Genetic Analysis of Patients with Nausea and Vomiting in Pregnancy and hyperemesis gravidarum.

Admin	
Protocol ID	2023-XXX
Panel	No Panel Assigned
PI	Benjamin Brooks Signed 01/05/2023 12:46 PM MST **No COI Reported**
Campus	UT
PI Type	Faculty/Staff - Faculty
Department	MSBS
PI Institution	
Co-PI's	XXXXXXX 01/05/2023 Signed 01/09/2023 11:00 AM MST YYYYYYYY 01/05/2023 Signed 01/20/2023 2:01 PM MST ZZZZZ 01/05/2023 Signed 01/10/2023 10:10 AM MST
External co-PIs	AAAAAAA
Full Review	Completed / 02/03/2023 5:00 PM MST
Full Review	Completed / 02/22/2023 5:00 PM MST
Full Review	Completed / 02/22/2023 5:00 PM MST
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Review Type	Full Review
Approval Status	Full Review Approved
Submitted By	Benjamin Brooks
Date Received	01/20/2023
Date of Completion	
Date Approved	04/03/2023
Final Approval Date	04/03/2023
Approval Expires	02/01/2025
Proposed Start Date	01/03/2023
Proposed End Date	01/31/2024
Date Closed	
Type of Research	Student Research
Funding Source	
Sponsor	
Sponsor Contact	
Sponsor Address	
Sponsor Email	
Sponsor Phone	
Consent Waived	Not Requested
Waiver of Documentation of Informed	

Consent	Not Requested
Regulatory Agency	None
Subjects	• Minors (under age 18)
Other Subjects Type	
Total Number of Subjects	50
Searchable Keywords	

Pre-Protocol Questionnaire	01/05/2023 Pre-Protocol Questionnaire.pdf
Reviewer Notes	03/01/2023 Full Review Review Notes.pdf 03/20/2023 Full Review Review Notes.pdf 03/20/2023 Full Review Review Notes.pdf 03/27/2023 Full Review Review Notes.pdf 03/27/2023 Full Review Review Notes.pdf 03/27/2023 Full Review Review Notes.pdf 03/27/2023 Full Review Review Notes.pdf 03/27/2023 Full Review Review Notes.pdf 03/27/2023 Full Review Review Notes.pdf 03/27/2023 Full Review Review Notes.pdf 03/27/2023 Full Review Review Notes.pdf 03/28/2023 Full Review Review Notes.pdf 03/28/2023 Full Review Review Notes.pdf 03/28/2023 Full Review Review Notes.pdf 03/28/2023 Full Review Review Notes.pdf 03/30/2023 Full Review Review Notes.pdf 03/30/2023 Full Review Review Notes.pdf 04/03/2023 Full Review Review Notes.pdf 04/03/2023 Full Review Review Notes.pdf 04/03/2023 Full Review Review Notes.pdf 04/03/2023 Full Review Review Notes.pdf
Consent Form	04/03/2023 Minor consent form GDF15 v3.1.docx 04/03/2023 Full consent Form GDF15 v3.1.doc 04/03/2023 Genetic_Analysis_of_Patients_with_Nausea_and_Vomit...
Grant Application Docs	01/20/2023 The effect of GDF15 in Hyperemesis Gravidarum Gran...
Notifications	01/23/2023 Revisions Required: IRB #2023-005.pdf 03/07/2023 Revisions Required: IRB #2023-005.pdf 03/20/2023 IRB #2023-005 Re-Review Email to Members.pdf 03/27/2023 Reviewer Revisions Required - IRB ID: 2023-005.pdf 03/31/2023 Automatic Reviewer Reminder Notice - IRB ID: 2023-... 04/03/2023 Revisions Required: IRB #2023-005.pdf 04/03/2023 Full Board Approved: IRB #2023-005.pdf 04/03/2023 Add One More Form: IRB #2023-005.pdf
Approved Application Sections	04/03/2023 Approved Application Sections Start Here.pdf

Personnel

PI

Benjamin Brooks (01/05/2023)

Responsibilities

1. What is the Campus Location for the Principal Investigator?

Answer:

Ivins

Co-PI's

XXXXXXXX (01/05/2023) No Allow Edit

Responsibilities

1. What is the Campus Location for the Principal Investigator?

Answer:

Ivins

Amanda Brooks (01/05/2023) No Allow Edit

Responsibilities

1. What is the Campus Location for the Principal Investigator?

Answer:

Ivins

YYYYYYYY (01/05/2023) No Allow Edit

Responsibilities

1. What is the Campus Location for the Principal Investigator?

Answer:

Ivins

Project Description

Briefly state the objective(s) and procedures associated with this project in the space provided.

NOTE: Incomplete or unclear information will delay IRB review and approval.

Answer:

GDF-15 is associated with hyperemesis gravidarum (HG) and Nausea and Vomiting in Pregnancy (NVP). Growth/differentiation factor-15 (GDF-15 is a member of the transforming growth factor β superfamily. Four alleles, two alleles in the mother, and two alleles in the child (in utero) could contribute to the severity of HG. The interplay of how these four alleles contribute to the severity of symptoms in patients with HG is not fully characterized. We hypothesize that the child's genotype (in utero) contributed to the severity and morbidity of the HG (and NVP) for the mother during the pregnancy with that child. The severity of symptoms will be assessed utilizing the mother's retrospective reporting. Our objective is to add to the existing body of literature addressing the topic of HG. We will perform a cohort analysis of mothers and children of pregnancies that were associated with HG. The procedure will be to collect cheek swabs from mothers, and children. This procedure has been performed in over 200 medical students without any adverse effects. This sampling technique has minimal discomfort, if any, but could possibly cause pain, bleeding, or irritation to the mother or the child(ren). The sample will be PCR amplified and will be sequenced the DNA to determine the genotypes from the four alleles. An analysis of the interplay between the alleles will be compared to symptom severity, as reported by the mother, electronically.

