SCI and CellNetix Launch Gene Sequencing Program

Advances in cancer research have given oncologists many new and remarkable preventive, diagnostic and therapeutic tools. The newest tool is gene sequencing, which the Swedish Cancer Institute (SCI) has added to its arsenal in the fight against cancer.

Thanks to a partnership with CellNetix, SCI cancer specialists are now able to use gene sequencing to identify a tumor’s “fingerprint.” Using this information, they personalize their patients’ treatment plans based on the identification of abnormalities in specific cells - no matter where the cells or tumors are located.

This is a significant and exciting change in the approach to cancer care, which for years primarily focused on the anatomic location of a tumor to develop a treatment plan, rather than the tumor’s molecular makeup.

SCI and CellNetix have strategically selected a “hotspot” panel of 68 genes for sequencing. These genes represent the most relevant mutations in many different cancers, including those found in the brain, breast, colon, ovaries, skin and lungs, as well as other types of tumors. The panel also includes genes found in blood cancers, such as leukemia and lymphoma. The genes were selected as being the most actionable in regards to promising treatments and outcomes.

“Gene sequencing has opened the door to new therapies that zero in on the abnormal cancer cells and leave healthy cells alone,” says Anna B. Berry, M.D., director of molecular pathology at CellNetix. “The reports we provide SCI’s cancer specialists will include a wealth of information about treatment options and available clinical trials.”

(continued on page 2)

Prevalence of Non-Alcoholic Fatty Liver Disease Tied to Rise in Obesity, Diabetes and Metabolic Syndrome

Non-alcoholic fatty liver disease (NAFLD) is one of the newer additions to the list of reasons physicians should be promoting weight loss and exercise with their patients. Researchers who analyzed data from three nationwide surveys conducted between 1988 and 2008 presented some startling findings at the International Liver Congress in 2011. They showed that the prevalence of NAFLD doubled. Some liver specialists estimate the overall prevalence of NAFLD will increase to 40 percent of the population by 2020 and to 50 percent by 2050. The researchers also discovered that the percentage of chronic liver disease (non-alcoholic steatohepatitis/NASH) related to NAFLD increased from 46.8 percent during the first survey period (1988-1994) to 75.1 percent by the 2005-2008 survey period. Additionally, the frequency of liver transplant for NASH/cirrhosis has increased five-fold over the last decade — a trend which is expected to continue.

These trends are understandable within the context of the growing number of people who are obese, particularly visceral obesity, and have metabolic syndrome. NAFLD is seen in up to 87 percent of those with diabetes. At least 50 percent of those with high serum triglyceride or low HDL cholesterol levels have NAFLD.

(continued on page 6)
Why is gene sequencing important?
Cancer patients want to beat cancer and get on with their lives as soon as possible. Being able to identify the best treatment — right from the start — is the most efficient way to treat cancer. A gene-sequencing report identifies treatment options that have been effective for other patients with a similar gene abnormality, as well as available clinical trials of investigational therapies. Because SCI is one of the largest clinical-trial facilities on the West Coast, SCI patients have access to many of these treatments that may not be available elsewhere.

The information gained through gene sequencing helps avoid potentially ineffective treatments and gets the patient on the road to recovery more quickly.

“Gene sequencing and the study of tumor genes is not new to Swedish, or to the Ivy Center for Advanced Brain Tumor Treatment at the Swedish Neuroscience Institute, which has been mapping brain-tumor genes since 2009,” says Thomas Brown, M.D., executive director of SCI. “What is new at SCI is a step-by-step approach that expands the use of gene sequencing to benefit more patients with cancer. We are fortunate to have a tremendous number of cancer treatment options — many drug therapies, sophisticated surgical procedures and an extensive array of radiation technologies. Gene sequencing gives us the ability to more efficiently incorporate those options into highly personalized treatment plans.

“The goal is to use gene sequencing to develop the most effective treatment plans that will help minimize side effects, improve our patients’ quality of life during and after treatment, and ensure the best possible outcomes.”

Go to www.swedishcancerinstitute.org for more information about personalized medicine at the Swedish Cancer Institute. To refer one of your patients or to request a second opinion, please call 1-855-XCANCER.

How does personalized medicine work?

