Protocol including Statistical Analysis Plan

Official Title: Effect of Antibiotics on Enteric Neurons and Glia (YAL-138) v1.2

NCT Number - NCT05834036

IRB approval date: November 6, 2025

SCIENCE FOR THE BENEFIT OF HUMANITY

Institutional Review Board
Sarah J. Schlesinger, MD, Chair
Dale Miller, BA CIP
Sr. IRB Specialist (212) 327-8411
Vanessa Smith, BA MPS, CIM, CIP
Sr. IRB Specialist, (212) 327-8410
Hospital Bldg., Room 201 Box 331

ClinicalTrials.gov
National Library of Medicine
8600 Rockville Pike
Bethesda, MD 20894

Re: Effect of Antibiotics on Enteric Neurons and Glia, NCT05834036, IRB ID YAL-1038

Dear Representative of ClinicalTrials.gov:

Thank you for your communication regarding project, Effect of Antibiotics on Enteric Neurons and Glia under NCT05834036, IRB ID: YAL-1038.

This letter is to confirm that the uploaded Study Protocol and Statistical Analysis Plan PDF/A document is the original, pre-specified Study Protocol and Statistical Analysis Plan document approved by the Rockefeller University Institutional Review Board. Our institution utilizes an IRB application format, rather than a separate Protocol and/or Statistical Analysis Plan. Please do not hesitate to contact me if I may be of further assistance.

Sincerely,

Sarah J. Schlesinger, MD
Chair, Institutional Review Board
Associate Professor of Clinical Investigation
Senior Attending Physician
Laboratory of Chemical Biology and Signal Transduction
The Rockefeller University

Study Application (Version 1.12)

1.0 General Information

***Please enter the full title of your study::**
Effect of antibiotics on submucosal enteric neurons and glia in the lower gastrointestinal tract.
***Please enter the study short title:**
Antibiotics effects on enteric neurons and glia. * This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.
Is this Study using Subject Management?
(•) Yes ( ) No

2.0 Add departments

2.1 List departments associated with this study:

- **Please choose at least two labs/departments. Your main lab/dept. should be the primary lab listed, e.g. your HOL's lab.**
- **All protocols must also list "Rockefeller University Hospital (RUH)" as a secondary lab/dept.**
- **You may also list additional, lab/dept(s) if appropriate to include RU collaborators.**
- **If your lab/department is not listed in the 'Add Department' dropdown menu, please contact RUH IT at hospital_informatics@rockefeller.edu to arrange for the new lab to be added to the listing.**

Is Primary?	Department Name
(•)	**RUH** - Laboratory of Mucosal Immunology (Mucida)
( )	**RUH** - Research Facilitation Office (Facilitation)

3.0 Assign key study personnel(KSP) access to the study

3.1 * Please add a Principal Investigator for the study:

Name	Role	Training Record
Aydin, Begum, PhD	**Principal Investigator**	View Training Record

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Name	Role	Training Record

3.0 Assign key study personnel(KSP) access to the study

No Additional Investigators have been added

B) Research Support Staff

Name	Role	Training Record
Fry, Rebecca Stanton, MSN FNP	**Facilitator**	View Training Record

3.3 *Please add a Study Contact:

Name	Role	Training Record
Aydin, Begum, PhD	**Study Contact**	View Training Record
Fry, Rebecca Stanton, MSN FNP	**Study Contact**	View Training Record

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

4.0 Rockefeller University Conflict of Interest

4.1 Investigator Financial Conflict of Interest All KSP must complete an annual certification of their Significant Financial Interest ("SFI") disclosures in the University's online Research Administration System at https://RAS.rockefeller.edu. Disclosures also must be updated in connection with new human subjects research protocols ("Research Certification"), and within 30 days of discovering or acquiring a new SFI. To avoid delays in the IRB review process, when prompted by an email from rascoi@rockefeller.edu requesting an updated Research Certification, KSP should click on the Research Certification link contained in that email notification, or go to https://RAS.rockefeller.edu, to (a) review and update his or her SFI disclosures or certify that he/she has no updates, as appropriate, and (b) indicate whether any of his/her SFI disclosures are reasonably related to the design, conduct, or reporting of the research protocol. If a KSP discloses a SFI that might constitute a conflict of interest with respect to the proposed protocol, he or she must e-mail a copy of the Lay Summary of the draft protocol to Teresa Solomon, Esq. (solomot@rockefeller.edu). Doing so will facilitate addressing COI issues in step with the development of the study protocol. Non-compliance or tardiness in making or updating COI disclosures will result in a delay in IRB review. Institutional Conflict of Interest:

As early as possible the PI (or a designee) preparing a clinical research protocol must review a list of entities in which The Rockefeller University has an Institutional Financial Interest at https://icoi.rockefeller.edu/account/login.php. If the proposed study involves any entity on that list, the PI (or designee) must notify Teresa Solomon, staff to the FCOI Committee, by e-mail solomot@rockefeller.edu and Sarah Schlesinger, Chair of the IRB, by email: schless@rockefeller.edu, provide the name(s) of the entities and a copy of the Lay Summary. Doing so will facilitate addressing institutional COI issues in step with the development of the study protocol. Failure to take steps to review and address potential institutional conflicts of interest will delay the IRB review process.

5.0 External Personnel

5.1 List external personnel who will be working on the study:

Name	Institution	Telephone	E-mail	Role
Yelina Alvarez	Janssen Immunology	650 269 2708	yelina.alvarez@gmail.com	Consultant

6.0 Delegation of Authority

6.1 Enter authorized activities for all Rockefeller University personnel named on the study.

Activity Codes:

1. Informed consent **
2. Inclusion / exclusion criteria
3. Medical/medication history *
4. Perform Physical Exam *

4a. Write / Sign LIP orders *

5. Skin assessments and photos
6. Study drug dispensing *
7. Study drug administration *
8. Study drug reconciliation
9. Study drug compliance
10. Administer study questionnaire(s)
11. Participant recruitment
12. Perform assays
13. Specimen / sample analysis
14. Lumbar puncture *
15. Femoral line placement *
16. Central line placement *
17. Insulin clamp procedure *
18. Leukapheresis *
19. Sigmoidoscopy *
20. Fat biopsy *
21. Skin biopsy *
22. Conduct sleep study
23. Diet design and preparation
24. Nutritional assessment and counseling
25. Addition of PABA to food
26. Data analysis
27. Data review
28. Data management
29. Maintain regulatory documents / files
30. Complete CRF's

Add up to three additional authorized activities specific to this study (do NOT add activities that have previously designated codes):

31:	Facilitator
32:	
33:	

Activity Codes Continued:

34. Behavioral Testing
35. Bod Pod
36. Bone Marrow Aspiration *
37. Neuropsychological Testing *
38. Conduct Focus Group
39. Conduct Smell Study
40. Genetic Counseling *
41. Apply EEG Electrodes **
42. Olfactometer Test
43. Study Participant Teaching
44. Resting Energy Expenditure
45. Source Document Review & Correction
46. Medical Photography
47. See 4a
48. Adverse Event Assessment
49. Clinical Trial Registration
50. Study Support Drug Dispensary
51. Internal Monitoring
52. Randomization

Enter delegation of authority for Rockefeller University Key Study Personnel:

NOTE:

* Indicates procedures requiring the individual complete specific credentialing **BEFORE** the activity may be added to their delegated activities.

** Indicates procedures requiring the individual complete specific training **BEFORE** the activity may be added to their delegated activities.

Name	Title	Authorized Activities	Start Date	End Date
Alvarez, Yelina, MD/PhD	PI	1, 2, 3, 4, 4a, 10, 12, 13, 19, 26, 27, 28, 30	11/14/2022	05/24/2024
Dowd, Kathleen, BSN, RN, CCRC	Facilitator	6,31	11/14/2022	04/17/2024
Olufeko, Oluwatobi Temitope, MPH, MA, CCRC	Facilitator	31	07/18/2023	10/03/2025
Aydin, Begum, PhD	Co-Investigator	12, 13, 26, 27, 28, 30	04/17/2024	05/24/2024
Burgos-Rivera, Genesis, BA	Facilitator	31	04/17/2024	10/03/2025
Aydin, Begum, PhD	PI	12, 13, 26,27,28, 30	05/24/2024	
Alvarez, Yelina, MD/PhD	Consultant	26,27,49	05/24/2024	05/24/2024
Dowd, Kathleen, BSN, RN, CCRC	Facilitator	31	05/22/2024	10/03/2025
Fry, Rebecca Stanton, MSN FNP	Facilitator	31	10/03/2025	

Enter delegation of authority for additional Rockefeller University Key Study Personnel:

Name	Title	Authorized Activities	Start Date	End Date
No results found				

Enter the authorized activities for External Personnel:

Name	Title	Authorized Activities	Start Date	End Date
No results found				

7.0 Study Description

7.1

Study Classification

Full Review

7.2

* Submission Request Category

Note: For each submission, please designate the level of review, or "Submission Request Category" you are requesting. When completing this field, please indicate the level of review you are requesting for the specific submission you are working on.
For example, if you are submitting an Expedited Amendment request to change the Key Study Personnel on your existing Full Board study, you should select "Expedited Review" in both the Amendment Submission Form and Study Application. The IRB will confirm an Expedited review of the Amendment submission is appropriate, and the overall study will remain classified as a full Board review. Please see the help bubble for guidance.

To submit a request for a Not Human Subjects research determination, please exit this form and select the "Not Human Subjects Research Determination" form under Create a New Study.

- ○ Exempt from Review
- ○ Exempt with Limited Review
- ○ Expedited Review
- ◉ Full Review

7.3 *** Lay Summary**

Please provide a summary of your study in lay language that is easily understood by a non-scientist. The summary should be no more than half a page (500 words or less) and should contain a clear statement of the rational for the study.

Please click on the help bubble to get the information on " How to use iRIS text editor."

Please provide a summary of your study in lay language. The summary should be no more than a half page (500 words or less) and should contain a clear statement of the rationale for the study.

The interactions between bacteria and their products with the intestinal tissue are important for maintaining a healthy and balanced system. Alterations in gut bacteria communities have been associated with various human pathologies. Our lab and others have found that mice treated with short and long-term antibiotics exhibit a transient yet profound loss of neurons in the more superficial submucosal and deeper muscularis plexi in the intestine accompanied by slow motility. Glia cells also depend on microbiota for their maintenance. In humans, antibiotic use has been associated with disorders of gut-brain interactions (DGBI) such as irritable bowel syndrome however whether there are changes in the enteric neurons and glia cells remain unknown. Therefore, we propose to further characterize the neurons and glia populations in the human distal colon after a single antibiotic course. We expect that our study will reveal glia and neuronal subtypes that are susceptible to changes in the bacteria populations and depend on microbial products for their maintenance. Our findings will guide future DGBI studies to ascertain the physiological effects that such loss has on intestinal healthy balance.