03/16/2023 1:12 PM MDT

Does the study involve storage or banking of human specimens or identifiable private information for use in future studies (e.g., submission to a repository)?

Answer: Yes
✔No

Does the study involve genetic testing or DNA/RNA extraction?

Answer: ✔Yes
No

Please describe:

The procedure will be to collect cheek swabs from mothers and children. The sample will be PCR amplified and will be sequenced the DNA to determine the genotypes from the mother's alleles and the child's alleles (in utero). An analysis of the interplay between the alleles will be compared to symptom severity as reported by the mother. Cells from the swab will be lysed, and PCR on the GDF-15 gene will be performed. The PCR sample will be sequenced by the procedure described below.

03/16/2023 1:13 PM MDT

GENETIC TESTING and/or DNA/RNA EXTRACTION
(Please note page where these issues are discussed in the Informed Consent documents.)

Test results wil:

Answer:
be given directly to subjects
be given to treating physicians
✔not be given outside the research.

Please describe the testing/extraction process:

Answer:

The sample collection will be performed by a student doctor or the study participant. The sample will be collected by cheek swab. Briefly, a sterile cotton tip swab or a swab specifically designed for buccal cell collection will be used to swab the buccal membranes on both sides of the mouth for 30 seconds. The swab will be placed into a lysis/storage buffer. The sample can be stored for up to one week at -20C (facilities at RVU MOB research lab). After standard genomic DNA extraction protocols using the Invitrogen Pure Link Genomic DNA prep kit (or similar product), the sample will be amplified using PCR (performed either at the RVU- UT facility in MOB or in the biochemistry lab at Southern Utah University under the supervision of external CO-I Jessica Pullan, Ph.D. and assistant professor of chemistry at SUU.

03/16/2023 1:14 PM MDT

Please describe the arrangements for storage of DNA/RNA samples:

Answer:

The samples from genomic preparation and PCR will be stored at SUU at -20C (standard DNA storage conditions) until sequence results are obtained. Samples could be stored at RVU MOB temporarily if they are acquired and processed at RVU. The sample will be disposed of by autoclaving and then using standard, university-approved biosafety protocols (incineration by external collection).

03/16/2023 1:14 PM MDT

Please describe the duration of storage:

Answer:

The duration of the storage will be one week. If trouble occurs with the DNA sequencing, then the sample will be rerun. The sample could be stored for up to one month while the DNA sequencing is performed.

03/16/2023 1:14 PM MDT

DATA COLLECTION METHODS

Will audio taping or videotaping of subjects occur?

Answer:
Yes
✔No

Will any of the following instruments/methods be used?

Answer:
Interview
Anonymous Surveys/Questionnaires
✔Identifiable Surveys/Questionnaires
Full consent Form GDF15 v3.1.doc (Consent Form) (Existing)
Minor consent form GDF15 v3.1.docx (Consent Form) (Existing)
Genetic_Analysis_of_Patients_with_Nausea_and_Vomit... (Consent Form)

Focus Groups
Standardized (published) Tests/Assessments
Not Applicable

Are you planning on using RVU institutional data (e.g. student information, grades, test scores, evaluations,

assessment data) for your research?

Answer: Yes
✔No

Will the records or specimens be collected from RVU?

Answer: ✔RVU only
RVU and other institutions
Other institutions only
Study does not involve records or specimen collection

Project Details

***Specific Aims* – State the specific scientific objectives of the research:**

Answer:

Nausea and vomiting during pregnancy (NVP) occur in 70-80% of pregnancies [5]. However, 0.3–3.6% of pregnant patients experience the most severe form of NVP, hyperemesis gravidarum (HG), with debilitating symptoms [5]. A recently developed consensus definition for hyperemesis gravidarum, also referred to as the Windsor Definition, includes the start of symptoms in early pregnancy (before 16 weeks gestational age); nausea and vomiting, at least one of which severe; inability to eat and/or drink normally; strongly limits daily living activities [6]. HG is further characterized by intractable vomiting, especially during the first trimester, which is challenging to treat and often leads to hypovolemia and weight loss.

HG is the most significant cause of early pregnancy hospitalization in the United States [7]. Patients with HG are commonly hospitalized due to weight loss that exceeds 5% of pre-pregnancy weight, dehydration, electrolyte imbalance, arrhythmias, and acid-base balance disturbance. HG can also be a driving factor in developing metabolic disorders, including acute kidney injury [8]. Despite the prevalence and significant morbidity associated with HG, high-quality research is still lacking in its primary etiology, treatment, and prevention. Most studies are limited by too few participants, biases, and uncontrollable confounding variables [9]. Furthermore, stigma, improper management, and lack of investment have all impeded care for these patients [10]. A significant benefit would be a genetic marker to identify at-risk individuals and pregnancies.

The study aims to characterize further the GDF-15 genetic influence of the mother and infant on NVP/HG disease severity. The state of the literature is that GDF-15 influences the severity of HG/NVP with some indication that the child's genotype, in utero, impacts disease severity. This study will attempt to characterize further the influence of the child's genotype while in utero on the disease severity in the mother.

