Medical University of South Carolina
Protocol

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THE CORE CENTER FOR CLINICAL RESEARCH, IMPROVING MINORITY HEALTH IN RHEUMATIC DISEASES

CONTENTS

A. SPECIFIC AIMS

1. Build on existing infrastructure to recruit and retain a well-characterized population of human subjects with systemic lupus erythematosus (lupus; SLE),systemic sclerosis (scleroderma; SSc), and vasculitis and unaffected control subjects for research purposes.

2. Establish and maintain a database containing demographic, social, environmental, genetic and clinical data from existing and prospectively recruited SLE,SSc and vasculitis subjects in Aim 1 so that that information can be easily retrieved by investigators for research purposes.

3. Collect, process, and store biologic material (urine, serum, cells, DNA, RNA, and tissue) obtained from the SLE, SSc, vasculitis, and unaffected subjects in Aim 1 and to track those specimens using appropriate biologic tissue management software.

4. To link clinical and genetic data from Aim 2, specimen data from Aim 3, and clinical laboratory data from the clinical electronic data warehouse into a common research data mart that can be queried for research purposes.

B. BACKGROUND AND SIGNIFICANCE

The Medical University of South Carolina Division of Rheumatology and the Core Center for Clinical Research (hereafter named “CCCR”) research base have a track record of successful translational research in scleroderma and lupus. The Division has a very dedicated patient population that participates readily in interventional and observational studies. We have also been historically successful in recruiting healthy controls willing to volunteer in order to help find answers to the many unknown questions surrounding autoimmune diseases. This study will develop a leading-edge Clinical and Community Resource Core through collaborative relationships with MUSC’s SCTR Bioinformatics Program. This Core will be responsible for providing well characterized subjects (both diseased and normal controls) linked to high quality clinical phenotype, biological specimens, and genetic information for research studies.

C. PRELIMINARY STUDIES

The Division of Rheumatology at MUSC is currently collecting longitudinal data and biospecimens from patients with lupus and healthy controls (SLE Database HR 15014 and SLE in Gullah Health Study HR 10852) and collecting cross-sectional biospecimens from patients with scleroderma and healthy controls (Rheum Repository HR 18881), all of which has led to the advancement of knowledge about the diseases and many publications.

The SLE Database Study was initiated under the original MCRC grant (now the CCCR). Approximately 453 mostly African American patients with SLE are currently enrolled for longitudinal study. However, funding for this study ended in June 2011. Also, during this period,

the Division maintained a database of 923 SSc subjects with ongoing collection of skin fibroblasts and bronchoalveolar lavage fluid, peripheral blood cells, and serum. The SLE in Gullah Health (SLEIGH) study has also enabled the collection of clinical data and specimens on 745 Gullah patients and controls.

Lupus and scleroderma are both complex autoimmune diseases, known to have a genetic component. We have seen evidence of high heritability within our local lupus cohort (HR 10852) with a 26.6% prevalence of patients coming from multi-affected families [1]. Current evidence suggests that perhaps as many as 100 genes contribute to the genetic risk for autoimmune diseases like lupus and scleroderma, each gene having at most a modest effect size [2]. The DNA samples which are collected as part of the SLEIGH (HR 10852), the Lupus Clinic Database (HR 15014), and CLu (HR 6926) Studies, in conjunction with the detailed clinical data collected on each study participant, have been a valuable part of the rapidly advancing international studies of the genetics of autoimmune diseases. We have, through our membership in two large international Lupus Genetics Consortiums (the Large Lupus Association Studies (LLAS) group and the International Consortium on the Genetics of SLE), as well as 27 collaborations with external investigators at 23 different universities, medical centers, and other institutions contributed to the intense effort underway to discover genetic associations with rheumatic diseases, refine the effects at these loci, and ultimately come to understand the biological mechanisms underlying them. In contrast to lupus and scleroderma, due in part to the rarity of vasculitis, the heritability and genetic risk of these disorders is still poorly defined and not well understood. The significant morbidities of these disorders and limitations of current therapy are compelling reasons to advance knowledge of the genetics and associated physiologic vulnerabilities of these disorders.

