Official Title:	A Pilot Proof of Concept Study of the Effects of Administration of a Short Chain Fatty Acid (SCFA) Supplement in Rheumatoid Arthritis Inadequate Responders (EASi-RAIR)
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Research Subject Informed Consent Form

Title of Study:	A pilot proof of concept study of the Effects of Administration of SCFA in Rheumatoid Arthritis Inadequate Responders (EASi-RAIR) s22-01526
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1. About volunteering for this research study

You are being invited to take part in a research study. Your participation is voluntary which means you can choose whether or not you want to take part in this study.

People who agree to take part in research studies are called “subjects” or “research subjects”. These words are used throughout this consent form. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. You may also decide to discuss this study and this form with your family, friends, or doctor. If you have any questions about the study or about this form, please ask us. If you decide to take part in this study, you must sign this form. We will give you a copy of this form signed by you for you to keep.

2. What is the purpose of this study?

The purpose of this research is to study Short Chain Fatty Acids (SCFAs), bacterial fermentation products that are naturally found at varying concentrations in your gut, and how it affects the abundance of microorganisms in your gut, as well as T regulatory cells in your blood. SCFAs are metabolites that are known to change the immune response in animal models of inflammation. This study is important because we hypothesize that changes in the gut microbiome and the regulatory immune response may improve treatment of rheumatoid arthritis.

SCFAs are not an FDA-approved treatment for RA or for any other condition. We are not studying SCFAs as a treatment for your condition. We only want to see the effect of SCFAs on the microorganisms in your gut and on certain blood measures.

We are asking you to take part in this research study because you have been diagnosed with rheumatoid arthritis (RA), which is an autoimmune disorder, and you are taking methotrexate (MTX) as part of your standard of care treatment plan.

You do not have to take the SCFA oral supplement. If you prefer, you can proceed with the next medication suggested by your treating physician but will continue to follow the schedule of activities detailed in section 4 of this document.

3. How long will I be in the study? How many other people will be in the study?

Your expected duration in the study is approximately 2 months with an OPTIONAL additional visit at about 12 months. The expected duration of the entire study is at least 5 years. About 65 people will be in this study.

4. What will I be asked to do in the study?

If you choose to take part in the study, we will ask you to sign this consent form before you have any procedures with the study staff that are part of the study. You will be asked to participate in a total of 3 study visits over 2 months.

Study drug overview

The SCFA supplement is an over-the-counter supplement that comes in a soft gel capsule. You will receive the supplement at your study visits at the visit location. You will take two capsules (1000mg) by mouth three times daily, preferably, with meals. If you miss a dose, the dose can be taken within 3 hours of the missed dose with or without food. Otherwise you can just wait until next dose. Do not double up on dose if missed previous dose.

You will be continuing methotrexate (MTX) as part of your standard of care with your treating physician.

If you do not want to take the SCFA oral supplement and want to proceed with the next medication your physician suggests; you will continue the standard of care with your treating physician and adhere to the schedule of activities below. You will be considered a control participant.

STUDY VISITS

The procedures at each study visit are listed below.

Visit 1

- Review and sign this informed consent form
- The study doctor will review your demographics (such as: age, race, and gender), medical and medication history
- Complete the disease Activity Score Calculator for Rheumatoid Arthritis (DAS28) and Multidimensional Health Assessment Questionnaire (MDHAQ) to record the severity of your disease. Joint counts will be used to measure tender joint and swollen joint counts.
- Approximately 5 tablespoons of blood sample will be collected for laboratory tests and markers of inflammation
- Urine sample will be collected for laboratory tests
- Stool sample collection. We will provide you with a collecting kit ahead of time that includes a stool collection frame and bowl. You will be asked to collect stool from a single bowel movement and mail it back or bring the sample back to the research site.
- All adverse events will be documented.