There are five steps that a patient follows to participate in the Personalized Medicine Program at the Swedish Cancer Institute.

**Step 1.** Agree to share information. Some patients voluntarily agree to have their anonymous genomic sequencing data and information about their treatments and results stored in a database. These patients are contributing to research efforts aimed at increasing the survival and cure rates for other patients with cancer.

**Step 2.** Collect a tissue sample. A small tissue sample is collected through a biopsy or surgery.

**Step 3.** Sequence the genes. Pathologists at CellNetix use sophisticated equipment to pull out the DNA and identify the tumor’s genomic fingerprint and gene abnormalities. They also collect additional information about the tumor using a variety of other tests.

**Step 4.** Analyze the data. In about 10-14 days, the cancer specialist receives a report from CellNetix that lists treatments that have been effective with other patients who have the same cell abnormalities. The report also references clinical trials of investigational treatments that might be appropriate. Because SCI is one of the leading sites on the West Coast for clinical trials, cancer specialists are participating in more than 100 studies of new drugs, therapies or procedures at any given time. This gives patients access to many treatments that may not be available elsewhere.

**Step 5.** Personalize treatment. The cancer specialist evaluates the report — along with the patient’s medical history, drug tolerance and surgical limitations — and creates a personalized treatment plan.

The Newest Members of the Swedish Medical Staff

The following individuals joined Swedish during the first quarter of 2014. We invite you to view their online profiles at www.swedish.org/physicians.

- Michael Erickson, M.D. *Family Medicine*
- Andrew Graustein, M.D. *Critical Care/Hospitalist*
- Janice Gupta, D.O. *Rheumatology*
- Jennifer Ham, CNM *Midwifery*
- Traci Hiegel, M.D. *Pediatrics*
- David Hildebrand, M.D. *Pediatrics*
- Michael Janssen, M.D. *Internal Medicine*
- Glen Kiyonaga, M.D. *Family Medicine*
- Rajneet Lamba, M.D. *Internal Medicine/Hospitalist*
- Jesse Dean Matthews, M.D. *Internal Medicine/Hospitalist*
- Kenneth Mayeda, M.D. *Family Medicine*
- Kelly McKittrick, CNM *Midwifery*
- Laura MacPherson, CNM *Midwifery*
- Lahar Mehta, M.D. *Neurology*
- Kimberley Middleton, M.D. *Physical Medicine & Rehabilitation*
- Raya Mawad, M.D. *Hematology*
- Sonam Nyatsatsang, M.D. *Infectious Disease*
- Joan Olson, M.D. *Internal Medicine*
- Katherine Ritchey, D.O. *Internal Medicine/Hospitalist*
- Jon Welch, M.D. *Allergy & Immunology*
- Rodney Yen, DPM *Podiatry*
- Song Zhao, M.D. *Medical Oncology*
Diagnosing celiac disease in children can be one of the bigger challenges for primary-care providers and pediatricians. The typical presentation of diarrhea and belly pain can be symptomatic of many things. On the other hand, patients may be completely asymptomatic.

“Fortunately, we are blessed with very good screening tools,” says Jonah Essers, M.D., MPH, a pediatric gastroenterologist with Swedish Pediatric Specialists at Swedish/First Hill and Swedish/Issaquah. “A screening blood test, bundled together with a physical exam and other specialized tests, can help us narrow down the differential diagnosis. It can also help us determine whether we are confident ruling out celiac (a negative result) or whether we have additional work to do (a positive result).”

Even with the screening blood test, however, the diagnosis can be a bit tricky because some children with celiac do not have elevated immunoglobulin A (IgA) anti-tissue transglutaminase antibodies (IgA-tTG), which may erroneously turn diagnostic reasoning to other possibilities, such as Crohn’s disease, ulcerative colitis, intestinal infection, food allergies or a thyroid condition.

Children with any positive finding, as well as those with a negative finding with clinically suspicious symptoms, will benefit from a referral to a pediatric gastroenterologist. With the appropriate resources to closely manage these patients, these specialists are often able to come to a conclusive diagnosis through treatment regimens.

To consult or refer a patient or to request a second opinion, please call 206-215-2700 (Swedish/First Hill) or 425-313-7088 (Swedish/Issaquah).