7.4

*** Public Health Impact Statement**

Provide a brief plain language statement (100 words or less) of the value of the research proposed and its potential impact on population health. Additional instructions located in Help.

Anti-microbials have been associated with Disorders of Gut Brain Interactions (DGBIs). We propose to study the effects that antibiotic use has on the number and type of neuron and glia cells in the gut. A better understanding of these effects will lead to the development of new therapeutic interventions and prevention strategies.

8.0

Clinical Trial Registration

8.1

Clinical Trial Registration

The types of studies listed below must be registered at **Clinical Trials website** before enrolling the first participant in order to be in compliance with federal regulations and preserve the opportunity to publish the study in journals that adhere to the **ICMJE guidelines**. Please check the answer that best applies.

- ○ Study involves testing of FDA regulated drugs or biologics (See HELP)
- ◉ Study is funded by the NIH, and meets the definition of a "clinical trial" (see HELP)
- ○ Study meets the ICMJE definition of a "clinical trial" (See HELP)
- ○ Additional funding agency or journal requires clinical trial registration
- ○ None of the above

If you selected 1, 2, 3, or 4 you must register your trial with ClinicalTrials.gov through the Rockefeller University institutional account. Please contact the Clinical Research Support Office x7408 for assistance.

9.0 Study Overview/Summary

9.1 * Who initiated this study?

Please specify one:

- (•) Principal Investigator Initiated
- ( ) Industry Initiated
- ( ) Other

9.2 *Are other institutions involved in the study?

- (•) No
- ( ) Yes

9.3 * Is this a multi-site trial using a single IRB (sIRB) review arrangement? Please see help bubble for definition.

- ( ) Yes (•) No

9.4 * Who (What) is to be studied?

- [x] Human Subjects - including coded samples and/or data with links to Identifiers
- [ ] Deidentified Samples - unable to be linked to identifiers by receiver
- [ ] Data Only - unable to be linked to identifiers
- [ ] Identifiable samples or data for exemptions (per 104 (s)(4))

9.5 *Study Type:

- (•) Interventional
- ( ) Observational

9.6 The initial date of IRB approval/determination was:

12/01/2022

9.7 * What is the expected duration of the study?

7 years

9.8 * Are any of the following agents to be used in the study?

Check all that apply:

- [ ] FDA Approved Drug
- [x] FDA Approved Drug for Off-Label Purpose (This might require an IND)
- [ ] Investigational New Drug
- [ ] Biologic Agents
- [ ] Nutritional Supplements
- [ ] Placebo
- [ ] Vaccines
- [ ] No Agents
- [ ] FDA Exemption to use Study Drug

Please indicate whether your application to the FDA for use of the investigational drug is planned or has been submitted by checking the box below.
Include a description of the status of the FDA submission in the text box.

- [ ] Planned
- [ ] Submitted

9.9 * Are investigational devices to be used in the study?

- ( ) Yes
- (•) No

9.15 Special Research Procedures

Does the study propose to directly involve participants in the following special research procedures?

- [ ] Recombinant DNA
- [ ] Gene Therapy
- [ ] Fetal Tissue
- [ ] Embryonic Stem Cells
- [ ] Induced Pluripotent Stem Cells
- [ ] CRISPR-Cas9

If any item is checked, please see Help for details.

9.16 * Radioactive Isotopes Involved

Will participants be exposed to any radiation other than routine x-rays solely for clinical care purposes?

- ( ) Yes
- (•) No

10.0 Interventional

10.1 *Interventional, please specify:

- (•) Open Label
- ( ) Single Blind
- ( ) Double Blind
- ( ) Other

11.0 Study Phase:

11.1 Study Phase:

Select where applicable

- ( ) Phase 0
- ( ) Phase I
- ( ) Phase I/II
- ( ) Phase II
- ( ) Phase III
- ( ) Phase IA
- ( ) Phase IB
- ( ) Phase IIA
- ( ) Phase IIB
- ( ) Phase IB/IIA
- ( ) Phase IIB/IIIA
- ( ) Phase IIIA
- ( ) Phase IIIB
- (•) N/A

12.0 Objectives and Rationale

12.1 * Overview

Briefly state the ***purpose of this study***. Give enough background and rationale to provide both scientists and lay members of the IRB and ACCTS with the basis for exposing human participants to the risks involved.

The enteric nervous system (ENS) has been recognized as the “second brain” as it can regulate enteric physiology without central nervous system input. Similar to the central nervous system, it is composed of multiple neuron populations whose main functions are gut motility, secretion, and absorption [3, 10]**.** In addition to the neurons, the ENS contains glia cells whose main role is neuroprotection but also contribute to normal gut motility [11]. Several studies have demonstrated that the microbiota and the ENS have an intimate relationship that begins *in utero,* and it is critical for its normal development [3]. Neurons can recognize bacteria and their products [12, 13]. Our lab and others have shown neuronal loss after enteric infections and antibiotic (Ampicillin) treatment in the muscularis layer, that results in delayed transit time in animal models [5, 7]. Hence, communication between the microbiota and the ENS is important to maintain normal gut motility. Disorders of Gut-Brain Interactions (DGBIs) are quite common, among these are Irritable Bowel Syndrome (IBS defined by Rome IV criteria as abdominal pain associated with a change in consistency and frequency of bowel movements) and the constipation predominant subtype (less than 3 bowel movements per week) is the most prevalent, which is also the most common motility disorder that our mouse models of infection and antibiotics treatment exhibit [14]. IBS has been associated with dysbiosis and a recent study demonstrated that antibiotic use immediately before or after screening colonoscopy increased the risk of developing IBS [9, 15]. In addition, dysfunction of submucosal neurons in IBS has been previously reported but whether there are changes in neuron numbers or neuron characteristics has not been

explored [16]. While there have been prospective studies that have explored the effects of antibiotics in patients treated for Helicobacter Pylori, there have been other investigators who have focused on the long term effects of antibiotics in healthy volunteers [17,18]. Therefore, similar to our animal models, we propose that humans experience a profound and transient loss/alteration of neurons in the setting of antimicrobial use associated dysbiosis that manifest as DGBIs, most notably the constipation subtypes. This proposal will address **whether antimicrobial use leads to quantitative and qualitative changes in the populations of submucosal neurons and glia cells in human subjects**.
We will test this hypothesis in a prospective study in which healthy participants will be asked to take the commonly used antibiotic amoxicillin twice a day for 7 days, and colon tissue biopsies will be obtained before and after treatment. We will then process and analyze the human tissue using techniques already established in the lab that will include confocal microscopy to visualize structural changes, single nuclei RNA sequencing, 16S ribosomal bacteria RNA sequencing and metabolomics analysis.

12.4 * Engaging Stakeholders: Describe any plans to engage other stakeholders (Scientists, practitioners, patients, advocacy groups, etc.) for hypothesis generation, or feasibility purposes.

Since this is a human subjects protocol we plan to engage the assistance of Rockefeller Hospital Research Support Office for protocol development, and recruitment of participants. We will need the assistance of a pharmacist to dispense the antibiotics. The hospital staff will assist with volunteers' visits and the endoscopic procedures. In the lab, one postdoc will assist with planning sequencing strategy. Staff from metabolomics, genomics and bioinformatics research support cores will also assist in this project.

Because we will only recruit healthy participants for this study, we will not engage any patients' groups.

12.5 * Hypothesis

Describe the ***research hypothesis*** in a single sentence.

Antimicrobial use leads to quantitative and qualitative changes in the populations of submucosal neurons and glia cells in human subjects.

12.6 * Aim(s)

Indicate how you will ***address the hypothesis*** (e.g., to compare groups, to estimate a parameter, to ascertain feasibility). Since the sample size determination is usually based on the primary aim only, the primary aim should be sufficient to justify the study.

Aim1: Characterize the changes of submucosal neurons and glia cells before and after course of antibiotics in humans.

12.7 * Primary Outcome(s)

Indicate which ***variable(s)*** will be assessed to judge the primary specific aim. Give measurement units, if applicable.

Total number of colonic submucosal neurons and glia cells in humans before and after course of antibiotics.

12.8 * Secondary Outcome(s)

Indicate which ***additional variable(s)*** will be assessed to judge the secondary outcome(s). Give measurement units, if applicable.

a. Gene expression profiles in the mucosa and submucosa compartments in humans before and after course of antibiotics.

b. Gut microbiota changes in humans after course of antibiotics.

c. Gut metabolites changes in humans after course of antibiotics.

12.9 * Methods and Procedures

Please provide a description of the laboratory and clinical analyses and procedures that will be performed. Include the role of external collaborators and consultants when appropriate. Please refer to Help text for Guidance.

One set of samples will be studied: Colorectal sample tissue and stool from amoxicillin-treated participants. All samples will be collected from RUH volunteers.

Ten 18–75-year-old participants will be divided into two groups of 5 and matched in age +/- 5 years, race, sex, and gender.

There will be five (5) study visits:

Study Visit 1 (Screening Visit) (approximately 2 hours; Out-Patient Visit)

- Consent process
- Medical History
- Targeted physical exam (focus on GI, cardiac and respiratory)
- HIV test
- POC Pregnancy test for women of childbearing age
- Labs: venipuncture to collect CBC, Comprehensive metabolic panel, PT/PTT, INR for a total of 10 ml blood (2 tsps.).
- Instructions will be provided in preparation for Visit #2. The following will be included:

a. adhere to a clear liquid diet the day prior to the scheduled flexible sigmoidoscopy. A clear liquid diet sheet with examples will be given to each participant.
b. The evening prior to the flexible sigmoidoscopy, participants will cleanse their bowels with a tap water enema. A plastic bottle and K-y jelly will be given to the participants to take home.
c. a sealed commercial stool collection kit (DNA Genotek) that includes specimen collection instructions, toilet accessory, collection tubes, and spatulas will be given to the participants to collect stool prior to the procedure. The participant will bring the stool sample during visit #2, +/- 2 days.
c. NPO after midnight the day of the procedure but encourage sips of water.

Further instructions will be given to participants on how to avoid prebiotics and probiotics during the study and to notify the PI if they need to take any antimicrobials or any new medications, start a new diet, have enteric infections during the study as these may result in their exclusion from the study.

