Northwell Health

Campus: Zucker Hillside Hospital

Consent for Participation in a Research Study

Study Title: MicroRNAs in neural-derived extracellular vesicles as biomarkers in first episode schizophrenia

Principal Investigator: Juan Gallego, MD, MS

Sponsor: National Institutes of Mental Health

About this research
You are being asked to participate in a research study.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Important Information
This information gives you an overview of the research. More information about these topics may be found on the pages that follow.

Why am I being asked to provide my consent?	This is a research study, which is different from personal medical care. Scientists do research to answer important questions which might help change or improve the way we do things in the future.
Do I have to join this research study?	No. Taking part in this research study is voluntary. You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled.
Why is this research study being done?	The purpose of this research study is to identify changes in tiny molecules floating in blood called Neural-derived Exosome (NDE) MicroRNAs (miRNAs) in patients with schizophrenia compared to healthy volunteers and to evaluate whether these changes are associated with improvement of symptoms after treatment with either aripiprazole or risperidone for 12 weeks.
What will happen to me during the study?	If you choose to participate in this study, you will attend several study visits over 12 weeks. You will have research visits every week for the first month and then every other week until the end of the study. At the start of the study, you will have an electrocardiogram (EKG, a heart test) and provide a urine sample for drug screening. You will be asked questions about your symptoms at every research visit also will have tests of thinking and memory at the beginning and at the end of the study. You

	will have a blood draw at the beginning and end of the study to measure the tiny molecules (miRNAs) and a blood draw at weeks 0, 4, 8, and 12 to measure antipsychotic medication levels.
How long will I participate?	Your participation will last approximately 12 weeks.
Will taking part expose me to risks?	The most frequent side effects (occurring in 10% or more of participants) reported for risperidone and aripiprazole, as per FDA-approved labeling, include: somnolence, increased appetite, fatigue, insomnia, sedation, tremors, restlessness, vomiting, cough, constipation, drooling, dry mouth, abdominal pain, dizziness, nausea, anxiety, headache, nasal congestion, and rash. Blood collection carries risks of bruising and infection at the puncture site.
Are there any benefits to participation?	You will not have direct benefit from participating in the study, but you will likely feel better with the treatment with risperidone or aripiprazole provided by your treating psychiatrist.

Please review the rest of this document for details about these topics and additional things you should know before making a decision about whether to participate in this research.

Introduction
You are being asked to join a research study. The purpose of a research study is to answer specific questions.

You do not have to be in this study to receive medical care. You should ask questions before you decide if you want to participate. You can also ask questions at any time during the study.

Why is this research study being done?
The purpose of this research study is to identify tiny molecules floating in blood called Neural-derived Exosome (NDE) MicroRNAs (miRNAs) in Blood profiles of patients with schizophrenia compared to healthy volunteers and evaluate change scores of blood NDE miRNAs as predictors of response to 12 weeks of treatment with aripiprazole or risperidone. You are invited to participate in this study because you have been diagnosed with a first-episode psychotic disorder.

How many people will take part in this study?
This research study aims to enroll approximately 160 people (80 with a first-episode psychotic disorder and 80 healthy volunteers), and we expect about 80 to complete the full 12 weeks.

How long will you be in this study?
If you choose to take part in this study, you will do baseline assessments at the beginning of the study. After baseline assessments, participants will be followed up to the 12th week. Follow-up visits are scheduled on week 1, 2, 3, 4, 6, 8, 10 and 12. After completion of study procedures on week 12, your participation in this study will be concluded. Days of the week will vary slightly due to scheduling availability or any missed visits.

What will happen in this research study?
You will be receiving treatment with either aripiprazole or risperidone, as prescribed by your treating psychiatrist. Follow-up assessments of your clinical symptoms will occur weekly on the first month and then every other week until the end of the study.

These assessments will include questions about your diagnosis, current medications and dosages, current symptoms and will utilize the following questionnaires:

- Structured Clinical Interview for DSM-5 Research Version (SCID-5-RV) to confirm your diagnosis.
- Your psychiatric symptoms will be assessed using Brief Psychiatric Rating Scale (BPRS), the scale for the Assessment of Negative Symptoms (SANS), the Clinical Global Impression (CGI), the Columbia-Suicide Severity Rating Scale (C-SSRS), the Patient Health Questionnaire-9 (PHQ-9), the Generalized Anxiety Disorder-7 (GAD-7) and the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0)
- The presence of adverse effects will be assessed using the Systematic Assessment for Treatment Emergent Events - Specific Inquiry (SAFTEE-SI), the Barnes Akathisia Rating Scale (BARS) and the Simpson-Angus Scale (SAS)
- Your mental function will be assessed using the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery

We will also monitor your general side effects to medication, vital signs, and substance use. At the start of the study, you will have an electrocardiogram (EKG, a heart test).