D. RESEARCH DESIGN AND METHODS

Design & procedures

Aim 1: The Study Coordinator will be directly involved in the recruitment and retention of study subjects and controls, and work closely with clinicians who have identified potential subjects and be responsible for entering those individuals who agree to take part in the study. For those patients who have given informed consent, data regarding their medical, social, family and medications history as well as lab results will be retrieved from the medical record for their initial visit. Longitudinal data will be obtained following each clinic visit attended by that individual. Participants will be asked to complete questionnaires about their physical health, and medical history. They may also be asked to complete questionnaires about their home and work environment, diet, sleep, social history, and ob/gyn history for females. For individuals who have not attended a clinic within the previous year, information will be sought by secure fax, telephone, mail or secure electronic means following a signed release of medical information. The collection of longitudinal data and samples from existing SLE/SSc/vasculitis patients will provide the opportunity for studies focused on the nature of disease progression. In order to retain subjects for the studies, the coordinator and other members of the study

team will maintain relationships with the subjects through phone calls, email, a newsletter and attendance at lay organization meetings to report on study progress. Control subjects will be recruited by means of advertisement in strategically placed print media at MUSC or community engagement activities (e.g. health fairs). Electronic versions of the media may be used on MUSC platforms like the Division website or social media sites like Yammer, Facebook, etc. Also, in collaboration with the SCTR Biomedical Informatics group, a recruitment tool will be developed that identifies patients with the diagnosis of SLE,SSc, or vasculitisprior to the clinic visit (Pro00015492).

Aim 2: A REDCap database will be maintained into which lupus,scleroderma and vasculitis patient and healthy control demographic, social, familial, genetic, environmental, and clinical data will be entered. In collaboration with database managers from the Bioinformatics group, a Common Data Dictionary will be maintained for semantic integration. The REDCap database will be accessible from any web browser using Shibboleth secure login. Thus, new study participants will have their demographic, social, familial, environmental, genetic, epigenetic and clinical information entered into the REDCap database either during or after study visits in the clinic. Lab data will be obtained by the Study Coordinator after the study visit and entered into the database.

Aim 3: Tissue databases containing sample location, type, and quantity linked to patients will be maintained in the CCCR Biorepository secure tissue management software (TisueMetrix (TMX), AIM Inc., Toronto, Ontario, Canada). Biologic material (serum/plasma and urine) will be collected during visits from SLE, SSc, and vasculitis patients described in Aim 1 and processed and stored by the CCCR Biorepository. Skin biopsy and/or cheek cell specimens will be collected on an as-needed basis and similarly stored for SSc patients only. Samples will be stored in tubes with sample type (i.e. - urine, serum, DNA), study ID, and collection date integrated into the label to provide the ability for single tube location tracking using TMX software. Samples will be stored in the CCCR Biorepository using -80°C freezers with emergency backup power and temperature/power monitoring. Skin fibroblasts will be isolated from skin punch biopsies obtained from the involved forearm skin of SSc-ILD patients positive for D1398G and from age-, sex-, and race-matched healthy adult donors. This procedure can be performed during a normal clinic visit, outside a standard of care visit, or in the Research Nexus by the patient's rheumatologist or one of the study-approved rheumatologists qualified to perform skin biopsies.

Aim 4: The strengths of REDCap will be utilized with a common data dictionary that will facilitate pooling of data and representation for research queries. Automated, secure data connections between Epic and the REDCap database created by the SCTR Biomedical Informatics Center will allow the import of relevant data from the EMR based on pre-defined criteria by the study team. Electronic health record worksheets will be encorporated into the visit workflow for rapid data entry by clinicians. The data entered are clinically relevant classification criteria and activity/damage scores that can be automatically carried forward in clinical notes to improve patient care as well as facilitate transfer of data to REDCap as discrete data fields. Enhanced recruitment and eligible patient identification may be done through the

creation of an alert mechanism that will automatically detect eligibility criteria already present in the electronic medical record during registration and email alerts to study team members.

Data analysis

Methodological and biostatistical expertise for research studies utilizing the Clinical and Community Methodology Core resources will be provided by a team of biostatisticians in the Division of Biostatistics and Epidemiology. Their role will include:

1. Data management, including overseeing data integrity processes for existing and new longitudinal clinical research databases, preparing analytic databases, assisting with data sharing processes, and Data and Safety Monitoring reporting, as needed.

2. Biostatistical collaboration, including the provision of design and analysis support to emerging research studies, assisting investigators with clinical research design, data analysis, and dissemination of findings, and participation in project review and selection processes.