03/16/2023 1:15 PM MDT

***Background and Significance* - Briefly sketch the background leading to the present proposal. Describe the contributions that the study will make to the health of human beings and/or to the scientific data base, using documentation from the literature where appropriate. Although it is helpful for the Board to have a decent understanding of the basis for conducting a research project, it is not necessary to have a full-blown literature review or extensive background and rationale for the proposed research plan or activity.**

Answer:

A genomic analysis using GWAS has indicated that GDF-15 plays a role in the disease severity of NVP and HG. Numerous studies have expanded to support this original study1,2,3,4. The role of the infant's genotype, in utero, in the disease has not been fully characterized. Here, we seek to identify the role of the infant. By identifying the role, doctors could have a predictive tool in which Mothers would have NVP/HG and potentially the disease severity. Further, this could lead to future directions where the burden of disease could be lessened.

Sources:
1. Fejzo MS, Fasching PA, Schneider MO, et al. Analysis of GDF15 and IGFBP7 in Hyperemesis Gravidarum Support Causality Analyse von GDF-15 und IGFBP-7 bei Hyperemesis gravidarum unterstützt Kausalhypothese.
2. Fejzo MS, Fasching PA, Schneider MO, et al. Analysis of GDF15 and IGFBP7 in hyperemesis gravidarum support causality. *GeburtshilfeFrauenheilkd*. 2019;79(04):382-388.
3. Cruickshank T, MacDonald TM, Walker SP, et al. Circulating growth differentiation factor 15 is increased preceding preeclampsia diagnosis: implications as a disease biomarker. *J Am Heart Assoc*. 2021;10(16):e020302.
4. Prajapat R, Jain S, Vaishnav MK, Sogani S. Structural Modeling and Validation of Growth/Differentiation Factor 15 [NP_004855] Associated with Pregnancy Complication-Hyperemesis Gravidarum. *J Krishna Inst Med Sci JKIMSU*. 2020;9(3). 5. Einarson TR, Piwko C, Koren G. Quantifying the global rates of nausea and vomiting of pregnancy: a meta analysis. J Popul Ther Clin Pharmacol. 2013;20(2):e171–83.
6. Jansen LAW, Koot M, Hooft J, Dean C, Bossuyt PMM, Ganzevoort W, et al. Grooten, Iris. The Windsor Definition for Hyperemesis Gravidarum: a multistakeholder International Consensus Definition. Eur J Obstet Gynecol Reprod Biol. 2021:266. https://doi.org/10.1016/j.ejogrb.2021.09.004.
7. London V, Grube S, Sherer DM, Abulafia O. Hyperemesis Gravidarum: A Review of Recent Literature. PubMed. 2017;100(3-4):161–71. https://doi.org/10.1159/000477853.
8. Popa SL, Barsan M, Caziuc A, et al. Life-threatening complications of hyperemesis gravidarum. Exp Ther Med. 2021;21(6):642. https://doi.org/10.3892/etm.2021.10074.

9. Boelig RC, Barton SJ, Saccone G, Kelly AJ, Edwards SJ, Berghella V. Interventions for treating hyperemesis gravidarum. Cochrane Database Syst Rev. 2016;11(5):CD010607. https://doi.org/10.1002/14651858.CD010607.pub2 PMID: 27168518.
10. Maslin K, Dean C. Nutritional consequences and management of hyperemesis gravidarum: a narrative review. Nutr Res Rev Published online September. 2021;16:1–. https://doi.org/10.1017/S0954422421000305.

03/16/2023 1:15 PM MDT

***Preliminary Studies* - Summarize preliminary studies conducted by the investigator pertinent to this proposal. State "none" if applicable.**

Answer:

PI Brooks led an investigation using a survey of HG/NVP patients where the severity and treatments were assessed.

Assessment of management approaches for hyperemesis gravidarum and nausea and vomiting of pregnancy: a retrospective questionnaire analysis
Rachel Mares, Adelene Morrow, Haley Shumway, Isain Zapata, David Forstein & Benjamin Brooks
BMC Pregnancy and Childbirth volume 22, Article number: 609 (2022)

The survey will be the same survey from this paper.

***Investigator Experience* - Provide a brief synopsis of the Principal Investigator's (and/or faculty mentor's) expertise, experience, and capability to perform this research. Please DO NOT PASTE CV in this answer section. You may attach a copy of the curriculum vitae or research background of the principal investigator on the protocol page by uploading under "Files" at the bottom of the page.**

Answer:

PI Brooks has a doctoral degree in molecular biology, where PCR, DNA sequencing, and genetic analysis were

performed. Additionally, PI Brooks has over 60 publications. PI Brooks led an investigation using a survey of HG/NVP patients where the severity and treatments were assessed.

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Experimental Design and Methods **- Detailed protocol for this project / subject-related studies.**

Methods and Procedures - Describe the procedure (s) in sequential detail. Clearly identify any experimental element of the study. Include a thorough description of any investigational drugs, therapeutic procedures, monitoring techniques, test procedures or medical devices.

