Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: **H-56296**
Status: Approved
Initial Submit Date: 10/24/2024
Approval Period: 12/5/2024 - 11/13/2025

Section Aa: Title & PI

A1. Main Title

MAGNET: MAKING GENOMICS ACCESSIBLE FOR NEWBORNS IN TEXAS

A2. Principal Investigator

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A3a. Financial Conflict of Interest

Does any member of study personnel (Investigator (including investigator's spouse and/or dependent children)) that are involved in the design, conduct, or reporting of the research have a Significant Financial Interest (SFI) that would reasonably appear to be affected by the research for which funding is sought and/or associated with an entity/business that would reasonably appear to be affected by the research?

No

Section Ab: General Information

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A5. Funding Source:

Organization: NATIONAL INSTITUTES OF HEALTH (NIH)

A5a. ESP2 proposal(s) linked to this protocol:

A6a. Institution(s) where work will be performed:

BCM: Baylor College of Medicine

A6b. Research conducted outside of the United States:

Country:
Facility/Institution:
Contact/Investigator:
Phone Number:

If documentation of assurances has not been sent to the Office of Research, please explain:

A7. Research Category:

A8. Therapeutic Intent

Does this trial have therapeutic intent?
No

A9. ClinicalTrials.gov Registration

Does this protocol/trial require registration on ClinicalTrials.gov due to it: meeting the definition of an Applicable Clinical Trial, being required under the terms and conditions of an award, or being proposed to be published in ICMJE journals?
No, this clinical is not a clinical trial, or does not meet the definition of an Applicable Clinical Trial, or does not need to be registered under the terms and conditions of an award, or is not a clinical trial with results intended to be reported in an journal belonging to the ICMJE. Registration is not required.

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

Birth defects, including structural and functional anomalies, are the leading cause of neonatal mortality and a significant cause of pediatric hospitalizations worldwide, affecting about 7.9 million children annually. In developed countries, congenital anomalies account for approximately 13% of NICU admissions. Genetic origins are suspected in 30% of these cases, with half of the sick neonates lacking an identified genetic cause. Advances in molecular technologies, such as whole-genome sequencing (WGS), have transformed the diagnosis and treatment of genetic disorders in neonates. Rapid WGS has provided diagnoses in 36% to 57% of infants, significantly influencing clinical decision-making. However, many NICUs in Texas lack resources for comprehensive genetic evaluation. Without a genetic diagnosis, families remain uninformed about recurrence risks, and medical decisions may be made without genomic insights. To address these gaps, we will use an an academic virtual consultation platform, called Consultagene (www.consultagene.org) to reach the under-resourced NICUs at the Texas-Mexico border and other parts of Texas, aiming to provide low-cost genetic testing and improve genomic care for vulnerable neonatal populations in NICUs in Texas. Consultagene was developed at BCM to improve access to genomic care and education for individuals with limited access to a genetics specialist. This virtual platform offers comprehensive services, including patient scheduling, medical document sharing, interpretation of genetic test results, tele-genetic counseling, and educational videos for patients and healthcare providers, which are available in multiple languages including Spanish.

Section D: Purpose and Objectives

The purpose of this protocol is to:

1. Deliver virtual genetic evaluation through Consultagene and low-cost trio whole genome sequencing (WGS) RNAseq, and metabolomic studies for critically-ill newborns in under-resourced NICUs at the Texas-Mexico border, particularly in El Paso and Rio Grande Valley (RGV) and other parts of Texas.

2. Determine the effectiveness of Consultagene in under-resourced NICUs via surveys and clinician interviews.

Section E: Protocol Risks/Subjects

E1. Risk Category

Category 1: Research not involving greater than minimum risk.

E2. Subjects

Gender:
Both

Age:
Adult (18-64 yrs), Infant/Toddler (0-36 mos), Premature Infant (<37 weeks gestational age)

Ethnicity:
All Ethnicities

Primary Language:
English, Spanish

Groups to be recruited will include:
Both patients and healthy, non-patient, normals

Which if any of the following vulnerable populations will be recruited as subjects?
Children, Employees or lab personnel

Vulnerable populations require special protections. How will you obtain informed consent, protect subject confidentiality, and prevent undue coercion?
Parents will provide informed consent for participation of their children in the study. This would prevent undue coercion of this vulnerable population. Subject confidentiality would be maintained by coding of all specimens. Family participation would be entirely voluntary.

To protect employees' participating in interviews, the study team will ensure confidentiality by anonymizing responses and storing data securely. Participation will be voluntary, with verbal consent obtained (see section S). Interviews will take place in a private setting.

