



HMRI *insights*

Huntington Medical Research Institutes

New Non-Intrusive Sleep Apnea Treatment

Clinical Trials Set to Proceed with Prototype Device

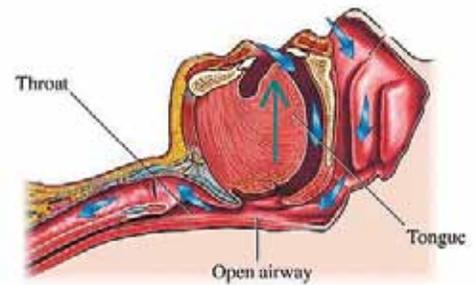
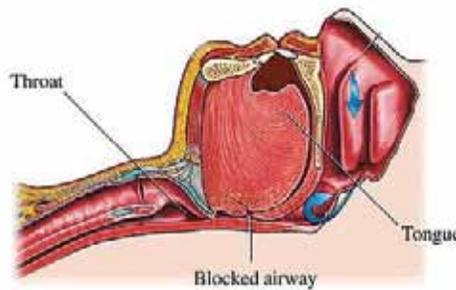
HMRI has developed a new non-intrusive treatment for obstructive sleep apnea (OSA). The new technology compactly fits into a dental appliance such as the "bite guard" now utilized for the treatment of bruxism



Dr. Douglas McCreery with prototype

(nocturnal grinding of teeth). It contains an infra-red sensor which detects the position of the tongue in the mouth. If the tongue falls toward the back of the mouth, a slight electrical stimulation would cause the person to move the tongue forward again, with the goal of eventually "training" the tongue to move itself into the forward position when it falls back. This is all accomplished without disturbing sleep in any way.

"The airway obstruction in OSA is caused by two things," Dr. Douglas McCreery, director of HMRI's Neural Engineering program and designer of the device, explained. "First, it's caused by the tongue partially falling back into



OSA is due to occlusion of the upper airway when the muscles collapse during sleep and the tongue base and soft pallet prolapse into the airway.

the airway, blocking the airway. Second, it's caused by lack of good muscle tone in some of the other muscles that surround the upper airway that are connected to the tongue. As it turns

out, if you move the tongue forward you get the tongue out of the way of the airway and that action tends to dilate the other muscles in the upper

continued page 8

Confocal Microscope:

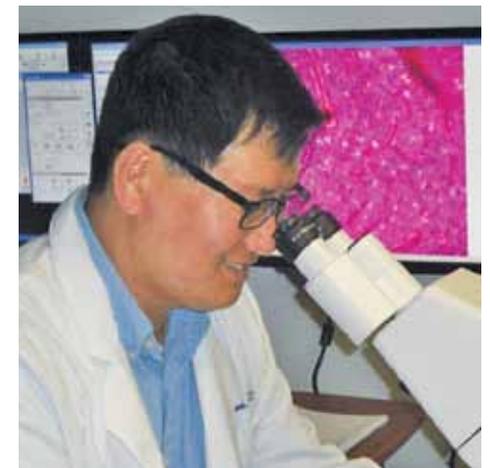
Enabling Reconstruction of 3-D Structures from Images

HMRI has just purchased a scientific instrument vital to its research—a Zeiss LSM 510 META confocal microscope. Half the funds for the purchase were provided by the Altadena Guild of Huntington Hospital, a major funding partner of HMRI for over 60 years. The microscope greatly enhances the ability of HMRI neural engineers and neurologists to conduct detailed in-house research.

"We received a great deal of assistance from the Altadena Guild to purchase this instrument, for which we are very grateful," said Dr. Douglas McCreery, director of HMRI's Neural Engineering program. "With the confocal microscope, we now have the ability to visually reach down into tissue and obtain a

three-dimensional reconstruction of all of the different cell types. Doing this same work with a conventional

continued page 3



Dr. Martin Han views brain tissue cells through confocal microscope.