Visit 2 (month 1)

- Review any changes to your medication history.
- Complete the disease Activity Score Calculator for Rheumatoid Arthritis (DAS28) and Multidimensional Health Assessment Questionnaire (MDHAQ) to record the severity of your disease.
- Joint counts will be used to measure tender joint and swollen joint counts.
- Approximately 5 tablespoons of blood sample will be collected for laboratory tests and markers of inflammation.
- Urine sample will be collected for laboratory tests
- Stool sample collection: We will provide you with a collecting kit ahead of time that includes a stool collection frame and bowl. You will be asked to collect stool from a single bowel movement and mail it back or bring the sample back to the research site.
- All adverse events will be documented.

Visit 3 (month 2: OPTIONAL)

- Same as visit 2

Visit 4 (up to month 12: OPTIONAL)

- Same as visit 2

Tests may be run looking at different genes and their relationships in the body to better understand their role in rheumatoid arthritis and response to treatment. This is called genomic research. However, no genetic testing will be performed in a certified lab to diagnose your predisposition to conditions you don't currently know you have. These genetic tests will not be released to you and do not have direct clinical relevance to you individually.

OPTIONAL SAMPLE STORAGE FOR FUTURE STUDY-RELATED RESEARCH

We are asking permission to store leftover blood, urine, and stool from the samples collected during your visits, to be used for future research related to this study.

Only authorized study personnel will have access to your samples and information. The samples will be coded so that they do not contain information that can identify you. Only your study doctor will have the code that links you to your specimens and information. No information identifying you will be shared in any publications based on the future research.

The samples will be stored in the lab of Dr Scher, located at the NYU Langone Orthopedic Hospital, 301 E17th St, Room 1611, New York, NY 10003. Samples will be stored indefinitely unless you withdraw your permission in writing.

Any identifiable private information or specimens collected and/or used for the purposes of this research will not be used or distributed for future research studies.

If you agree to sample storage, you can change your mind at any time. You should send a written request to the study doctor and ask to have your samples destroyed. If your samples have not been used, they will be destroyed.

☐ Checking this box indicates my permission to have the remaining samples of blood, urine, and stool that are left over from the study be stored for future study-related research

☐ Checking this box indicates I DO NOT give my permission to have the remaining samples of blood, urine, and stool that are left over from the study be stored for future study-related research

5. What are the possible risks or discomforts?

The possible risks associated with this study are listed below.

Risk of SCFA:
SCFA is a normal gut metabolite. As such, no risks are expected other than those from ingestion of concentrated fatty acids, namely gastrointestinal intolerance (including pain and bloating) and (possibly) diarrhea. If you experience any of these symptoms, please tell us.

Blood Drawing:
Risks of venipuncture include bruising, pain at site of phlebotomy, fainting, and rarely infection.

Stool Sample Collection:
Potential contamination of surfaces or other people is the major risk of stool collection procedure, which may transmit infectious diseases to animals and individuals.

Urine Sample Collection
No identifiable risks.

Loss of Privacy and Confidentiality:
As with participation in any research study, there is always a risk that confidential or private information can be compromised. To minimize this risk, the study team will de-identify patient samples and replace identifying information, such as your name, with a bar code label that will not be associated with any date or identifiable information to the you (for example birthday or street address). Samples will be stored in the PI's lab. Only Dr. Scher and his research team will have access to them.

6. Can I be in the study if I am pregnant or breastfeeding?

If you are currently pregnant, you will not be able participate in the study since you cannot take MTX while pregnant.

If you become or you think you have become pregnant during the study, you must tell the principal investigator right away and must tell your obstetrician or other health care provider caring for you during your pregnancy that you took part in this study.

7. What if new information becomes available?

During the course of this study we may find more information that could be important to you. This includes information that might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

8. What are the possible benefits of the study?

You are not expected to benefit from taking part in this study. The benefits of SCFA in patients with rheumatoid arthritis, if any, are currently unknown.

We hope the information gained will help us better understand the effects of SCFA in patients with RA.

9. What other choices do I have if I do not participate?

You have the choice not to take part in the study. Your decision will not affect the care you receive for your condition.

