INTERVENTIONAL
RESEARCH PROTOCOL TEMPLATE
(HRP-503a)

INSTRUCTIONS

This template should be used by biomedical and social-behavioral researchers conducting research which subjects are assigned to receive one or more interventions so that the researchers can evaluate their effects. (e.g. clinical trials, CBT, Behavioral Modification studies, or randomized outcome studies)

STUDY INFORMATION

Title of Project: The effect of dietary fiber-supplemented food on glycemic response in human: a pilot study (short title: High-fiber food and glycemic response)

Principal Investigator:

Name: Liping Zhao

Division & Department: Department of Biochemistry and Microbiology, School of Environmental and Biological Sciences

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PROTOCOL VERSION AND DATE: Version #2; September 27, 2017

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1.0 Research Introduction

1.1 Purpose/Specific Aims

To characterize the effect of food supplemented with dietary fiber on glycemic response in humans

A. Objectives

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To characterize the effect of food supplemented with dietary fiber on postprandial blood glucose levels. This pilot study will generate data to facilitate the development of a high dietary fiber dietary intervention for an upcoming study that aims at improving gut microbial profile and functions to improve glycemic control in patients with type 2 diabetes.

B. Hypotheses / Research Question(s)

We hypothesize that food supplemented with dietary fiber will reduce postprandial glycemic response as compared to a standard meal tolerance test (white bread with 50 g of available carbohydrates). Further, the impact of supplemented food, although with the same amount of dietary fiber, will vary due to differences in cooking procedures and serving temperatures.

1.2 Research Significance *(Briefly describe the following in 500 words or less):*

The gut ecosystem has now been regarded as the foundation for human health, with developing strategies to promote and maintain gut homeostasis as one of the key priorities in recent medical research. Dysbiosis (an imbalance of beneficial and detrimental microbes) has long been associated with metabolic diseases, notably obesity and type 2 diabetes. To date the mechanisms by which the gut microbiome impacts on host health have not been fully elucidated, but the literature points to short-chain fatty acid (SCFA) production from bacterial carbohydrate fermentation as a key microbial function that is essential for humans and the deficiency of which may lead to deleterious metabolic sequelae. SCFAs confer direct benefits to humans, e.g. butyrate is the primary energy substrate for colonocytes and a wide range of SCFAs function as signaling molecules that modulate inflammation and appetite regulation (1). SCFAs also impact on the gut ecosystem *per se*. By modulating gut luminal pH, SCFAs create a selective pressure against acid-intolerant bacteria (notably opportunistic pathogens) and therefore an acidity-driven shift in overall gut microbial structure (2).

Dietary fiber is the primary source of fermentable carbohydrates for the gut bacteria and thus dietary fiber supplementation is commonly used in microbiota-targeted dietary interventions. There is some evidence for increased dietary fiber intake to positively impact on metabolic outcomes in patients with type 2 diabetes (3, 4). A single dietary fiber type, however, is unlikely to confer universal benefits. The human gut microbiota is highly variable across individuals, with different capacities for fermenting dietary fiber of various physiochemical properties. Accordingly, it is logical to tailor microbiota-targeted dietary interventions based on each individuals gut microbial functions (a separate project that we are currently pursuing). From a population health perspective, dietary fiber fortification of everyday food products should consist of a broad range of dietary fiber types so that most individuals would be able to benefit from at least some of the ingredients.

We have developed two dietary fiber mixes, one consists of different bran as sources of insoluble dietary fiber (sorghum bran, corn bran, wheat bran and oat bran; Insoluble Mix) and the other one consists of two soluble dietary fiber (inulin and Fibersol-2®; Soluble Mix). The work proposed here will explore the effect of these two Mixes on glycemic response in human. This pilot study is part of the food/meal development for an upcoming study that will explore the effect of a gut microbiota-targeted dietary intervention program on glucose homeostasis in patients with type 2 diabetes.

1.3 Research Design and Methods

OVERVIEW. This is a pilot study to characterize the effect of food supplemented with dietary fiber on glycemic response in human. Participants will test 6 food items (plus a control food for comparison) with postprandial glycemic response monitored using a continuous glucose monitoring system. The study will be conducted at the Cook-Douglass Student Health Center and Harvest Café at New Jersey Institute for Food, Nutrition & Health (IFNH). There will be an eligibility screening and group assignment visit, and 14 food testing visits over 4 weeks (Figure 1).