E3. Pregnant woman/fetus

Will pregnant women and/or fetuses (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E4. Neonates

Will neonates of uncertain viability or nonviable neonates (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E5. Children

Will children be enrolled in the research?
Yes

Section F: Design/Procedure

F1. Design

Select one category that most adequately describes your research:
e) Specimen/laboratory experiment

Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.
We propose to recruit 40 newborns every year from various NICUs in Texas for WGS, RNAseq, and metabolomics. The primary outcome will be effectiveness of Consultagene, defined as difference in diagnostic yield compared to usual care. Secondary outcomes will include 1) change in clinical care attributable to genomic results measured by adapting the harmonized measure from the Clinical Sequencing Evidence-Generating Research (CSER) consortium; and 2) caregivers' experience with and perceptions of genomic sequencing and Consultagene assessed with validated measures of caregiver outcomes. Data will be collected via Consultagene, surveys, and qualitative interviews.

A stepped wedge cluster-randomized trial design will be used to implement the program and to evaluate the effectiveness of Consultagene (primary outcome) in providing genomic care to newborn infants in the RGV and El Paso. The Consultagene platform will be implemented in nine under-resourced NICUs, matched into cohorts based on size (number of beds), and rural/urban status. Based on those characteristics, we will have cohort triads (three NICUs each) which will be simultaneously randomized to the time at which the intervention is implemented.

Inclusion Criteria:

Inclusion criteria: Undiagnosed infants from 0-90 days of age, with a diverse group of phenotypes and strongly suspected to have genetic disorders will be recruited. Samples from biological parents will be obtained whenever available.

Clinicians will be included for interviews who use the Consultagene portal for the MAGNET study.

Exclusion Criteria:

Exclusion criteria include: (1) abnormal noninvasive prenatal testing (NIPT) suggesting chromosomal abnormality; (2) abnormal amniocentesis results, (3) abnormal newborn screening indicating an inborn error of metabolism; (4) abnormal FISH results for aneuploidy (trisomy 18, 13, or monosomy X); (5) Down syndrome; (6) dysmorphic features in the absence of other congenital anomalies; (7) isolated birth defects such as myelomeningocele, cleft lip/palate, cardiac septal defects, isolated congenital diaphragmatic hernia, etc.; (8) birth defects due to known teratogens i.e., alcohol, Isotretinoin, etc.; (9) multiple congenital anomalies associated with maternal diabetes; (10) VACTERL association; and (11) hemodynamically unstable newborns needing transport for higher level of care.

F2. Procedure

We will execute broad reliance agreements and contracts with the NICUs participating in the study after IRB approval. Baylor IRB will serve as the IRB of record for all participating sites. SMART IRB agreement will be used as the basis for reliance. An amendment will be submitted to add each participating site after the reliance agreements are established and before work commences at each site. BCM staff will conduct the research on sites.

Based on the established inclusion and exclusion criteria, when a neonate seen by our NICU partners at level III/IV units is ascertained to need genetics consultation, the provider (neonatologist or nurse practitioner) will inform the BCM research coordinator and establish care for that patient through Consultagene portal as a peer-to-peer consultation journey. This study is based on peer to peer referral which means that patients will not be able to sign up themselves in the study. Providers will enter individuals' data into Consultagene after informed consent is obtained. Consent will be obtained by BCM research personnel and, where included in individual hospital contracts, by research coordinators at participating institutions. The research team will only obtain consent after reliance agreements have been established with different institutions.

Families accepted in the study will be contacted by the study team at BCM for video education on research study, virtual evaluation of the neonate and multi-omic study, including WGS, RNAseq, and metabolomics study. Board-certified medical geneticists and counselors at BCM will perform remote genetic evaluations using iPads at the bedside, with assistance from the local provider/research coordinator. Additional evaluations will cover various systems, and photographs will be taken with parental permission.

Research photographs taken for clinical assessment will be securely managed to protect participant privacy and confidentiality. The images will be stored on encrypted devices or secure servers, accessible only to authorized research personnel. The purpose of these photographs is to document physical features relevant to the study, enabling researchers to make accurate clinical assessments during virtual evaluations. Any identifiable information will be removed or obscured when sharing images in reports or presentations, ensuring that the photographs are used strictly for research and clinical evaluation purposes. Families will opt in for specific use of photos as per the informed consent form. The photos will not be destroyed unless the subject withdraws from the study.