Specific analytical plans for studies based on data collected in this project will be submitted separately as data requests that will be reviewed by the CCCR Executive Committee or the Methodology Core.

Research instruments

Demographic information, social and family history, medical history, and medication lists are collected as part of standard care, and this information from the clinical visit will be added to the research database. In addition, brief research-specific questions will be asked of the study participants at the visit, over the phone, by mail, or through electronic REDCap questionnaires. The MCRC Database Questionnaire in its entirety is attached.

Limitations and alternatives

The richness of the data contained within the Clinical and Community Resource Core and the ability of future investigators to compare characteristics of SSc,SLE, and vasculitis patients with unaffected controls will be limited if inadequate unaffected individuals are willing to participate in the study by providing information or biologic samples. Since the Division of Rheumatology has a very dedicated patient population that participates readily in interventional and observational studies, and who bring our recruitment efforts to the attention of unaffected friends and family members, we do not anticipate this being a problem.

There is no alternative method or source of biologic samples required.

Hazards to personnel

Hazards to study personnel include those inherent in handling and transporting body fluids collected in the study.

E. PROTECTION OF HUMAN SUBJECTS

1. RISKS TO THE SUBJECTS

a. Human Subjects Involvement and Characteristics

Clinical data will be obtained from adult and pediatric SSc,SLE, and vasculitis patients who are seen in the facilities served by the Division of Rheumatology & Immunology and who have given informed consent. Children aged 10-17 will also provide assent. Currently, 290 scleroderma, 396 lupus, 19 incomplete lupus/overlap, and 141 control volunteers are enrolled in the study. We anticipate the enrollment of up to 150 additional lupus, 150 additional scleroderma, 100 vasculitis patients and 150 control volunteers each to maintain the longitudinal cohort and ensure proper matching for disease participants with controls. We will exclude children below 6 years of age, but there is no upper limit on the age eligibility. Although not selected for sex or ethnic background, the ratio of women to men in the MUSC Rheumatology Clinics is approximately 3:1, closer to 9:1 in patients with SLE, and African Americans are disproportionately affected by SLE and SSc. No special groups of individuals (such as prisoners, pregnant women, fetuses, or persons unable to give informed consent) are required in this study.

Of the participants in the main study, a subset drawn from scleroderma patients and unaffected controls will be asked to consent to one or both of two additional procedures, designed to collect genetic material for analysis. We expect to separately consent 100 scleroderma patients and 100 control subjects for skin biopsy. Some participants who have difficult venous access may be asked to have DNA collected by cheek swab or by saliva collection.

Targeted/Planned Enrollment Table: Recruitment of existing and new SLE and SSc patients and unaffected controls

	Sex/Gender		
Ethnic Category	Females	Males	Total
Hispanic or Latino	0	0	0
Not Hispanic or Latino	1156	204	1360
Ethnic Category: Total of All Subjects*	1156	204	1360
Racial Categories			
American Indian/Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	768	106	874
White	389	97	486
Racial Categories: Total of All Subjects	1156	204	1360

Inclusion/Exclusion Criteria

<u>Scleroderma patients</u>
Inclusion:
- Age ≥ 6 years
- Diagnosis of SSc as defined by American College of Rheumatology (ACR)/European League Against Rheumatism criteria

Exclusion:
- Being a prisoner or institutionalized individual
- Unwilling or unable to give informed consent

Exclusion from skin biopsy:
- Age <18
- Being a prisoner or institutionalized individual
- Unwilling or unable to give informed consent

<u>Lupus and incomplete lupus patients</u>
Inclusion:
- Age ≥ 6 years
- Patient with diagnosed SLE defined by having at least 4 of the 11 American College of Rheumatology Revised Criteria for the Classification of SLE,
- Iincomplete lupus defined by a practitioner as having lupus or incomplete lupus despite not having 4 ACR criteria.

