Permission to Take Part in a Human Research Study

Do not sign this consent if today's date is later than the stated expiration date above.

Title of Research Study: Examining the Effects of Popular Diet Intervention on Epigenetics

Investigator: Dr. Melinda Ring, MD, FACP; Lifang Hou, MD, PhD; Brian Joyce, PhD

Supported By: This research is supported by The Osher Center for Integrative Medicine and the Center for Population Epigenetics at Northwestern University.

Key Information:

The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary.

Why am I being asked to take part in this research study?

You are being asked to take part in this research study because you are a healthy young adult of normal body weight. You are in general good health and have no significant dietary limitations. This Consent Form document has important information about the reason for the study, what you will do if you choose to be in this research study, and the way we will use the information collected through this study. You are being given this information to help you decide if you would like to participate in the study.

If you have any questions, you can ask the study investigator and/or staff.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The purpose of this study is to test the effectiveness of dietary interventions that have the possibility to improve markers of gut health and improve general well-being. This study will allow healthcare professionals to learn how dietary interventions involving fasting can affect health. Food is increasingly recognized as important to treating and preventing disease. Juice fasting has quickly become one of the most popular self-prescribed dietary interventions in the United States. A wide variety of juice fasts are available in the popular market, the most popular variation is the three-day juice and vegetable fast. The purpose of this study is to assess the effects of a 3 day juice fast on certain markers of age-related disease and bio-markers of longevity. In particular, this study will assess certain epigenetic markers. Epigenetics are how the environment (including diet) can change the way that genes are expressed (whether genes are active or inactive) without changing the genes themselves. This study will also look at the body's microbiome- especially the bacteria that live in our gut- and how the body handles carbohydrates and sugar in the diet.

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How long will the research last and what will I need to do?

We expect that you will be in this research study for 21 days. Total time commitment for the 21-day period is estimated at 6.5 hours, not including actual consumption of food and beverages. The time allotted may vary depending on amount of time participants require for sample collection and recording. You will also need to have access to adequate food storage, such as a refrigerator.

While you are in the study you will be required to do the following:

Dietary intervention: For 3 days during the study you will be required to follow a specific diet which may include a juice fast. We refer to this as the period of dietary intervention. You will also have dietary restrictions for the 3 days before and after this intervention.

Diet diary recording: Includes documenting all consumed food and beverages during the periods of dietary restriction and dietary intervention (overall time commitment: 3.0 hours).

Biomarker collection: At four points in the study a small amount of blood will be collected on campus by the research assistant using a finger prick along with measures of blood pressure, weight and waist circumference. You will be asked to self-collect saliva at home using a tube and a cheek swab, and stool using a wipe for collection four times (overall time commitment: 3.0 hours).

Daily check-in: You will be contacted by the research staff daily during the diet portion of the study for a check-in. During the 3 days of dietary intervention, you will also respond to a brief validated measurement survey online about how you are feeling. (overall time commitment: 0.5 hour).

More detailed information about the study procedures can be found under the section **What happens if I say "Yes, I want to be in this research"?**

Is there any way being in this study could be bad for me?
The risk to participants during this study is expected to be minimal. The assigned dietary interventions over short periods are generally safe, but may cause some minor discomfort during the study period. Similarly, biological sample collection may cause some minor discomfort.

More detailed information about the risks of this study can be found under **"Is there any way being in this study could be bad for me? (Detailed Risks)"**

Will being in this study help me in any way?
We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include health benefits from the dietary intervention. You will also receive meals during the 3-day intervention. Participants will be compensated $50 at the third visit and $50 at the fourth visit for the study.

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What happens if I do not want to be in this research?
You can choose not to participate in this research, and it will not be held against you. There will be no penalty to you or loss of benefits to which you are otherwise entitled, if you choose not to participate in this study. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment to which you are otherwise entitled.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

Who can I talk to?
If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at 312-503-5192.

This research has been reviewed and approved by an Institutional Review Board (IRB). You may talk to them at (312) 503-9338 or irb@northwestern.edu if:
- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be studied?
We expect about 30 people here at Northwestern will be in this research study.