Urine Toxicology:

At the start of the study, you will provide a urine sample to test for drugs and to help rule out medical conditions that can cause psychosis. The results will be shared with your treating doctor and included in a research progress note in your electronic medical record. A positive drug test will not automatically exclude you from the study, but you cannot participate if you have a moderate or severe substance use disorder (other than nicotine) or a mild substance use disorder for substances other than nicotine, cannabis, or alcohol.

Pregnancy:

You cannot participate in this study if you are currently pregnant or become pregnant during the study. For participants recruited from the inpatient unit, we will review pregnancy test results from your routine clinical care. For participants recruited from outpatient settings, we will ask you about your pregnancy status.

Blood Draws:

At your first visit (week 0), we will draw blood from your arm two times: one blood draw (about 2 tablespoons) to study your genes (DNA) and one blood draw (about 2 tablespoons) to measure tiny molecules called miRNAs. We will also draw blood at weeks 4 and 8 to check your medication levels. At your last visit (week 12), we will draw blood one time (about 2 tablespoons) to measure

the miRNAs again. The miRNA samples will be sent to the University of Alabama at Birmingham for analysis with only a code number and collection date—no information that identifies you like your name or date of birth will be included.

Genetic Testing:

We will collect one blood sample (about 2 tablespoons) at the beginning of the study for genetic testing called whole genome sequencing. This means we will look at your DNA to understand how genes might affect psychosis and treatment response. Your genetic sample and data will be stored permanently at the Boas Center Biorepository at Northwell Health. We will NOT give you any genetic results. Your genetic samples may be used for future research on mental health. You can stop allowing us to use your sample at any time. If your sample hasn't been tested yet, we will destroy it. If it has been tested, we will make it anonymous so no one can tell it's yours. All samples have your name removed before testing and are stored in locked freezers. Federal law (GINA) protects you from discrimination by health insurance companies and employers based on genetic information.

Storage of Your Blood Samples:

Blood samples collected for this study will be stored long-term (indefinitely) at the Boas Center Biorepository at Northwell Health. This special storage facility has freezers that are monitored 24/7 and have backup power in case of emergencies. De-identified samples (with only a code number, no name) will be sent to the University of Alabama at Birmingham for miRNA analysis.

These samples may be used for future research on mental health conditions, subject to IRB approval. You can request that your samples be destroyed at any time by contacting Dr. Gallego (see contact information at the end of this form). If samples have already been sent for analysis, we will destroy all information linking you to your sample, making it anonymous.

Details for the study procedures are shown below.

Timepoint (End of Week N)	0	1	2	3	4	6	8	10	12
Informed consent	X								
Med Eval, EKG, Utox, SCID-5-RV	X								
BPRS/SANS/CGI/CSSRS	X	X	X	X	X	X	X	X	X
Vitals/weight	X	X	X	X	X	X	X	X	X
SAFTEE-SI	X	X	X	X	X	X	X	X	X
SAS, BAS	X	X	X	X	X	X	X	X	X
Simpson-Dyskinesia Scale	X								X
PHQ-9, GAD-7, WHODAS 2.0	X	X	X	X	X	X	X	X	X

Antipsychotic levels	X				X		X		X
MATRICS Cog Battery	X								X
Blood collection for NDE microRNA analysis	X								X
Genetic Testing	X								

What are the risks of the research study? What could go wrong?

Risks directly associated with study treatment:
The main risks to participants are: 1) risks of blood collection, 2) risks of loss of confidentiality, 3) risks associated with genetic testing, and 4) risks of other study procedures.

Risks associated with blood draws include getting a bruise where the needle goes in. There's also a very small chance of getting an infection at that spot. Rarely, people might feel dizzy or faint when their blood is drawn. Please know that only trained staff will take your blood.

Risks of loss of confidentiality We work very hard to keep your study information private. However, there's a small chance that your personal information could accidentally be seen by unauthorized individuals.