HMRI Marks 60th Anniversary with Diamond Jubilee Tea

On Tuesday, August 28, Huntington Medical Research Institutes (HMRI) celebrated its 60th anniversary in the best way possible - with an afternoon Tea honoring its partner through the years: the Altadena Guild of Huntington Hospital. The event was held at the University Club of Pasadena and drew close to 100 attendees, including many longtime members of the Altadena Guild, HMRI board members, researchers and VIP guests.

HMRI President Dr. William Opel opened the program with a historical look back at the relationship between HMRI and the Altadena Guild. Tribute remarks followed from a distinguished list of HMRI board members, staff and



Altadena Guild members Nancy Zachariasen (left) and Helen Posthuma with MHRI board member Dr. Larry Jones.

researchers: Dr. Marylou Ingram, Dr. Michael Harrington, Dr. Larry Jones, Dr. Brian Ross, retired researcher Dr. William Agnew and HMRI Director of Development Diane James.

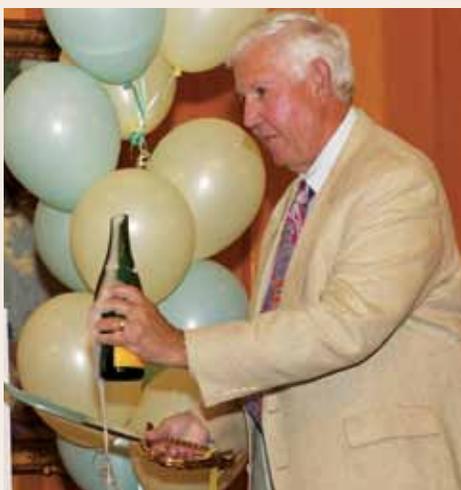
While the temperature outside was well over 100 degrees, inside the University Club's main dining room, the group enjoyed conversation while harpist Carolyn Sykes provided background music. The menu included assorted tea sandwiches, fresh fruit tarts and scones.

Throughout the event, Opel invited Altadena Guild past presidents, home tour chairs, golf tournament chairs, and other special friends to stand and be recognized. A PowerPoint presentation in the background also offered recognition and thanks. "As an organization, and individually, we are pleased to have the privilege of supporting HMRI and its research," commented Guild President Debbie Williams. "We are in awe of the outstanding accomplishments of these gifted scientists and physicians."

The highlight of the Tea proved to be the opening of a bottle of champagne with a saber by HMRI board member Roger Engemann - something that he said Napoleon did at the end of a campaign. He then asked everyone to join him in a celebratory toast to HMRI. Since a 60th anniversary is considered a Diamond Jubilee Anniversary, each of the Altadena Guild members was



Dr. William Opel opens program with historical perspective.



As Napoleon did following a campaign, Roger Engemann used a saber to open a bottle of champagne.

presented with a "diamond ring" key chain by the table captain. A representative from HMRI was seated at each table to make these presentations. As they left, guests also received a 60th anniversary commemorative leather bookmark.

The recognition for the Altadena Guild members was appropriate and fitting. HMRI was founded in 1952 and the Altadena Guild has been fundraising for the organization since the beginning. "To date, the Guild's annual home tours, fashion shows and other philanthropic endeavors have raised approximately \$2 million on behalf of HMRI," commented Opel. "It is with deep appreciation that we honor the Guild and also credit them for introducing many other friends and benefactors who support HMRI directly."

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microscope is extremely laborious and time-consuming, which is what we had to do prior to the confocal microscope.”

A confocal microscope allows examination of a specimen in such a way that extremely high detail is obtained. Specific molecules can be isolated and examined by placing fluorescent dyes within antibodies which attach themselves to the molecules. A laser is used to cause the dyes to “light up” and be seen within the microscope.