What happens if I say "Yes, I want to be in this research"?
If you decide to participate in this research study, you will be asked to read and sign this study consent form. This consent form should be signed only after all of your questions are answered. Once consented, you will be registered to the study. You will be randomly assigned (i.e., by chance, like flipping a coin) to a specific dietary intervention. The three possible groups are: Juice Fasting, Juice in Addition to Normal Diet, and Caloric Restriction Diet. If in the Juice Fasting group, you will be given vegetable/fruit pressed juices and be instructed to engage in a three-day juice fast. If in the Juice in Addition to Normal Diet group, you will be given the same juice for three days but continue with an ad lib diet in addition to the juice. If in the Caloric Restriction Diet group, you will be on a 900 kcal-per-day diet for three days (matching the calories of juice fasting) using packaged food that we will provide. You will have an equal (1:1:1) chance of being in any group. You will be notified on the day of your baseline visit which group you are assigned to. See below for nutrition facts and ingredients.

Diet Intervention

You will take part in 9 days total of diet intervention. The first three days you will follow an elimination diet to prepare for your diet intervention. The elimination diet is outlined in your provided "Study Diet Guide" and includes limiting sugar, alcohol, caffeine, gluten and dairy. After your 3-day elimination diet you will begin your assigned diet intervention. You will be provided any food to be consumed during your 3-day diet intervention. You are to consume only the food outlined on your "Study Diet Guide" during this period. Finally, you will complete 3-days post-

intervention reintroduction diet. Again, the information for reintroducing your normal diet will be outlined in the "Study Diet Guide."

Nutrition information for provided food and drink

Juice Menu (Delivered by Pressed Vibrance)

Name	Calories	Ingredients
Astound, 16oz	140	Spinach, Kale, Romaine, Cucumber, Fennel, Parsley, Celery, Lemon, Apple, Ginger, Turmeric
Delightful Greens, 16oz	170	Kale, Spinach, Cucumber, Romaine, Parsley, Celery, Ginger, Lemon
Connective, 16oz	120	Aronia Berry, Spinach, Romaine, Cucumber, Parsley, Lemon, Ginger
Mindful, 16oz	130	Spinach, Kale, Romaine, Cucumber, Parsley, Celery, Swiss Chard, Lemon, Lime, Ginger, Apple
Nourishment, 16oz	120	Aronia Berry, Spinach, Kale, Romaine, Cucumber, Parsley, Celery, Lemon, Turmeric, Ginger, Wheatgrass, Broccoli Sprouts, Sunflower Sprouts
Aronia Crunch, 16oz	140	Apple, Celery, Lime, Aronia Berry

Caloric Restriction diet

~900 Calorie Plant-Based Daily Meal Plan (Delivered by KitchFix)	**Calories**
Loaded Cauliflower Mash (No Bacon) + Strawberry Cashew Yogurt + Power Green Veggie Quinoa Bowl	881
Herbed Root Vegetable Side + Spice Roasted Sweet Potato Side + Paleo Blueberry Muffin + Broccolini	879
Paleo Blueberry Muffin + Loaded Cauliflower Mash (No Bacon) + Spice Roasted Sweet Potato Side + Power Green Veggie Quinoa Bowl	889
Strawberry Cashew Yogurt + Herbed Root Vegetable Side + Tomato and Roasted Garlic Soup	862

Name	Calories *(Calories from fat)*	Ingredients
Loaded Cauliflower Mash (No Bacon), 141.7 g	75 *(25)*	Cauliflower, scallions, almond, nutritional yeast, parsley, thyme, rosemary, garlic, salt, black pepper
Strawberry Cashew Yogurt, 198.4 g	453 *(292)*	YOGURT cashew, raw honey, lemon, coconut water, vanilla extract, psyllium, salt STRAWBERRY strawberry, lemon, honey, salt GRANOLA almonds, sunflower seeds, pecans, cashews, almond flour, maple syrup, clover honey, coconut oil, flax seed, vanilla extract, cinnamon, sea salt