Exclusion:
- Being a prisoner, mentally ill patient, or institutionalized individual
- Unwilling or unable to give informed consent

Vasculitis patients
Inclusion:
- Age ≥ 6 years
- Patient meeting either the revised International Chapel Hill consensus criteria or the American College of Rheumatology Classification criteria for primary vasculitis

Exclusion:
- Being a prisoner, mentally ill patient, or institutionalized individual
- Unwilling or unable to give informed consent

Unaffected controls:
Inclusion:
- Age ≥ 6 years
- No diagnosis of SSc, SLE, vasculitis or other connective tissue disease

Exclusion:
- Being a prisoner or institutionalized individual
- Unwilling or unable to give informed consent

Exclusion from skin biopsy:
- Age <18
- Being a prisoner or institutionalized individual
- Unwilling or unable to give informed consent

Unaffected controls will be matched to SSc patients based on age (control age = patient age +/- 5 years), race, and gender.

As part of the consenting process for skin biopsy, exclusion criteria will be reviewed with the potential study participant, and if any pre-existing exclusion criteria is identified the subject will not be enrolled.

Choice of study population

Minority populations and women: SLE and SSc disproportionately affect African Americans and women, so it is important to include these populations in the study. Conversely, the rarity of the vasculitides and the relatively recent recognition of disease incidence in some forms of vasculitis in minority patients, and disease severity and poor outcomes particularly in African-American patients are compelling reasons to focus on this population in the study. Participants will be drawn from existing and future patients and the majority of data collected will derive from surveys, tests and procedures that are done as part of normal care for which there will be no payment. Adults with SSc and healthy controls will be invited to volunteer to donate additional biologic samples (skin biopsy), for which a modest compensatory payment will be made.

Children: Minors who are affected by SLE,SSc, or vasculitis will be invited to participate in the study with the appropriate parental/guardian consent, but will be excluded as subjects for skin biopsies. SLE and many of the vasculitides are found at lower rates among children than observed in adults whereas SSc is rare in children. Minors will be re-contacted and asked to re-consent to participating in this research when they reach adulthood.

Research Setting

Study participants will be recruited from existing and future scleroderma (SSc),lupus (SLE) and vasculitis patients seen in the facilities served by the Division of Rheumatology & Immunology. Unaffected control participants will be recruited by placing advertisements in a number of strategically-selected print/website media (e.g. – The Catalyst). Affected and unaffected participants will also be recruited from the annual Scleroderma Patient Education Conference and annual Lupus Patient Education Event; both sponsored by MUSC. Data collection will be carried out in the facilities served by the Division of Rheumatology & Immunology (existing and new SSc/SLE/vasculitis patients), REDCap survey, and the Research Nexus (unaffected controls)..

b. Sources of Materials

Clinical Data will be obtained from existing records of patients followed longitudinally and from newly created clinical records for new patients attending the outpatient clinics. Classification criteria, activity and damage indices that clinically characterize patients with SLE,SSc, or vasculitis will be recorded in the medical record per standard of care or facilitated through a data collection instrument in the patient note. This instrument collects clinically relevant information in discrete data elements that will allow clinicians to follow the progress of their patients and also record data in a fashion that is amenable to research. These data elements are part of routine clinical care and quality metrics in our clinic. Database questionnaires will be completed by patients at the time of clinic visits, on the patient's own time via an emailed/mailed/electronic secure survey, or soon after the clinic visit. Consented participants may fill out electronic questionnaires before clinic visits. Although the database questionnaires will be completed specifically for research purposes, the majority of data will be obtained from history, physical examination, laboratory testing and diagnostic procedures performed in the medical care of the subjects.

For healthy controls: medical, family, social, OB/GYN (for females only) will be obtained from the patient. Two database questionnaires (SF-36 and CSQ) will be completed by patients at the time of clinic visits, on the patient's own time via an emailed/mailed/electronic secure survey, or soon after the clinic visit. Consented participants may fill out electronic questionaires before clinic visits.

Plasma, serum, cells and genetic material will be isolated from blood and/or cheek swabs/saliva collected from SLE,SSc and vasculitis patients and the healthy controls as part of the clinical database project. The patient's rheumatology physician associated with the research

study or a trained phlebotomist will collect up to 95cc of blood for research purposes for the CCCR biorepository (see section 5 below), to be transported either directly or through the Research Nexus to the CCCR Biorepository for processing and storage. Blood collected from subjects may be obtained simultaneously with blood being drawn for standard clinical monitoring, however the study blood will be used for research purposes only. With permission, blood may be drawn for research purposes in the absence of testing required for clinical monitoring. The study coordinator conducting the study visit may ask the participant (typically those with difficult venous access) to provide a sample of cells from inside their cheeks using a buccal swab or a small amount (approximately 2cc) of saliva. During a clinic visit, children who are not required to provide blood for normal medical care will not be asked to give blood for research purposes and could be asked to provide saliva or cheek cells from a swab for DNA testing. Healthy controls will most likely not be having clinical monitoring lab work done, and therefore will be compensated for their time and effort in undergoing the blood collection.