Medical records from EMR systems or documentation provided by the referring physicians will be reviewed. Medical records include prenatal, birth, and family history, radiologic and other imaging studies, echocardiogram, laboratory studies, and subspecialty consult reports for the neonates, etc for appropriate phenotyping. Blood or buccal samples from the infant and buccal samples from both parents will be collected for rapid trio GS and sent to Baylor Genetics in Houston via fedex. The WGS results will be available within 5-7 days. The first-tier evaluation focuses on detecting genetic variants, and the results will be returned through a detailed clinical report. If the first-tier testing does not provide a diagnosis, second-tier investigations, including RNA sequencing and metabolomics, may be pursued. RNA sequencing can be done on blood or skin biopsy dependent on gene expression of relevant gene(s). Skin biopsy would be completely optional.

Return of Results (ROR): Once rapid WGS results are available, a clinical report will be sent to the referring physicians, and a follow-up virtual visit will be arranged for result disclosure via Consultagene with the provider/research coordinator and family. BCM staff will communicate results and offer comprehensive genetic counseling, along with providing family support resources and disease-specific information in the family's preferred language. Recommendations for additional diagnostic studies, current therapies, clinical trials, and referrals to subspecialists or tertiary care centers for life-saving interventions will be provided to the physicians. Families will also be directed to rare disease registries and natural history studies if available for participation. Inheritance patterns, recurrence risks, and reproductive options will be discussed. Inconclusive or non-diagnostic results will also be shared with the families through the same process. A detailed report of the genomic findings and recommendations will be sent to the physicians and families, and incorporated into medical records.

The impact on patients, families, and clinicians will be evaluated through surveys and interviews.

Caregiver surveys: We will administer baseline (at enrollment) and ROR (~2 weeks after results are disclosed) surveys to the primary caregiver of all referred newborns. All surveys will be available in English and Spanish. They will be

programmed in REDCap for electronic administration, but caregivers who prefer will be able to take the survey via phone or secure video call with a research assistant. Caregivers will be compensated $20 per survey, for a total of $40 for the baseline and RoR surveys.

Clinician interviews: We will survey each clinician who makes a referral through the Consultagene platform at the time of their first referral (baseline). We will administer clinician followup surveys on an annual basis. Clinician qualitative interviews will be conducted 6-12 months after implementation; all clinicians who make a referral will be invited to participate. Interviews will focus on barriers and facilitators to using the Consultagene platform, satisfaction with and suggested improvements, and perceived fidelity to the intervention. We will reach out to eligible clinicians via email and/or phone to request their participation in an interview. Informed consent will be obtained using a verbal consent statement as approved by the Institutional Review Board. Interviews will generally take place over the phone or via secure video conferencing that is approved for communicating protected health information. Local interviews will be conducted in person when feasible. Interviews may take up to 1 hour, depending on how much the interviewee has to say about the topic. Interviews will be audio-recorded with the interviewee's permission, transcribed by Rev, a transcription provider with whom we (Center for Medical Ethics & Health Policy at BCM) already have a Business Associate Agreement in place. Personally identifying information will be stripped from the transcripts before beginning analysis. Data will be maintained on secure and encrypted computers and in locked offices at BCM.

DNA Banking: DNA samples will be coded to protect personal identification and will be banked at Baylor College of Medicine indefinitely. Baylor will keep the DNA samples until the research is complete or until it is completely used. The coded DNA samples without any identifying information may be shared with other qualified investigators if they are also studying the genetics of birth defects in children. The PI will review all such requests. Coded samples will be transferred only after ensuring that the investigators have IRB approval for the study. MTA will need to be in place before samples are transferred.

Section G: Sample Size/Data Analysis

G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?

Local: 410 Worldwide: 410

Please indicate why you chose the sample size proposed:

Primary Outcome Power Calculation: One of the relevant indicators of the clinical impact is percentage of babies who need genetic screening getting diagnosis. Based on the current published estimates, we anticipate that about 10% of babies at NICU will need genetic screening, and 60% of those babies will likely need to be evaluated by genomics. Currently, none of the 9 participating clinics have performed any WGS or RNA sequencing (baseline). We estimate that about 1/10 of babies who need screening get genetic diagnoses based on the use of other diagnostic methods such as karyotype and chromosomal microarray analysis available to the neonatologists. After the program of genetic screening or Consultagene platform is established and implemented, we expect that all babies who need genetic screening (10/10) or need further genomics evaluation (~6/10) (60%) will receive it. And about 50% of those getting genomics evaluation will get a diagnosis, i.e., 30% of babies who need genetic screening will get a diagnosis.