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Power Green Veggie Quinoa Bowl, 326.0 g	353 *(188)*	QUINOA quinoa, arugula, broccoli, asparagus, kale, mustard greens, parsley, salt SAUCE VERTE basil, arugula, EVO, garlic, red onion, lemon, capers, dijon, red fresno pepper, salt
Herbed Root Vegetable Side, 226.8 g	222 *(34)*	Parsnip, carrot, turnip, redskin potato, high-oleic sunflower oil, parsley, salt, black pepper
Spice Roasted Sweet Potato Side, 226.8 g	229 *(20)*	Sweet potato, chili powder, paprika, coconut oil, salt
Paleo Blueberry Muffin, 62.0 g	162 *(106)*	MUFFIN almond flour, coconut flour, banana, almond butter, almonds, baking powder, salt, baking soda, vanilla extract, coconut oil, maple syrup, coconut milk, pastured eggs, cinnamon, blueberries
Broccolini, 226.8 g	81 *(8)*	Broccolini, garlic, salt, black pepper, lemon zest, chili flake
Tomato and Roasted Garlic Soup, 453.6 g	187 *(57)*	SOUP tomato, vegetable broth, onion, red bell pepper, garlic, carrot, cashew, tomato paste, olive oil, basil, salt, black pepper, chili flakes GARNISH basil

See supplemental brochures for full nutrition information.

Food and drink delivery. Any food or drink that you would receive for the intervention will be delivered directly from the manufacturer to your place of residence or another location specified by you. The date and time of the deliveries will be arranged with you to ensure that you receive and are able to promptly refrigerate your food or drink.

Cheek swab collection. The research assistant will rub the inside of each of your cheeks with a swab for about 15 seconds each. This procedure will happen each time you come into the lab.

Saliva samples. The research assistant will provide you with training and written instructions in how to provide saliva samples and give you a kit that will contain all materials needed for saliva collection. The procedure is simple. You will let saliva build in your mouth, place the end of a small straw in your mouth, and let the saliva that has built up in your mouth flow through the straw into a plastic tube. Once collected, you will promptly label the plastic tube, place it in a sealed container, and refrigerate it. You will collect four saliva samples during the duration of the study. The first will be collected on the first day of the study, the second on the first day of your specific diet intervention, the third at the conclusion of your specific diet intervention, and the final on the last day of your participation in the study. The samples will be collected by the research assistant each time you come into the lab.

Blood spot collection. The research assistant will clean your finger with alcohol and then prick it with a sterile, disposable, widely available micro-lancet commonly used by diabetics. Five drops of whole blood will be collected on standardized filter paper. We will collect the first blood sample on the first day of the study, the second on the first day of your specific diet intervention, the third at the end of your dietary intervention, and the last 14 days after resuming your usual diet. These blood spots will be used to assess whether diet impacts on how your genes get expressed.

Stool sample collection. The research assistant will provide you with a pre-moistened wipe and written instructions on how to collect the sample at home. You will collect four samples during the duration of the study. You will collect the first sample on the first day of the study, the second just before beginning your diet intervention, the third at the end of your diet intervention, and the last just before your final lab visit. You will then be asked to provide the sample to the research assistant at your next visit.

Questionnaires and Diet Diary
At your initial visit you will be asked to complete a series of questionnaires about your normal diet history. Additionally, you will be asked to complete a quality of life questionnaire at the same points in time that you are collecting your saliva and stool samples.

During the periods of diet restriction and intervention (9 days), you will be asked to maintain a diet diary of any food and beverages you consume. Additionally, you will be contacted daily by the research assistant to ensure completion of the diet diary. During the diet intervention period, you will also be asked to fill out a brief online survey each day about how you're feeling.

After your diet intervention is complete and your last-samples have been collected, your participation in the study will be complete. The research assistant will contact you regarding

your compensation for completing the study. In addition, we will send all participants a Thank You letter/email for study participation and provide participants with the option to be notified with research results and publication information that results from the study upon study termination.

What are my responsibilities if I take part in this research?
If you take part in this research, you will be responsible to:
- Complete food frequency and quality of life questionnaires prior to participation
- Complete blood spot, cheek swab, stool, and saliva specimen samples at four points over the course of the study
- Adhere to the provided diet for the 3-day dietary intervention and the 6 days of restricted diet
- Participate in food recall call with Research Assistant
- Report any additional food/beverage items consumed to research assistant

What happens if I say "Yes", but I change my mind later?
You can choose to leave the research study at any time, and it will not be held against you. Choosing to withdraw from this study will not result in any penalty to you or loss of benefits to which you are otherwise entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment to which you are otherwise entitled.