Urine will also be requested from SLE, SSc, vasculitis and healthy control participants, in the amount of up to 40cc.

DNA will be isolated from blood (SLE, SSc, vasculitis, healthy controls), buccal swabs (if needed) and saliva collected (if needed) if the study subject provides additional optional informed genetic consent.

Genome-wide association studies (GWAS) and those involving whole genome/exome sequencing may be conducted to examine genetic differences that exist in the complete set of human genes and the association between these differences and health conditions. Information relevant to GWAS will be sent to the National Institutes of Health (NIH) GWAS database called dbGAP (Database of Genotypes and Phenotypes). No identifying information will accompany this data.

Skin Biopsies will be obtained from patients with scleroderma and healthy controls. Samples will be obtained by 3-4 mm punch biopsies of the forearm from outpatients in the Rheumatology Clinic and unaffected volunteer participants. Little risk will be involved. No unaffected volunteers or patient groups in this study will have an impaired ability to give voluntary informed consent. The date of biopsy, subject's age, gender, ethnicity, race, diagnosis, and name will be recorded for statistical purposes if the participant is not already part of the CCCR longitudinal cohort. The biopsy and descriptive data will be obtained specifically for research purposes. A separate informed consent will be obtained for this procedure and modest compensatory payment will be provided for all having the skin biopsy completed.

c. Potential Risks

Clinical data collection risks loss of patient confidentiality. Since database questions may concern psychological issues there is, therefore, the risk that anxiety concerning mental health will be increased. The risks of drawing blood include temporary discomfort from the needle

stick, bruising and infection; fainting is possible but rare.

Skin biopsy: Risks are associated with the numbing injection and the skin puncture. Slight pain will be felt with the anesthetic injection and there may be temporary bleeding and bruising. Side effects for the anesthetic are rare and temporary, and include allergic reactions such as itching or burning at the injection site or difficulty breathing. The risk of infection is very small. A small scar may be seen for a few months and may be permanent.

DNA analysis: Data will be coded prior to analysis. This code will be used to label the sample which links the sample to identifying information; this code will be known only to study personnel. There is a risk that in the course of the study deleterious genes may be discovered that are believed to predispose an individual to disease. This information will not be shared with the individual, or with any family members who may also be impacted by the gene. If prevalent, gene markers may become associated with a specific demographic group.

Additional risks include the unauthorized release of information collected and stored for research purposes and biologic samples stored with identifying information.

2. ADEQUACY OF PROTECTION AGAINST RISKS

a. Recruitment and Informed Consent

Study participants will be recruited from existing and future SSc,SLE, and vasculitis patients in the facilities served by the Division of Rheumatology & Immunology and information about the study will be provided at educational events for the public. Unaffected control participants will be recruited by placing advertisements in a number of strategically selected print/website media (e.g. - The Catalyst). Both case and control populations will also be recruited utilizing MyChart recruitment capabilities via EPIC EMR. This process involves the use of previously approved recruitment report – Pro00015492 – in order to search for patients with and without rheumatic diseases seen by MUSC. Only patients that have provided future research contact permissions will be contacted in this manner to be recruited for the study.

Written or electronic (eConsent via REDCap survey format on computer or tablet) informed consent to obtain and use **clinical data and specimens** will be requested by the research staff. The study coordinator will introduce him or herself to the potential participant during the course of a normal outpatient clinic visit, describe the study in further detail including the possible discomforts of the procedure(s), the purposes for which the samples are being taken, and that s/he will not personally benefit from the results. Any questions that the patient might have will be answered by the study staff as appropriate. The participant will be informed that consent to donate specimen(s) at this time will in no way obligate him/her to do so at a future date, nor affect his/her care in any way. The study coordinator will guide the participant through the consent, asking open-ended questions to assess their comprehension of the study procedures. This process will be conducted in a closed room within the clinic to ensure a proper, private environment.