Because the microscope can also reach downward within a specimen, specific detail can be viewed which cannot be obtained with a conventional light microscope. “For a conventional microscope, specimens must be cut into thin sections,”

explained Dr. Martin Han, biomedical engineer and staff scientist in HMRI’s Neural Engineering program. “Whenever you cut tissue sections, you sacrifice a little bit of detail of the top and bottom. When you can examine it all together in one specimen, you preserve much of the existing tissue as it is, instead of losing 5 to 10 percent of everything you cut.”

The microscope has already been put to immediate use within HMRI. In research dealing with neurological implants, it is being used to view the results of long-term implantation. “On a cellular level, we are studying the interaction between the brain and the device we put into the brain,” said Han. “Prior to having the confocal microscope, we did some work using a confocal micro-

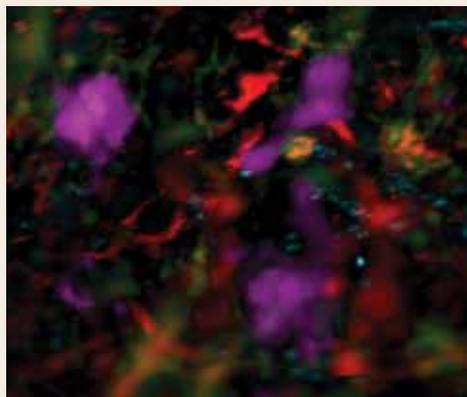
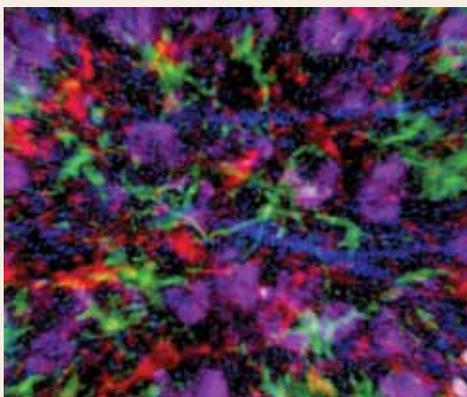
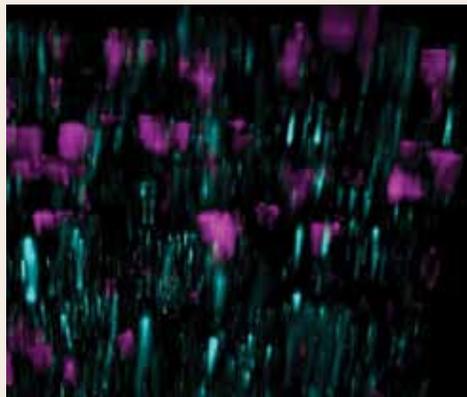
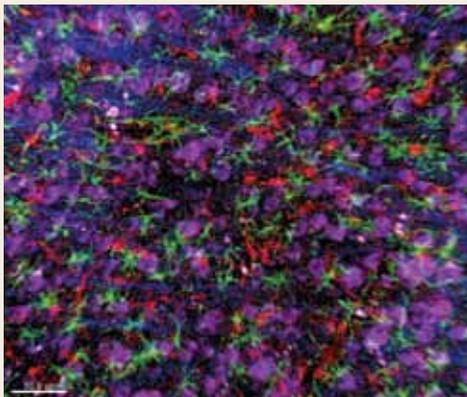
scope at Caltech. The advantage of our new microscope over others is that it is motorized. We would have to manually scan a large area which took a long time and was very expensive. Now, we can automate the moving of one area to the next. It saves a lot of time and reduces human error.”

“Having the equipment here, I can actually turn it on, leave it on for 24 hours, and let it scan whatever it needs to scan for an indefinite period,” added Haison Duong, HMRI Neural Engineering research associate “That increases the workflow quite a bit. I can basically calibrate all the settings and let it work on its own.”

