funded in part by the UW — Madison Institute for Clinical and Translational Research Award, made possible through a grant from the National Institutes of Health. In addition to Dr. Gapinski, the study’s principal investigators are John Dopp, PharmD, assistant professor at the UW — Madison School of Pharmacy, and Barbara Morgan, PhD, professor at the UW — Madison School of Medicine and Public Health, in the Department of Orthopedics and Rehabilitation.

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But patient compliance is not the only issue. Further complicating the health effects of OSA is that the condition also adversely affects cardiovascular health.
Award from Department of Defense Helps Advance Evidence-based Nursing

Aurora Health Care is currently collaborating with the Department of Defense on a new study that uses technology to enhance provider knowledge and the use of best practices in daily patient care. With funding from the U.S. Army Medical Research and Materiel Command and its Telemedicine and Advanced Technology Research Center (TATRC), Aurora is studying the use of specific electronic tools, such as electronic health records, to enhance daily processes for improved decision-making and positive patient outcomes.

A primary aspect of the study is to create a process through which patient care information can be easily entered and accessed by nurses using an electronic tool – which could replace more traditional care that is solely based on knowledge that the nurse gathers at the bedside. Incorporating a faster electronic tool for documentation and communication could increase the amount of time available for direct patient care.

Led by principal investigator Mary Hook, PhD, PHCNS-BC, the study is aimed at early detection and collaboration, with the goal of enhancing evidence-based practices in patient care. TATRC will provide more than $450,000 in the first year and potentially about $1.5 million over three years to support the study.

Dedicated Research Supports Accreditations

The Aurora Health Care Metro Region received a three-year accreditation from the Commission on Cancer, an honor only given to programs with innovative, productive research departments. Accredited programs annually diagnose and treat approximately 80 percent of new cancer cases.

Judy Tjoe, MD, Wendy Mikkelson, MD, and Julie Kepple, MD, were awarded a three-year accreditation from the National Accreditation Program for Breast Center (NAPBC). It is bestowed upon organizations dedicated to improving quality of care for patients with diseases of the breast.

Excellence in Scientific Innovation

In October 2012, representatives from Aurora Health Care were invited by Oracle to attend the 2012 Prix Galien USA Forum in New York City. The annual event is hosted by the Galien Foundation, which fosters, recognizes and rewards excellence in scientific innovation in human health. The Galien Forum brings together industry, academia and government leaders to discuss pressing issues in research. Aurora participated in clinical research trials developed by the following companies who were final candidates for the Prix Galien USA 2012 Awards: Abbott, Biogen Idec and Acorda Therapeutic.

Left to right: Randall Lambrecht, PhD, Senior Vice President of Research and Academic Relations; Rachel Roller, Senior Vice President, Government Affairs; Colonel Karl E. Freidl, PhD, (Ret.) Former Director, TATRC

Left to right: Representing Aurora at the 2012 Prix Galien USA Forum were Sara Planton, Director, Clinical Trials Research; Margaret Hamburg, MD, Commissioner of US Food and Drug Administration; and Randall Lambrecht.