The patient will be given time to read the consent form and consider their options. If they agree to participate, the study coordinator will ask the patient to sign the standard participation consent and a HIPAA form. We anticipate unaffected volunteers will telephone the study coordinator in response to a print/web advertisement and if willing to participate, they will be asked to attend a scheduled appointment at the Research Nexus, where the consenting process will be as for SLE/SSc patients.

The study coordinator will also assess if the participant prefers to use the paper copy or eConsent. If, for any reason, the eConsent is not available, the paper version will be used. If the eConsent is chosen by the participant then the coordinator will open the informed consent document and HIPAA via the REDCap eConsent project website. This involves the coordinator logging into the study-specific REDCap eConsent project and opening the consent survey. A security and privacy measure built into the eConsent project involves an automatic log-out of the REDCap database before the patient can view the consent/HIPAA documents. This allows the participant to only view/edit the documents presented to them. The consent and HIPAA documents uploaded to the eConsent project are the exact same documents provided in paper copy.

Once the participant has the informed consent open on a computer or tablet, they are able to scroll through (using mouse or finger) and read the document in its entirety, just as they would an article on a website. The study coordinator will guide the participant through the consent, asking open-ended questions to assess their comprehension of the study procedures. As the participant finishes reading sections of the document that require initialing or signature to provide consent for specific procedures, they are given the ability to do so by clicking on a link stating “add signature.” Each of these links provides verbiage identical to the paper consent form indicating the procedures for which they are being consented. These initials and signatures are completed by using their finger (tablet) or the mouse (computer) and accepting the changes by clicking “save signature.” Only the portions of the document that require the initials or signature of the participant will be provided to the participant, ensuring that they will not sign, initial, or date the improper portion of the document (e.g. – signing on the line for the person obtaining consent). The study coordinator will then be allowed to print their name, sign and date the form independent of the participant. The “submit” button is then pressed at the bottom of the screen by the study coordinator which then automatically opens the HIPAA document for the same review and signature/initialing process as above. Just as for paper copy consenting above, the eConsent process will be conducted in a closed room within the clinic to ensure a proper, private environment. The study coordinator may also elect to conduct the eConsent process over the phone with the subject if they are willing.

All participants will receive copies of the appropriate consent forms and HIPAA notice.

Data collection will be carried out in the Rheumatology clinics mentioned above, via REDCap survey, or the Research Nexus. Skin biopsies will be performed at the time of the clinic/Research Nexus visit.

Minors will be re-contacted and asked to re-consent to participating in this research when they reach adulthood. If participants wish to withdraw their samples, they will be instructed to contact the Principal Investigator and notify him/her of their wish. Any unanalyzed samples donated as a part of this study will then be destroyed only upon request. If the participant does not request to have data and specimens destroyed, they will still be kept in order to be utilized for future research assuming proper consent has been provided to do so. Documentation of withdrawal and destruction will be completed and recorded in the appropriate location(s).

The database paper forms and other study-related documents are secured in a locked cabinet accessible only to the database entry personnel and investigators. The electronic database storage is on an MUSC server with access limited by password to investigators.

b. Protection against Risk

Access to the electronic databases containing participant clinical data and stored on an MUSC server will be limited by password to investigators associated with the study. The risk to psychological anxiety will be diminished by informing the subject that there are no "right or wrong" answers to the survey questions.

Experienced MUSC professionals will perform the **blood collection and skin biopsies** (phlebotomist and CCCR experienced physicians, respectively) in the outpatient clinic or Research Nexus. Any emergencies will be handled promptly. Bruising and bleeding will be controlled by direct pressure or application of a stitch to the biopsy site. Risks of infection will be minimized by use of aseptic technique, sterile dressing, and instruction of the subject in care of the puncture wound.

All tissues and cells provided to investigators will be de-identified to ensure **confidentiality protection**, including only the date of collection, gender, age, race, and diagnosis when required. The clinical databases are password protected and allow restriction of identifiers to study personnel only. Patients must give consent for their de-identified research specimens or data to be used by other investigators or it is not shared.

3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

This study is not expected to directly benefit individual subjects, but is likely to yield generalizable knowledge which contributes to the field.

4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

The potential benefits to society of the study outweigh the risks involved. SSc and SLE place a disproportionate burden on the African American community. Vasculitis has been understudied in minority patients, including African American patients, despite poorer outcomes in some disorders. The clinical impact and the molecular and cellular mechanisms leading to SSc, SLE,

and vasculitis are poorly understood. Our results may increase the understanding of the pathogenesis and allow intervention in the disease processes with more effective therapies. In addition, the establishment of a large and rigorously collected database of SSc/SLE/vasculitis patients will provide a rich source of data for future approved investigators.