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Food Testing		
	Panel A	Panel B
Week 1	White bread (Control)	White bread (Control)
	Dietary fiber mix in water	Dietary fiber mix in water
Week 2	Waffle (hot)	Sponge cake
	Waffle (room temperature)	Crispbread
Week 3	Pancake (hot)	Vegetable smoothie
	Pancake (room temperature)	Fruit smoothie
Week 4	Muffin	Muffin

Eligibility Screening
- Informed consent
- Medical and medication history
- Inclusion/exclusion criteria

Group Assignment
Fasting glucose concentration (finger prick)

< 100 mg/dL
Non-Diabetes Group

≥ 100 mg/dL
Prediabetes/ Diabetes Group

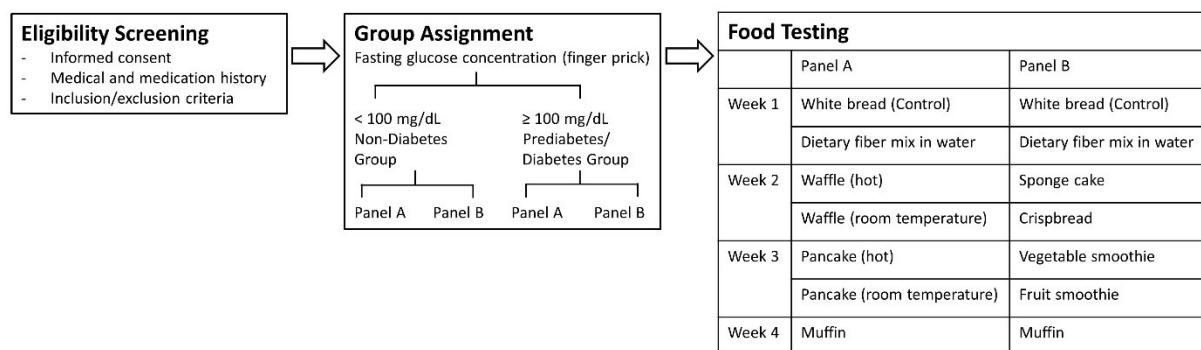Panel A   Panel B   Panel A   Panel B

Figure 1. Study design.

RECRUITMENT. Prospective participants will be recruited through advertisements on Rutgers University website and email lists (Attachment 3A), and flyers on the Rutgers University campuses (Attachment 3B). Interested individuals will be asked to contact the research team by phone, during which a research officer will provide an overview of the study and describe the broad selection criteria. Prospective participants will be invited to attend a screening visit to establish eligibility. The final selection will be contingent upon the individuals meeting all eligibility criteria and are deemed capable of complying with the protocol.

ELIGIBILITY SCREENING. Prospective participants will attend the eligibility screening visit after an overnight fast of at least 8 h. They will meet a member of the research team at IFNH, who will provide a detailed description of the study, including the rationale, aim, expected outcomes and significance of the research, the experimental procedures, what is required from the participants, and the benefits and risks associated with the study. Written informed consent (Attachment 4) will be obtained prior to the eligibility screening process. All information collected during the screening process will be documented in the screening checklist (Attachment 7). Specifically a Research Officer will record medical history and current medications and assess eligibility. Patients with type 2 diabetes who are receiving nutritional management and/or oral hypoglycemic medications may be eligible for the study, however those who are receiving insulin treatment or other injectable prescription medication will be excluded. A full list of inclusion and exclusion criteria is available in Section 4.2.

GROUP ASSIGNMENT. Upon confirmation of eligibility, the Research Officer will measure fasting blood glucose concentration (FBG) by performing a finger prick test (ACCU-CHEK® Aviva Plus, Roche Diabetes Care, Indianapolis, IN). Participants who are clinically diagnosed with impaired glucose tolerance or type 2 diabetes (diet-controlled and/or on oral hypoglycemic medications) will be assigned to the Prediabetes/Diabetes group irrespective of their finger prick test results. , For participants who are not diagnosed with diabetes, those with FBG < 100 mg/dL will be assigned to the Non-Diabetes group, and those with FBG ≥ 100 mg/dL will be assigned to the Prediabetes/Diabetes group based on classification guidelines from the American Diabetes Association (5). Participants will also be asked to sign up for one of the testing panels: 1) Panel A will test one control food (white bread) and six fiber-supplemented food (dietary fiber mix in water, hot waffle, room temperature waffle, hot pancake, room temperature pancake and muffin); or 2) Panel B will test one control food (white bread) and six fiber-supplemented food (dietary fiber mix in water, sponge cake, crispbread, vegetable smoothie, fruit smoothie and muffin). Finally, the Research Officer will collect information to complete the participant profile, including anthropometry measurements (height and weight), and demographics and contact details.