Upon review of lab results and if the participant meets eligibility criteria, the PI will contact the study participant to schedule the flexible sigmoidoscopy. The participant will be instructed to adhere to a clear liquid diet the day before the procedure, to self-administer the tap water enema in the evening prior to the procedure, and not to eat or drink anything (except sips of water) after midnight the day of the procedure.

VISIT #2: Procedure Visit (2 to 21 days after screening visit) (approximately 2 hours; Day Patient Visit)

- Stool sample will be collected and stored in the refrigerator.
- Vital signs pre- and post-procedure. Post-procedure, vital signs will be taken immediately after the procedure, then 30 minutes after the procedure, and 1hr after the procedure.
- POC Urine Pregnancy test for women of childbearing age.
- Stool consistency and frequency questionnaire will be given to the participant to complete.
- Oral diazepam 5 mg pre-procedure will be offered and administered based on the patient preference and PI evaluation. Oral diazepam takes 30 - 60 minutes to take effect.
- Tap water enema upon arrival followed by additional 1 or 2, 200ml tap water enemas if the participant still has solid debris after a bowel movement.
- Flexible Sigmoidoscopy Procedure
    - The sigmoidoscope is advanced to the beginning of the descending colon (about 24 cm) and up to 20 biopsies will be obtained with Boston Scientific Jumbo forceps (max diameter of 2.8mm), each biopsy will be 2-2.8 mm in size, one in each quadrant, spaced 2-3cm throughout the sigmoid colon.
    - Tissue specimens will be placed in sterile specimen cups containing normal saline.
- Observation for one-hour post-procedure (for signs of bleeding or distress) and evaluation by nursing and PI to determine when ready for discharge.
- Breakfast
- Post-procedure Instruction sheet given prior to departure.

In the event a mass, polyp, or ulceration is found, a copy of the images obtained during the sigmoidoscopy and a letter with the examination findings will be given to the participant and they will be instructed to follow-up with their Primary Healthcare Provider.

The participant will be asked to return in two weeks for Visit #3 and instructions on avoiding the addition of new probiotics, prebiotics or drastic dietary changes will be given. In addition, participants will be instructed to notify us if he/she starts any antimicrobial medication including antifungals, or developed any intestinal infection.

VISIT #3: Medication Visit (14 to 21 days after visit 2) (approximately 1 hour; Outpatient Patient Visit)

- Medical History
- Targeted physical exam (focus on GI, cardiac and respiratory)
- POC Urine Pregnancy test for women of childbearing age
- Participants will be randomized to receive a 7-day supply of amoxicillin 875mg capsules to be taken every 12 hours. Medication will be dispensed and provided during the visit.
- Participants will be given a diary to record medication intake times.
- Participants will be given a plastic bottle and K-y jelly to self-apply a tap water enema at home on the night prior to the procedure.
- A sealed commercial stool collection kit (DNA Genotek) that includes specimen collection instructions, toilet accessory, collection tubes, and spatulas will be given to the participants to collect stool prior to the next procedure. The participant will bring the stool sample during Visit #4, +/- 2 days.

- Same instructions provided in preparation for Visit #2 will be provided in preparation for Visit #4.
- Same as in Visit #2 participants will be asked to avoid any new prebiotics, probiotics, or drastic dietary changes and to notify investigators if new anti-microbial medications were started or they developed an intestinal infection.

VISIT #4: Procedure Visit (5-9 days after initiation of antibiotics) (approximately 2 hours; Day Patient Visit)

Same as Visit #2. This visit could also occur after 5 Days of antibiotics in volunteers who cannot tolerate a 7-day course of amoxicillin. Participants that cannot tolerate at least 5 days of antibiotics will be excluded from the study, replaced with other participants, and provided partial compensation.

- Medication diary will be collected.
- Stool sample will be collected and stored in the refrigerator.
- Vital signs pre- and post-procedure. Post-procedure, vital signs will be taken immediately after the procedure, then 30 minutes after the procedure, and 1hr after the procedure.
- POC Urine Pregnancy test for women of childbearing age.
- Stool consistency and frequency questionnaire will be given to the participant to complete.
- Oral diazepam 5 mg pre-procedure will be offered and administered based on the participant's preference and PI evaluation. Oral diazepam takes 30 - 60 minutes to take effect.
- Tap water enema upon arrival followed by additional 1 or 2, 200ml tap water enemas if the participant still has solid debris after a bowel movement.
- Flexible Sigmoidoscopy Procedure
- The sigmoidoscope is advanced to the beginning of the descending colon (about 24 cm) and up to 20 biopsies will be obtained with Boston Scientific Jumbo forceps (max diameter of 2.8mm), each biopsy will be 2-2.8 mm in size, one in each quadrant, spaced 2-3cm throughout the sigmoid colon.
- Tissue specimens will be placed in sterile specimen cups containing normal saline.
- Observation for one-hour post-procedure (for signs of bleeding or distress) and evaluation by nursing and PI to determine when ready for discharge.
- Breakfast
- Post-procedure Instruction sheet given prior to departure.
- In the event a mass, polyp, or ulceration is found, a copy of the images obtained during the sigmoidoscopy and a letter with the examination findings will be given to the participant and they will be instructed to follow-up with their Primary Healthcare Provider.
- The participant will receive a sealed commercial stool collection kit (DNA Genotek) that includes specimen collection instructions, toilet accessory, collection tubes, and spatulas to collect stool prior to the next procedure. The participant will bring the stool sample during visit #5, +/- 2 days. similar to Visits #1 and # 3 to collect stool prior to Visit #5.
- Same as in Visit #3 participants will be asked to avoid any new prebiotics, probiotics, or drastic dietary changes and to notify investigators if new anti-microbial medications were started or they developed an intestinal infection.
- Participants will be given a plastic bottle and K-y jelly to self-apply a tap water enema at home on the night prior to the procedure.

VISIT #5: Procedure Visit (21 to 30 days after Visit #4) (approximately 2 hours; Day Patient Visit)

- Stool sample will be collected and stored in the refrigerator.

- Vital signs pre- and post-procedure. Post-procedure, vital signs will be taken immediately after the procedure, then 30 minutes after the procedure, and 1hr after the procedure.
- POC Urine Pregnancy test for women of childbearing age.
- Stool consistency and frequency questionnaire will be given to the participant to complete.
- Oral diazepam 5 mg pre-procedure will be offered and administered based on the patient preference and PI evaluation. Oral diazepam takes 30 - 60 minutes to take effect.
- Tap water enema upon arrival followed by additional 1 or 2, 200ml tap water enemas if the participant still has solid debris after a bowel movement.
- Flexible Sigmoidoscopy Procedure
- The sigmoidoscope is advanced to the beginning of the descending colon (about 24 cm) and up to 20 biopsies will be obtained with Boston Scientific Jumbo forceps (max diameter of 2.8mm), each biopsy will be 2-2.8 mm in size, one in each quadrant, spaced 2-3cm throughout the sigmoid colon.
- Tissue specimens will be placed in sterile specimen cups containing normal saline.
- Observation for one-hour post-procedure (for signs of bleeding or distress) and evaluation by nursing and PI to determine when ready for discharge.
- Breakfast
- Post-procedure Instruction sheet given prior to departure.
- In the event a mass, polyp, or ulceration is found, a copy of the images obtained during the sigmoidoscopy and a letter with the examination findings will be given to the participant and they will be instructed to follow-up with their Primary Healthcare Provider.

Lab Procedures

Sample processing and analysis.

A total of 20 biopsies will be obtained per participant: 4 will be used for tissue immunostaining and remaining 16 will be used for single nuclei sequencing. Tissue obtained from each region will be separated: four biopsies will be pinned and fixed in 4% paraformaldehyde overnight, followed by washing, permeabilization, and staining of the tissue with the neuronal antibody ANNA-1 and anti-Sox10 which is a glia antibody. We will image the samples with a confocal microscope, and we will count the neurons and glia. Sixteen biopsies will be snap frozen in liquid nitrogen and stored in a -80C freezer. Once several samples have been collected, we will defrost them and further process them into single nuclei suspensions that will be utilized to generate sequencing libraries with the 10X Chromium platform. We will sequence the nuclear RNA to determine the expression of multiple genes in the human intestine. Of note, we do not know what the nuclei yield will be for the pooled 16 biopsies obtained per participant, our target nuclei count will be about 20,000 in total. We will enrich the desired populations by staining the nuclei with anti-NeuN and anti-Sox10 to sort the neurons and glia populations respectively. We do not know what will be the proportions of the different cell types for this particular protocol, however, based on other studies we expect small proportion of glia and neurons thus making it necessary to pool samples from several participants. We will not sequence the human DNA.

We will isolate bacterial DNA from the stool and perform 16S ribosomal RNA sequencing for which we have an optimized protocol in our lab. Moreover. we will identify and measure stool metabolites via Liquid Chromatography- Mass Spectrometry at RU Proteomics Core.

NOTE:

This study will follow the NYSDOH guidelines regarding COVID-19 testing throughout the course of the study. Any participant that reports experiencing COVID symptoms and has a positive SARS-Cov-2 PCR test will not be able to undergo the flexible sigmoidoscopy procedures until 5 days after symptom onset provided that symptoms are resolved. For example, if a participant develops COVID while taking antibiotics, he/she will have to wait until symptom resolution to undergo follow up flexible sigmoidoscopy.

We will also follow RU COVID-19 clinic policies.

Study is closed to enrollment as of May 24, 2024.

12.10 * Data Analysis

Describe method(s) of data analysis.

In this pilot study, with 10 iparticipants, we will assess the change in the outcomes between baseline and follow up using a paired sample t-test. While exploratory, we will be able to detect a 1.3 standard deviation change in outcomes pre versus post, with greater than 80% power, holding Type I Error to 5%.

12.11 * Explain the rationale for the choice of statistical measures and the number of participants proposed for the study, including the power calculations when applicable.

Assuming we can enroll 10 patients, we will have over 80% power to detect a 1.3 standard deviation difference in continuous outcome measures and a 38% absolute difference in proportions (assume base rate of 50%). This pilot study will also provide observed effect size for use in the design of future analysis.

12.12 * Will samples be coded?

(•) Yes ( ) No

If Yes, Please describe coding scheme consistent with GCP. If samples will not be coded, please provide justification for this proposed departure from GCP practice.

Samples from participants seen at RUH will be coded with the alphanumeric IRB approval followed by
P (denotes participant), and then a consecutive number starting with 001.

For example: YAL-10xx-P-001, YAL-10xx-P-002, YAL-10xx-P-003, etc.

If available, upload the Data and Sample Sharing Management Plan approved by RU IT.