We do not have prior data on intra-class correlation for NICUs, but we expect it to be large. Specifically, we use different sizes of the cluster (4, 5, 6) i.e. number of babies per NICU requiring genetic screening from whom data will be collected in each time step. Additionally, difference of the correlation values are employed (0.5, 0.6, 0.7). As the intervention effect is anticipated to be large (change from 10% to 30%), we have very high power to detect this change (range from 0.8585 to 99.98).

We will survey 1 caregiver per newborn (n=200).

We will survey each clinician who makes a referral through the Consultagene platform at the time of their first referral (baseline). We will administer clinician followup surveys on an annual basis. Clinician qualitative interviews. About 10 clinicians will be interviewed ~12 months after implementation; all clinicians who make a referral will be invited to participate. Interviews will focus on barriers and facilitators to using the Consultagene platform, satisfaction with and suggested improvements, and perceived fidelity to the intervention.

G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?

Primary outcome: Descriptive statistics (proportion and 95% CI) will be presented for each NICU and for all NICUs at each time point. Approximately 40 babies will be recruited per year over 5 years. Cluster or NICU effect will be taken into account when calculating overall data (proportion and 95% confidence intervals). To compare changes before and after intervention (the percent of babies with a diagnosis based on genetic evaluation over the total number of babies suspected to have a genetic diagnosis), mixed-effects model will be used to take into account both time effect and clustering (NICU) effect.

Secondary outcomes: Descriptive statistics (proportion and 95% CI, mean, standard deviation, median, range) of all studied variables collected in caregiver surveys will be examined. Descriptive data will be presented for each NICU and for all NICUs at each time point.

Clinical Outcomes: We will calculate descriptive statistics on patient clinical presentations, such as HPO terms and clinical diagnoses, to characterize the clinical presentation of the patient population, as well as on institutional features of the NICU, such as care level and geographic location, to characterize features of the care setting. Additionally, we will calculate descriptive statistics on clinically relevant laboratory outcomes, such as the turnaround time and outcome (diagnostic versus non-diagnostic) of each test in the multi-'omics pipeline and the combined analyses for a particular patient. We will use logistic regression analysis to calculate the odds of WGS diagnosis based on clinical characteristics.

Section H: Potential Risks/Discomforts

H1. Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:

The research involves no more than minimal risk to the subjects. Parents will provide informed consent for participation of their children in the study. We will avoid any undue inducement to participation in this vulnerable population by thoroughly explaining the risks and benefits of the research and sequencing and ensuring that caregivers are aware of alternatives to participation. Complications of blood sampling such as bleeding, pain, bruising, and infection at site can occur. For the optional skin biopsy, pain, bleeding, and infection involving the biopsy site may be experienced by study participants. The risk is minimized with local anesthetic such as lidocaine. Skin biopsies limited to 2-3 mm that do not require sutures and would be considered minimal risk. There is a small risk of loss of patient confidentiality, which the study personnel will make every effort to minimize. There is a risk of hearing unsettling information if the results of the genetic testing are conveyed to the research subject's parents. This risk will be minimized by study clinicians who are experts in disclosing such information. Non-paternity will not be reported to the participating families.

DNA data may be released to a research database. Neither the research subject's name nor any other identifiable information will be released. Because DNA sequences are unique to individuals, there is a small chance that someone could trace the information back to the research subject. At present there are only a few ways this could be done. First, if another sample from the research subject were available for comparison, a relatively small number of tests on that sample could be matched with the information in the database. Second, genetic information known to be from the research subject extracted from another database (e.g. a database of clinical test results) could be matched to the research database. Finally, a relative could compare their own DNA results with the information in the database and based on expected similarity infer which sample belonged to the research subject.

Survey and interview risks: Risks to participants posed by survey and interview participation are minor: participants may feel uncomfortable or experience fatigue answer questions, and there is the potential for loss of confidentiality.

H2. Data and safety monitoring plan

Do the study activities impart greater than minimal risk to subjects?

No

H3. Coordination of information among sites for multi-site research

Is the BCM Principal Investigator acting as the SPONSOR-INVESTIGATOR for this multi-site research?

Yes

Is BCM the COORDINATING CENTER for this multi-site research?

Yes

If the answer to EITHER of the questions above is "Yes", please complete the following questions:

If this is a multicenter study and the BCM PI is an INVESTIGATOR with responsibilities of SPONSOR or if BCM is the COORDINATING CENTER, describe the management of information among the sites related to participant protections. Your description should include reporting of unanticipated problems, protocol modifications, IRB and/or institutional approvals, and interim results among the sites.