The eligibility screening and group assignment visit will take approximately 1 h to complete.

FOOD TESTING. In the morning of each testing day, participants will attend IFNH between 8 and 10 am after an overnight fast of at least 8 h. They will be required to consume all the study food provided under supervision. The

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amount of white bread to be consumed will contain 50 g of available carbohydrates (3-4 slices of bread), and the amount of fiber-supplemented food to be consumed will contain 60 g of dietary fiber mix (approximately 2 waffles, 2 pancakes, 2 slices of sponge cake, 2 serves of crispbread, 2 muffins or 300 ml of smoothies). Participants may leave the research facility after consuming the food, and they will be instructed to refrain from eating and drinking (except water) for the next 3 h. Each food will be tested twice over two consecutive days, with all testing to be completed in 4 weeks (Figure 1). Each food testing session will take approximately 30 min to complete.

Postprandial glycemic response will be assessed by changes in blood glucose concentrations, to be monitored using a continuous glucose monitoring system (CGM; FreeStyle Libre Pro, Abbott Diabetes Care, Alameda CA). On the first day of food testing, a sensor will be placed on the participant's arm by our Study Physician or other members of the research team trained by the sensor supplier (Abbott Diabetes Care). The sensor will stay on the participant's arm until the end of the study (the sensor will be replaced after 14 days as per manufacturer instructions). Participants will be asked not to take the sensor below 3 ft (1 m) of water and not to submerge the sensor in water for more than 30 min to prevent sensor malfunction. Should there is a need to take off the sensor prior to the intended wear duration, the sensor has fallen off or there is question about proper functioning of the sensors, participants should contact the research team and attend our facility to check the sensors and replace them if necessary. At completion of the last food testing, participants are required to return to IFNH for removal of the CGM sensor anytime between 3 h after the last food item is consumed and the end of the week.

SAFETY MONITORING. All food ingredients will be sourced from local commercial suppliers and the dietary fiber mixes will be prepared in-house at the Food Innovation Center of Rutgers University (a facility that operates under constant USDA inspection). The dietary fiber mixes will undergo microbial count testing at EMSL Analytical (Piscataway, NJ). All meals will be prepared at Harvest Café of IFNH where all managers are ServSafe certified. CGM data will be reviewed by our Research Physician who, with written consent from the participants, will communicate directly with their primary healthcare provider(s) should there be a need for medical care adjustment.

1.4 Preliminary Data

Our research group focuses on using dietary interventions, primarily dietary fiber supplementation, to restore and maintain a healthy gut microbiota as a key strategy to improve metabolic health. In a cohort of children with Prader-Willi syndrome (a genetic form of obesity) (6), we showed that a diet enriched in non-digestible carbohydrates induced significant weight loss and metabolic improvements, an effect associated with structural changes of the gut microbiota. Importantly, germ-free mice that received fecal microbiota transplantation derived from participants post-intervention exhibited a more favorable metabolic profile and glycemic control as compared to those animals that received pre-intervention fecal material, which provided direct evidence for the gut microbiota to causally contribute to the host glucose homeostasis.

In two cohorts that we have recently completed, a comparable 3-month high dietary fiber regimen was able to significantly reduce HbA1c in adults with type 2 diabetes (under review with Nature). Below are the HbA1c data from the GUT2D (participants were institutionalized; Figure 2A) and the QIDONG studies (participants were under free-living conditions; Figure 2B).

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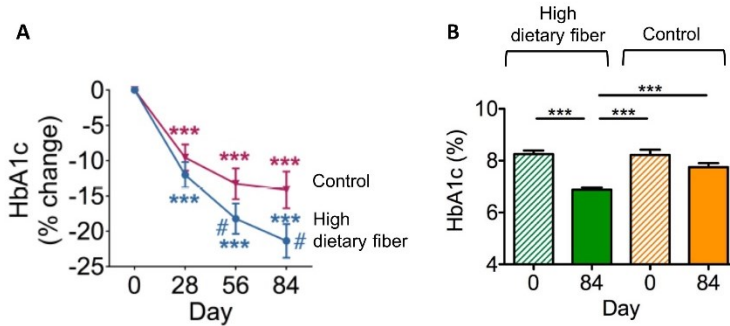
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Figure 2. The effects of a high dietary fiber regimen on HbA1c in patients with type 2 diabetes in the GUT2D (A) and QIDONG (B) cohorts.

