Sickle Cell Today

USA Comprehensive Sickle Cell Center

Volume 14 Issue 1 April 2017

TABLE OF CONTENTS

USA Comprehensive Sickle Cell Center
Main Office (251) 470-5893
Fax (251) 470-5895
Clinical Research (251) 471-7703
Pediatric Clinic (251) 405-5147
Adult Clinic (251) 470-5890
Community-based Program (251) 432-0301

Sickle Cell Disease: Sleep Quality and Pain

William A. Broughton, MD, Professor of Medicine
Division of Pulmonary/Critical Care and Sleep Medicine, University of South Alabama

Disturbance of sleep is common in sickle cell disease (SCD). One study suggests that 93% of those afflicted with SCD experience recurrent or chronic pain. Most SCD patients (83%) also report not sleeping well. There is a well-studied relationship between poor sleep and the degree to which pain is experienced in many conditions. What is clear is that pain always disrupts sleep. What is unclear in SCD is whether disrupted sleep makes the pain experience worse.

If we think that poor quality sleep might be associated with a worse pain experience and we know that sleep disruption worsens SCD sufferer's self-efficiency (a person's belief that they can cope with life's challenges), it seems reasonable to do all one can to optimize sleep quality. What can you do? First, you should consider specific medical disorders.

- *Sleep apnea syndrome* is common and is easily diagnosed. If you snore loudly, wake up gasping and choking, or others report that you stop breathing during sleep; you should see a sleep specialist to see if special testing is needed.
- *Restless legs syndrome (RLS)* is a feeling of discomfort in the legs that begins when you become immobile before sleep. Most people experience the need to continuously move their legs. The discomfort usually resolves after sleep onset and is always gone in the morning. There is no test for RLS. There are specific medicines that will relieve it. Ask your doctor.

Second, there are several things you can do on your own to improve your sleep quality. The following interventions require only some thoughtfulness and minor life-style modifications.

- Use caffeine intelligently. Caffeine lasts about 6 hours in your system. Studies show that caffeine use before bed makes it harder to fall asleep and will make you get up to urinate more frequently at night. You should avoid caffeine-containing drinks for at least 6 hours before sleep and perhaps consider avoiding it altogether.
- If you take "fluid pills"/diuretics, do your best not to take them right before bed. Usually the effects of these drugs last for about 6 hours. Try to take your last dose in the mid-afternoon at the latest.
- Keep a regular sleep/wake schedule – plan your sleep onset and wake time near the same times every day. Your brain has a built-in 24-hour clock for sleep and wake; try to take advantage of it.

Continue on 2

Visit the Comprehensive Sickle Cell Center website at:
http://www.usahealthsystem.com/sicklecellcenter

- Sleep in a dark and quiet environment. The noise and flashing light of TV disturbs sleep. Try setting the sleep timer or turning the TV off. If you need background noise to sleep, try a white noise generator. These are cheap and can assist in sleep onset and maintenance.
- If you awaken during sleep, do not check your clock or phone for the time. If it is still dark outside, go back to sleep. Knowing the time only makes you worry about how much time is left for sleep. That knowledge often makes it more difficult to go back to sleep.
- Do not nap during the day. We can only sleep so much in a 24-hour period and "using up" our sleep drive can result in sleep-onset insomnia, mid-sleep awakenings, or early morning awakenings.
- Limit your "screen-time" (cell phones, LED TVs, etc.) before bed. These devices emit a blue light frequency that tells your brain that it is still daytime and inhibits sleep onset. Some devices have a function to turn off the blue light spectrum (an app called f-LUX for Android / the built-in Night-Shift function for Apple iOS devices). Use these apps to lessen incoming blue light frequencies from your device or just try laying off the gaming and Facebook before bed.
- Give yourself some "downtime" to relax before bed. If you worry while waiting for sleep, make a list of your worries and what actions you plan to take – then put it aside.
- A hot bath/shower before bed also helps you get to sleep.

With all this talk about sleep quality and its effect on pain and self-efficiency, it is easy to think that sleeping pills might be the answer. They are not! Almost all sedative use leads to habituation (they become less effective with time) and dependence. Getting off these drugs can be a painful and difficult experience. Almost all of the studies in the sleep literature suggest that life-style changes work better than regular sleeping pill use. Many think "herbal/natural" remedies like melatonin can help – they are mostly ineffective. Melatonin has specific uses but it is not intended as a sleeping pill and works poorly. It can also disrupt the scheduling of your sleep – avoid it!