Another area of research utilizing the microscope is that of migraine headaches. “I plan to use the confocal microscope to look at the fine cellular localization of particular molecules that are involved in a model of migraine that we’re studying,” said Dr. Michael Harrington, director of HMRI’s Molecular Neurology program. “The reason we need a confocal microscope is that if I have two different molecules in the same cell, and they’re in different regions of the cell, there’s no way a regular microscope will unequivocally let me know where things are. That’s why we need the confocal microscope: we need what we refer to as sub-cellular localization.”

In addition to the microscope itself, an attached computer and software is utilized for three-dimensional renderings after observation. Such renderings make it possible to view specimens from multiple angles, and also “stitch” together different images to create one all-encompassing image.

Due to the capability of bringing detailed research completely in-house, it is expected that the LSM 510 META confocal microscope will earn back its purchase price rather quickly. “It will pay for itself within a year, just based on what it costs us per hour to go to another facility,” noted Duong.



Images of brain cells in a thin slice of tissue, taken with the new Zeiss LSM 510 confocal microscope. The brain cells have been stained with dyes that reveal each cell type with a different color: nerve cell bodies (magenta); branches of nerve cells (blue); astrocyte cells (green); microglia cells (red). The latter two are supporting cells that help the neurons. These images make it possible to correlate changes in the tissue surrounding the implants with changes in the implants’ ability to record signals from the nearby nerve cells. The goal is to design implants that can record these signals for many years.

Automation Advances Laboratory: New Equipment Enhances Critical Tissue Engineering Research



Dr. Marylou Ingram and Brenda Ward, research associate, observe robotic fluid handling by Biomek 4000.



New Synergy H1 Microplate Reader and Biomek 4000.

As our world becomes a faster-paced environment, life sciences have turned to automation to reduce costs and create more efficient operations. Thanks to a grant from the Roy E. Thomas Foundation, researchers in the HMRI Tissue Engineering laboratory have recently acquired two new instruments that will allow them to streamline workflow through automation and spend more time on the discovery process in their

search for new anti-cancer drugs.

With the new Biomek 4000 Laboratory Automation Workstation, our Tissue Engineering program has the ability to increase production of tumor histoids – living human mini-tumors – used in testing new anti-cancer drugs. Producing the large number of tumor histoids required for drug testing would be virtually impossible without robotic fluid handling offered by the Biomek

4000. Much of the exorbitant cost of developing new anti-cancer drugs is attributed to the use of unreliable and inefficient test systems during screening of potential new drugs and can cost upwards of \$1 billion to bring one new drug to market.

The grant from the Roy E. Thomas Foundation also enabled the purchase of a second essential piece of equipment, the Synergy H1 Hybrid Multi-Mode Microplate Reader. Placed next to the Biomek 4000 robotic system, this temperature-controlled programmable plate reader is used for spectrophotometric analysis of tumor histoids within their droplets. Both pieces of equipment are housed within a laminar flow tissue culture hood, a requirement for maintaining the integrity of sterile cultures.

“We are absolutely delighted, to say nothing of relieved and grateful, to have the important new equipment which will allow us to advance to a new phase of our research,” said Dr. Marylou Ingram, senior research scientist with the Tissue Engineering & In Vitro Systems program. “The grant from the Roy E. Thomas Foundation could not have been more timely or important to our research.”



HMRI Receives Top Rating

Charity Navigator, one of the nation’s premier charity evaluators, has honored HMRI with its coveted 4-star rating. Only 25 percent of charities evaluated receive the four out of a possible four stars that indicate an organization adheres to good governance and other best practices, and consistently executes its mission in a fiscally responsible way.

In this competitive philanthropic market, Charity Navigator highlights the outstanding work of efficient and ethical charities with the goal of providing donors with information needed to give them greater confidence in the charitable choices they make.

Golf Tournament Celebrates 60 Years Of Research Excellence

On Monday, October 22nd, the forecast called for rain throughout the Southland. You wouldn't know it if you were among the golfers gathered at Annandale Golf

Engemann were the tournament's major sponsor. Lending their support as tournament sponsors were Tom Boyle and Wendy Lees, Symes Automotive Group, and the Emelco Foundation.