<table>
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<tr>
<th>Symptoms Associated With Celiac Disease in Children</th>
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<tbody>
<tr>
<td>• Abdominal bloating and pain</td>
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<tr>
<td>• Chronic diarrhea</td>
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<td>• Vomiting</td>
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<td>• Constipation</td>
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<td>• Pale, foul-smelling or fatty stool</td>
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<td>• Irritability</td>
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A Word About Genetic Testing for Children

Genetic testing for celiac disease can be very expensive and will not necessarily be conclusive, except for a negative test result. If the test is negative for the genetic marker, the child is not predisposed to celiac.

A positive genetic test is a little more complicated. Whether the child develops celiac is not pre-ordained. Many people harbor the marker, but never get the disease. Parents seeing a positive test result may be eager to introduce a gluten-free diet, which would unnecessarily rob their children of many important nutrients in foods.

Therefore, genetic testing is a course of action that should be taken after thoughtful discussion with a pediatric gastroenterologist.

GAINS™ Program Addresses Feeding and Weight Gain Problems in Children

Pediatric Growth and Integrated Nutrition at Swedish
Swedish/First Hill and Swedish/Issaquah
Phone: 206-215-GAIN (4246)

The Growth and Integrated Nutrition Service at Swedish, known as GAINS, is a multidisciplinary program. The team includes physician specialists in pediatric gastroenterology, surgery and neonatology, nurses, dietitians, behavioral specialists and feeding therapists. Team members work collaboratively on behalf of patients who are referred to the program.

The program specializes in infants and children younger than six years of age who have problems with feeding or weight gain, such as:

- Breastfeeding difficulties
- Malnutrition
- Failure to thrive
- Slow growth
- Low birthweight

Team members are available for consults and second opinions, and will provide full assessments and specific recommendations for your patients.

(continued on page 4)
Living With Achalasia — Like Seahawk Malcolm Smith

Earlier this year, Yahoo Sports published an article regarding this year’s Super Bowl MVP, Malcolm Smith, as not only achieving recognition for his Super Bowl performance, but also dealing with a swallowing disorder known as achalasia.

Achalasia is a rare disorder with a prevalence of 10 cases per 100,000 individuals. Men and women are equally affected and it is usually diagnosed between the ages of 25 to 60 years. The disease often comes on slowly and is gradually progressive with problems swallowing solids and liquids, and the unintentional movement of undigested food particles back up into the mouth (bland regurgitation). Patients also often complain of a burning sensation in their chests. Other symptoms may include hiccups, difficulty belching and occasionally weight loss.

The condition can be seen with radiology studies including a barium esophagram that shows a dilated or larger than normal caliber of the esophagus with a narrowing or tightness at the lower esophageal sphincter. An upper endoscopy or camera study is often performed to closely evaluate the esophagus and stomach. It is ultimately diagnosed with high-resolution esophageal manometry, which is a technique for evaluating esophageal motor dysfunction or movement disorders of the esophagus.

Once diagnosed, there are different treatment options to consider based on medical history, age and patient preference, including surgery, dilation to open up the lower esophageal sphincter or botox injection to relax the muscle of the lower esophageal sphincter.

Malcolm Smith’s story opens a public conversation about the importance of identifying swallowing disorders. Often patients will have symptoms that are present for years prior to seeking medical attention. It is important, however, to diagnose the condition earlier rather than later because early intervention may prevent worsening dilation of the esophagus.

If you would like to refer or consult on a patient with a preliminary diagnosis of a swallowing disorder, please call the Swedish Digestive Health Network at 1-855-411-MyGI (6944).

Case Study: Celiac disease in 22-month-old child

A 22-month-old boy was referred to the GAINS program (Growth and Integrated Nutrition Service at Swedish) for failure to thrive (FTT), iron deficiency anemia and food refusal.

For the last month, the patient subsisted on mostly oatmeal, cereal and apple juice. He began refusing most other solid foods. He also was having watery, non-bloody diarrhea two-to-three times per day and occasional vomiting after meals.

His primary-care provider sent a very thorough and appropriate workup for FTT, including screening blood, urine and stool tests. Except for iron-deficiency anemia and a low albumin, all testing was non-revealing, including the most common screening test for celiac disease, the immunoglobulin A (IgA) anti-tissue transglutaminase antibody (IgA-tTG).