In the GUT2D cohort, high dietary fiber intake induced shifts in the overall structure of the gut microbiota (Figure 3A) that was driven by an increased abundance of a guild of acetate- and butyrate-producing bacteria (Figure 3B). The dramatic reduction of fecal pH from 6.82 ± 0.07 at baseline to 6.36 ± 0.11 at the end of the 3-month intervention, together with trended increase in overall fecal SCFA content, supported that a high dietary fiber regimen was effective in increasing bacterial carbohydrate fermentation, and these were associated with improvements in glucose homeostasis and overall metabolic profiles of patients with type 2 diabetes.
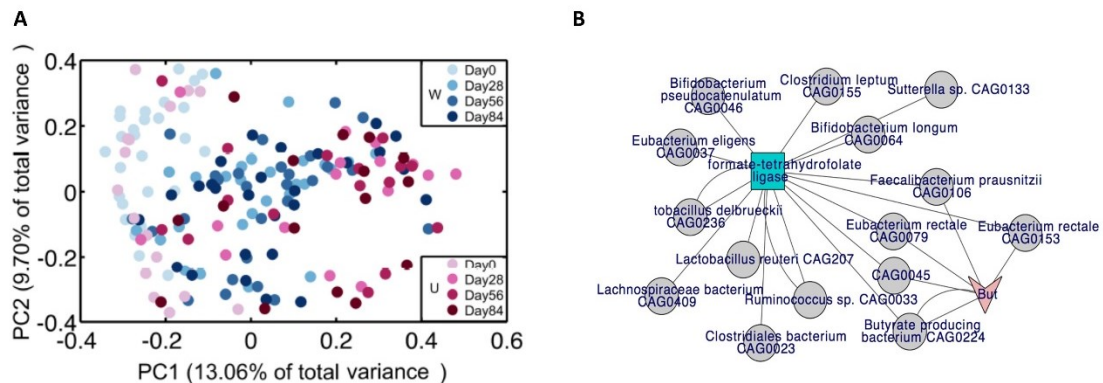

Figure 3. Changes in the overall gut microbial structure (A) and the guild of short-chain fatty acid producers promoted by the high dietary fiber intervention (B). U = control group and W = high dietary fiber group.

1.5 Sample Size Justification
No power calculation is performed for this pilot study. We aim to have 5 completers in the Non-Diabetes and 5 in the Prediabetes/Diabetes group, for each of the test panel (i.e. a total of 20 completers). This sample size is comparable to those used in published pilot studies on bran products. Steinert et al (7) used 10 participants (healthy, overweight and obese) to examine the effect of oat bran on glycemic response; Sheflin et al (8) used 7 participants (3 in control and 4 in experimental group) to examine the effect of heat-stabilized rice bran on gut microbiota and metabolites.

1.6 Study Variables
A. Independent Variables, Interventions, or Predictor Variables
The independent variable will be type of food: white bread vs dietary fiber mix in water, waffle, pancake, sponge cake, crispbread, vegetable smoothie, fruit smoothie and muffin.

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B. Dependent Variables or Outcome Measures
The outcome measure will be postprandial blood glucose concentration.

1.7 Drugs/Devices/Biologics
N/A

1.8 Primary Specimen Collection
N/A

1.9 Interviews, Focus Groups, or Surveys
N/A

1.10 Timetable/Schedule of Events

	Sept 2017	Oct 2017	Nov 2017	Dec 2017	Jan 2018	Feb 2018
Staff/student training, departmental setup, research material development	▓					
Recruitment		▓	▓			
Eligibility screening and group assignment		▓	▓			
Food testing		▓	▓	▓		
Data analyses				▓		
Write up, results dissemination and record archiving					▓	▓