Version	Title	Category	Expiration Date	Document Outcome	View Document

No Document(s) have been attached to this form.

13.0 Participants of Study

13.1 Specify age range of participants:

* Minimum Age:

18

* Maximum Age:

75

Please note: If the age of participants indicated is less than 18 years old, you will be prompted to attach a Pediatric Assent form later on in the submission process. A link to the Pediatric Assent form can be found in the Help link to the right, or this form can be downloaded later on in the submission process.

13.2 * Indicate the gender(s) of the participants:

- [x] Female
- [x] Male
- [x] Unknown
- [x] Not Reported

13.3 * Indicate projected enrollment by race and ethnicity. See Help for disease/volunteer population demographics.

Ethnic Category	Sex/Gender			
	Females	Males	Unknown or Not Reported	Total
Hispanic or Latino	4	2	0	6
Not Hispanic or Latino	3	1	0	4
Unknown (individuals not reporting ethnicity)	0	0	0	0
Ethnic Category: Total of All Subjects*	7	3	0	10
Racial Categories				
American Indian/Alaska Native	0	0	0	0
Asian	2	1	0	3
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	2	1	0	3
White	3	1	0	4
More Than One Race	0	0	0	0
Unknown or Not Reported	0	0	0	0
Racial Categories: Total of All Subjects*	7	3	0	10

13.4 Exclusion of Protected Groups:

***Research involving human participants should be designed/conducted to be as broadly inclusive as possible regarding sex, gender, race, age, and ethnicity. Exclusions regarding**

these characteristics require an explanation of the rationale and justification.

Will participants of a specific sex/gender/race/ethnicity/age or other protected group characteristic be excluded from participation?

○ Yes ◉ No

13.5 Vulnerable Populations

Indicate whether any of the following populations will be included in the study:

- ☐ Children
- ☐ Pregnant Women
- ☐ Cognitively Impaired Persons
- ☐ RU Employees
- ☐ RU Students
- ☐ Other:

13.6 *What is the total number of evaluable participants you plan to enroll at Rockefeller University Hospital over the course of the entire study?

10

13.7 * What is the total number of participants who will need to sign consent *at Rockefeller University Hospital over the course of the entire study* to result in the desired number of evaluable participants?

20

13.8 * What is the total number of participants you plan to sign consent *at Rockefeller University Hospital in the next year?*

0

13.9 * What will be the total number of evaluable participants *at all sites over the course of the entire study?*

10

13.10 Inclusion Criteria

Please list participant inclusion criteria:

Order Number	Criteria
1	18-75 years old of different sex and races.

13.11 Exclusion Criteria

Please list participant exclusion criteria:

Order Number	Criteria

1	Rockefeller University Students and Employees
2	Allergy to penicillin, amoxicillin, augmentin, ampicillin, and other antibiotics in the penicillin family
3	Pregnancy or fertility treatments
4	Usage of antibiotics, antifungals or antivirals within three months prior to participation
5	Change in dietary habits within the last three months prior to participation such as transitioning from high fat western diet to primarily plant based diet, initiation of ketogenic, paleo or any other weight loss regimen.
6	Acute (in the past 30 days) or chronic enteric infections, including C. difficile.
7	Chronic gastrointestinal disorder including inflammatory bowel disease, celiac disease , irritable bowel syndrome, chronic constipation or diarrhea
8	Active neuropsychiatric disorder that requires anti-psychotic ie typical and atypical antipsychotics as well as anti-epileptics, levodopa, rivastigmine or any other neuropsychiatric medication with dopaminergic and cholinergic effects.
9	Myocardial infarction or cerebrovascular accident in the six months prior to participation
10	Coagulation disorders
11	Chronic immunosuppressive medication (systemic) usage
12	Anti-coagulation and anti-platelet agents such as plavix, warfarin, heparin, direct oral anticoagulants. Low dose Aspirin does not constitute an exclusion criteria.
13	Prior episode of C. difficile infection.
14	Prosthetic heart valves or any other conditions that require pre-procedure antibiotics.
15	Currently receiving chemotherapy
16	Any medical, psychological or social condition, in the opinion of the investigator, would jeopardize the health or well-being of the participant, interfere with their participation in the study, or confound the results of the study.

14.0 Schedule of Events/Study Plan

14.1

Instructions:<u>New Studies:</u>

- **A Schedule of Events is required for all new studies involving interactions with human subjects.**
- **The iRIS Study Plan will not be accepted for new protocols.**
- **A template Schedule of Events is available on the IRB Website. For any new study, populate the template with the visits and procedures for the study.**
- **The content of the Schedule of Events should be consistent with any descriptions of study procedures that may be in the protocol text and informed consent.**
- **Attach the completed Schedule of Events document to the Submission Form in the Schedule of Events section.**

Existing Studies: For existing studies, investigators may elect to update the existing Study Plan OR may replace the Study Plan with a Schedule of Events, following the instructions above for new studies.

Attach the Study Plan (an option only for studies with pre-existing Study Plans):

No Study Plan Templates have been associated.

*** What is the total number of outpatient visits for all participants projected for the next year?**

0

*** What is the average length of each outpatient visit (in hours)?**

0

*** What is the total number of Day Patient visits for all participants projected for the next year?**

0

*** What is the average length of each Day Patient visit (in hours)?**

0

*** What is the total number of inpatient days for all participants projected for the next year?**

0

15.0 Investigational and Support Medications

15.1 List all the investigational medications

See Help for link to Rockefeller University Research Pharmacy web page for additional information.

View Details	Drug Name		FDA Approved	IND Number
	Trade Drug Name:	Amoxil		
⊟	**Generic Drug Name:**	Amoxicillin	Yes	
	Investigational Drug Name:			

Trade Drug Name:	Amoxil
Generic Drug Name:	Amoxicillin
Investigational Drug Name:	

Identify the name of the manufacturer or source of investigational drug/biologic:	USAntibiotics
Is the Drug FDA Approved:	Yes
Is an IND necessary	No
IND Number	
Who holds the IND:	N/A
IND details:	
Are you currently using this IND in another research project?	No
If yes, list the IRB Number(s):	
Dose Range:	875mg
Frequency:	Twice a day

Trade Drug Name: Valium

⊟ **Generic Drug Name:** Diazepam Yes

Investigational Drug Name:

Trade Drug Name:	Valium
Generic Drug Name:	Diazepam
Investigational Drug Name:	
Identify the name of the manufacturer or source of investigational drug/biologic:	Pfizer
Is the Drug FDA Approved:	Yes
Is an IND necessary	No
IND Number	
Who holds the IND:	N/A
IND details:	
Are you currently using this IND in another research project?	No
If yes, list the IRB Number(s):	
Dose Range:	
Frequency:	

15.2 * **Will the study involve the use of a placebo?**

○ Yes ◉ No

15.3 Study support medications are medications that will support the conduct of the study. Please list all support medications to be used in the study (include all prescription drugs, over the counter drugs herbs, and supplements).

Amoxicillin 875mg q12 hours PO
Diazepam 5mg once pre-procedure.
Fleet Enema

16.0 Consent Procedure

16.1 * **This study will use the following types of informed consent:**

- [ ] Informed Consent Form Standard - a standard consent form with instructions for adapting it to your study
- [ ] Consent Form Genetic- a consent form designed for a study where genetic testing (as defined by NYS law) is to be done in the CURRENT study
- [x] Consent for studies including genome wide sequencing
- [ ] Pediatric Assent Form (To be used in addition to Consent) for Pediatric patients
- [ ] Other (e.g., waivers, electronic informed consent)

Links to the **Standard Consent, Genetic Testing Consent** and the **Pediatric Assent** forms can be found in the Help link to the right, or these forms can be downloaded later on in the submission process.

16.2 * **Indicate the consent process to be used. (See Help for CCTS SOP)**

Describe how the required information is being presented to participants (consent form, orally, information sheet, etc.). Attach a copy of what is being presented to participants (usually the ICF and Assent forms).

Prior to the initiation of any study related procedures, the potential subjects will be given a copy of the most recent IRB stamped and approved informed consent to read. Additionally, the PI or study staff member who has been designated to consent will discuss the specifics of the study including but not limited to the purpose of the research, procedures, time commitment, required tasks, test article or device, alternative treatments, benefits, risks, confidentiality etc. in a comprehensible (non-scientific) manner, using language readily understandable by the subject. Subjects will be told that participation is voluntary and that, if they do not consent, they will not be penalized. The person consenting will assure the voluntariness of the subject.

Describe the circumstances under which consent will be obtained, where the process will take place and any waiting period between informing the prospective participant and obtaining consent.

A private, confidential setting will be provided for the potential subject to read and discuss the informed consent free from coercion, undue influence or constraints of time. All subjects will be given a chance to ask questions and express concerns. They will be given the option to take the consent home and discuss it with family, friends, and /or health care providers. After a subject and the person conducting the consenting signs and dates the consent, the subject will be given a copy of the signed informed consent form. An enrollment note will be written in the source document as to who obtained consent, how, when, were questions asked and answered, and that a copy of the informed consent was given to the subject.

Describe the experience of the investigators designated for this task in the DOA in obtaining consent from participants.

Y. Alvarez has demonstrated competency in consenting subjects for participation in research studies. This competency is based on attending a consenting class which includes regulations, the do’s and don’ts, and didactic role-playing. It also includes observing the consenting process as performed by an experienced consenter and then consenting a participant to participate in a research study while being observed by the experienced consenter.

How will it be determined that the participants or the participants' authorized representatives understand the information presented?

The "Teach Back" method will be used in the clinical research setting to ask research participants to repeat or “teach back” the information, concepts and directions that the staff member has attempted to convey to the subject. This method is used to assess comprehension and retention of protocol requirements, adverse event information, risks and benefits, and the subject's rights described in the Informed Consent process.

If English is not the participants' native language, how will written and/or verbal translation be provided?

For unexpected or isolated subjects who are candidates for this study, but for whom English is not a primary language, a translator provided through Pacific Interpreters will be used to facilitate the explanation of the study.

Will any participants be cognitively impaired so that they may not have the capacity to give consent?

○ Yes ◉ No

For participants where it has been determined that they lack the capacity to give consent, describe the provisions for obtaining consent from the participants' legally authorized representative.

16.3 * Based on the demographics, will this study's participant population require foreign language consent form?

◉ Yes ○ No

If Yes, please list the language(s):

Spanish

16.4 * This study's consent procedure will require the following waivers: (See Help for additional information.)