On initial evaluation, the boy appeared cachectic with a protuberant abdomen. His weight was three standard deviations below the mean and his linear growth was mildly stunted. Based on this exam, we admitted him to the pediatric ward for nutritional rehabilitation and diagnostic testing.

We sent additional celiac markers, including the IgA and IgG (immunoglobulin G) anti-gliadin antibody panel, both of which returned elevated. He underwent esophago-gastroduodenoscopy (EGD), which revealed diffuse duodenitis. On microscopy, he had complete loss of duodenal villi and a lymphocyte-expanded lamina propria, the characteristic lesion seen in celiac disease.

He was immediately placed on a gluten-free diet. A nasogastric (NG) tube was inserted and, in conjunction with our pediatric dieticians, the patient began nutritional rehabilitation with an age-appropriate formula. He was also started on iron-replacement therapy. Within five days, his diarrhea started to wane and his vomiting ceased. He was discharged home after a seven-day admission.

In follow up, the patient began eating solid food spontaneously within four weeks, at which time his NG tube was removed. His weight returned to the 20th percentile within four months. Six months after diagnosis, now at 28 months of age, our patient enjoys hot dogs, French fries, gluten-free pizza, and even broccoli!

About the Author

Jonah Essers, M.D., MPH, received his medical degree from Columbia University College of Physicians and Surgeons in New York City. He completed his pediatric residency at George Washington University Children’s National Medical Center in Washington, D.C., and his fellowship in pediatric gastroenterology at Harvard University, Children’s Hospital Boston. He is board certified in pediatrics and pediatric gastroenterology. Dr. Essers sees patients at the Swedish Pediatric Specialties clinics at Swedish/First Hill and Swedish/Issaquah.
Case Study: Achalasia variant

Leslie H. Price, M.D., gastroenterologist, Swedish Gastroenterology

A 61-year-old female presented to clinic with solid and liquid dysphagia of two years duration. She localized the symptoms to the upper and mid substernal region. There was no associated chest pain or nasal or oral regurgitation. She had nausea without emesis and reflux with frequent throat clearing despite taking 40 mg of esomeprazole daily. She said her symptoms were alleviated with pureed food, frequent deglutition and liquids. Despite these attempts, however, she reported a weight loss of 10 pounds over approximately seven months.

The patient has multiple medical problems, including:

- Crohn's ileocolitis (treated with Humira®)
- A history of ileocolonic resection
- Myelodysplastic syndrome
- A history of deep venous thrombosis
- Asthma
- Adrenal insufficiency secondary to steroid use
- A history of seizure
- Hypothyroidism
- Depression
- Fibromyalgia
- Thoracic outlet syndrome
- Carpal tunnel syndrome
- Peripheral neuropathy
- Hypovitaminosis D

Her current medications include:

- Esomeprazole (40 mg daily)
- Diltiazem (240 mg daily)
- Rabeprazole (20 mg at night)
- Hydrochlorothiazide (12.5 mg daily)
- Montelukast (10 mg daily)
- Levothyroxine (0.88 mg daily)
- Buproprion XL (150 mg daily)
- Methadone (10 mg tid and 20 mg every evening)
- Adalimumab (40 mg every two weeks)
- Prednisone (5 mg daily)
- Zolpidem (10 mg qHS)
- Eszopiclone (3 mg qHS)
- Mirtazapine (45 mg qHS)
- Several vitamins

She also takes as-needed medications, including metaxalone, hydromorphone, oxycodone/APAP, ipratropium/albuterol inhaler, valacyclovir, trazodone, and several topical creams.

A previous work-up at another clinic included an esophagogastroduodenoscopy with mild gastritis, biopsy with gastropathy, and multiple spastic contractions of the esophagus with biopsy negative for eosinophilic esophagitis. A 20-mm balloon dilator was inflated at the gastroesophageal junction and dragged through the esophagus, without symptom relief.

After seeing her at our clinic, we scheduled her for an esophageal manometry, which revealed normal upper esophageal sphincter relaxation from a borderline low baseline. There was normal peristaltic initiation and progression of the skeletal muscle. Esophageal body contraction was rapid, with almost uniformly simultaneous sequencing and merging of contraction segments. The lower esophageal sphincter was normotensive, but relaxation was abnormal with intrabolus esophageal compartmentalization between the contraction sequence and the abnormal relaxation of the lower esophageal sphincter.