Please note that you may change your mind and "take back" (revoke) this consent at any time. Even if you revoke this consent, the Principal Investigator may still use or share health information that was obtained about you before you revoked your consent as needed for the purpose of this study. To revoke your consent for the use of your health information, you must do so in writing to: Melinda Ring MD, Osher Center for Integrative Medicine at Northwestern University, 150 East Huron Avenue, Suite 1100, Chicago, Illinois 60611. Unless you revoke your consent, it will not expire.

If you withdraw from the study, you will be contacted by the Research Assistant to ascertain reason for withdrawal (information collected for study accrual reporting), provide you with the option to be notified with research results and publication information that results from the study upon research completion, and to address any remaining questions/concerns you may have about your experience in the research study. This call tends to take approximately five minutes, but can take as long as needed to ensure that you have all of your questions/concerns addressed.

Detailed Risks: Is there any way being in this study could be bad for me?
This research may hurt you in the following ways:
Diet intervention: Fasting and juice cleanse diets over short periods are generally safe, but may cause some minor discomfort during the study period. For those on restricted intake diets, several minor adverse effects may occur and include constipation, headache, muscle cramps, diarrhea, general weakness, and rash. Most of these are short-lived, and are generally alleviated by adequate fluid intake and other minor diet modifications. The restricted diet may lead to decreases in glucose levels.

Blood spot: There is a small risk that the puncture associated with the blood spot may cause bruising or infection at the site of the needle insertion.

Weight, height and waist circumference measurements: There is no physical risk involved in measuring weight, height, and waist circumference but there is a risk of embarrassment or

discomfort at being measured in your underclothes.

Behavioral and psychological questionnaires: These carry a minimal risk for emotional discomfort and stress.

This study involves the use of your identifiable, personal information and there is a chance that a loss of confidentiality could occur. The researchers have procedures in place to lessen the possibility of this happening. See the section below titled: "**What happens to the information collected for the research?**"

Will it cost me anything to participate in this research study?
Taking part in this research study will not lead to any costs to you, including the costs of food and drink delivery.

What happens to the information collected for the research?
Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. The Principal Investigator and the Investigator's study team may give information about you to the researchers for this study and other University staff associated with the study. Organizations that may inspect and copy your information include the IRB and other representatives of this institution and study monitors and auditors who make sure that the study is being done properly.
Please note that any research information shared with people outside of Northwestern University will not contain your name, address, telephone or any other direct personal identifier unless disclosure of the direct identifier is required by law [except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigator's office]. Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission.
Your name and the address you provide will be shared, without any research information, with the manufacturers of the food or drink (depending on your random assignment) for the purposes of delivery only.
The results of this study may also be used for research, publications, or presentations at scientific meetings. A unique code number will be assigned to you that will link to some of your identifiers. This is maintained in locked offices and a password protected database at the Northwestern University Department of Medical Social Sciences. It is accessible only by staff on the Northwestern University study team.

Can I be removed from the research without my OK?
Involuntary withdrawals will be initiated when participants report experiencing an adverse medical event (e.g., fainting or other health effects that may be related to fasting and caloric restriction). You will be notified by the research assistant if you are removed from the study.

What else do I need to know?
If you become ill or get injured as a result of this study (medications, devices or procedures), you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.

The university will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back

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for care required because of a bad outcome.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

If you agree to take part in this research study, we will pay you $100 in gift card form for your time and effort. This amount is pro-rated for research visit completion, with $50 being paid for the third sample collection and $50 for the fourth.

If you would like to be notified of study results, please contact the research team at 312-503-5192.

Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

I agree	**I disagree**	
_____	_____	The researcher may contact me in the future to see whether I am interested in participating in other research studies by the Principal Investigator of this study.
_____	_____	The researcher may retain any leftover blood or tissue samples taken during the study. These samples may be used for other research not related to this study. These samples will be retained in non-identifiable form, meaning that there will be no information associated with the blood or samples that will allow anyone to readily ascertain my identity.

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____

Signature of Participant Date

_____

Printed Name of Participant

_____ _____

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Signature of Person Obtaining Consent Date

_____

Printed Name of Person Obtaining Consent