10. Will I be paid for being in this study?

You will be paid $40 in either prepaid gift card or prepaid debit card for each *completed visit* at baseline, 1, and 2 months and additional optional 12-month visit. If you complete all study visits, you will receive a total value of $160. Reimbursements may be made available for travel expenses, such as parking reimbursement, where appropriate. You may receive up to $40 for travel expenses per visit.

As is required by the laws that apply to NYU Langone, in order for you to receive a payment (i.e. check, ClinCard, or bank gift card), you need to give the study staff either your Social Security number or your Alien Registration number and will be asked to complete an IRS W9. If you do not have either of these numbers or are not willing to complete the IRS W9, you may be in the study but will not receive any payment.

You must let us know immediately if/when the total research payments presently equal or are likely to exceed $600.00 total (not including travel reimbursements) for this calendar year. If your total payments (for one or more studies) reach $600.00, please tell the PI on page 1. However, you are required to report to the IRS all payments made to you by NYU Langone for your participation in any research for this calendar year, even payments under $600.00.

In order to receive payments for your participation in research, you may need to provide your Social Security number. This is because NYU Langone is required to report to the Internal Revenue Service (IRS) any amounts that are paid to research participants that are equal to or greater than $600.00. If you will receive payments in any amount by a check, you will need to provide your Social Security number or Alien Registration number and will be asked to complete an IRS W9. If you do not have either of these numbers or are not willing to complete the IRS W9, you may be in the study but will not receive any payment.

The samples collected in this study will never be used for commercial profit.

11. Will I have to pay for anything?

We will provide the SCFA supplement to you free of cost.

You will not have to pay for anything to be in this study.

You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study, or if your insurance agrees in advance to pay. This includes the costs of MTX. If you have health insurance, the cost of these services will be billed to your insurance company. If your insurance does not cover these costs or you do not have insurance, these costs will be your responsibility.

12. What happens if I am injured from being in the study?

For medical emergencies contact 911. If you think you have been injured as a result of taking part in this research study, tell the principal investigator as soon as possible. The principal investigator's name and phone number are listed at the top of page 1 of this consent form.

There are no plans for the NYU Grossman School of Medicine or Medical Center to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

13. When is the study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped or your participation ended at any time by your physician, and/or the principal investigator without your consent because:

- The principal investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The principal investigator has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. Leaving the study will not interfere with your future care, payment for your health care or your eligibility for health care benefits.

14. How will you protect my confidentiality?

Your medical information is protected health information, or “PHI”, and is protected by federal and state laws, such as the Health Insurance Portability and Accountability Act, or HIPAA. This includes information in your research record as well as information in your medical record at NYU Langone Health. In compliance with NYU Langone Health policies and procedures and with HIPAA, only those individuals with a job purpose can access this information.

Medical information created by this research study may become part of your medical record. We may include your research information in your medical record for several reasons, including for the billing of services provided in connection with the study, to securely document any medical services you receive, and so that other members of the NYU Langone Health community who may treat you have access to important information about your health.

You have a right to access information in your medical record. In some cases, when necessary to protect the integrity of the research, you will not be allowed to see or copy certain information relating to the study while the study is in progress, but you will have the right to see and copy the information once the study is over in accordance with NYU Langone Health policies and applicable law.

15. HIPAA Authorization

As noted in the Confidentiality section above, federal law requires us, and our affiliated researchers, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions. We are asking for your permission (authorization) to use and share your health information with others in connection with this study- in other words, for purposes of this research, including conducting and overseeing the study.

Your treatment outside of this study, payment for your health care, and your health care benefits will not be affected even if you do not authorize the use and disclosure of your information for this study.

What information may be used or shared with others in connection with this study?

All information in your research record for this study may be used and shared with those individuals listed in this section. Additionally, information in your medical record that the research team believes may be important to the study may be accessed by those listed here. This includes, for example, results from your physical examinations, laboratory tests, procedures, questionnaires, and diaries.