Questions remain. We know pain disrupts sleep but we are unsure if sleep disruption significantly worsens pain in SCD. Until we know for sure, it seems most reasonable to do those things that can improve sleep. If you do these things while you try to control pain with your doctor's assistance, you are more likely to achieve your best sleep and optimum daily function.

Maintaining Your Health with Sickle Cell Disease

Jessica L. King, CRNP
University of South Alabama Comprehensive Sickle Cell Center

Typically when we think of maintaining health, we go to the old adages of eating right, drinking plenty of water, and getting regular exercise and plenty of sleep, all of which are important. Years ago, going to the doctor's office regularly for a checkup was not associated with maintaining optimal health; instead, people thought it signified that you were either overly concerned with your health or that your health was getting worse.

However, now we know that regular visits with your health care provider can help identify potential health risks, find ways to prevent problems, and screen for a problem early so that intervention can occur. Individuals living with sickle cell disease (SCD) are no different from anyone else; they, too, can develop common problems such as diabetes, hypertension, asthma, and arthritis. In addition, individuals with SCD also face a unique set of challenges concerning their health, such as increased risk for dehydration, pain crisis, and infection.

Listed below are some specific ways that your sickle cell health care provider can help you stay well:

- Provide routine and specific immunizations such as the Pneumococcal, Influenza and Meningococcal vaccines to prevent infection;
- Assist with scheduling annual eye exams with an ophthalmologist (used to screen for potential sickle cell related eye disease that if identified early can be monitored and treated appropriately to prevent blindness);
- Assist with scheduling bi-annual lung function testing (used to screen for potential lung problems such as asthma);
- Obtain routine blood work and urine samples (used to screen for and manage anemia, kidney, and liver function problems);
- Order X-rays if you are having joint pain to screen for potential bone-related problems that can occur with SCD and, if needed, assist in the referral to an orthopedic surgeon;
- Provide education regarding the importance of adequate nutrition and hydration and its relationship in the prevention of pain crisis;
- Provide education regarding available medical treatment options for pain prevention and treatment;
- Provide education regarding exercise recommendations;

- Provide medical letters for international travel so that you can take any needed medications to your destination;
- Provide supportive counseling to assist with preparing for educational and vocational goals as well as direct patients to the available community resources.

Outpatient care for adults living with SCD is available at the University of South Alabama Physicians Group, Mastin Professional Building, Suite 102, 2451 USA Medical Center Drive, Mobile Alabama, 36617. Adult patient clinics are now available on Monday, Tuesday, Thursday, and Friday's from 8:30am-12pm. For adult new patient appointments, please call T'Shemika Perryman, RN at (251) 470-5893 or 470-5875. To schedule a follow-up appointment, call (251) 470-5890.

Outpatient care for pediatric SCD patients is provided at the Strada Patient Care Center, Suite 1F, 1601 Center Street, Mobile, Alabama, 36604. Pediatric clinics are held on Tuesdays and Fridays from 8am-12pm. To schedule an appointment for your child with a pediatric SCD provider, call (251) 410-5437.

Pediatric to Adult Care Transition:

EmPowering and EnAbling ExCellence Together

T'Shemika Perryman, RN, P.A.C.T. Coordinator
University of South Alabama Comprehensive Sickle Cell Center