2.0 Project Management

2.1 Research Staff and Qualifications

Principal Investigator Dr Liping Zhao (BSc, MSc, PhD) is the Eveleigh-Fenton Chair of Applied Microbiology in the School of Environmental and Biological Sciences and he leads the Program of Human Microbiome in Nutrition and Health at IFNH. Dr Zhao's research applies molecular and genomic tools in understanding systems biology and predictive manipulation of the gut microbial communities, with his recent research primarily focuses on using dietary interventions to restore and maintain a health gut microbiota as a key strategy to improve metabolic health. Dr Zhao's research group in China successfully used a high dietary fiber intervention to induce significant weight loss and metabolic improvements in children with obesity (6) and in adults with type 2 diabetes (manuscript under review in Science). Adopting an integrated metagenomics-metabolomics approach, Dr Zhao identified a functional guilds of carbohydrate-fermenting bacteria that may be pivotal to a healthy gut microbiota, which provides an important basis for optimizing dietary fiber supplementation to improve metabolic outcomes. Dr Zhao leads experimental design and research material development for this study.

Co-Investigator Dr Yan Lam (BSc, MSc, PhD) is an Assistant Research Professor of the laboratory of Dr Liping Zhao (Principal Investigator; mentor) at the Department of Biochemistry and Microbiology. Dr Lam's initial training was in nutritional biochemistry followed by professional qualification and practice in clinical dietetics in Australia. Her broad research interest is to understand how diet impacts on health, with the ultimate aim of developing evidence-based nutritional advice to improve metabolic wellbeing. Dr Lam's recent research primarily focuses on investigating the role of dietary factors on the gut microbiota and how that influences clinical metabolic risk factors. With experience in successfully leading clinical trials to completion at the Pennington Biomedical Research Center of Louisiana State University and at the University of Sydney in Australia, Dr Lam participates in experimental design and research material development, and will oversee staff/student training and day-to-day running of this study.

Co-Investigator Dr Tingting Chen (PhD) is a Postdoctoral Research Associate of the Zhao laboratory at the Department of Biochemistry and Microbiology. Dr Chen was awarded her PhD in Food Science from Purdue University in 2016. Her research primarily focuses on understanding the molecular mechanisms by which dietary

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fiber modulates the gut microbiota using a model of *in vitro* fermentation with human fecal inoculum. Dr Chen leads the development of dietary fiber mix.

Co-Investigator Dr Peggy Policastro (PhD, RDN) is the Director of Behavioral Nutrition and Health/Dining Services at IFNH. Dr Policastro has extensive experience in nutritional analysis and menu planning. She will oversee the development of fiber-supplemented food.

Co-Investigator Dr David Krol (MD, MPH) is the Medical Director of the New Jersey Healthy Kids Initiative. As our Research Physician, he will review the CGM data throughout this trial as part of our safety monitoring protocol, and contact the participants and their primary care or other main treating physician (with consent) to discuss alterations in medical treatment plan should the need arises.

Graduate Student Ying Wang will assist with participant recruitment, scheduling, conducting food testing visits, data entry and analyses.

Graduate Student Yongjia Gong will assist with participant recruitment, scheduling, conducting food testing visits, data entry and analyses.

2.2 Resources Available
FACILITIES. All procedures will be conducted at IFNH. The Cook-Douglass Student Health Center is equipped with interview rooms for eligibility screening visits. The dietary fiber mix will be prepared at the Food Innovation Center and stored at IFNH until use. Harvest Café will prepare all the test food and provide seating for food consumption.

GLUCOSE MONITORING DEVICE. The FreeStyle Pro, the continuous glucose monitoring system, will be purchased from Abbott Diabetes Care. The Abbott technical support team will provide training to the research team on the sensor application and data download procedures, and ongoing technical support throughout the study.

RESEARCH TRAINING. All investigators and research personnel will complete the Collaborative Institutional Training Initiative (CITI) training. Those who will work in the clinical research facilities will also be required to complete the Lab Safety/Biological Safety/Blood Borne Pathogens Training from Rutgers Environmental Health & Safety.

2.3 Research Sites
- Cook-Douglass Student Health Center, New Jersey Institute for Food, Nutrition & Health
- Harvest Café, New Jersey Institute for Food, Nutrition & Health

3.0 Multi-Site Research Communication & Coordination
N/A

4.0 Research Data Source/s

4.1 Primary Data-Subjects and Specimens
Male and female individuals

4.2 Subject Selection and Enrollment Considerations
A. Recruitment Details
Recruitment will start in October 2017 (pending IRB approval). Prospective participants will be recruited through advertisements on Rutgers University website and email lists, and flyers on Rutgers University campuses. Interested individuals will be asked to contact the research team by phone, during which a research officer will provide an overview of the study and describe the broad selection criteria. Prospective participants will be invited to attend a screening visit to establish eligibility. The final selection will be

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contingent upon the individuals meeting all eligibility criteria and are deemed capable of complying with the intervention protocol.