[The description of investigational medical devices should include information on each important component, ingredient, principle of operation, and anticipated developmental changes in the device. On a separate page describe and address issues associated with the device presenting "Significant Risk" or "Non-Significant Risk"]

Answer:

This is a retrospective cohort analysis to identified mother and child(ren) with associated clinical diagnosis of HG in at least one pregnancy, physician diagnosed. The cohort will be comprised of women of childbearing age who have had successful pregnancies that were diagnosed with HG. Inclusion to the cohort includes patients with a diagnosis of HG during a single pregnancy, the ability to provide informed consent, the ability to provide a DNA sample, mothers with access to the genotype of their children, ability to provide information electronically. Subjects will be excluded from the study if: mothers were not diagnosed with HG during pregnancy, participants are unable or unwilling to provide informed consent, mother who are unable to provide information electronically, mother or child are unavailable for genotyping. This descriptive study aims to determine heterogenous alleles or homogenous alleles in symptomatic women and their association with the children through sequencing of the GDF-15 gene. The procedure will collect cheek swabs from mothers and child(ren), isolate genomic DNA, and sequence GDF-15 DNA amplified by PCR to determine the genotypes from the mother's two alleles, and child's two alleles. A student doctor or the study participant will perform sample collection. The sample will be collected by cheek swab. Briefly, a sterile cotton swab or buccal-specific swab will be vigorously rubbed on the buccal surfaces of the oral cavity for 30 seconds before being placed into a lysis/storage buffer. De-identification will occur using an ID number. Samples will be labeled with the ID. All laboratories beyond RVU will only have an ID number. Samples collected at the RVU clinic by students will be under the supervision of one of the PIs as well as the parents. De-identification will occur by PI while the student is collecting the sample or when the sample is received. The PI will de-identify electronically gathered information. Identifying information after the collection of the sample and electronic data collection will be destroyed. The sample can be stored for up to one week at -20C (in the SUU Biochemistry lab or at RVU MOB research lab). All samples will be destroyed after sequencing by defacing the label and disposing of them as a biosafety hazard. After standard genomic DNA extraction protocols using the Invitrogen Pure Link Genomic DNA prep kit (or a similar kit), the sample will be amplified at the RVU facility or Southern Utah University biochemistry lab under the supervision of external CO-I Jessica Pullan, Ph.D. and assistant professor of chemistry at SUU. A professional sequencing facility will be used for all sequence analyses. Data collected electronically from the mother regarding pregnancy will be analyzed against the genotype of the mother, the child and combined (mother and child) genotypes. An analysis of the interplay between the alleles will be compared to symptom severity reportedretrospectively by the mother electronically.

Sources:

1. Fejzo MS, Fasching PA, Schneider MO, et al. Analysis of GDF15 and IGFBP7 in Hyperemesis Gravidarum Support Causality Analyse von GDF-15 und IGFBP-7 bei Hyperemesis gravidarum unterstützt Kausalhypothese.

2. Fejzo MS, Fasching PA, Schneider MO, et al. Analysis of GDF15 and IGFBP7 in hyperemesis gravidarum support causality. *Geburtshilfe Frauenheilkd*. 2019;79(04):382-388.

3. Cruickshank T, MacDonald TM, Walker SP, et al. Circulating growth differentiation factor 15 is increased preceding preeclampsia diagnosis: implications as a disease biomarker. *J Am Heart Assoc*. 2021;10(16):e020302.

4. Prajapat R, Jain S, Vaishnav MK, Sogani S. Structural Modeling and Validation of Growth/Differentiation Factor 15 [NP_004855] Associated with Pregnancy Complication-Hyperemesis Gravidarum. *J Krishna Inst Med Sci JKIMSU*. 2020;9(3).

5. Mares R, Morrow A, Shumway H, Zapata I, Forstein D, Brooks B. Assessment of

management approaches for hyperemesis gravidarum and nausea and vomiting of pregnancy: a retrospective questionnaire analysis. *BMC Pregnancy and Childbirth* volume 22, Article number: 609 (2022)

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***Data Analysis and Data Monitoring* - Describe plans for statistical analysis of data when appropriate. If a data safety monitoring committee is appropriate to protect the safety and/or welfare of subjects, describe its operation (e.g., membership, stopping rules and frequency of review).**

Answer:

Electronically gathered disease severity data will be correlated with genotypic variant of the mother, child, and combined using linear regression. Demographic statistics will be reported. Additional statistical analysis will be reported as necessary for publication. This protocol poses little risk to subjects from sampling or the data analysis. The results will not be deidentified. Only summary data will be reported and no individual data will be published or presented.

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***Data Storage and Confidentiality* – Describe where the research data will be stored during the study and how it will be secured. The investigator must take necessary steps to maintain confidentiality of data. This includes coding data and choosing an appropriate and secure data storage mechanism which will prevent unauthorized access to data. State who will have access to the data. If data with subject identifiers will be released, specify the person (s) or agency to whom the information will be released and the purpose of the release.**

Answer:

Data will be stored securely (password protection) on the RVU OneDrive. Access will be given to the data administrator to deidentify. Only PIs will be given access. No individuals with access to the identified data should be involved with the data analysis.

03/16/2023 1:17 PM MDT

***Setting* - Describe briefly where the study will be conducted, e.g., private outpatient clinics, physicians offices.**

NOTE: If other institutional review committees (IRBs) or approvals are required, note them by name, affiliation and contact person. Also, be aware that the approval of other involved institutions' IRBs must be obtained before initiation of the project (but are not essential for RVU IRB review to begin).

Answer:

The following sites will be used to conduct the study.

1. RVU Research Facility in MOB in Southern Utah. Patient samples will be collected here and genomic DNA preparation/PCR can be performed here.
2. Southern Utah University Molecular Biology Lab. Genomic DNA preparation/PCR can be performed here.
3. University of Utah DNA Sequencing Core facility. DNA sequencing will be performed here.
4. RVU COMs. Data analysis will be performed at RVU facilities.

Are other IRBs involved in the approval of this project?