BCM PI will be responsible for assuring protocol compliance and conduct safety reviews quarterly. Based on the review, the PI will determine whether the study should continue unchanged, require amendment or should close to enrollment. BCM PI will be responsible for reporting all adverse events to the IRB involving risks to subjects or others.

Children suspected to have genetic disorders of unclear etiology will be recruited at RGV and El Paso. No recruitment is anticipated through BCM. Children of all ethnicities will be part of the study. Both English and non-English speaking children will be enrolled. Parents will provide informed consent for participation of their children in the study. This would prevent undue coercion of this vulnerable population. Family participation would be entirely voluntary. Identifying information will be kept confidential by all reasonable means. The study will comply with all Federal and local privacy laws

and regulations. Subject confidentiality would be maintained by coding of all specimens. All subject identifiers as defined by HIPAA will be protected and assigned ID numbers so that identities are not traceable outside the study. BCM will have the key to identify subjects who are assigned a code and the key will be kept confidential.

PHI will be accessible only to the study staff at RGV, El Paso, and BCM. The health information by which subjects can be identified will be stored in a password-protected spreadsheet and shared via BCM's officially sanctioned service for secure online file sharing.

When research is conducted in collaboration with outside entities or organizations, the PI must obtain the necessary approvals from those entities. The BCM IRB may request documentation that such approvals have been obtained. Please list and describe the planned sites for this multi-site research for which the BCM PI is either Sponsor-Investigator and/or Coordinating Center. Sites that do not meet the requirements for inclusion in section A6a of the protocol summary and BCM informed consent documents should be listed here.

We will execute broad reliance agreements with the NICUs participating in the study. Baylor IRB will serve as the IRB of record for all participating sites. SMART IRB agreement will be used as the basis for reliance. For sites that do not have an IRB in place, a Letter of Support by the institution will be added to the protocol. Mission Regional Medical center in the Rio Grande Valley does not have an IRB in place at present. A letter of Support by the institution is provided in section S. A BCM local research coordinator will be present to facilitate the study.

The BCM Coordinating site will be responsible for overall data management, monitoring, general oversight of conduct of the project, and communication between researchers at BCM, El Paso, and RGV. BCM site will be responsible for meeting regulatory obligations, such as obtaining informed consent, overseeing the implementation of the approved protocol, and reporting unanticipated problems and study progress.

Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.

Without a definitive diagnosis, neonates with rare diseases often have no access to disease-specific intervention or opportunities for clinical trials to alleviate the disease process. Subjects can receive a genetic diagnosis by participating in this study. Detailed counseling for disease management will be provided by the study staff to the family once diagnosed, including discussion of current therapies/clinical trials/medications, referral to subspecialty services including palliative care, and if needed, prompt referral to tertiary care center in select cases for life-saving interventions.

Describe potential benefit(s) to society of the planned work.

The study will deliver high level genomic care to infants in NICUs in under-resourced and underserved regions of Texas.

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.

The anticipated benefits outweigh potential risks. The risk-to-benefit ratio remains low.

Section J: Consent Procedures

J1. Waiver of Consent

Will any portion of this research require a waiver of consent and authorization?

No

J1a. Waiver of requirement for written documentation of Consent

Will this research require a waiver of the requirement for written documentation of informed consent?

Yes

Explain how the research involves no more than minimal risk to the participants, and the specifics demonstrating that the research does not involve procedures for which written consent is normally required outside of the research context.

Waiver of requirement for written documentation of consent is requested for Clinician surveys and interviews. Individuals typically do not sign to participate in interviews/surveys outside of the research context. Clinicians will be interviewed approximately 6-12 months after implementation of the study. Interviews will focus on barriers and facilitators to using the Consultagene platform, satisfaction with and suggested improvements to Consultagene, and perceived fidelity to the intervention. We will reach out to clinicians via email and/or phone to request their participation in an interview. Informed consent will be obtained using a verbal consent statement as approved by the Institutional Review Board. The script is included in section S. Verbal consent will be recorded on audio (will be transcribed as well) and documented as such.

Verbal consent will be audio-recorded before beginning the interviews. Some participants may feel uncomfortable or upset while discussing their experiences, but they will have the option to skip questions they do not wish to answer. Although there is a slight risk of a confidentiality breach, patient data will be stored securely on a HIPAA-compliant BCM platform. The study staff will take every possible measure to minimize these risks.

J2. Consent Procedures

Who will recruit subjects for this study?