L-R: Denise Allen, Vickie Miller and Wendy Cobleigh (with their caddy) took the trophy for Women's Flight Overall Winners. Vickie also captured the award for Women's Closest to the Pin.



L-R: Frank Davis, Bryant Davis, Ed Freeman and Dave West were the Men's Flight Overall Winners.

Club in Pasadena. For the HMRI Lynn Smith Founders' Classic, it was a beautiful fall day – just perfect for golfing!

Part of HMRI's year-long 60th anniversary celebration, the golf tournament brought together a "Who's Who" of Pasadena philanthropy as supporters and sponsors. HMRI board member Ann Hall served as tournament chair. Serving as honorary co-chairs were Michael C. Doyle, HMRI's board chairman, and H. Thomas Boyle, Annandale's club president. Mr. and Mrs. Roger

A number of corporate and business sponsors were also involved, including Wells Fargo Home Mortgage, Sullivan Curtis Monroe Insurance Services, Cooperative of American Physicians and Citizens Business Bank.

The day began with arrivals and registration at 9:30 a.m. Guests were greeted by a distinguished group of gentlemen in blue blazers and grey slacks. The "A" list greeters included HMRI President Dr. William Opel. Lunch on the commons followed, sponsored by Huntington Hospital and HMRI Board Chairman Mike Doyle. After golf, guests enjoyed a cocktail reception sponsored by Davis Wright Tremaine LLP and PBWS Architects. The day concluded with an awards dinner with all proceeds from the tournament benefitting HMRI.

Twenty-three foursomes vied for awards for Men's, Women's and Mixed Flights. The day also included contests for Men's and Women's Closest-to-the-Pin, Men's and Women's Longest Drive, and two separate Hole-in-One prizes – one for \$10,000 in cash, and one for a Cadillac.

Congratulations to the award winners, and thanks to all who made the HMRI Lynn Smith Founders' Classic the perfect celebration for 60 years of research excellence.

HMRI Lynn Smith Founders' Classic Winners:

Men's Flight

Frank Davis, Bryant Davis, Ed Freeman and David West

Ladies' Flight

Denise Allen, Vickie Miller and Wendy Cobleigh

Mixed Flight

Theresa D'Andria, Frank Tamburo, Christopher Kopecky and Joe Jardino (Thomas & Bette Coleman Foundation)

Closest to Pin #9

Men's – Tony Solano - 9' (Symes Automotive Group)

Ladies' – Vickie Miller – 4'5"

Long Drive #6

Men's – Greg Greenwood (Symes Automotive Group)

Ladies' – Rita Whitney (Wells Fargo Home Mortgage)



Patsy Grant and Jim Griesgraber of Wells Fargo Home Mortgage sponsored a gold-level foursome and tee sign.

Guild Fashion Show Benefits HMRI

The Altadena Guild of Huntington Hospital recently made a generous donation of \$6,500 to HMRI following its "Fall Fashion Fun" event held at Macy's Pasadena. Proceeds from the event will support the various research projects currently underway at HMRI. Proceeds also benefit the Constance G. Zahorik Appearance Center at the hospital.



Guild model Diana Trujillo walks the runway in style.

HMRI Colorectal Research Fund: *Advances in Surgical Treatment Applauded*

For 20 years, Paula Welch-Forrest led a reclusive lifestyle complete with clinical depression, low energy, a lack of self-esteem and virtually no zest for life. In 2012, Dr. Howard Kaufman, colorectal surgeon and HMRI researcher, changed all of that. Suffering from numerous colorectal problems and unable to get a proper diagnosis or successful treatment, Forrest was eventually referred to Kaufman.

"By the time I met Dr. Kaufman, I had already been told I had the colon of an 80-year-old," said 49-year-old Forrest. "Dr. Kaufman was so kind and asked me questions that no other physician had bothered to ask. He also listened carefully to what I had to say in order to put all of the pieces of the puzzle together." Forrest sensed right away that she finally had met the right physician whose extensive research and experience made him one of the top experts in his field.