Answer: Yes

✔No

***Laboratory Methods and Facilities* - Indicate where specific laboratory tests will be performed; e.g., hospital chemistry laboratory, investigators' laboratory, radiology clinic, etc. If None, state N/A**

Answer:

1. The University of Utah DNA Sequencing Core facility. DNA sequencing will be performed here.

01/23/2023 8:53 AM MST

Estimated Period of Time to Complete the Study **– Describe the stages and total time of subject participation as well as overall time for the entire study (start to completion). Also, if study involves more than one visit, describe time range estimates for each visit (e.g., 20-30 minutes; 2 – 3 hrs, etc.). Where possible use a table or "bullet-point" format to clearly illustrate the flow of activities and procedures.**

Answer:

Descriptive data will be retrospectively obtained. Identifying patients will take 3-6 months. Sample gathering for the cohort will take 2 months. For each individual subject sampling will be completed within 5 minutes. The sample will be delivered to SUU withing 24 hours. Data processing will take 3-4 months. We anticipate overall completion of one year (in case additional samples are required after data analysis to power the study).

03/16/2023 1:18 PM MDT

Human Subjects **- Describe the characteristics of the research population**

Description of subjects **is to include the projected sample size, plans for the selection of subjects, and inclusion and exclusion criteria.**

Answer:

This is a cohort analysis of retrospectively identified mother and child(ren) with an associated pregnancy that was diagnosed with HG. Up to fifty sets [mother and child] will be collected. The inclusion of the patients require a diagnosis HG during a single pregnancy by a physician.

03/16/2023 1:19 PM MDT

Sample Size: **Number of subjects to be enrolled in this study at this site. Approximately ____ subjects at ____ sites in the U.S. will be enrolled in the study overall. For Clinical Trial studies, indicate number of subjects to be randomized.**

Answer:

This is a descriptive study and does not afford a power analysis. Descriptive statistics will be used to characterize the findings. Our objective is to add to the existing body of literature addressing the topic of HG. Fifty sets [mother and child] will be collected.

03/16/2023 1:19 PM MDT

Describe both *Inclusion / Exclusion Criteria*. BE SPECIFIC! Also, if children (persons under age 18) are excluded from this study provide scientific justification for such exclusion. Include physical, mental, cognitive, medical, and other relevant Inclusion and Exclusion criteria.

Answer:

Inclusion criteria for the study will include
· The inclusion of the patients in the sample include patients with a diagnosis HG during a single pregnancy.
· Participants who are mothers must have access to the genotype their child(ten).
· Participants must be able to provide informed consent
· Participants must be able to provide DNA samples
· Participants who are mother must be able provide data electronically
Exclusion criteria:
· Mothers who do not have a physician diagnosis of HG
· Mothers and/or children who are unable or unwilling to provide informed consent
· Mothers who are unable provide data electronically

· Mothers and child both must be available for genotyping
· Mothers who have moral or religious values that will not allow them to participate in this research

The inclusion of the patients and child in the sample include patients with a diagnosis HG or NVP during a single pregnancy.

03/16/2023 1:19 PM MDT

Describe intended gender or sex, age range, intended racial and ethnic distribution. If any vulnerable subjects are involved in this study (e.g., those with limited autonomy or decision-making capabilities) are included, justification must be provided.

Answer:

Inclusion criteria for the study will include

- The inclusion of the patients in the sample include patients with a diagnosis HG or NVP during a single pregnancy.
- Participants who are mothers must have access to the genotype their child(ten).
- Participants must be able to provide informed consent
- Participants must be able to provide DNA samples
- Participants who are mother must be able to fill out survey

Exclusion criteria:

- Participants who are the mother who do not have a diagnosis of NVP or HG
- Participants who are unable or unwilling to provide informed consent
- Mothers who are unable to complete survey
- Mothers and child both must be available for genotyping

Additional criteria will be considered upon or during the pilot study.

03/02/2023 7:35 PM MST

Identify the source(s) from which you will obtain your study population.

Answer:

In our initial survey on HG/NVP, word of mouth and social networking sites (Facebook HG support groups) were used to get samples. A sufficient number are local for this pilot study.

Describe plans for *recruitment of subjects*. All materials (e.g., flyers, ads, emails, letters, postings, handouts, etc.) to be used for recruiting subjects must be submitted to the IRB for review. Please upload recruitment materials under the "Files" tab at the bottom of your protocol page.

Answer:

Electronic data gathering on HG/NVP, word of mouth and social networking sites (Facebook HG support groups) were used to get samples. A sufficient number are local for this pilot study.

03/16/2023 1:20 PM MDT

Risk/Benefit Assessment and Informed Consent:

Describe the level of risk, and if more than minimal, describe how this research holds the prospect of a direct benefit for the subjects. If there is NO direct benefit to subjects, state such in protocol and in the consent documents.

Answer:

The risk to the patient is a HIPPA-related information breach. The risk of a breach is minimal. The consequence of a brief would stigma by associates resulting from a breach is minimal. There is no direct benefit to the participants of the study but rather to the population at large. This will be stated in the consent. The information returned to the patient would not be specific. The information will not be distributed to subjects and would be aggregated for the scientific and medical community to deliver and regulate as needed.

This will be stated in the consent.

The information returned to the patient would not be specific and not from the administrators of this survey. The information will not be distributed to patients and would be aggregated for the scientific and medical community to deliver and regulate as needed.

03/16/2023 1:21 PM MDT

Describe how the anticipated benefit justifies the risk.