B. Source of Subjects

We expect most of the participants will be employees or students of Rutgers University, although we would also anticipate prospective participants from the wider community via word-of-mouth.

C. Method to Identify Potential Subjects

An advertisement will be placed in the Rutgers University website and email lists (Attachment 3A). Flyers will be posted on the Rutgers University campuses (Attachment 3B).

D. Subject Screening

Prospective participants will attend an eligibility screening visit at IFNH after an overnight fast of at least 8 h. They will meet a member of the research team who will decide eligibility based on the following criteria:

- **Inclusion Criteria**
  - Aged between 18 and 55 years
  - Understand and be able to follow written and oral instructions in English
  - Provide written informed consent

- **Exclusion Criteria**
  - Receiving insulin for diabetes treatment
  - Receiving injectable prescription medicine
  - Self-reported allergy or intolerance to any ingredients in the test food
  - Any conditions deemed by the investigators that would prevent participation in the study, e.g. participation in past or active clinical research that may interfere with study outcomes, at the discretion of the investigators
  - Any conditions deemed by the investigators that would compromise the individual's ability to complete the study, e.g. serious psychiatric conditions, at the discretion of the investigators

E. Recruitment Materials

Please see Attachment 3.

F. Lead Site Recruitment Methods

N/A

4.3 Subject Randomization

Participants will not be randomized. They will be assigned to the Non-Diabetes group if their FBGs are < 100 mg/dL, and to the Prediabetes/Diabetes group if their FBGs are ≥100 mg/dL. At participant's choice, they will sign up to one of the two testing panels (see Section 1.3).

4.4 Secondary Subjects

N/A

4.5 Number of Subjects

    A. Total Number of Subjects

    24

    B. Total Number of Subjects If Multicenter Study

    N/A

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C. Require Number of Subjects to Complete Research

20 (5 each in Panel A Non-Diabetes group and Prediabetes/Diabetes group, same two groups for Panel B)

D. Feasibility Of Recruiting

We expect to recruit the majority of our participants from the New Brunswick campus of Rutgers University. With a relatively flexible study schedule and no particularly stringent eligibility criteria, we do not anticipate difficulties in engaging interest in the Rutgers community. We expect a recruitment rate of 4-6 participants per week over 4-6 weeks including an estimated attrition rate of 20%.

4.6 Consent Procedures

A. Consent

- **Documenting Consent**

Please see Attachment 4.

- **Waiver of <u>Documentation</u> Of Consent**

N/A

- **Waiver or <u>Alteration</u> of Consent <u>Process</u>**

N/A

B. Consent Process

- **Location of Consent Process**

The Consent Process will take place at the Cook-Douglass Student Health Center of the New Jersey Institute for Food, Nutrition & Health

- **Ongoing Consent**

N/A

- **Individual Roles for Researchers Involved in Consent**

Co-Investigators Dr Yan Lam and Dr Tingting Chen, or graduate student Ying Wang (with supervision) will conduct the consent process to explain all aspects of the study and answer any questions the prospective participants may have. Dr Lam, Dr Chen or Ying Wang will sign the consent form.

1. Consent Discussion Duration

It is expected that the consent discussion will last approximately 30 min.

2. Coercion or Undue Influence

In order to minimize the possibility of coercion or undue influence, the consent process will not be conducted by research personnel who have any known relationship or conflict of interest with the prospective participants.

3. Subject Understanding

Throughout the consent process the prospective participants will be encouraged to ask any questions should they feel the need to do so. The consent process will be divided into a series of small sections. Members of the research team will summarize each section, use probe questions to check for sufficient understanding before proceeding to the next section.

4.7 Special Consent/Populations

N/A

4.8 Economic Burden and/or Compensation for Subjects

A. Expenses

The participants will likely incur expenses when they travel to our research facilities.

B. Compensation/Incentives

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Participants will be paid up to $60. The compensation is based on the amount of time that the participants is expected to spent in our research facilities and is calculated according to the minimum wage in New Jersey in 2017. They will have to successfully complete all food testing sessions to receive full compensation. The payment schedules are as follow:

- $20 when they complete Week 2
- $40 when they return the CGM sensor at the end of the study

Should participants choose to withdraw from the study, no pro-rata payment will be made other than the ones scheduled above.