With a diagnosis of colonic inertia, a condition that occurs when muscles or nerves in the colon fail to function effectively, Kaufman performed a laparoscopic total abdominal colectomy. Sometimes known as an ileorectal anastomosis, the surgery involves removal of the large intestine from the ileum (lowest part of the small intestine) to the rectum. The end of the small intestine is then attached to the rectum.

"Ms. Forrest was a wonderful and cooperative patient who was anxious to resolve her long-standing medical issues. I'm pleased that she

recovered so well from the procedure and is moving forward with her life," stated Kaufman.

Since her surgical procedure, Forrest's lifestyle has changed considerably.

She has become an active, social person who no longer hides out from the world. Her family and friends barely recognize the new persona but are delighted. "My husband calls me his 'social butterfly' now and tries to keep up with my schedule," commented Forrest. "I was too embarrassed to speak out about my medical problems before, but now I

want to 'shout it from the rooftops' so others like me have hope."

In addition to a private practice and serving as medical director for Huntington Hospital's Cancer Center, Kaufman is director of the Colorectal Research program at HMRI where he passionately pursues new technologies in his field. He was one of the early pioneers of minimally invasive surgery for Crohn's disease and was the first surgeon on the west coast to perform colon resections laparoscopically through a tiny single incision.

"I cannot sing the praises of Dr. Kaufman enough," said Forrest. "Every time I receive a compliment regarding my renewed health, I tell them that Dr. Kaufman literally saved my life. I'm asking everyone to show their appreciation by sending a donation to HMRI for the Colorectal Research Fund. I'm proud to be able to honor Dr. Kaufman in this way so others can experience the same successful outcome."



Dr. Kaufman with patient Paula Welch-Forrest

HMRI Researcher Inspires Youth

"Thank you so much for coming to our science fair and teaching us about the human brain. It looked really strange but was so cool!"

"Thank you for inspiring [us] with science. The fact I found most interesting is that neurologists do not know the causes of brain diseases. I will look into becoming a neurologist."

"I learned so much from you about our brain. My dad was amazed that I knew so much."

These are but a few of the many accolades expressed in "thank you" letters received by Dr. Michael Harrington, HMRI's director of Molecular Neurology, following his presentation at a reverse science fair at Holy Redeemer Middle School in Montrose. Harrington was one of a number of physicians, researchers



Dr. Michael Harrington emphasizes connection between brain and spinal nerves.

and engineers invited to participate in this annual event to give 7th and 8th graders an opportunity to understand science and medicine "up close and personal."

Beth Cohen, Holy Redeemer's science teacher, acknowledged that Harrington's presentation regarding the brain is the most popular which is why she invites him back every year. "He truly knows how to inspire these kids and pique their curiosity," she noted. "His style is very real rather than sounding like a text book." The classroom presentation included viewing a real human brain followed by an explanation of the function of the brain and the mystery of brain diseases such as Alzheimer's, Parkinson's and migraine.

"As a researcher, I feel we have a moral and social responsibility to share information with our youth through science education," noted Harrington. "I thoroughly enjoy this annual opportunity to interact with our young people."

HMRI Honors Long-Service Employees

Last fall, HMRI hosted its annual Long-Service Employee Anniversary Luncheon. The following were honored in five-year increments:

30 Years:

Marylou Ingram, In Vitro Systems/
Tissue Engineering

20 Years:

Frank Davis, Business Office

10 Years:

Todd Franklin, Business Office

Al Kowalewski, Neural Engineering

5 Years:

Xianghong Arakaki, Molecular
Neurology

Bernice Garza, Liver Center

Margaret Diamond, Administration

Mandy Lai, Business Office

Pom Sailasuta, MRS

To become a
research study participant in
migraine or aging research



contact

Dr. Michael Harrington

(626) 795-4343

Ext 218

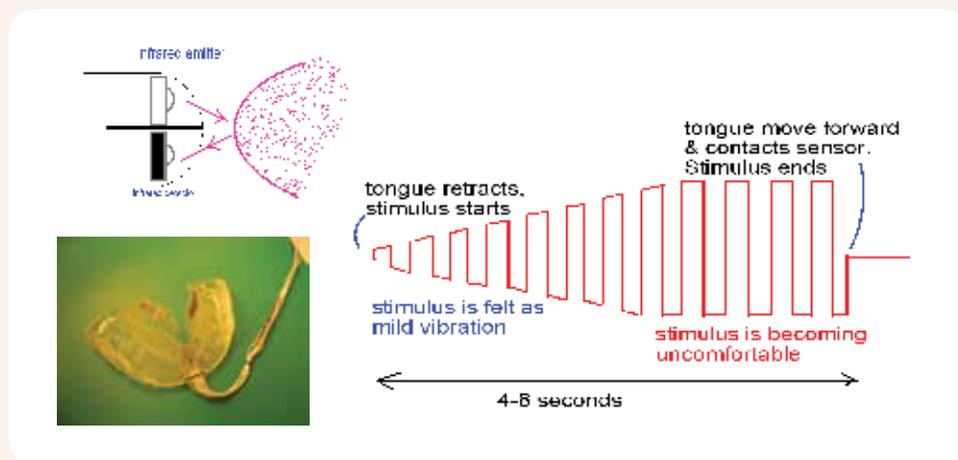
mghworks@hmri.org

airway. These actions make it possible for a person to breathe throughout the night without interruption.”

HMRI received a patent for the new technology on August 31, 2012. This patent provides a protection for the technology so that it can be licensed to commercial manufacturers for broad distribution.

Currently, the most common treatment for OSA is a technology called Continuous Positive Airway Pressure (CPAP) – a method by which air pressure is applied through a mask worn while sleeping. While this method is highly effective, it has been found that OSA patients using CPAP only use it 54 percent of the time due to discomfort and other issues. Five percent of users actually give up on the method leaving them with no treatment at all.

“Our objective was to find a way of treating OSA that was more acceptable



Electrical stimulation of the Hypoglossal nerve can move the tongue forward in the mouth and prevent it from blocking the airway.

to users than treatments such as CPAP,” McCreery said. “CPAP is 100 percent effective when used, but because the user must wear a hose and attachments that connect to the nose, people often find it intrusive and generally don’t like it. We set out to devise something with

the efficacy of CPAP, but that is more generally acceptable and that people will use 100 percent of the time. In your mouth, the device feels exactly like a bite guard – no difference whatsoever. It’s very comfortable.”

OSA is a treatable disorder in which

Volunteer Spotlight – Jeannette Martin



Since her retirement, Huntington Medical Research Institutes (HMRI) volunteer Jeannette Martin finds that life is still exciting and filled with challenges. She first learned of HMRI through her husband who invited her to attend its lectures and events. Coincidentally, her husband is a close friend of HMRI’s Chairman of the Board Mike Doyle, who originally introduced the

pair. Doyle, owner of Econolite, a traffic control systems company, was also her employer for 35 years while she served as vice president of human resources.

As she became more involved with HMRI, her talents became more apparent. “Jeannette Martin is living proof that good things come in small packages,” noted HMRI Development Officer Terry Garay. “She may be petite, but is easily one of the strongest and most effective leaders I have ever met. Thanks to her efforts, HMRI’s Event Committee produced stellar results.”

As event chair for HMRI’s Casino Night fundraiser on February 23 to celebrate its 60th anniversary, Martin energized a committee that turned researchers and friends into free-wheeling gamblers in a speakeasy ambiance. “We were grateful for the opportunity to create a successful fundraiser and ‘friend-raiser’ in order to provide HMRI with the crucial resources it needs,” enthused Martin.