○ Waiver of one or more elements of informed consent, 45 CFR 46.116(f)
○ Waiver of documentation of informed consent, 45 CFR 46.117(c)
◉ No waiver is requested

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

◉ Yes ○ No

☑ A CoC will be provided automatically as part of its funding mechanism with NIH
☐ The PI will apply independently to NIH for a CoC

Note to Investigator: If this study has a CoC, the Informed Consent document must contain CoC template language

16.6 * Does this study include video/audio recording, photography or other electronic recording of human participants?

○ Yes ◉ No

17.0 Recruitment and Advertising

For assistance consult CRSO to create a robust Recruitment Plan see Help.

17.1 * What is the plan for recruitment?

What is the plan for recruitment?

Overview: The CRROSS seeks to prescreen 25 healthy volunteers between the ages of 18-75 to achieve the overall goal of 15 evaluable participants.

Feasibility and Assessment:

Incentives:1) Altruism; 2) Interest in study topic 3) Compensation 4; 3) Return of (aggregate) results may be an incentive.

Challenges: 1) Overall impact of the Covid-19 pandemic may dissuade individuals from voluntarily participating in research studies; 2) Number of study visits and multiple flexible sigmoidoscopy procedures may be a deterrent.

Issues relevant to rapid accrual:

Positive: 1) Existing cohort of healthy volunteers in the repository*; 2)*Compensation amount.

Negative: 1) Candidates may not be interested due to perceived discomfort and burden of sigmoidoscopy preparation the day before the procedure, and/or embarrassment about the procedure; 2) Participants may not adhere to antibiotic treatment due to side effects 2) Potential for post procedure bleeding may dissuade some candidates from participating.

Projected Time to Accrual Completion (PTAC):

The research team plans to screen up to 1 *day per week* which translates to enrolling 2 volunteers a week.

Factors Affecting Predicted Time to Accrual Completion	Weeks
Research team plans to screen 2 participants 1 day per week = 2 volunteers screened per week (10 pax Add 2 weeks for overlap with current study, YAL-1027	11
Anticipated start up, add 1 2 weeks; *if assay not ready, add estimated time to readiness*	1
Add any vacation time when screen/visit capacity will be reduced	1
Recruitment is to occur during August? *add 2 weeks due to historical slowing*	N/A
Recruitment to occur across Dec Jan. time frame; *add 2 wks for unit closure*	N/A
Known anticipated maternity leave, other LOA of key staff – *add est. weeks lost capacity*	N/A
Staff or KSP changes – *add onboarding time*	N/A
Staff travel for major conferences – *add weeks lost capacity*	N/A
Institutional interruptions (graduation, symposium days, etc.) *add team estimate*	N/A
Projected Time to Accrual Completion (PTAC)	13

Recruitment Implementation:

Advertising- CRROSS will advertise on RU Classifieds, Craigslist and ResearchMatch. Volunteers will also be drawn from the Clinical Conductor Repository. If applicable, eligible participants from YAL-1027 may also be considered for this study.

Centralized Call Management – CRROSS will work with the research team to develop a protocol-specific pre-screening script based on IRB approved protocol eligibility criteria to prescreen volunteers who call 1800RUCARES. Potentially eligible candidates will be scheduled for the study team for further screening. CRROSS staff will also call volunteers based on Repository queries described above. Research teams are responsible to provide

timely updates on pre/screening outcomes by updating volunteers' Study Status in Cerner. The Recruitment team uses screening outcomes to review progress and strategy to keep enrollment on target.

17.2 *From the date of final IRB approval, how long will it take to complete enrollment of the study?

- ○ 6 Months
- ◉ 12 Months
- ○ 18 Months
- ○ 24 Months
- ○ More than 2 years (specify in years)

17.3 This Study

- ◉ Involves an intervention or comparison and a defined enrollment target
- ○ Is a natural history study with expected annual enrollment over many years
- ○ Is an exploratory mechanistic study
- ○ Other

17.4 This Study will enroll:

- ◉ Healthy volunteers
- ○ Individuals affected with a specific disease/disorder
- ○ Both

17.5 * Do you plan on using the Research Participant Repository (RKO-0648) ?

◉ Yes ○ No

17.6 * Are you screening or recruiting from or through a record review of an existing patient database of a healthcare provider?

○ Yes ◉ No

17.7 * Please describe how the Recruitment Plan addresses recruitment of the volunteers consistent with the demographics of the condition under study:

Both healthy men and women of all races between the ages of 18-75 years of age will be recruited.

17.8 * Do you plan to advertise directly to potential volunteers? (As opposed to relying on practitioner referrals or flyers to practitioners)

◉ Yes ○ No

17.9 * **Do you plan to use the free, web-based volunteer registry, ResearchMatch.org, as a recruitment tool?**

(•) Yes ( ) No

18.0 Research Participant Repository (RKO-0648)

18.1 This protocol, will be linked with the Research Volunteer Screening/Recruitment Data Repository run by the Recruitment staff and the Clinical Research Support Office (protocol RKO-0648-1008). In order to participate in the generation of the Repository the PI will enter into a Collector/Collaborator agreement regarding the Repository. The role of Collector/Collaborator is to contribute to the Repository the name, contact and demographic information, recruitment referral information, and screening outcome information, as well as appropriate protocol specific screening information, of volunteers who are screened by telephone or in person for entry into the protocol regardless of the screening outcome. In addition to screening volunteers for the PI's current study, verbal consent will be obtained from the volunteers regarding their willingness to be contacted in the future about possible additional research studies. This permission may be obtained by the Recruitment office staff through the central Call Center. If the PI receives calls directly from participants for initial prescreening, then the PI is responsible for collecting the required information and conveying it to the Recruitment staff for data entry. The consent or withholding of permission will be recorded in the Repository as will the name of the person who obtained the permission. A volunteer's permission or declination will not affect their eligibility for my current protocol, or future protocols. The Recruitment staff of the Clinical Research Support Office may gather the Repository information and request the verbal consent of the volunteer for re-contacting on my behalf as part of our recruitment plan. In order to benefit from the Repository, the PI will enter into a Recipient/Collaborator agreement with the Repository. The Recipient/Collaborator may receive from the Repository pre-screened lists of potentially eligible participants for his/her study as a means to facilitate recruitment. The Recruitment staff will prepare the Repository queries according to the protocol eligibility requirements and available Repository information, and may re-affirm permission to re-contact volunteers as necessary. The PI may use the information and names in the list from the Repository only for the current study and may not save the list to use for a future study of his/her own, nor may he/she share the list with colleagues for other studies."

19.0 Utilization of ResearchMatch.org

19.1 Utilization of ResearchMatch.org for Recruitment

Basic information regarding this tool:

- **ResearchMatch.org is a national electronic, web-based recruitment tool that was created through the Clinical & Translational Science Awards Consortium in 2009 and is maintained at Vanderbilt University. There is no cost for researchers at participating institutions in the ResearchMatch.org Network to use ResearchMatch.org. The Vanderbilt IRB provides oversight for ResearchMatch.org as a recruitment tool and this has been documented within the ResearchMatch.org IRB Letter of Understanding which was executed by Dr. Gotschlich in October, 2009. However, individual requests to use ResearchMatch.org as a recruitment tool must be submitted to this institutions' IRB.**

Registration:

- **This recruitment tool may be utilized once the PI or research staff registers for recruitment access through ResearchMatch.org and the Institutional Liaison provides approval.**
- **The ResearchMatch.org Institutional Liaison will review the study information and evidence of IRB approval. He/she will set the researcher's expiration date to mirror that of the study's IRB approval.**

Search Capability:

- **After being granted recruitment access, the researcher can search for appropriate matches amongst the non-identifiable ResearchMatch.org Volunteer profiles in the system. He/she can enter study inclusion/exclusion criteria in the ResearchMatch.org Search Builder which will yield a list of potential matches to the study's criteria.**

Contacting ResearchMatch.org Volunteers:

- **Once yielding a list of potential matches (ResearchMatch.org Volunteers), the researcher will send out IRB-approved content that will be the initial recruitment message that these volunteers receive about the study through ResearchMatch.org. The study's recruitment message will be inserted into the standard ResearchMatch.org electronic notification that informs possible matched Volunteers that he/she has been identified as a potential match for the study. The secure ResearchMatch.org clearinghouse will route this standard ResearchMatch.org email notification. These potential matching volunteers will have the option of replying yes, no, or not respond through a set of quick links available in this notification to the study announcement. THE CONTACT MESSAGE WILL NOT INCLUDE THE STUDY'S DIRECT CONTACT INFORMATION (e.g. EMAIL, PHONE). By responding yes, the Volunteer has authorized ResearchMatch.org to release his/her contact information to the researcher. The researcher will be responsible for managing this contact information as called for by this IRB-approved study protocol.**

Study Management in ResearchMatch.org:

- **Researchers (and the Liaison) can view information regarding his/her study's status in ResearchMatch.org (e.g. number of volunteers contacted for the study via ResearchMatch.org to date, response rate of volunteers, etc.). ResearchMatch.org will also be collecting aggregate data regarding the status of ResearchMatch.org volunteers within the study. Volunteers consent to this within the ResearchMatch.org Volunteer Agreement. This information will allow the researcher to indicate where the Volunteer currently stands within the recruitment process and thus will help the researcher monitor the utility and effectiveness of using this resource (e.g. Did not contact, Not eligible, Enrolled, Completed, etc.).**

20.0 Potential Benefits to Participants

20.1 * **Will participation in this study provide direct benefits to the participant?**

○ Yes ◉ No

21.0 Potential Risks to Participants

21.1 * **Describe any potential risks: physical, psychological, social, legal or other and assess their likelihood and seriousness. Indicate risks both to the participants and to the embryo or fetus if the participant is or may become pregnant. Please provide the potential risks below:**

Blood draw: Potential risks associated with venipuncture include discomfort or pain, ecchymosis, bleeding, nerve damage, phlebitis and infection at the needle insertion site. Additional risks include lightheadedness and a vasovagal response.

Diazepam: Potential risks associated with allergic reaction, drowsiness, loss of coordination, drug/drug interactions with other common medications (antidepressants, other anxiolytics), and alcohol.

Amoxicillin: Potential risk associated with mild to severe allergic reaction, anaphylaxis or hives, nausea, vomiting, and diarrhea (2%). Change in bowel habits and abdominal pain <1%. Vulvovaginal infection (2%). If participant develops vulvovaginal infection she will be given fluconazole course and advised to follow up with gynecology. Participant will not be able to complete last flexible sigmoidoscopy and will be given partial compensation. Antibiotic resistance (negligible). This will not be determined until participant requires another course of amoxicillin and even if he/she develop antibiotic resistance, it will be difficult to know if it was due to the antibiotic course during our study or due to pre-existing antibiotic resistance.