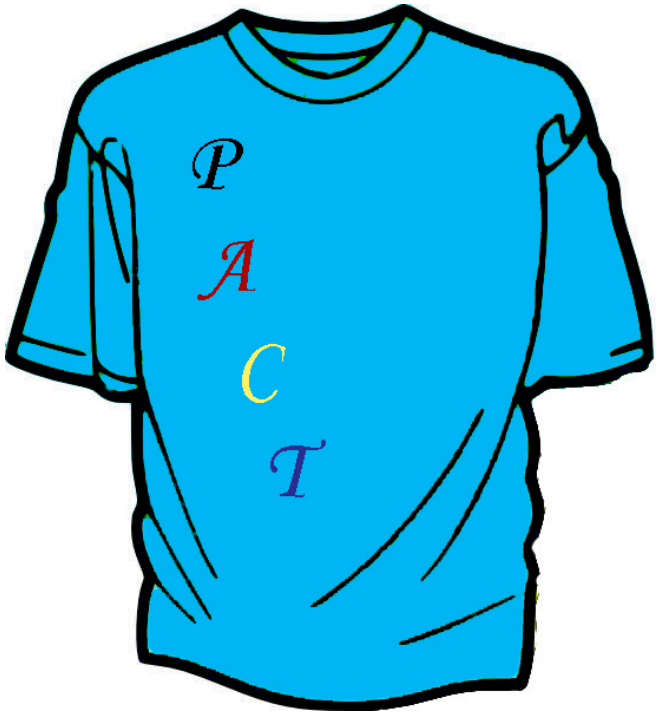
In September 2016, the USA Comprehensive Sickle Cell Center sponsored a contest asking participants in the Pediatric to Adult Care Transition (PACT) program to submit designs for a tee shirt that expressed their life's journey living with sickle cell disease. The winning design is to be displayed on the official PACT program tee shirt. Once completed, the tee shirt will be distributed to our PACT participants.

A major goal of PACT is to empower and enable our clients with sickle cell disease while encouraging excellence by working together. By participating in this contest and other planned activities, young persons will likely have an effective transition into adult health care.

Our judges had a difficult time deciding on one design, so there are two winners whose designs will be displayed on the shirts. They are Briah Sewell and Jesse Grayson. For their work, they received a $50 Visa gift card.

There were two other designs submitted by PACT participants that deserve an honorable mention. Those designs were submitted by Asiah Hope and Alasha Flott, who also received $50 Visa gift cards.

The final design of the tee shirt will be determined by a committee composed of PACT participants, including Ashlyn Cohen, Alasha Flott, Briah Sewell, Maxwell Harness, and Jada Cathcart. Please stay tuned for the September 2017 newsletter for the preview of the official PACT tee shirt!!



We're Hiring! City of Mobile Youth Summer Employment Program. Visit: **www.yes251.org**

New Hope for Prevention of Sickle Cell Pain Crises

Felicia L. Wilson, MD – Professor of Pediatrics
Director, Division of Hematology/Oncology, University of South Alabama

Sickle cell pain crises are the most common cause of emergency room visits and hospitalizations resulting in decreased quality of life and increased risk of death. They are variable in frequency, duration, and severity making them unpredictable and sometimes unbearable. Pain crises are the result of a complex interaction between blood cells including sickle red blood cells that carry oxygen, white blood cells that fight infection and are important in inflammation, platelets that cause blood to clot, and the lining of the blood vessels known as endothelium. P-selectin acts as a glue-like molecule causing sickle cells and white blood cells to stick to the vascular endothelium and also causing platelets to stick to the red cells and white cells. The adhesion of cells to vascular endothelium and to other cells creates blockages of blood flow known as vaso-occlusion. This process deprives the tissues of oxygen resulting in ischemia, multiorgan dysfunction, and pain. Now there is new hope for prevention of pain crises with a novel drug called crizanlizumab.

Crizanlizumab (SelG1 developed by Selexys Pharmaceuticals and acquired by Novartis Pharmaceuticals) is a humanized monoclonal antibody that blocks binding to P-selectin and the complex interactions described above. Results from the Phase 2 SUSTAIN clinical trial demonstrated that crizanlizumab prevents pain crises. The multicenter study enrolled 198 patients aged 16-65 years with all the common sickle cell genotypes (hemoglobin SS, SC, $S\beta^0$ thalassemia, and $S\beta^+$ thalassemia) who had 2-10 pain crises per year at baseline. Patients were randomized into three arms. High-dose crizanlizumab (5 mg/kg) was given to 67 patients, 66 patients received low-dose crizanlizumab (2.5 mg/kg), while 65 patients received placebo without drug. Patients received two loading doses given intravenously (IV) two weeks apart followed by IV infusion of doses every 4 weeks for one year. The primary outcome was the annual rate of pain crises also evaluating episodes of acute chest syndrome, hepatic and splenic sequestration, and priapism. Secondary endpoints included annual rate of days hospitalized, time to first and second pain crisis, and markers of hemolysis including hemoglobin, lactate dehydrogenase, haptoglobin, reticulocyte count, and indirect bilirubin.