Answer:

The benefit is early identification which will allow for early inventions for HG/NVP and information to the subject. The information returned to the patient would not be specific. The information will not be distributed to subjectss and would be aggregated for the scientific and medical community to deliver and regulate as needed.

03/16/2023 1:21 PM MDT

Describe how the anticipated benefit of this research is at least as favorable to the subjects as that to be received by available alternative approaches for the subjects.

Answer:

This study will add to the body of literature detailing possible diagnosis and informing possible treatment options for HG. Current approaches are limited to speculation on past pregnancies. With this descriptive study future therapeutic interventions could be identified that could benefit the mothers and their children.

03/16/2023 1:21 PM MDT

Describe any potential *RISKS OR DISCOMFORTS* in detail. Use evidence from clinical and/or animal studies to evaluate the level of potential hazards associated with participation in the research protocol. Indicate the methods for detecting adverse reactions. Describe the procedures for protecting against or minimizing potential risks (e.g., confidentiality, reputational injury, direct injury or harm to subject, etc.) and assess their effectiveness. Discuss why the risks to the subjects are reasonable in relation to proposed benefits to mankind. Be sure to describe any anticipated adverse events that might occur during the course of the study.

Answer:

HiPPA violations associated with the survey could pose a risk to the patient. (loss of privacy)
The benefits include to society as a whole and potentially to the individual if validated.

03/02/2023 7:36 PM MST

***Payment/Compensation* - Describe any financial payments for subject participation (e.g. compensation for time and travel). Indicate any partial payment schedule for less than complete study participation. Recall that payments cannot be perceived as coercive (overpayment for time and effort). Remember: payments are NOT benefits.**

Answer:

Participants will not be compensated for the pilot study.

***Subject Costs* - Describe any anticipated costs to research subject. If none, state such.**

Answer:

The partcipants will be donating time to collect the sample (~1 hour).

***Literature Cited* – If any, the references should be limited to relevant and current literature pertinent to the proposed research.**

Answer:

1. Fejzo MS, Fasching PA, Schneider MO, et al. Analysis of GDF15 and IGFBP7 in Hyperemesis Gravidarum Support Causality Analyse von GDF-15 und IGFBP-7 bei Hyperemesis gravidarum unterstützt Kausalhypothese.
2. Fejzo MS, Fasching PA, Schneider MO, et al. Analysis of GDF15 and IGFBP7 in hyperemesis gravidarum support causality. *Geburtshilfe Frauenheilkd*. 2019;79(04):382-388.
3. Cruickshank T, MacDonald TM, Walker SP, et al. Circulating growth differentiation factor 15 is increased preceding preeclampsia diagnosis: implications as a disease biomarker. *J Am Heart Assoc*.

2021;10(16):e020302.
4. Prajapat R, Jain S, Vaishnav MK, Sogani S. Structural Modeling and Validation of Growth/Differentiation Factor 15 [NP_004855] Associated with Pregnancy Complication-Hyperemesis Gravidarum. *J Krishna Inst Med Sci JKIMSU*. 2020;9(3).

5. Einarson TR, Piwko C, Koren G. Quantifying the global rates of nausea and vomiting of pregnancy: a meta analysis. J Popul Ther Clin Pharmacol. 2013;20(2):e171–83.
6. Jansen LAW, Koot M, Hooft J, Dean C, Bossuyt PMM, Ganzevoort W, et al. Grooten, Iris. The Windsor Definition for Hyperemesis Gravidarum: a multistakeholder International Consensus Definition. Eur J Obstet Gynecol Reprod Biol. 2021:266. https://doi.org/10.1016/j.ejogrb.2021.09.004.
7. London V, Grube S, Sherer DM, Abulafia O. Hyperemesis Gravidarum: A Review of Recent Literature. PubMed. 2017;100(3-4):161–71. https://doi.org/10.1159/000477853.
8. Popa SL, Barsan M, Caziuc A, et al. Life-threatening complications of hyperemesis gravidarum. Exp Ther Med. 2021;21(6):642. https://doi.org/10.3892/etm.2021.10074.

9. Boelig RC, Barton SJ, Saccone G, Kelly AJ, Edwards SJ, Berghella V. Interventions for treating hyperemesis gravidarum. Cochrane Database Syst Rev. 2016;11(5):CD010607. https://doi.org/10.1002/14651858.CD010607.pub2 PMID: 27168518.
10. Maslin K, Dean C. Nutritional consequences and management of hyperemesis gravidarum: a narrative review. Nutr Res Rev Published online September. 2021;16:1–. https://doi.org/10.1017/S0954422421000305.

01/20/2023 12:36 PM MST

Do you ever intend to publish or present (oral, poster, or written) the results of this project?

Answer: ✔Yes. *Please remember to fill out the Attestation form on iNET if you present or publish any of your work.
No

Funding

Indicate the category of the sponsor:

☐ **Local Government**

☐ **State Government**

☐ **Federal Government**

☐ **Industry or Pharmaceutical Company**

✔ **Non-Profit Foundation/Institution**

Name of Foundation/Institution:
Southern Utah University awarded an internal grant to Jessica Pullan to complete the sequencing of the DNA.

☐ **RVU Intramural Grant**

Please upload entire grant application and supporting documents:

Answer:
The effect of GDF15 in Hyperemesis Gravidarum Gran... 01/20/2023 (Grant Application Docs)

Informed Consent

Is a signed Informed Consent document being used?