Who may use and share information in connection with this study?
The following individuals may use, share, or receive your information for this research study:

- The research team, including the Principal Investigator, study coordinators, and personnel responsible for the support or oversight of the study
- Governmental agencies responsible for research oversight (e.g., the Food and Drug Administration or FDA).
- Health care providers, including your doctors and others who provide services to you in connection with this study, and laboratories or other individuals who analyze your health information in connection with this study.
- Other study sites involved in the research

Your information may be re-disclosed or used for other purposes if the person who receives your information is not required by law to protect the privacy of the information.

What if I do not want to give permission to use and share my information for this study?
Signing this form is voluntary. You do not have to give us permission to use and share your information, but if you do not, you will not be able to participate in this study.

Can I change my mind and withdraw permission to use or share my information?
Yes, you may withdraw or take back your permission to use and share your health information at any time for this research study. If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. To withdraw your permission, send a written notice to the principal investigator for the study noted at the top of page 1 of this form. If you withdraw your permission, you will not be able to stay in this study.

How long may my information be used or shared?
Your permission to use or share your personal health information for this study will never expire unless you withdraw it.

16. Electronic Medical Record and Release of Study-Related Information

What is an Electronic Medical Record?
An Electronic Medical Record (EMR) is an electronic version of your medical chart within NYU Langone Health. An EMR is simply a computer version of a paper medical record.

If you are or have been a patient at NYU Langone Health in the past, you have an EMR at NYU Langone Health. Information from your research participation will be added to this EMR.

If you have never been a patient at NYU Langone Health, you may not have an EMR at NYU Langone Health. In connection with your participation in this study, an EMR will be created for you. The purpose of your EMR at NYU Langone Health will be to facilitate this research study and allow the researchers to maintain information arising from your participation in this research study. The creation of this EMR is a requirement of your participation in this study. In order to create your EMR, the study team will need to

obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility, for example, your name, the name of your primary doctor, the type of insurance you have, your date of birth and other health-related information.

What may be placed in the EMR?
Information related to your participation in the research (e.g., laboratory tests, research-related notes, imaging studies, and clinical procedures, etc.) will be placed in your EMR maintained by NYU Langone Health.

This information will be accessible to other members of the NYU Langone workforce that are not part of the research team. Information within your EMR may also be shared with others who NYU Langone Health has determined may appropriately have access to your EMR (e.g. Health Insurance Company, disability provider, etc.).

Will I have access to research-related information within the Electronic Medical Record?

The 21st Century Cures Act allows patients increased access to their EMR. If you agree to participate in this study, this means that any research-related information placed in your EMR will be available to you immediately.

As a research participant, this means that you have immediate access to any research-related information that is placed in your EMR before the researchers have had an opportunity to review the information.

The research-related information that will be available to you immediately are as follows:

- Results that may be placed in the medical record: none

Access to research-related information within your EMR can be found through NYU Langone Health's patient portal, MyChart.

In this study, some research-related information will never be made available to you in your EMR. This information will not be accessible in your EMR because the information is specific to this research and is not part of your medical history and clinical care.

- Results that will not be placed in the medical record: biospecimen testing

17. The Institutional Review Board (IRB) and how it protects you

The IRB reviews all human research studies – including this study. The IRB follows Federal Government rules and guidelines designed to protect the rights and welfare of the people taking part in the research studies. The IRB also reviews research to make sure the risks for all studies are as small as possible. The NYU IRB Office number is (212) 263-4110. The NYU School of Medicine's IRB is made up of doctors, nurses, scientists, and people from the community.

18. Who can I call with questions, or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on top of the page 1 of this consent form. If a member of the research team cannot be

reached or you want to talk to someone other than those working on the study, you may contact the Institutional Review Board (IRB) at (212) 263-4110.

When you sign this form, you are agreeing to take part in this research study as described to you. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer.

Name of Subject (Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date

Witness to Consent of Non-English Speaking Subjects Using the "Short Form" in Subject's Spoken Language

Statement of Witness

As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

Name of Witness (Print)	Signature of Witness	Date