Patients who received high-dose crizanlizumab had a 45.3% lower annual rate of pain crises compared to the placebo group ($p=0.01$). Median times to first and second crises were two to three times longer in the high-dose crizanlizumab group compared to the placebo group ($p=0.001$ and $p=0.02$ respectively). For patients receiving concomitant hydroxyurea, the annual crisis rate was 32.1% lower with high-dose crizanlizumab than the placebo group. These treatment effects were significant. Further analysis did not show a significant difference in acute chest syndrome, hepatic and splenic sequestration, priapism, median rate of days hospitalized, and markers of hemolysis. Overall the drug was well tolerated. No detectable antibody response to crizanlizumab developed in any patients. Adverse events were similar in all groups and included headache, back pain, nausea, and arthralgia.

These results are exciting because prevention of pain crises could improve quality of life, decrease organ damage, and potentially decrease the risk of death among patients with sickle cell disease. To date, hydroxyurea remains the only drug ever approved for prevention of sickle cell disease complications including pain crises, acute chest syndrome, and the need for blood transfusions. It has been nearly 20 years since its FDA approval for individuals 18 years of age and older. More recently, the TWiTCH trial demonstrated that hydroxyurea could be used for primary stroke prevention in children. Hydroxyurea requires daily oral dosing with at least monthly monitoring of blood counts making adherence challenging. In addition, some patients are not able to tolerate hydroxyurea leaving them with no treatment options. Since crizanlizumab is only administered monthly, adherence may improve.

The University of South Alabama participated in the SUSTAIN study with Dr. Felicia L. Wilson as the principal investigator, Drs. Imran and Siddiqui as co-investigators, and Andretta McCovey, RN, CRA as the nurse coordinator. Future direction depends on evaluation by the Food and Drug Administration (FDA) to approve crizanlizumab after evaluation of current data or determine that further study is necessary. Results of the SUSTAIN study have been published in the New England Journal of Medicine. Since the study was restricted to patients 16-65 years, we are interested in performing this study in younger children. Long-term follow-up studies are needed to determine if crizanlizumab can improve survival. Until then, we have new hope for a novel drug for prevention of sickle cell pain crises.

The Big Surprise: Part II

Johnson Haynes, Jr., MD
Director, University of South Alabama Comprehensive Sickle Cell Center

The Big Surprise: Part I was published in the 2016 September edition of Sickle Cell Today. Log on to http://www.usahealthsystem.com/sicklecellcenter to follow this story and to view other editions of Sickle Cell Today.

Mike and Isabella are tested for sickle cell disease. Visits to the doctor's office seemingly had become a way of life, thought Isabella. But if that was required to better understand how Aria had inherited sickle cell trait, it was more than worth the visit. Dr. Trammel had referred Mike and Isabella to a local internist, Dr. Hayes, for their testing. When they went to see Dr. Hayes and requested being tested for sickle cell, Dr. Hayes himself looked a little stunned and asked why? The young couple told him that their daughter had been recently diagnosed with sickle cell trait on her newborn screening test and that they needed to be tested to determine who passed this gene to her. Dr. Hayes told them this test was a send out to a reference lab and it would take a week to ten days to get the results. While both were anxious to know their results, they had no choice but to wait. As the days passed, Aria was well and with her hardy appetite, was gaining weight and growing "like a weed." Her beautiful smile, rosy cheeks and plump little legs made the couple feel they had the most beautiful little girl in the world. With three days left before having their test results, Mike was getting anxious. Isabella assured Mike all would be well. Seemingly as quickly as she said that, the pain under the left lower rib cage flared again. This time it was worse than ever and she felt dizzy every time she would try to stand. Both were frightened but Mike knew he had to hold things together and get Isabella to the local hospital. When they arrived, Isabella was rushed back. She was pale and sweaty with a weak pulse. The doctor in the emergency room said Isabella's blood pressure was low and she needed fluids. An IV was placed immediately and stat lab work was sent. On the exam, the doctor felt a mass in the area where Isabella was experiencing severe pain. It felt like a big spleen. The labs returned and Isabella was found to be severely anemic with a low platelet count and white blood cell count. The doctor told Mike that Isabella would need a blood transfusion urgently but was stable. Mike told the emergency room doctor that Dr. Hayes was their primary care doctor and he had the nurse page Dr. Hayes because Isabella was going to be admitted. Mike and Isabella were so afraid, not just for them, but for Aria. What if something were to go wrong, thought Isabella. This time Mike assured Isabella all would be well. Dr. Hayes came in and admitted Isabella. With her transfusion and pain medicine she felt better and the dizziness resolved. Dr. Hayes obtained special x-rays of Isabella's stomach and indeed her spleen was enlarged. There were no other findings. He told the couple he wasn't sure why her spleen was enlarged and that he would need to do more testing and would consult a blood/cancer specialist, Dr. Hernandez, to assist in figuring this all out. "Cancer specialist," Mike asked? Dr. Hayes tried to calm their fears and asked them not to worry. They assured Dr. Hayes they would try but they were afraid. The young couple embraced each other with Aria nestled in their arms, in silence. A couple of days passed and the test for sickle cell came back. Mike's test was negative and to everyone's surprise, Isabella's results came back confirming that she actually has a form of sickle cell disease called, sickle-beta-plus thalassemia. Dr. Hernandez reviewed all the findings and concluded that Isabella's hospitalization could be explained by a condition called splenic sequestration crisis. This explains why her blood counts dropped and why she has been having the recurring pain under the left side of her ribs. Isabella asked, "What does this mean? Am I going to be ok? Is Aria going to be ok?" For the first time, Mike felt so vulnerable, so helpless, and so uncertain. Physically, Isabella's pain had resolved and her blood counts and blood pressure were back to baseline. Dr. Hernandez recommended that Isabella be discharged and to make a follow up appointment to see him at his office in one week. At that time he would go over all of their concerns and questions. Mike, Isabella and Aria left the hospital feeling better that Isabella did not have cancer but in a state of disbelief that she has a form of sickle cell disease. Rather than going home, Mike thought a stop by the local ice cream parlor would hopefully bring a little joy to Isabella as she indulged in a double scoop of her favorite ice cream, jamoca, almond fudge.