PI
PI's staff

Describe how research population will be identified, recruitment procedures, any waiting period between informing the prospective participant and obtaining consent, steps taken to minimize the possibility of coercion or undue influence and consent procedures in detail.

Newborns with suspected genetic disorders will be referred to Consultagene (www.consultagene.org) by the neonatologists and nurse practitioners. The informed consent will be obtained in subjects' preferred language by the NICU team before submission of clinical information into Consultagene. The research team will only obtain consent after reliance agreements have been established with their institution. Infants with a diverse group of phenotypes will be considered for recruitment. Diagnostic studies from NICU including echocardiogram, cranial ultrasound, brain MRI, X-rays, laboratory evaluation, and other consultations will be reviewed and analyzed. These would be uploaded by the neonatologists in the Consultagene portal. Once the baby is accepted in the study by the BCM study team, the demographic information of the baby which is also submitted into Consultagene portal by the NICU providers will be available to the local research coordinators, employed by BCM. The BCM research coordinators in the Rio Grande Valley and El Paso will then contact the family and meet with them in the NICU and review the details of the study with them. Buccal samples on both parents will also be collected whenever feasible. A medical release will be obtained from all families to ensure appropriate access to medical information required for the genomic analysis.

Clinicians will complete a survey at their first referral through the Consultagene platform, followed by annual surveys. Twelve months post-implementation, about 10 clinicians will be interviewed to gather feedback on platform use, satisfaction, and potential improvements.

Are foreign language consent forms required for this protocol?

No

J3. Privacy and Intrusiveness

Will the research involve observation or intrusion in situations where the subjects would normally have an expectation of privacy?

No

J4. Children

Will children be enrolled in the research?

Yes

J5. Neonates

Will non-viable neonates or neonates of uncertain viability be involved in research?

No

J6. Consent Capacity - Adults who lack capacity

Will Adult subjects who lack the capacity to give informed consent be enrolled in the research?

No

J7. Prisoners

Will Prisoners be enrolled in the research?

No

Section K: Research Related Health Information and Confidentiality

Will research data include identifiable subject information?

Yes

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.

Yes

Specific information concerning alcohol abuse:

No

Specific information concerning drug abuse:

No

Specific information concerning sickle cell anemia:
No

Specific information concerning HIV:
No

Specific information concerning psychiatry notes:
No

Demographic information (name, D.O.B., age, gender, race, etc.):
Yes

Full Social Security #:
No

Partial Social Security # (Last four digits):
No

Billing or financial records:
No

Photographs, videotapes, and/or audiotapes of you:
Yes

Identifiable biospecimens
Yes

Will identifiable biospecimens be stored for future research?
Yes

If yes, is the storage of biospecimens optional for subjects?
No

Will identifiable private information be stored for future research?
Yes

If yes, is the storage of information optional for subjects?
No

Questionnaire, Survey, and/or subject diary
Yes

Other:
No

At what institution will the physical research data be kept?
Baylor College of Medicine

How will such physical research data be secured?
The hard copies related to subject identification will be kept in a locked file cabinet at Baylor College of Medicine.

At what institution will the electronic research data be kept?
The research data will be kept in a secured password protected Baylor College of Medicine drive

Such electronic research data will be secured via BCM IT Services- provided secured network storage of electronic research data (Non-Portable devices only):
Yes

Such electronic research data will be secured via Other:
No

Will there be anyone besides the PI, the study staff, the IRB and the sponsor, who will have access to identifiable research data?
Yes, identify the classes of the persons:
Patient's physicians

Please describe the methods of transmission of any research data (including PHI, sensitive, and non-sensitive data) to sponsors and/or collaborators.

All specimens will be coded to protect identity of the individuals and subject-specific information with personal identifiers will be stored in a secure electronic database. All subject identifiers as defined by HIPAA will be protected and assigned ID numbers so that identities are not traceable outside the study. BCM will have the key to identify subjects who are assigned a code and the key will be kept confidential. The health information by which subjects can be identified will be stored in a password-protected spreadsheet. Identifying information will be kept confidential by all reasonable means and shared with study personnel via BCM's officially sanctioned service for secure online file sharing. PHI will not be reused or disclosed to or shared with any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

Will you obtain a Certificate of Confidentiality (COC) for this study?

Yes

Please further discuss any potential confidentiality issues related to this study.

All subject samples will be coded. Consent forms will be assigned code numbers at the time of consent and sample acquisition. Personal identifying information will be recorded in a secure database and documents will be stored in a secure file cabinet at Baylor. Identifiable subject-specific data will not be reported in any public format nor will it be reported to any third party.