The compensation will be paid in the form of gift cards.

4.9 Risks to Subjects

A. Description of Subject Risk

The finger prick test and the use of CGM sensor both involve piercing of the skin which may cause infection. However infection is rare.

Participants may experience gastrointestinal symptoms (e.g. bloating, flatulence, diarrhea, constipation or cramping) when they consume the fiber-supplemented test food. These discomforts are common, however, these discomforts are minor and they should not last longer than a few hours.

B. Procedures for Risks to Embryo, Fetus, and/or Pregnant Subjects

N/A

C. Risks to Non-Subjects

N/A

D. Assessment of Social Behavior Considerations

- **Reasonably Foreseeable Risks**

N/A

- **Risk Of Imposing An Intervention On Subject With Existing Condition**

N/A

- **Other Foreseeable Risks**

N/A

- **Observation And Sensitive Information**

N/A

E. Minimizing Risks

Participants will be advised to drink enough fluids throughout the food testing day (approximately eight 8-ounce glasses of fluid a day) to avoid constipation.

F. Certificate of Confidentiality

N/A

G. Potential Benefits to Subjects

Participants will receive reports of their daily fluctuations of blood glucose level throughout the study.

H. Provisions to Protect the Privacy Interests of Subjects

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Should any participants desire not to interact with or provide personal information to specific members of the research team, they may report such a need to the Principal Investigator and the arrangement of the research personnel will be adjusted accordingly. Participants will not be required to provide a reason if they desire not to do so. Should changing of the research personnel is not possible, the Principal Investigator will discuss with the participants about alternative solutions.

In order to ensure the protection of personal health information of the participants, there will be no identifiable information on any of the data collection instruments. Each participant will be assigned a unique identification code. A master code identifier which links the identification code and personal information (name, date of birth and contact information) will be maintained separately from the study data. Only the Principal Investigator and approved research personnel who have a specific need for identifiable information will have access (e.g. Study Physician to communicate directly with participants and/or their primary physicians; research student/staff to schedule appointments). All data and materials collected during this study are for research purpose only, and the data will be kept in strict confidence. No information will be given to anyone without permission from the participants.

I. Research Team Access To Subject Data
A code will be assigned to every participant and the collected data will be recorded using the participant's unique code for identification purposes. Only the Principal Investigator, Study Physician and research staff/student who schedule appointments will have access to the master code identifier and be able to re-identify the participants if necessary. Each member of the research team will only be able to have access to the subsets of study data (in de-identified form) that are relevant to his/her scope of work.

4.10 Secondary Data – Records/Chart Reviews/Databases/Tissue Banks/etc.
N/A

4.11 Chart/Record Review Selection
N/A

4.12 Secondary Specimen Collection
N/A

5.0 Special Considerations

5.1 Health Insurance Portability and Accountability Act (HIPAA)
N/A

5.2 Family Educational Rights and Privacy Act (FERPA)
N/A

5.3 NJ Access to Medical Research Act
N/A

5.4 Code of Federal Regulations Title 45 Part 46 (Vulnerable Populations)
N/A

6.0 Research Data Protection and Reporting

6.1 Data Management and Confidentiality

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A. *Data analysis plan*: Statistical analyses will be performed using the SPSS Statistics Software Package. Analysis of variance with Tukey's post-hot test (two-tailed) will be used for intra-and inter-group comparisons of postprandial blood glucose concentration (area-under-curve). Independent-samples t test (two-tailed) will be used to analyze variations in other participant characteristics. Statistical significance will be accepted at p value < 0.05.

B. *Quality control*: All research personnel will complete CITI training and be knowledgeable about Good Clinical Practice (GCP), relevant regulations and policies. The Principal Investigator will ensure adherence to the study protocol, regulatory requirements, GCP standards at all times. Team meeting will be held on a regular basis to review adherence to study protocol, and to discuss any incidents of failures of protocol compliance, keeping adequate and accurate records, and reporting of adverse events.