Mike and Isabella are educated on sickle cell disease. By the time the next week passed, there were lots of questions for Dr. Hernandez when Mike and Isabella arrived at his office. Isabella had been doing well with no recurrence of the pain. Life as she knew it had returned to its routine but she needed to know how often would this kind of thing happen? Dr. Hernandez told her there was no way to predict this but if her blood counts should drop as they had with the last admission, she would need her spleen removed. In anticipation of this he advised Isabella to start receiving a series of immunizations that would protect her from various infections if her spleen had to be removed. She agreed to getting started with her vaccines as soon as possible. She then wanted to know how she could have gotten sickle cell disease. Dr. Hernandez explained to her that both her parents had to be carriers of the sickle trait for her to have the disease and that her parents and siblings should also be tested. The more they learned about sickle cell, the more they were baffled. As Isabella recounted her life, she could recall an occasional pain in her stomach area but not anything like she had experienced since living in Castle Rock. Dr. Hernandez said while he could not be a 100% certain, but that the severe symptoms may have been precipitated by the higher altitude. Mike chimed in and said, "We will move back home; anything that will keep my family safe." Dr. Hernandez told them the same thing could happen in Mississippi and that with time, Isabella's body would adapt to the change in altitude. Then, what about Aria? "Is she going to have the same problem?" Dr. Hernandez said, "Aria does

not have sickle cell disease. She has sickle cell trait and will likely never have any problems. Most importantly is to let her know that she has sickle cell trait and if her future spouse does not have the trait, there is a 50% chance with each of her pregnancies, her children will also have sickle cell trait. Of even greater concern is that if she marries someone with the trait there is a 50% chance that with each pregnancy, the child will have sickle cell disease. The question that plagued Isabella the most was the most difficult to ask, "How long will I live?" Dr. Hernandez explained that sickle-beta-plus thalassemia tends to be the mildest form of sickle cell disease and that survival, as best we know, closely parallels that of the general population. This provided some relief to Isabella. Dr. Hernandez thought for one visit, they were off to a good start regarding the young couples understanding of what sickle cell trait and disease entails. He further assured them he would be there for them and to approach their bright futures with an open mind. He went on to tell Isabella there are some routine tests he likes to monitor annually in all of his sickle cell patients and that if there is anything ever of concern he would notify her and bring her back in. Other than this, he would like to see her in follow up every six months for now. As the young couple left they felt somewhat better but still less certain about their futures, whether or not they would have more children, and would they stay in Castle Rock. For now they took peace in what they had, family, and decided they would do whatever was required to make sure their family was healthy and happy.