Martin is no stranger to the magnitude of the resources offered by HMRI. Several years ago, her adult son was diagnosed with hepatitis C. She knew immediately that she wanted him to be seen at HMRI’s Liver Center under the auspices of Dr. Myron Tong. Her trust was already deeply rooted in the Center’s programs, and she felt confident he would receive the best medical advice and innovative treatments available.

In her leisure time, Jeannette continues to pursue her hobby of painting china plates and vases as well as porcelain ornaments, which she gives away as gifts. She also enjoys travel and managing a menagerie of rescue dogs and cats at home. “With everything that I do, I still find my role with HMRI to be the most meaningful,” stated Martin. “I’m proud to contribute to a mission that will impact medical technology for generations to come.”

the upper airway collapses during sleep, causing cessation of breathing for several seconds at a time, numerous times throughout the night. The disorder affects 9 percent of working-age women and 24 percent of working-age men - and it is estimated that only one in five persons afflicted with OSA receive effective treatment. It is hoped that this new technology will significantly increase those numbers.

OSA has a number of negative medical ramifications. Those afflicted suffer frequently interrupted sleep, which causes fatigue during waking - usually working - hours. In addition to constant tiredness, research has indicated that increased risk of cardiovascular disease is associated with OSA as well as a markedly increased mortality rate relative to the general population.

McCreery emphasized that the as-yet-named device is not ready for use in

patient treatment. A prototype device has been developed and McCreery will soon be seeking permission to proceed with clinical trials. When needed funding for the trials is obtained, clinical trials will start with non-OSA participants to finalize issues such as comfort and acceptability. Once that phase is completed, trials will then move forward with OSA sufferers. These trials will be conducted in partnership with a neurologist or pulmonologist whose input and analysis will be critical to the outcomes.

Since joining HMRI in 1979, McCreery has been the principal investigator or co-principal investigator of 18 research grants and contracts from the National Institutes of Health. He participated in the development of the vagus-nerve-stimulating electrode, which has now helped more than 30,000 people afflicted with epilepsy. McCreery and his team have been instrumental in defining pro-

cedures and criteria for safe therapeutic stimulation of neural tissue - data which has been used by the FDA for the certification of implantable medical devices. These include the deep brain stimulator manufactured by Medtronic, which has been utilized in the treatment of more than 50,000 patients with Parkinson's disease.

McCreery is enthusiastic about the development of this new technology for the treatment of OSA. "Looking at the incidence of this disease and the number of people that are not getting treatment, along with the number of people that are somewhat reluctant to use or don't adapt well to CPAP, we are confident that we have the ability to find a way to get more people on board," McCreery concluded. "It would be of great benefit to have a larger percentage of the population receiving acceptable, effective treatment."

YOUR SUPPORT...OUR GRATITUDE

HMRI's 60th Anniversary 2013 Casino Night Celebration



Proceeds from this event benefit HMRI's Scientific Equipment Fund.

Thank you for honoring our physicians and scientists. Your support could help fund the next medical breakthrough.



Jeannette Martin, *Event Committee Chair*

Event Committee

Judy Bolenbaugh	Bobbie Miller
Joan Branin	Persephone Oliver
Cindy Carlburg	Halaine Rose
Wray Cornwell	Maureen Savage



Partners In Discovery (September to December, 2012)

Special thanks to philanthropic partners whose generous support helps HMRI improve health and enhance life through medical research.

Major Donors

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Memorial and Tribute Gifts Received (September to December, 2012)

Honor someone special — perhaps a favorite physician or a researcher, or make a memorial gift to remember a special individual

Tribute gifts honored:

Mr. and Mrs. Wray C. Cornwell
Ms. Molly Cummins
Dr. Howard Kaufman
Dr. and Mrs. William Opel
Dr. Brian D. Ross
Mr. Grant Stein
Dr. Myron Tong

Memorial gifts remembered:

Mrs. Margaret Bailey
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