Risks associated with genetic testing include that this private genetic information could get out. If that happened, it might (though this is rare) affect things like your health insurance, your job, or your personal privacy. Additional genetic risks include:

- Your genetic information is shared with your biological relatives, so findings could potentially affect them too, even though we won't tell you or them the results
- You might feel anxious or worried about having your genes studied, even though we won't tell you the results
- Your samples will be stored permanently, which slightly increases privacy risks over time, though we have safeguards in place
- Your samples might be used for future studies on mental health that we can't describe yet, because we don't know what questions scientists will ask in the future

Risks of other study procedures. With some of the other things we ask you to do, like answering questions, you might find them annoying, uncomfortable, or even upsetting. Remember, you don't have to answer any questions you don't want to, and you can always ask for a break.

What are the benefits of this research study?
There is no direct benefit to you for participating in this study. The results of this study may be of future benefit to society as a whole and to future patients with illnesses similar to yours, by increasing knowledge about the biological basis of psychiatric illness.

Are there any costs for being in this research study?

This research study is funded by the National Institutes of Mental Health. You will not have any added costs from being in this study. All study-related visits and procedures will be given to you at no cost. Neither you nor your insurance company will be billed for your participation in this research.

Will you receive any payments for participating in this research study?
You will be paid up to $275 for your participation in the study. You will receive $50 for completing the baseline visit (Week 0) and $50 for completing the final visit (Week 12). You will receive $25 for each of the intermediate visits at weeks 1, 2, 3, 4, 6, 8, and 10. Payment will be provided in cash or via ClinCard at the end of each completed visit. If you are under 18 years old, payment will be given to your parent or legal guardian.

If the total payment you receive from Northwell Health, during this year, is equal to $600 or more, the payment is required to be reported to the IRS. If you participate in other Northwell Health studies, it is possible your payment could end up totaling $600. If this occurs, the payment you receive on this study will be reported to the IRS. In this case, you will be issued a 1099 form and be required to provide your social security number at that time for reporting purposes. You will also be responsible for reporting this income while filing your tax return.

What happens if you are injured because of the research?

For medical emergencies, call 911 or go to the nearest Emergency Room. If you believe you have been injured because of this research study, tell Dr. Gallego right away. His contact information is at the end of this form.

You will receive medical care from Northwell Health if you are injured from research procedures like blood draws, genetic testing, the EKG, or the thinking and memory tests. However, Northwell Health may bill your insurance company for this care. You will be instructed to use your own health insurance in the event of research-related injuries. You may be responsible for costs like deductibles, co-payments, and any costs not covered by your insurance. Northwell Health will not pay you money for research-related injuries, but will provide the medical care you need.

Will my biospecimens be used to create a marketable product? And if so, will I receive payment?
If this research produces a marketable product, there are no plans for you to receive any money.

What are your rights as a research participant?
Your participation in this project is voluntary. If you do not join the study, you will not be penalized or lose benefits to which you are entitled. If you join the study, you may withdraw at any time without prejudice to your future care at the Northwell Health System. Follow-up examinations may be needed to ensure your well-being.

How We Monitor Your Safety:
Your safety is very important to us. We monitor it in several ways:

- Dr. Gallego and the study team (including Kelly Garcia) will check on your safety at every visit
- Dr. Raphael Braga, a psychiatrist not involved in the study, will review any serious side effects within 48 hours
- A Data and Safety Monitoring Board (a group of independent experts who are not part of this study) will review safety information from the study twice a year

Could you be taken off the study before it is over?
It is also possible that your participation in this study may end without your consent. This decision may be made by a researcher, study sponsor, or the Institutional Review Board (IRB- the committee that oversees research at this institution).

Reasons for withdrawal may include:

- failure to follow instructions,
- failure to show up for study visits,
- it is not in your best interest to continue on this study, or
- the study is stopped.
- your doctor decides to change your medication to something different from aripiprazole or risperidone
- the study team or an independent safety monitor determines it is not safe for you to continue
- you lose the ability to make decisions for yourself during the study
- you develop a substance use problem that makes you ineligible

If you decide to leave the study before 12 weeks have passed, we might offer you a chance to do a final check-up. This check-up would involve a blood test (for microRNA) and some brain games, just like the ones you'd do at Week 12. You don't have to do this final check-up to leave the study; it's totally up to you.

What happens if new information is learned?
You will be told of any new findings that may change your decision to continue to participate. Your consent to continue participating in this study may be obtained again.

What will happen with the information we collect as part of this research study?
Any identifiable study information about you will be kept private and separated from the collected data. Your name, date of birth, address, and any other identifiable information will not be shared outside of the researchers directly involved in this study without your permission (except when required by law or for regulatory oversight). Your research records will be private to the extent allowed by law.