Answer: ✔Yes

No

What is the reading grade level of the consent document?
8th grade

Please upload consent forms:

Answer:

Genetic_Analysis_of_Patients_with_Nausea_and_Vomit... 04/03/2023 3 (Consent Form) (Existing)
Full consent Form GDF15 v3.1.doc 04/03/2023 (Consent Form)
Minor consent form GDF15 v3.1.docx 04/03/2023 (Consent Form)

04/03/2023 9:57 AM MDT

Will a Certificate of Confidentiality be requested from NIH?

Answer: Yes
✔No

Does the consent form tell the subject of situations where the PI may voluntarily comply with state laws? (e.g. reporting of child abuse, elder abuse, or immediate danger to self or others)?

Answer: Yes
✔No

Has the confidentiality statement been modified to be consistent with the Certificate of Confidentiality protections (if not applicable, leave blank)?

Answer: Yes
No
✔Not Applicable

Does the consent form include HIPAA Privacy Rule Information for the use of Protected Health Information (PHI)?

Answer: ✔Yes
No

Correspondences

Publicationss

Project Reports

Year	Status	Due Date	Date Received	Date Approved	Submitted By
2	Due	12/21/2024			

Total # Subjects Enrolled Since Last Project Report:
Total # Subjects Enrolled in Study to Date:
Total # Subjects Who Have Died: 0
Total # Subjects Who Have Completed Study:
Total # Subjects Still Active:
Continuation Status:
Unforeseen/Adverse Events: None
Describe Unforeseen/Adverse Events:
Additional Comments:

Cont Review Form

If any subjects were withdrawn by the PI, please provide the reasons subjects were withdrawn (during this reporting period):

If any subjects self-withdrew, please provide the reasons for their decision (during this reporting period):

SUBJECT ENROLLMENT: GENDER

Gender Distribution of Study Subjects - Female:

Gender Distribution of Study Subjects - Male:

Gender Distribution of Study Subjects - Other:

SUBJECT ENROLLMENT: ETHNICITY

Ethnic Distribution of Study Subjects - Black:

Ethnic Distribution of Study Subjects - Native American/American Indian:

Ethnic Distribution of Study Subjects - Asian:

Ethnic Distribution of Study Subjects - Caucasian (White):

Ethnic Distribution of Study Subjects - Native Hawaiian/Pacific Islander:

Ethnic Distribution of Study Subjects - Other/Unknown Origin:

CONSENT DOCUMENT STATEMENT:

Was informed consent obtained on all human subjects?

Options: Yes - All Subjects Consented
No - Some Subjects Did Not Consent
No - Waiver of Informed Consent was Granted by the IRB

SERIOUS ADVERSE EVENTS

Did any serious adverse events (SAEs) occur since you last reported on this study?

Options: Yes
No

SUBJECT COMPLAINTS

Did research subjects register any complaints about this study since the most recent IRB Progress Report was filed?

Options: Yes
No

Has anything occurred since initial IRB review and approval which may have altered the risk/benefit relationship?

Options: Yes
No

Has any new literature or findings been reported since you last reported on this study which would significantly impact the design of this study or the risks associated with this study?

Options: Yes
No

No Panel Assigned

Tracking Status: No Status Recorded

1	Approved	02/20/2024	02/01/2024	02/02/2024	Benjamin Brooks

Total # Subjects Enrolled Since Last Project Report:	
Total # Subjects Enrolled in Study to Date:	10
Total # Subjects Who Have Died:	0
Total # Subjects Who Have Completed Study:	
Total # Subjects Still Active:	
Continuation Status:	Actively Enrolling new subjects
Unforeseen/Adverse Events:	None
Describe Unforeseen/Adverse Events:	
Additional Comments:	

Cont Review Form

Date of FIRST subject enrollment:

Answer: 03/14/2023

Date of MOST RECENT subject enrollment:

Answer: 10/31/2023

If any subjects were withdrawn by the PI, please provide the reasons subjects were withdrawn (during this reporting period):

Answer:

NA

If any subjects self-withdrew, please provide the reasons for their decision (during this reporting period):

Answer:

NA

SUBJECT ENROLLMENT: GENDER

Gender Distribution of Study Subjects - Female:

Answer: 100

Gender Distribution of Study Subjects - Male:

Answer: 0

Gender Distribution of Study Subjects - Other:

Answer: 0

SUBJECT ENROLLMENT: ETHNICITY

Ethnic Distribution of Study Subjects - Black:

Answer: 0

Ethnic Distribution of Study Subjects - Native American/American Indian:

Answer: 0

Ethnic Distribution of Study Subjects - Asian:

Answer: 0

Ethnic Distribution of Study Subjects - Caucasian (White):

Answer: 100

Ethnic Distribution of Study Subjects - Native Hawaiian/Pacific Islander:

Answer: 0

Ethnic Distribution of Study Subjects - Other/Unknown Origin:

Answer: 0

CONSENT DOCUMENT STATEMENT:

Was informed consent obtained on all human subjects?

Answer: ✔Yes - All Subjects Consented
No - Some Subjects Did Not Consent
No - Waiver of Informed Consent was Granted by the IRB

Copies of the executed consent forms are maintained at:

Answer: with investigators

Briefly describe any problems you have encountered in obtaining and documenting informed consent from participants:

Answer:
none

SERIOUS ADVERSE EVENTS

Did any serious adverse events (SAEs) occur since you last reported on this study?

Answer: Yes
✔No

SUBJECT COMPLAINTS

Did research subjects register any complaints about this study since the most recent IRB Progress Report was filed?