5. PERIPHERAL/PILOT STUDIES USING CCCR FOR RECRUITMENT ASSISTANCE

Investigators may wish to utilize the CCR Core for recruitment assistance (including PHI), biospecimens, protocol creation and/or community engagement. For those investigators wishing to obtain any form of the previously mentioned information or services, the following process will occur:

a. A formal request through a REDCap survey will be provided by the investigator;

b. As part of this submission, an approved human subjects IRB protocol specifically describing the use of the CCR Core as a recruitment service must be provided; separate informed consent process must be included in study protocol;

c. A review of the biorepository request for ethical and scientific consideration as well as proper research protocol will be completed by the CCCR Executive Committee,

- This committee is comprised of the PI (Oates) and Co-Directors (Silver, Gilkeson, & Nietert);
- If approval is not granted, the biorepository request with either be edited by the requestor or the request will be closed;

d. Upon approval through the Executive Committee, CCR Core will then identify potential participants within the CCCR Biorepository via pilot/peripheral study inclusion/exclusion criteria

- All potential participants must have prior consent for future research contact through CCCR informed consent, or
- Prior consent via general MUSC consent for future research contact, or
- Direct referral from patient provider;

e. The CCR Core lead coordinator will conduct a consent/HIPAA document review for this list of potential participants. This includes all CCCR (and previous MCRC) consents and HIPAA documents to ensure no issues have occurred. If issues have occurred, data and/or specimens will not be allowed for dispersal.

f. If there are no consent/HIPAA issues, the CCCR Biorepository lab manager will then be provided a list of CCCR participants to disperse specimens.

- If only clinical data and/or recruitment assistance has been requested, the lead coordinator will then provide a list of potential participants, with no consent/HIPAA issues, to the requesting PI.

F. REFERENCES/LITERATURE

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G. CONSULTANTS

Jihad Obeid, MD will work with Dr. Oates to leverage the translational research infrastructure that the South Carolina Clinical and Translational Research Institute (SCTR) is developing for the Clinical Data Warehouse (CDW). As Associate Director of the SCTR Medical Informatics Program and Principal Investigator on the IRB submission for the CDW, Dr Obeid has worked recently with others on the approval of the general framework for the use of the CDW for driving biomedical research projects such as the MCRC. The creation of a comprehensive research data mart for systemic lupus erythematosus,systemic scleroderma, and vasculitis linking clinical phenotypic data with genomic and biospecimen data presents a novel approach that will require significant support from the expertise of the SCTR Informatics team.

H. FACILITES AVAILABLE

The Clinical and Community Resource Core for the CCCR will utilize services of the **South Carolina Clinical & Translation Research Institute (SCTR)** for study participant visits (Research Nexus), specialized molecular core laboratory services (Research Nexus Laboratory).

The **Rheumatology Clinics** will be used for patient visits, at which existing and new patients with SLE, SSc,and vasculitis will be invited to participate in the study. Information and biologic data customarily collected as part of normal care during these visits will comprise a significant proportion of the data collected for this study, as well as tissue samples from skin biopsies.

Biomedical Informatics Center has a dedicated team of software engineers and support services, who have assisted in the development and installation of several research infrastructural systems essential to this study including: REDCap (Research Electronic Data Capture) - a secure web application designed exclusively to support data capture for research studies; the i2b2 (Informatics for Integrating Biology and the Bedside) workbench – a secure interface used to access the clinical data warehouse; and CCCR Biorepository TMX software. The Epic Research Team has and will assist in developing clinically relevant data collection and recruitment tools in Epic.

All study personnel have secure personal **offices** with telephone, computer and internet access and adequate desk and file storage space to support the project. Print, copy, and fax capabilities are provided by a shared Xerox multifunction machine and by personal printers.

The Division of Rheumatology and Immunology provides **administrative support** for research purchasing and word processing.

I. INVESTIGATOR BROCHURE

N/A

J. APPENDICES

CCCR Database survey instruments:

- LUPQOL,
- SF36,
- CSQ,
- SleepQualitySurvey
- Patient Global Assessment