Flexible sigmoidoscopy: Potential risks include intestinal perforation, infection, and bleeding at the biopsy sites.

Privacy Risk: Potential loss of privacy if there is a breach of the RU hospital computer system.

Gene expression: Potentially the participant's identity can be unveiled.

22.0 Procedures to Minimize Risks

22.1 * Describe the procedures for protecting against or minimizing any potential risks, and include an assessment of their likely effectiveness. Include a discussion of confidentiality safeguards, where relevant, and arrangements for providing medical treatment, if needed.

The sigmoidoscopy will be performed by an experienced, trained, and credentialed physician.

In the event of a perforation, the participant will be stabilized (placed on a stretcher, the emergency medical response system will be activated, support therapies such as intravenous hydration and oxygen will be provided as needed, vital signs monitored), and the participant will be transferred to the Weill Cornell Emergency Room for further management. The participant's Primary Care Provider will be notified of any change in the participant's medical condition.

Blood draws will be performed by trained professionals using sterile equipment.

Participants will be asked about their medication allergies, current medications and substance use history prior to administering diazepam and amoxicillin.

Participants will be observed for 30-60min after procedure and advised to avoid operating a vehicle and/or heavy machinery for the rest of the day.

Participants who cannot tolerate taking the antibiotic will be assessed by Dr. Alvarez and may be removed from the study. If required, a referral to a primary care physician or clinic will be made.

To minimize the risk of *C.difficile* we have selected a short antibiotic course and we will exclude participants currently receiving chemotherapy or are taking immunosuppressive medications.

If any participant develops C.difficile infection and/or vulvovaginal infection, treatment will be prescribed by Dr. Alvarez and participant will be asked to follow up with Primary Care provider.

Participants personal information will be maintained in password protected electronic medical records protected in Rockefeller's network. Access of patient data from remote computer will only be done while in Rockefeller University's VPN.

23.0 Alternative Methods or Treatments

23.1 * **Describe alternative methods or treatments for the disease(s) under study, if any, that were considered and why they will not be used:**

There are no alternative methods or treatments that will allow the investigator to conduct the study.

24.0 Data and Safety Monitoring

This section describes the Data and Safety Monitoring Plan (DSMP) required of each protocol undertaken at the CCTS according to HRPP and NIH policies Notice 98 -084 and Notice 00-038, as cited in Help Sections below. Depending on the level or risk and trial phase, some protocols will need Data and Safety Monitoring Boards.

24.1 * **Overall Risk Classification**

An estimate of risk is necessary to evaluate the adequacy of the planned monitoring. The HELP section provides guidance in making the risk assessment.

Read the risk definitions and examples of risk in the HELP section and select the risk category that best describes the current study.

If your assessment differs from the definitions the HELP section, describe any factors that modify your judgment of the overall risk in the text box after the risk designation.

- ○ MINIMAL RISK
- ○ LOW RISK
- ◉ MODERATE RISK
- ○ SIGNIFICANT RISK

Please provide any optional description(s):

24.2 Protocols Involving Minors

The chance of direct benefit to the child, or to understanding a disorder not otherwise understood, may be major factors in justifying more than minimal risk in research involving children.

Based on the above definitions, please specify your study's risk classification below:

- ○ NOT GREATER THAN MINIMAL RISK (the risk of daily life to a healthy child living in a safe environment) 45 CFR 46.404
- ○ GREATER THAN MINIMAL RISK WITH DIRECT BENEFIT TO PARTICIPANT; 45 CFR 46.405
- ○ GREATER THAN MINIMAL RISK, NO DIRECT BENEFIT, BUT BENEFIT TO UNDERSTANDING OF PARTICPANT'S DISORDER; 45 CFR 46.406
- ○ RESEARCH NOT OTHERWISE APPROVED PRESENTING OPPORTUNITY TO UNDERSTAND, PREVENT OR ALLEVIATE SERIOUS PROBLEM AFFECTING CHILDREN 45 CFR 46.407 (cannot be approved by IRB; requires public comment)

24.3 DSMB

1. The NIH requires that all SIGNIFICANT RISK protocols have a **Data and Safety Monitoring Board** and provide information about the expertise and independence of that Board
2. Phase III trials require a Data and Safety Monitoring Board,
3. A DSMB may be appropriate for some Phase I and II protocols. (See Help for examples.)
4. It is the investigator's responsibility to report to the IRB, the findings and recommendations of the DSMB as they become available.

Please specify:

- ○ A DSMB is required for this study
- ◉ A DSMB is not required for this study
- ○ Unsure

If a DSMB is not required, but is being constituted for other reasons, please explain:

24.4 * **Safety Review**

Select one:

- ◉ Safety Review is conducted as follows: Laboratory results for research volunteers will be reviewed in a timely manner, usually within 24 hours of receipt by a licensed practitioner. The potential clinical significance of any abnormal finding will be documented in the medical and research record(s), and an appropriate plan or referral developed. The PI's review of safety issues at research team rounds will be documented in the meeting minutes.
- ○ Protocol Specific

24.5 Monitoring

Monitoring Personnel: See Help Bubble to the right.

Internal Monitoring

The PI or his/her designee shall conduct internal monitoring to assure the safe and proper conduct of the protocol and all the elements list above in monitoring, following the general principles of quality management. The intensity and frequency of internal monitoring will depend on the protocol risk to participants, the experience of the PI and research team, rate of enrollment, and specific details of the protocol.

Internal monitoring of informed consent and eligibility documentation will be conducted by the research team shortly after enrollment begins. Internal monitoring activities will be documented by logs, meeting minutes or other systematic means.

Specify the research team members who will conduct the internal monitoring of the study (see Help for who may monitor):

Internal Monitoring

The PI or his/her designee shall conduct internal monitoring to assure the safe and proper conduct of the protocol and all the elements list above in monitoring, following the general principles of quality management. The intensity and frequency of internal monitoring will

depend on the protocol risk to participants, the experience of the PI and research team, rate of enrollment, and specific details of the protocol.

Internal monitoring of informed consent and eligibility documentation will be conducted by the PI shortly after enrollment begins. Internal monitoring activities will be documented by logs, meeting minutes or other systematic means.

Specify the research team members who will conduct the internal monitoring of the study (see Help for who may monitor):

The PI will be shown how to perform internal monitoring.

For new investigators: Internal monitoring should be conducted at least monthly by new investigators until there are essentially no findings to correct at each review.

External Monitoring

* Is external monitoring planned for this protocol?

- ○ Yes
- ◉ No
- ○ Unsure

If external monitoring is planned, please specify (see Help for who may monitor):

- ○ (Significant Risk) External monitoring will occur at least every six weeks unless there is no enrollment
- ○ (Moderate Risk) External monitoring will occur at least quarterly
- ○ (Low or Minimal Risk) External monitoring will occur at least annually

If external monitoring is planned, please specify the name of the monitor:

- ☐ Note that copies of external monitoring reports must be supplied to the IRB and the CRSO as soon as they are made available

Additionally, audits of the research records of minimal, moderate or significant-risk protocols may be performed by the CRSO staff on a random basis or as part of a prospectively identified auditing plan.

24.6 Adverse Event Classification

Adverse events are classified by definition, severity, and association with the investigational trial.

Definition of an Adverse Event
Any unfavorable or unintended sign (including abnormal lab findings), symptom or disease temporally associated with the use of a medical treatment or procedure, or protocol, regardless of whether it is considered related to the medical treatment or procedure or protocol.

Definition of a Serious Adverse Event
Any unanticipated event that involves the following:
- o results in death
- o is life-threatening
- o requires hospitalization or prolongs existing hospitalization
- o results in persistent or significant disability/incapacity
- o is any medical event which requires treatment to prevent one of the outcomes listed above

Other events can be classified as "serious adverse events" at the discretion of the PI.

Definition of Anticipated/Expected Adverse Event

Any adverse event, which has been reported in the Investigator's Brochure, package insert, safety reports, clinical protocol, consent form or listed in the NCI agent-specific Expected Adverse Event List[3], is classified as an expected adverse event. The investigator must provide the available data of known adverse events and toxicities that have been associated with the study drug, device, intervention, or procedures. This information helps to define the level of risk of the trial and enables safety monitoring. A minimal risk trial may not have any defined risks and a statement to that effect is sufficient to meet the DSMP requirements.

Definition of an Unanticipated/Unexpected Adverse Event
Any adverse event that is not consistent with the known, predicted possible effects of the research protocol. An unexpected adverse event varies in nature, intensity or frequency from information on the investigational product provided in the Investigator's Brochure, package insert, safety reports, clinical protocol, or listed in the consent form.

Definition of an Unanticipated Problem (UaP)
A UaP is an event or circumstance that meets all the following three criteria: [1] the nature, severity, frequency of the event(s) or information was not expected in the descriptions in the study documents or the characteristics of the participant population being studied; [2] there is a reasonable possibility that the procedures involved in the research caused or are linked in a significant way to the problem; [3]the event or information suggests that the research places particpants or others at a greater risk of harm than was previously known or recognized (including physical, psychological, economic, or social harm.

Grade and Relatedness of Adverse Events:

Adverse Events are graded for severity and scored for relatedness to the protocol, according to a published scale. Several standardized AE Reporting scales are available. (See Help for links to these scales.)

* Please indicate the scale you intend to use:

- ○ CTC v2.0 (http://ctep.info.nih.gov/reporting/ctc.html)
- ○ CTCAE v3.0 (http://ctep.info.nih.gov/protocolDevelopment/electronic_applications/docs/ctcaev3.pdf)
- ○ CTCAE v4.0 (http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf)
- ◉ CTCAE v5.0 (https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf)
- ○ AIDS Clinical Trials Group (http://aactg.s-3.com/)
- ○ Other

24.7 Reporting Adverse Events

All AEs will be reported to the IRB at least annually.

Reporting Serious AEs

☑ Serious Adverse Events, (SAEs) will be reported to the IRB according to policy, within two working days of identification of the SAE.

Select all that apply:

☐ SAEs will be reported to the Sponsor and or ESCROW

SAEs will be reported to the sponsor within how many days of the event?

☐ SAEs will be reported directly to the FDA, per 21 CFR 312

SAEs must be reported directly to the FDA within 7 days of the event by the investigator/sponsor.

☐ SAEs will be reported to another entity

Describe:

Reporting Unanticipated AEs:

Select all that apply:

☑ UAEs will be reported to the IRB

UAEs that are related and greater than moderate severity must be reported to the IRB according to policy, within two working days of identification of the UAE.