Will information about the subject's participation be included in subject's medical records?

Yes

Please further discuss any potential confidentiality issues related to this study.

The subjects will receive CLIA-lab reports for whole genome sequencing. This would be included in their medical records.

Section L: Cost/Payment

Delineate clinical procedures from research procedures. Will subject's insurance (or subject) be responsible for research related costs? If so state for which items subject's insurance (or subject) will be responsible (surgery, device, drugs, etc). If appropriate, discuss the availability of financial counseling.

Subject's insurance will not be responsible for research related costs.

If subjects will be paid (money, gift certificates, coupons, etc.) to participate in this research project, please note the total dollar amount (or dollar value amount) and distribution plan (one payment, pro-rated payment, paid upon completion, etc) of the payment.

Dollar Amount:

40

Distribution Plan:

Subjects will be paid $20 for each survey (total of $40 for the two surveys via Clincard). The first survey would be completed on Visit 1 and the second survey would be completed two weeks after the return of results.

Section M: Genetics

How would you classify your genetic study?

DNA diagnostic study

Discuss the potential for psychological, social, and/or physical harm subsequent to participation in this research. Please discuss, considering the following areas: risks to privacy, confidentiality, insurability, employability, immigration status, paternity status, educational opportunities, or social stigma.

There is a risk of hearing unsettling information if the results of the genetics testing are conveyed to the research subject's parents. Non-paternity will not be reported to the participating family. There is a small risk of loss of patient confidentiality. However, study personnel will make every effort to minimize the risk.

DNA data may be released to a research database. Neither the research subject's name nor any other identifiable information will be released. Because DNA sequences are unique to individuals, there is a small chance that someone could trace the information back to the research subject. At present there are only a few ways this could be done. First, if another sample from the research subject were available for comparison, a relatively small number of tests on that sample could be matched with the information in the database. Second, genetic information known to be from the research subject extracted from another database (e.g. a database of clinical test results) could be matched to the research database.

Finally, a relative could compare their own DNA results with the information in the database and based on expected similarity infer which sample belonged to the research subject.

Will subjects be offered any type of genetic education or counseling, and if so, who will provide the education or counseling and under what conditions will it be provided? If there is the possibility that a family's pedigree will be presented or published, please describe how you will protect family member's confidentiality?

Formal genetic counseling will be provided to the study participants by the genetic counselors and geneticists at BCM.

Section N: Sample Collection

SAMPLE: Blood

What is the purpose of the sample collection?

DNA and RNA collection for genetic studies.

For blood draws, specify the amount drawn, in teaspoons, at each visit and across the course of the subjects entire participation time.

For babies, ~2 ml will be drawn for genetic studies. Additional 2 ml may be collected if RNAseq studies are planned based on the GS results.

Is there the possibility that cell lines will be developed with this sample?Yes

Sample will be obtained from:

Pathology, Clinical Labs, Research Labs

Will the sample be stripped of identifiers?

No

If sample will be released outside the hospital:

Will sample be released to anyone not listed as an investigator on the protocol? Will the information be identifiable, coded or de-identified?

Yes, coded samples may be transferred after formal Materials Transfer Agreement

Will sample material be sold or transferred to any third parties? Will the information be de-identified?

The transfer would be done only after formal material transfer agreement. Samples will not be sold

If sample will be banked for future use:

Where will the sample be banked and for how long?

Samples will be banked indefinitely at Baylor College of Medicine

Does the banking institution have an approved policy for the distribution of samples?

Yes.

If the entire sample will NOT be used during the course of this research study:

Will the remaining tissue be discarded? If not what will be done with the remaining sample after study completion and how long will the sample be kept?

The remaining tissue will not be discarded. The samples would be kept indefinitely

Will samples be made available to the research subject (or his/her medical doctor) for other testing?

No

If a subject withdraws from the study:

Will subject have the option to get the remaining portion of their sample back?

No

Will samples be destroyed? If not, will they be kept anonymously? What will happen to the sample if the subject revokes authorization?

Samples will be kept encoded. If a subject withdraws from the study, their samples will be destroyed.

Will data obtained from their sample be deleted? What will happen to the sample if the subject revokes authorization?

The data collected may not be deleted. The sample will be destroyed if the subject revokes.

Will study data or test results be recorded in the subject's medical records?

Yes

Will results of specific tests and/or results of the overall study be revealed to the research subject and or his/her doctor?
Yes, all positive and negative results will be revealed to the research subject and their doctors. The CLIA reports will be available to upload into EMR system.