Answer: Yes
✔No

Has anything occurred since initial IRB review and approval which may have altered the risk/benefit relationship?

Answer: Yes
✔No

Has any new literature or findings been reported since you last reported on this study which would significantly impact the design of this study or the risks associated with this study?

Answer: Yes
✔No

Notifications

Notifications 02/02/2024 Continuing Review Approved Notification.pdf

✔ PI: Benjamin Brooks Signed 02/01/2024 12:29 PM MST **No COI Reported**

- Co-PI's: XXXXXX
- Co-PI's: YYYYYYY
- Co-PI's: Amanda Brooks

No Panel Assigned

Tracking Status: Completed

Modifications

Adverse Events

Event / Date	Status / Comments / Files	Submitted By

No Adverse Events Found.

Deviations

Status	Deviations File/Comments	Submitted By
No Deviations Found		

Reviewer Comments

Full Review: Review Completed, Due date 02/03/2023 5:00 PM MST

Will send to ZZZZZZZZZZZ first after revision submitted.

Full Review: Review Completed, Due date 02/22/2023 5:00 PM MST

Edit consent form:
Confusing sentence structure

Page two of the consent 1st paragraph last line needs to be rewritten. Confusing
Page two second paragraph needs rewrite (confusing)
Typos need to be fixed.
Doesn't mention how long the data will be kept
Probable need to substitute "follow the direction given you on how to correctly take the medicine" for compliant.
Needs more description that this is a two part study. The survey in part one and depended on answers you may be asked to participate in part two consisting of cheek swabs. Although they are minor risks do exist so they need to be listed

I believe there is a corruption of the data if you are surveying someone that knew someone.
How is the population of interest identified?

Full Review: Review Completed, Due date 02/22/2023 5:00 PM MST

- no review text -

Full Review: Review Completed, Due date 02/28/2023 5:00 PM MST

Many revisions are required including:
1) updated inclusion/exclusion criteria (Is it just mothers or babies/infants?/children). This needs to be clarified
2) Consent form describes study investigating role of protein but I don't see any methods involving protein analysis
3) Why are mom/dad and child being sampled? Wouldn't you only need DNA from mom and child? What is the purpose of this study? That was not clear. Are you assessing DNA contribution from child and how that affects this disorder in pregnant women or are you assessing the interactions between the genotypes?
4) Grammatical/spelling errors throughout

Full Review: Review Completed, Due date 02/28/2023 5:00 PM MST

- no review text -

Full Review: Review Completed, Due date 02/28/2023 5:00 PM MST

- no review text -

Full Review: Review Completed, Due date 02/28/2023 5:00 PM MST

I agree with the decision of the IRB committee that this study needs further revisions for the reasons discussed during the review and the questions the committee members had around several aspects of this study.

Full Review: Review Completed, Due date 02/28/2023 5:00 PM MST

- no review text -

Full Review: Review Completed, Due date 02/28/2023 5:00 PM MST

- no review text -

Full Review: Review Completed, Due date 02/28/2023 5:00 PM MST

Qualtrics Survey Software -HG Project.pdf document has some minor grammar mistakes. "Do you feel like your symptoms cmpromised your overall enjoyment of pregnancy?" Just do a quick read-through to find others.

I could not read Minor consent form - GDF 15.pdf or Full consent Form GDF15.pdf. They were both blacked out with Qoppa Software stamped on the pdf. Maybe this is RVU software used for PDFs, and I don't have it downloaded because I am a student. If so, please ignore this.

Full Review: Review Completed, Due date 02/28/2023 5:00 PM MST

- no review text -

Full Review: Review Completed, Due date 03/27/2023 5:00 PM MDT

Will send to Gubler and Coleman first after revision submitted.

Full Review: Review Completed, Due date 03/27/2023 5:00 PM MDT

- no review text -

Full Review: Review Completed, Due date 03/27/2023 5:00 PM MDT

Many revisions are required including:
1) updated inclusion/exclusion criteria (Is it just mothers or babies/infants?/children). This needs to be clarified
2) Consent form describes study investigating role of protein but I don't see any methods involving protein analysis
3) Why are mom/dad and child being sampled? Wouldn't you only need DNA from mom and child? What is the purpose of this study? That was not clear. Are you assessing DNA contribution from child and how that affects this disorder in pregnant women or are you assessing the interactions between the genotypes?
4) Grammatical/spelling errors throughout

Full Review: Review Completed, Due date 03/27/2023 5:00 PM MDT

Thank you for clearing up my confusion about the study. I realize, now, what this pilot study is assessing. This will be very important to determine, what role, if any, a fetus' genotype has on HG/NVP. It will pave the way to additional research to help the parents make an informed decision about pregnancy and the potential risk associated with HG.

Full Review: Review Completed, Due date 03/27/2023 5:00 PM MDT

The inclusion criteria is incomplete. There are no ages for children in the criteria and it's vague that children will be included. Based on the age of children, an assent form should be included.

Full Review: Review Completed, Due date 03/27/2023 5:00 PM MDT

I agree with the decision of the IRB committee that this study needs further revisions for the reasons discussed during the review and the questions the committee members had around several aspects of this study.

Full Review: Review Completed, Due date 03/27/2023 5:00 PM MDT

I have reviewed the revision and think all issues have been adequately addressed.

Full Review: Review Completed, Due date 03/27/2023 5:00 PM MDT

- no review text -

Full Review: Review Completed, Due date 03/27/2023 5:00 PM MDT

- no review text -

Full Review: Review Completed, Due date 03/27/2023 5:00 PM MDT

- no review text -