The patient was diagnosed with a spastic disorder or variant of achalasia and scheduled for esophagogastroduodenoscopy with injection of botulinum toxin A, 100 units in 5 mL saline, injected in 1 mL aliquots starting at the lower esophageal sphincter and every 1 cm proximally in the spastic segment of the esophagus, with improvement. The patient was ultimately referred for Heller myotomy and more definitive therapy similar to achalasia treatment.

About the Author

Leslie H. Price, M.D., is board certified in internal medicine and gastroenterology. She received her medical degree from McGill University in Montreal, Quebec, Canada. She completed her residency in internal medicine at Virginia Mason Medical Center in Seattle, and her fellowship in gastroenterology at the University of New Mexico in Albuquerque. In her general gastroenterology and hepatology practice, she has a particular interest in gastrointestinal motility disorders. She sees patients at the gastroenterology clinics at Swedish/First Hill and Swedish/Issaquah.
Non-Alcoholic Fatty Liver Disease

Major contributors to an increased risk for NAFLD include:

- Weight
- Age
- Poor nutrition
- A sedentary lifestyle
- Ethnicity

Hispanics have a significantly higher risk of NAFLD when compared to non-Hispanic whites. Non-Hispanic blacks have a significantly lower risk. Other important risk factors, independent of obesity, include hypothyroidism, hypopituitarism, hypogonadism, sleep apnea and polycystic ovarian syndrome.

“Fatty liver disease generally should not be considered a benign condition,” says Anne Larson, M.D., FACP, AGAF, director of the Swedish Liver Center. “It can be progressive, leading to significant morbidity and mortality. As the obesity epidemic worsens, a greater percentage of the population will develop NAFLD/NASH, and NASH is projected to become the leading indication for liver transplant in the next several years.”

NAFLD shows a similar accumulation of fat and inflammation in the liver to that seen in alcohol-induced liver disease, but in individuals who drink little or no alcohol. Although, NAFLD can be asymptomatic and benign, it can also lead to progressive liver injury over time. There is no correlation between liver enzyme levels and progression or outcome. The most serious form, NASH, can lead to cirrhosis and liver cancer. Once cirrhosis and liver failure are present, patients may complain of fatigue, weakness, impaired judgment, confusion and trouble concentrating.

The relationship between NAFLD and chronic liver disease, liver fibrosis and cirrhosis has long been documented. NAFLD patients have an increased overall mortality compared to matched controls. Patients with NASH have an increased liver-related mortality rate. Studies show a close correlation between NAFLD and cardiovascular disease, which is the most common cause of death in patients with NAFLD/NASH. This suggests that increased cross screening may be indicated when evaluating patients for cardiovascular disease or liver disease.

Often, NAFLD is discovered incidentally through routine blood tests that show elevations in liver enzymes, such as alanine aminotransferase (ALT) or aspartate aminotransferase (AST), or imaging studies that show an enlarged or “fatty” liver.

When evaluating patients with suspected NAFLD, it is crucial to exclude competing causes of steatosis (fat) and co-existing common chronic liver diseases, such as hepatitis C virus. It is then necessary to stage the disease — is this benign steatosis or more progressive and severe disease? Liver biopsy is considered the gold standard, but there is growing interest in non-invasive methods (i.e., NAFLD Fibrosis Score, transient elastography). Liver biopsy should be considered in those at increased risk of having NASH and advanced fibrosis, or those in which competing or co-existing causes are suspected.

Treating NAFLD is a partnership between the patient’s primary-care physician and the liver specialists at the Swedish Liver Center. The treatment plan includes lifestyle changes, such as a balanced diet and increased physical activity, disease staging, and close monitoring.

If you suspect fatty liver disease, and would like to consult or refer a patient, please call the Swedish Liver Center at 206-215-1437 or 800-996-7426 (toll free).