Fact: In Alabama mandatory newborn screening for sickle cell, independent of racial designation, was implemented in 1988. Since 1988, 5-8% of all babies born in Alabama, racial designated as white, test positive for sickle cell trait.

Teenagers and Young Adults with Sickle Cell Disease

Your help is needed to learn more about the transition from pediatrics to adult care!!

Ardie Pack-Mabien, CRNP
University of South Alabama Comprehensive Sickle Cell Center

What is the purpose of this research study?
The purpose of this study is to learn more about the impact of participation in a transition program on the successful transition from pediatric doctors to adult care doctors. The study is being conducted by Ardie Pack-Mabien, a doctoral student at the University of Alabama at Birmingham, School of Nursing.

Note: Participation in this study is voluntary.

Who can voluntarily participate?

You can participate in this research study if:
- You are or your child is a teenager or young adult between the ages of 13 to 21 years with sickle cell disease;
- You are or your child is a current participant in the PACT program or has recently transitioned to adult care;
- You or your child can read and understand the English language.

Where will the study take place?

The study will take place in Mobile Alabama at:
- The Pediatric and Adult Sickle Cell Outpatient Clinics; USA Comprehensive Sickle Cell Center;
- The Sickle Cell Disease Association of America-Mobile Chapter.

What will happen if you decide to participate?

You will be asked to:
- Answer questions about yourself and the participation in the transition program;
- Participate in a group discussion on the movement from your current doctor to an adult care doctor;
- Give your thoughts on the results of this study to the researcher.

What are the benefits of taking part in this study?

- There may be no direct benefits for taking part in this study;
- Study participants will receive a $20 Visa gift card and parent(s) or caregiver will receive a Visa $15 gift card in appreciation for distance travel and time. Only parents of non-driving teens who provide transportation to and from the focus group discussion will be compensated.

For more information or to take part in this research study, please contact Ardie Pack-Mabien at (251) 470-5889 or (251) 582-4248 (numerical beeper).

Make a gift to the University of South Alabama Comprehensive Sickle Cell Center

I am a: (Please check all that apply) ❑ Friend ❑ Parent ❑ Grandparent ❑ USA Employee ❑ USA Alumni

Name(s): _____

Address: _____

City: _____ State: _____ Zip.: _____

Preferred Phone: (_____) Email: _____

I wish to make a gift to the University of South Alabama as follows:

Gift Purpose: ***(check all that apply)***

❑ I designate my gift to: Dr. Cecil L. Parker, Jr. Sickle Cell Disease Distinguished Lectureship Endowment

❑ This gift is in Honor/Memory (circle one) of: Please notify: _____

❑ Please credit this gift to: ❑ Me only ❑ My spouse & me. My spouse's FULL name: _____

Please list my/our name as follows: _____

Gift or Pledge Amount:

❑ I am making a one time gift of: $ _____

❑ I pledge $ _____ per month to be deducted from my Credit Card or Checking Account.

Please continue monthly deductions as follows:

❑ Until I provide notification to Stop OR ❑ Until _____ (month/year)

Gift Fulfillment:

❑ My check is enclosed (please make checks payable to USA - Parker Endowment Fund).

❑ Electronic Funds Transfer: (please send VOIDED CHECK with this form).

❑ Please charge my Credit Card:(check one) ❑ Visa ❑ MasterCard ❑ Discover ❑ AmEx

Card Number _____ Exp. Date _____ Name on Card _____

Matching Gift Information:

❑ I work for _____(company name) that has a corporate matching gift program and will match this gift. (Obtain appropriate forms from your HR department and mail to the USA Office of Health Sciences Development).

Signature: _____ Date: _____

To contact the USA Office of Health Sciences Development, call (251) 460-7032.
This form and gift payments should be returned to: University of South Alabama - Office of Health Sciences Development
300 Alumni Circle, Mobile, AL 36688-0002
rbanks@southalabama.edu

CLPARKLECT

Thank you very much for your consideration.

DMCLPARK

SCDA®
"Break The Sickle Cycle"®

USA™

SEPTEMBER
NATIONAL SICKLE CELL DISEASE AWARENESS MONTH

University of South Alabama
Comprehensive Sickle Cell Center
2451 USA Medical Center Drive, MCSB 1530
Mobile, AL 36617-2293

Non-Profit
U.S. Postage
PAID
Mobile, AL
Permit No. 506