☐ UAEs will be reported to the Sponsor

UAE will be reported to the sponsor within how many days of the event?

☐ UAEs will be reported to the FDA, per 21 CRF 312

UAEs will be reported to the FDA, per 21 CRF 312, within 15 days.

☐ UAEs will be reported to another entity

Describe:

24.8 Reporting Unanticipated Problems

☑ Unanticipated problems involving risks to participants or others will be reported to the IRB and the CRSO within five working days.

24.9 CLIA/CLEP

Only laboratory and research tests that are CLIA/CLEP certified or waived may be used to determine eligibility, shared with research volunteers, and used in clinical decision making.

Select if applicable:

☐ This study includes tests that are not CLIA/CLEP certified; the results of such tests will not be used in clinical decision making, or to determine eligibility, or shared with participants or their health care providers.

24.10 Tissue Repository

Human Tissue and Data Repositories collect, store, and distribute human tissue materials and or data for research purposes. Repository activities involve three components: (i) the collectors of tissue samples\data; (ii) the repository storage and data management center; and (iii) the recipient investigators.

* Select one:

- (●) I DO NOT intend to collect, store, and distribute human tissue materials for research purposes
- ( ) I DO intend to collect, store, and distribute human tissue materials for research purposes, therefore this protocol entails the Operation of a Tissue Repository. The IRB requires that the protocol specify the conditions under which data and specimens may be accepted and shared, and ensuring adequate provisions to protect the privacy of participants and maintain the confidentiality of data.

If you do intend to collect, store, and distribute human tissue materials, you will be asked to upload the following documents later on in the submission:

- A Sample collection protocol (for tissue collector collaborators to follow) and informed consent document for distribution to tissue collectors and their local IRBs.
- A Certificate of Confidentiality (to protect confidentiality of repository specimens and data).
- A Recipients Agreement describing the commitment of the recipient to preserve the anonymity of the samples shared.

25.0 Toxicity Management and Stopping Rules

25.1 * Describe any drug toxicity or other conditions under which the participation of a participant or the conduct of the study would be stopped in order to maximize safety (e.g., toxicity management and stopping rules):

If a participant develops an allergic reaction to diazepam, reaction will be immediately treated accordingly with severity of symptoms ie if patients develops rash he/she will be treated with Benadryl, if on the other hand patient develops anaphylactic shock, patient will be given epinephrine intramuscular injection and stabilized (placed on a stretcher, the emergency medical response system will be activated, other support therapies such as intravenous hydration and oxygen will be provided as needed, vital signs monitored), and the participant will be transferred to the Weill Cornell Emergency Room for further management. The participant's Primary Care Provider will be notified of any change in the participant's medical condition.

If patients develop allergic reaction to amoxicillin, he/she will also be instructed to cease the medication and call us and his/her PCP. He/she will be excluded from the study and advised to follow up with PMD.

If the participant cannot tolerate the fleet enema, he/she will be excluded. In addition, if he/she cannot tolerate the flexible sigmoidoscopy due to pain, he/she will be excluded.

If the participant has abnormal vital signs ie T>100.4, BP<80/50 or BP>140/90, HR<50 or HR>100 during any of the study visits, he/she will be excluded.

If a participant starts taking other antimicrobial medications he/she will be excluded from the study.

If a participant starts taking a medication that has adverse interactions with amoxicillin, he/she will be excluded from the study.

If a participant develops renal or liver disease that requires adjustment of amoxicillin dose, he/she will be excluded from the study.

*** Indicate withdrawal criteria and procedures below:**

If a participant cannot tolerate antibiotics he/she will receive partial compensation. If a participant cannot undergo flexible sigmoidoscopy due to discomfort he/she will receive

partial compensation. These participants will be excluded from the study. If a participant needs to take any other anti-microbial and/ or has an enteric infection while being in the study, he/she will be excluded. The PI will also determine whether other medical conditions developed during the study qualify as withdrawal criteria.

26.0 Compensation/Costs

26.1 *Will any compensation be offered to participants in return for their participation, e.g., direct payment, medical care, tests, etc.?

- ○ No
- ◉ Yes (Please describe)

Please Describe

Participants will receive $1100 for their participation and completion of the study.

- $300 for each completed sigmoidoscopy procedure
- $100 for completing a 7-day course of antibiotics

Participants will receive an additional $100 for completion of all study visit requirements.
If a participant only completes a portion of the study, they will receive partial compensation.

26.2 * Will there be any costs to participants associated with their participation in research?

- ○ Yes
- ◉ No

27.0 Bibliography

27.1 Enter your bibliography below:

1. Jacobson, A., et al., The intestinal neuro-immune axis: crosstalk between neurons, immune cells, andmicrobes. Mucosal Immunol, 2021. 14(3): p. 555-565.

2. Ye, L., et al., Enteroendocrine cells sense bacterial tryptophan catabolites to activate enteric and vagal neuronal pathways. Cell Host Microbe, 2021. 29(2): p. 179-196 e9.

3. Joly, A., F. Leulier, and F. De Vadder, Microbial Modulation of the Development and Physiology of the Enteric Nervous System. Trends Microbiol, 2021. 29(8): p. 686-699.

4. Heuckeroth, R.O., Hirschsprung disease - integrating basic science and clinical medicine to improve outcomes. Nat Rev Gastroenterol Hepatol, 2018. 15(3): p. 152-167.

5. Muller, P.A., et al., Microbiota-modulated CART(+) enteric neurons autonomously regulate blood glucose. Science, 2020. 370(6514): p. 314-321.

6. Neuvonen, M.I., et al., Intestinal Microbiota in Hirschsprung Disease. J Pediatr Gastroenterol Nutr, 2018. 67(5): p. 594-600.

7. Vicentini, F.A., et al., Intestinal microbiota shapes gut physiology and regulates enteric neurons and glia. Microbiome, 2021. 9(1): p. 210.

8. Kabouridis, P.S., et al., Microbiota controls the homeostasis of glial cells in the gut lamina propria. Neuron, 2015. 85(2): p. 289-95.

9. Vajravelu, R.K., et al., Risk for Post-Colonoscopy Irritable Bowel Syndrome in Patients With and Without Antibiotic Exposure: A Retrospective Cohort Study. Clin Gastroenterol Hepatol, 2021.

10. Furness, J.B., et al., Intrinsic primary afferent neurons and nerve circuits within the intestine. Prog Neurobiol, 2004. 72(2): p. 143-64.
11. Rao, M., et al., Enteric Glia Regulate Gastrointestinal Motility but Are Not Required for Maintenance of the Epithelium in Mice. Gastroenterology, 2017. 153(4): p. 1068-1081 e7.

12. Yarandi, S.S., et al., Intestinal Bacteria Maintain Adult Enteric Nervous System and Nitrergic Neurons via Toll-like Receptor 2-induced Neurogenesis in Mice. Gastroenterology, 2020. 159(1): p. 200-213 e8.

13. Obata, Y., et al., Neuronal programming by microbiota regulates intestinal physiology. Nature, 2020. 578(7794): p. 284-289.

14. Sperber, A.D., et al., Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study. Gastroenterology, 2021. 160(1): p. 99-114 e3.

15. Mars, R.A.T., et al., Longitudinal Multi-omics Reveals Subset-Specific Mechanisms Underlying Irritable Bowel Syndrome. Cell, 2020. 182(6): p. 1460-1473 e17.

16. Wouters, M.M., et al., Histamine Receptor H1-Mediated Sensitization of TRPV1 Mediates Visceral Hypersensitivity and Symptoms in Patients With Irritable Bowel Syndrome. Gastroenterology, 2016. 150(4): p. 875-87 e9.

17. Drokhlyansky, E., et al., The Human and Mouse Enteric Nervous System at Single-Cell Resolution. Cell, 2020. 182(6): p. 1606-1622 e23.

18. Dethlefsen, L., et al., The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing. PLoS Biol, 2008. 6(11): p. e280.

19. Jakobsson, H.E., et al., Short-term antibiotic treatment has differing long-term impacts on the human throat and gut microbiome. PLoS One, 2010. 5(3): p. e9836.

20. Ladirat, S.E., et al., Exploring the effects of galacto-oligosaccharides on the gut microbiota of healthy adults receiving amoxicillin treatment. Br J Nutr, 2014. 112(4): p. 536-46.

21. Suez, J., et al., Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT. Cell, 2018. 174(6): p. 1406-1423 e16

28.0 Appendices

28.1 Enter your appendices below:

None

29.0 Funding

29.1 * Do you have sufficient financial resources to support your study?

(•) Yes ( ) No

29.2 If this study is/was pilot funded, please specify dates of funding:

From date:

06/01/2022

To date:

12/31/2023

29.3 Source of investigational agents:

(•) N/A (no investigational agents)
( ) Provided by a pharmaceutical sponsor/partner with funding as described below
( ) Provided by a pharmaceutical sponsor/partner without additional funding
( ) Provided by investigator, participants, or other

29.4 Specify funding by Rockefeller University, industry sponsor and/or grant:

Search for a sponsor

	Sponsor	Funding
Rockefeller University	CTSA Pilot Grant	☐
Industry		
Grant		

Pilot Award		

29.5 List grants in which this study is named:

	PHS or Non-PHS	Program	Grant Number	Grant Name	From Date	To Date
No results found						

30.0 Clinical Services

30.1 *What is the general health status of your study group(s)?

- [x] Well/Minimally Ill
- [ ] Moderately Ill
- [ ] Severely Ill
- [ ] Other
- [ ] Not Applicable

If other than Well/Minimally Ill, please describe:

30.2 * Does your study group have special care needs?

( ) Yes (•) No

30.3 * Does your study have special equipment needs?

(•) Yes ( ) No

If Yes, please describe:

Sigmoidoscopy equipment.

30.4 * Will you require storage space on the clinical units for supplies to conduct this study?

( ) Yes (•) No

30.5 * Is special training of hospital staff required?

( ) Yes (•) No

31.0 Pharmacy Services

31.1 * Does the study require Pharmacy Services?

(•) Yes ( ) No

If Yes, please proceed to next section.

31.2 Types of pharmacy services required:

- [x] Dispensing
- [ ] Randomization
- [ ] Compounding
- [ ] Other

31.3 Dispensing:

- [ ] Sponsor supplied drugs
- [x] Pharmacy supplied drugs
- [ ] Other

31.4 Type of medication(s):

- [ ] Injectable
- [ ] Ophthalmic
- [ ] Inhalational
- [ ] Topical
- [ ] Suppository
- [x] Other

If Other, please specify:

Oral

32.0 Bionutrition

32.1 * Will study require patient meals?