Please identify all third parties, including the subject's physician, to receive the test results.
Subject and subject's physicians.

SAMPLE: Buccal Brushing

What is the purpose of the sample collection?
DNA collection for genetic studies.

For blood draws, specify the amount drawn, in teaspoons, at each visit and across the course of the subjects entire participation time.
N/A

Is there the possibility that cell lines will be developed with this sample?No

Sample will be obtained from:
Pathology, Clinical Labs, Research Labs

Will the sample be stripped of identifiers?
No

If sample will be released outside the hospital:

Will sample be released to anyone not listed as an investigator on the protocol? Will the information be identifiable, coded or de-identified?
Yes, coded samples may be transferred after formal Materials Transfer Agreement

Will sample material be sold or transferred to any third parties? Will the information be de-identified?
The transfer would be done only after formal material transfer agreement. Samples will not be sold

If sample will be banked for future use:

Where will the sample be banked and for how long?
Samples will be banked indefinitely at Baylor College of Medicine

Does the banking institution have an approved policy for the distribution of samples?
Yes

If the entire sample will NOT be used during the course of this research study:

Will the remaining tissue be discarded? If not what will be done with the remaining sample after study completion and how long will the sample be kept?
The remaining tissue will not be discarded. The samples would be kept indefinitely

Will samples be made available to the research subject (or his/her medical doctor) for other testing?
No

If a subject withdraws from the study:

Will subject have the option to get the remaining portion of their sample back?
No

Will samples be destroyed? If not, will they be kept anonymously? What will happen to the sample if the subject revokes authorization?
Samples will be kept encoded. If a subject withdraws from the study, their samples will be destroyed.

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Yes, all positive and negative results will be revealed to the research subject and their doctors. The CLIA reports will be available to upload into EMR system.

Please identify all third parties, including the subject's physician, to receive the test results.
Subject and subject's physicians.

SAMPLE: Skin

What is the purpose of the sample collection?
DNA and RNA collection for genetic studies.

For blood draws, specify the amount drawn, in teaspoons, at each visit and across the course of the subjects entire participation time.
N/A

Is there the possibility that cell lines will be developed with this sample?Yes

Sample will be obtained from:
Pathology, Clinical Labs, Research Labs

Will the sample be stripped of identifiers?
No

If sample will be released outside the hospital:

Will sample be released to anyone not listed as an investigator on the protocol? Will the information be identifiable, coded or de-identified?
Yes, coded samples may be transferred after formal Materials Transfer Agreement

Will sample material be sold or transferred to any third parties? Will the information be de-identified?
The transfer would be done only after formal material transfer agreement. Samples will not be sold

If sample will be banked for future use:

Where will the sample be banked and for how long?
Samples will be banked indefinitely at Baylor College of Medicine

Does the banking institution have an approved policy for the distribution of samples?
Yes

If the entire sample will NOT be used during the course of this research study:

Will the remaining tissue be discarded? If not what will be done with the remaining sample after study completion and how long will the sample be kept?
The remaining tissue will not be discarded. The samples would be kept indefinitely

Will samples be made available to the research subject (or his/her medical doctor) for other testing?
No

If a subject withdraws from the study:

Will subject have the option to get the remaining portion of their sample back?
No

Will samples be destroyed? If not, will they be kept anonymously? What will happen to the sample if the subject revokes authorization?
Samples will be kept encoded. If a subject withdraws from the study, their samples will be destroyed.

Will data obtained from their sample be deleted? What will happen to the sample if the subject revokes authorization?
The data collected may not be deleted. The sample will be destroyed if the subject revokes.

Will study data or test results be recorded in the subject's medical records?
Yes

Will results of specific tests and/or results of the overall study be revealed to the research subject and or his/her doctor?
Yes, all positive and negative results will be revealed to the research subject and their doctors. The CLIA reports will be available to upload into EMR system.

Please identify all third parties, including the subject's physician, to receive the test results.
Subject and subject's physicians.

Section O: Drug Studies

Does the research involve the use of ANY drug* or biologic? (*A drug is defined as any substance(other than food) that is used to elicit a pharmacologic or physiologic response whether it is for treatment or diagnostic purposes)

No

Does the research involve the use of ANY gene transfer agent for human gene transfer research?

No

O1. Current Drugs

Is this study placebo-controlled?

No

Will the research involve a radioactive drug?

No

Section P: Device Studies

Does this research study involve the use of ANY device?

No

Section Q: Consent Form(s)

Genetic study to determine the cause of birth defects in newborns in Texas

Section R: Advertisements

None