Referring Patients to Swedish

Swedish offers referring physicians multiple options for requesting a referral, including:

- Personalized referral services: 1-855-448-8094 (Monday through Friday, from 8 a.m. to 4 p.m.)
- Online referral form: www.swedish.org/refernow
- Secure fax: 206-320-2655

The Swedish Transfer Center is available seven days a week and 24 hours a day to facilitate patient admissions. The Transfer Center streamlines patient transfers, provides physician-to-physician consults between the referring and admitting physicians, offers access to all acute-care specialties and admissions to Ballard, Cherry Hill, First Hill and Issaquah. Call 1-866-470-4BED (4233).

To admit pediatric patients, please call the pediatric hospitalist at First Hill (206-969-7500) or Issaquah (206-969-7337).
Case Study: Fatty liver disease
Anne M. Larson, M.D., M.D., FACP, AGAF

Ms. X is a 52-year-old morbidly obese woman who was noted to have elevated liver enzymes in 2010. In addition to her morbid obesity (BMI 68), her medical history is significant for:

- Diabetes mellitus
- Hypertension
- Sleep apnea treated with CPAP
- Asthma
- Polycystic ovarian disease

An ultrasound evaluation noted the presence of a “fatty liver”. Her primary-care provider told her that she had fatty liver related to her weight and she needed to lose weight. No further liver evaluation was done at that time.

The patient attempted weight loss, but was unsuccessful. In consultation with her primary-care provider, she decided to pursue bariatric surgery. She was referred to a bariatric surgeon, who considered her an appropriate candidate for roux-n-Y gastric bypass. At the time of surgery, she was noted to have cirrhosis and was referred to a hepatologist at the Swedish Liver Center for further evaluation.

About the Author
Anne M. Larson, M.D., is the director of the Swedish Liver Center. Dr. Larson received her medical degree and also completed her residency in internal medicine from the University of Washington in Seattle. She completed a clinical fellowship in gastroenterology at the University of California, San Diego, before returning to the University of Washington to complete a senior fellowship in transplant hepatology. She is board certified in internal medicine, gastroenterology and hepatology. Her clinical interests include hepatitis, hepatocellular carcinoma, the diagnosis and treatment of liver disease, and liver transplantation.

When to Refer to Swedish
Swedish Liver Center, 1101 Madison St., Suite 850, Seattle, WA 98104
Phone: 206-215-1437 • 800-996-7426 (toll free) • Fax: 206-320-7431

Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in the U.S. Potential Causes/Association
- Obesity
- Diabetes Mellitus
- Dyslipidemia
- Metabolic Syndrome
- Medications

Symptoms of Liver Failure
- Fatigue
- Weakness
- Fluid accumulation
- Confusion, impaired judgment, trouble concentrating

The liver specialists at the Swedish Liver Center accept referrals and requests for second opinions to confirm a presumptive diagnosis of fatty liver disease. To consult or refer a patient, please call 206-215-1437 or 800-996-7425 (toll free).
Expanding Neuroscience Cranial and Spine Services in North Puget Sound Area

Providence Medical Group, Providence Regional Medical Center Everett and the Swedish Neuroscience Institute (SNI) have joined forces to expand cranial and spine care throughout the North Puget Sound area.

This partnership gives patients enhanced access to exceptional neuroscience care and technology. Whenever possible, care is provided in the community, close to home. When multiple sites are involved in a care plan, a shared electronic medical record system ensures continuity and seamless patient care. Using best-practice care pathways, the goal is to provide patients care that is both effective and efficient.

Please call 425-297-6400 for more information about the available services, or to consult or refer a patient directly to Providence Everett for cranial or spine care.

CME Course Listing – May – June 2014

Physicians from across the region and around the world come to Swedish Medical Center’s Continuing Medical Education (CME) courses to learn about new research and innovative treatment techniques.

For times and locations, go to www.swedish.org/cme or call 206-386-2755.

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<thead>
<tr>
<th>Course</th>
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<tr>
<td>Seventh Annual Iris and Ted Wagner Endowed Lectureship</td>
<td>Wednesday, May 21</td>
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<tr>
<td>Neurophysiologic Intraoperative Monitoring &amp; Clinical Neurophysiology</td>
<td>Friday, June 13</td>
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<tr>
<td>Update in the Care of the Acutely Ill Neurological Patient</td>
<td>Friday, June 6</td>
<td></td>
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<tr>
<td>Cardiology Update for Primary Care</td>
<td>Friday, July 11</td>
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Swedish Medical Center is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.