C. *Data handling:* The study data will include two key components: 1) a master code identifier that contains the personal information of the participants and the participant code assigned to them; and 2) study data files that contain all the de-identified data generated in this trial. Participants' hard copy files will be kept in locked cabinets only accessible by authorized research personnel in a secured building. Electronic files will be password-protected and stored on the university's secure server and will only be accessible to authorized research personnel. The master code identifier and the date files will be kept in two separate locations. The master code identifier is only accessible to the Principal Investigator, Study Physician and research staff who schedule appointments and the study data files are accessible to authorized research personnel who work in relevant components of the trial. Data in hard copies and the master code identifier will be kept for 6 years after study completion, thereafter they will be shredded. As data will then exist in de-identified form, the electronic data files will be kept indefinitely. The Principal Investigator will be responsible should receipt and/or transmission of data is required. All data transported/shared will be de-identified.

6.2 Data Security

A code will be assigned to every participant and the collected data will be recorded using the participant's unique code for identification purposes. The Principal Investigator, Study Physician and research staff/students who schedule appointments will be the only ones with access to the master code identifier. Participants' hard copy files will be kept in locked cabinets only accessible by authorized research personnel in a secured building. Electronic files will be password-protected and stored on the university's secure server and will only be accessible to authorized research personnel. The master code identifier and the data files will be kept in two separate locations. All personnel who will have access to data of any form will be required to complete CITI training and will only have access to the data during a specific duration deemed necessary by the Principal Investigator.

6.3 Data and Safety Monitoring

A. Periodic Data Evaluation

There will be a local Data and Safety Monitoring Committee composed of 3 Rutgers University faculty and staff members who are not directly involved with the study. The Committee will approve the protocol before the study is initiated, monitor study progress, and ensure that participant safety is addressed adequately. The Committee will receive monthly email updates on study progress and will meet at least once every 2 months. Additional meetings may be called if deemed necessary. Following each meeting, the Committee will provide written documentation regarding findings for the study as a whole and any relevant recommendations related to continuing, modifying or terminating the study. All recommendations will be submitted to the Principal Investigator. A copy of the recommendation will be provided to the Rutgers University IRB. A chairperson will be appointed to provide documentation on behalf of the Committee.

B. Type of Data Evaluated

The Committee will monitor recruitment, retention, adherence, and review participant safety including adverse events, proposed major protocol modifications, and reports of related studies as appropriate.

C. Collection of Safety Information
Safety information will be collected by research personnel at study visits or reported by the participants over the phone.

D. Frequency Of Data Collection
Safety data collection will start at the beginning of the first food testing visit and repeat after each study visit. However participants may contact members of the research team to report any potential adverse events anytime during the study.

E. Reviewer of Data
Members of the Data and Safety Monitoring Committee will review the data.

F. Schedule Of Review Of Cumulative Data
The Committee will receive monthly email updates on study progress and will meet at least once every 2 months. Additional meetings may be called if deemed necessary.

G. Tests for Safety Data
Pearson Chi-square tests (two-tailed) will be used to compare the safety data (e.g. number of reported adverse events) after consuming the control food (white bread) and each of the test food to determine whether the dietary fiber supplementation is causing harm comparing to an everyday food item.

H. Suspension of Research
Any serious adverse event that is life-threatening or results in death, that is possibly, probably or definitely related to the research protocol, will trigger an immediate suspension of the research.

6.4 Reporting Results
A. Sharing of Results with Subjects
See Section B below.

B. Individual Results
All participants will receive reports of their CGM data throughout the study, to be distributed via email after they have completed all the study visits.

C. Aggregate Results
All participants will receive aggregate results that summarize the overall findings of this study. The results will be in the form of a one-page summary that will be distributed via email after all data analyses are finalized.

D. Professional Reporting
Preliminary results will be presented in local and international academic conferences. The final study findings will be published in prestigious academic journals and the key findings will be disseminated to the public via press release.

E. ClinicalTrials.Gov Registration And Data Reporting
This study will be registered on ClinicalTrials.gov.

7.0 Data and/or Specimen Banking

Protocol Number: 18-074
Version: #2; September 27, 2017
PI Name: Liping Zhao
Protocol Title: The effect of dietary fiber-supplemented food on glycemic response in human: a pilot study

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De-identified electronic data will be stored on the university's secure server indefinitely. Data banked for future use will only be accessible by the Principal Investigator. Release of these data, irrespective of whether the Principal Investigator has ownership of the research project(s) that require the banked data, will need to obtain separate IRB approvals. When the banked data are transferred or shared, they will not be associated with any identifiable data, personal information of the research participants or the master code identifier for deciphering the codes.

8.0 Other Approvals/Authorizations
Pending approval from the Institutional Biosafety Committee.

9.0 Bibliography

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