(•) Yes ( ) No

If Yes, please specify:

Type of Diet	In/Outpatient	Pack Meal
Standard	[x] Inpatient [ ] Outpatient	(•) Pack Meal
Therapeutic	[ ] Inpatient [ ] Outpatient	( ) Pack Meal
Research Diet	[ ] Inpatient [ ] Outpatient	( ) Pack Meal
Formula Diet	[ ] Inpatient [ ] Outpatient	( ) Pack Meal

Nutrient(s) to be controlled (specify):

32.2 Will meal times be altered?

(•) Yes ( ) No

If Yes, please explain:

Participants have been asked to refrain from consuming any meals until the procedure is finalized.

32.3 Does the protocol require any of the following activities?

- [ ] Food Frequency Questionnaire
- [ ] Bod Pod/ Anthropometric Measurements
- [ ] Diet History/ Food Records
- [ ] Diet/ Nutrition Education

32.4 Will food be provided to caregiver, parent or significant other?

( ) Yes ( ) No

32.5 For metabolic diets, is diet homogenization required for nutrient analysis by independent lab?

( ) Yes
( ) No
( ) N/A

33.0 Clinical and Translational Research Facilitation Office

33.1 Indicate navigation assistance requested and/or received in the development of the study:

	Requested	Received
Protocol Development	☑	☑
Protocol Implementation	☑	☐
Protocol Conduct	☑	☐
ACCTS/IRB Submission	☑	☑

33.2 Indicate additional education assistance requested and/or received in the development of the study:

	Requested	Received

IND	☐	☐
IDE	☐	☐
Team Science Education	☐	☐
Study Progress Meeting	☑	☐
Investigator Responsibilities	☐	☐
Regulatory Binder/Folder	☑	☐
Source Documentation	☑	☐
Participant Involvement in Research	☐	☐

34.0 Clinical Research Support Office Resources (CRSO)

34.1 Indicate regulatory input assistance requested and/or received in the development of the study:

Regulatory Support/Design	Requested	Received
General, Vulnerable Populations, Minors, Group Harms	☐	☐
IND/IDE advice, assistance, and referral	☐	☐
Informed Consent/Assent	☐	☐
Data Safety Monitoring Plan	☐	☐
Clinical Trial Registration	☐	☐

Plan For Return of Research Results	☐	☐
Audit/Monitoring Service, Referrals, SOPs	☐	☐

34.2 Indicate recruitment assistance requested and/or received in the development of the study:

Recruitment of Participants	Requested	Received
Recruitment Planning and/or written Plan	☑	☑
Advertising Strategy, Content, Placement	☑	☑
Repository/Research Match Queries	☐	☐
Call Center/Prescreening/Scheduling	☐	☐
Cost Sharing for Advertising	☐	☐

34.3 Indicate community engaging assistance requested and/or received in the development of the study:

Community Engagement	Requested	Received
PHI Statement/Engaging Stakeholders Section	☐	☐
CEnR Navigation – fostering pt/community partnership	☐	☐
Outreach to community/partner/advocacy group/CE Studio	☐	☐

34.4 Indicate other assistance requested and/or received in the development of the study:

Other	Requested	Received

Survey design, fielding, validation	☐	☐
Data transfer and security planning	☐	☐

35.0

BERD: Biostatistics, Epidemiology and Research Design Resource

35.1 Indicate the Biostatistical assistance requested and/or received in the development of this study:

	Requested	Received
Development of experimental design	☑	☑
Power analysis/Sample size determination (# of subjects)	☑	☑
Navigation (Did Statistician participate in a navigation meeting)	☑	☑
Randomization schedule	☐	☐
Data analysis	☐	☐
Development of new statistical techniques for data analysis (Statistical research)	☐	☐
Protocol implementation	☐	☐
Other	☐	☐

35.2 If you are/will be using data analysis specify:

- [x] Exploratory
- [ ] Descriptive
- [ ] Hypothesis testing
- [ ] Statistical modeling
- [ ] Other

35.3 If you are/will be assisted with protocol implementation, specify:

- [ ] Publication
- [ ] Conference
- [ ] Other (type of dissemination)
- [ ] Grant(s)

35.4 Please select the Biostatistician on this Protocol:

- [x] Roger Vaughan, DrPH
- [ ] Caroline Jiang, MS
- [ ] Sandra Garcet, PhD
- [ ] Adam Qureshi, MA
- [ ] Other

36.0 Biomedical Informatics Resources

36.1 Indicate Bioinformatics assistance requested and/or received in the development of this study:

	Requested	Received
Microarray analysis	☐	☐
Pathway analysis	☐	☐
RNA-seq analysis	☐	☐
Bioinformatics training and consultation	☐	☐
Bioinformatics experimental design	☐	☐
HPC computing	☐	☐
Other	☐	☐

36.2 If you are/will be using pathway analysis software, specify:

- [ ] Ingenuity IPA
- [ ] David
- [ ] GSEA
- [ ] Other

36.3 If you are/will be using RNAseq analysis software, specify:

- [ ] Tophat
- [ ] Cufflinks
- [ ] Cuffdiff
- [ ] CummRbund
- [ ] STAR
- [ ] featureCounts
- [ ] DESeq2
- [ ] VOOM
- [ ] RNA-SeQC

If other, specify:

36.4 Indicate Medical Informatics assistance requested and/or received in the development of this study:

	Requested	Received
Data storage inside of iRIS	☐	☐
Redcap Database	☐	☐
Custom or Ad Hoc reports	☐	☐
Study plan creation	☐	☐
Specialize database or custom software	☐	☐
Other	☐	☐

37.0 HIPAA Form

37.1 A study's specific HIPAA form signed by the volunteer is required for institutions that are HIPAA covered entities so that they may communicate Private Health Information (PHI) to the Investigator.

Below, Memorial Sloan Kettering Cancer Center, New York-Presbyterian Hospital and Weill Medical College of Cornell University are listed so that that they may report laboratory results and X-ray readings respectively. If you foresee that any other entity may need to provide PHI then add them to the field highlighted in green.

37.2 Name of Study:

Effect of antibiotics on submucosal enteric neurons and glia in the lower gastrointestinal tract.

37.3 Principal Investigator:

Begum Aydin, PhD

37.4 Industry Sponsor:

If the funding source is industry please type in the sponsor here

Who may obtain, use, and/or disclose your health information?

The following persons and organizations may obtain, use, or disclose health information about you.

- The Principal Investigator(s) listed at the top of this form, and persons who assist the Investigator(s) in carrying out the research
- Each research site for this study, including The Rockefeller University, and the research management and support staff and the medical staff at each site
- Health care providers who have provided in the past, or currently provide, health care services to you
- Laboratories and other persons and organizations that will analyze your health information and/or biological samples as part of this study, including Memorial Sloan Kettering Cancer Center, New York-Presbyterian Hospital and Weill Medical College of Cornell University

Other entities that may need to provide PHI:

- Members and staff of the Institutional Review Board and other boards and committees that watch over research at The Rockefeller University
- Members and staff of The Rockefeller University's Office of Sponsored Research
- The sponsor(s) of the research, named above, and persons who watch over the research for the sponsor(s)
- The United States Food and Drug Administration, other government agencies, regulatory entities and Rockefeller University consultants that watch over the safety, effectiveness, and quality of research and/or fund The Rockefeller University Hospital
- Others (as described here):

What information will be obtained, used, or disclosed?

The persons and organizations listed above may obtain, use, and disclose:

- Information about you that is created or collected during the research study (but not including any HIV-related information)
- Health information in your medical records that is relevant to the research study (but not including any HIV-related information)
- **And**, if checked below:

___ HIV-related information (this includes any information indicating that you have had an HIV-related test or have HIV infection, HIV-related illness, or AIDS, as well as information that could indicate you may have been exposed to HIV)
___ Other information (as described here):

_____
_____
_____
_____

- Other information (as described here):

By signing this form, you give permission to the persons and organizations listed above to obtain, use and disclose your health information noted above.

How will your health information be used?

The health information noted above, as well as information shown by the boxes checked above (if any), may be obtained, used, and disclosed:

- to conduct the research study explained to you during the informed consent process; and
- to assure the quality, safety, and effectiveness of the research study

Please note that the persons and organizations listed above may re-use or further disclose your information if they are permitted by law to do so.

What are your rights?

It is your right to refuse to sign this authorization form. If you do not sign this form, you will not be able to participate in the research study. Your health care outside the study will not be affected. The payment for your health care and your health care benefits will not be affected.
If you sign this authorization form, you will have the right to withdraw it at any time except to the extent that the persons and organizations listed above:

- have already taken action based upon your authorization;
- need the previously collected information to complete analysis and reports of data for this research; or
- will continue to use and disclose previously collected information as permitted by the informed consent form signed by you (except as to HIV-related information, for which disclosure to new persons or organizations will not occur unless permitted by federal or state law).

If you withdraw the authorization, you will not be permitted to continue taking part in the research study. This authorization form will not expire unless you withdraw it. If you want to withdraw this authorization, please write to the above named investigators.
You have a right to see and copy your health information described in this authorization form in accordance with The Rockefeller University's policies; in certain circumstances where the integrity of the study will be affected, you will not be able to obtain your health records in this study until the study has been completed.
You will receive a copy of this form after you have signed it.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that such information may not be shared without your approval unless permitted by federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (212) 480-2493 or the New York City Commission of Human Rights at (212) 306-7450. These agencies are responsible for protecting your rights.

Your signature

I have read this form, and all of my questions have been answered. By signing below, I acknowledge that I have read and accept all of the information above.

Signature of participant or participant's legal representative

Date

Printed name of participant

Printed name of legal representative (if applicable)

Representative's relationship to participant

THE STUDY PARTICIPANT OR HIS OR HER PERSONAL REPRESENTATIVE MUST BE PROVIDED WITH A COPY OF THIS FORM AFTER IT HAS BEEN SIGNED.

38.0 End of Application Form

38.1 The study application form is complete.

The next step in the submission process is to gather attachments before proceeding to the submission form.

The following submission reports are generated in the Lab/Dept Reports menu, Submission Reports section:

- **Delegation of Authority** (if applicable, and if not previously generated)
- **HIPAA form** (if applicable)
- **CCTS Utilization Report** (required for all submissions)
- **Study Progress Report** (if the study has been managed in iRIS for a minimum of one year, generate the Progress Report from the report menu in iRIS. if the study has not been managed in iRIS for one year, complete the Progress Report located on the IRB website.)

All other required forms can be downloaded from the corresponding sections' help links above or from the IRB website.