We may use your de-identified (coded) data for future research and share it with trusted partners to process and study it. This data may be stored for a long time in secure databases used by researchers around the world. We will enter a few details (your first and last name, date of birth, city of birth and sex at birth) into a computer program on our computer to create a special code called a GUID. This identifying information is used only on our computer to create your code and is NOT sent to the NIMH Data Archive. The database will never receive your name, date of birth, or city of birth. After the GUID is created, your de-identified data (without your name or other direct identifiers) will be shared with the NIMH Data Archive, as required by our funding. Only approved researchers can access it. If we publish study results, we won't use your name or any details that could identify you.

To make sure the research is done properly, the Human Research Protection Program (a group of people that oversee research at this institution) may need access to information about your participation in this study.

Your data will be used and analyzed to answer scientific questions.

Who else will see your information?
Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside Northwell Health, except as detailed below.

Investigators will share information collected from this research study with:

- Study sponsor and/or its agents,
- Other researchers,
- Accrediting agencies,
- Clinical staff not involved in the study, who may be involved in participant's treatment, such as billing.
- De-identified blood samples (labeled only with a code number and collection date) will be sent to the University of Alabama at Birmingham for laboratory analysis.

The following reviewers may access your study and medical records to make sure that this study is being done properly:

- Representatives from Northwell Health's Human Research Protection Program (a group of people that oversee research at this institution)
- Representatives from federal and state government oversight agencies such as the Food and Drug Administration

We will do our best to protect the privacy of your records, but it is possible that once information is shared with people listed on this form, it may be released to others. If this happens, your information may no longer be protected by the federal law.

In the future, we may publish results of this study in scientific journals and may present it at scientific meetings. If we do, we will not identify you.

If the researchers learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

Will you be able to access your records?
If your research records are used for decisions related to your clinical care, then you have the right to review this information and request changes. This is limited to information about your treatment and does not include information related to procedures or tests that are for research purposes only. You may access this information only after the study analysis is complete. You have the right to know who has and who will see your records. To request this information, please call the Human Research Protection Program on 516-465-1910.

How long will your health information be kept?
There is no limit on the length of time we will keep your information for this research because it may be analyzed for many years. We will keep it if it is useful, unless you decide you no longer want to take part, or we close the study. You are allowing access to this information indefinitely.

Can you change your mind?
If you change your mind about being in the study, you may withdraw at any time. If you want us to stop collecting your health information, you need to send a letter to the researcher at the following address:

Juan Gallego, MD, MSc
The Zucker Hillside Hospital
75-59 263rd Street, Glen Oaks
New York, NY 11004

Your letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information. You may also need to leave the research study if we cannot collect any more health information. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

Will information about this study be available to the public?
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this website at any time.

Certificate of Confidentiality
To help us protect your privacy, this research is covered by a Certificate of Confidentiality from the US Department of Health and Human Services (DHHS). The Certificate of Confidentiality means that researchers cannot be forced to identify you, even under a court subpoena. The Certificate does not mean the Secretary of DHHS approves or disapproves of the project. It adds special protection for the research information about you. You should know, however, that researchers may provide information to appropriate individuals or agencies if harm to you, harm to others or child abuse becomes a concern. A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research.

However, if an insurer, employer or other person learns about your participation and gets your consent to receive research information, then the researchers will have to provide your information.

Does the investigator of this study receive money if you take part?
The investigators on this study receive money to conduct the study, but do not financially benefit from your participation. The money they receive is to pay them back for the costs of conducting the research study. Funding for this research study is provided by National Institutes of Health. If your doctor is an investigator for this study, she/he is interested in both your healthcare and the conduct of this research. You do not have to take part in a research study conducted by your doctor.

Who can answer your questions about this study?
If you have any questions about the study, or if you have questions about side effects or injury caused by research, you may call Dr. Gallego at (718)470- 4588. If you need emergency services, dial 911 or go to the nearest Emergency Room. If you have questions about your rights as a research participant, concerns about being in the study, or would like to offer input, you may contact the Office of the Institutional Review Board (the committee that oversees research at this institution) at (516) 465-1910.

Alternative options to be contacted:
We have found that it is often easier to reach participants for the purposes of scheduling and confirming research activities via text message or email. If you consent to allow us to contact you via text message or email, we will send you messages using the cell phone number and/or email address you provide below. Text messages will be sent to remind you of upcoming appointments and/or to request that you contact the study coordinator for additional information about the study. Examples of these messages include:

"Just a reminder that you have an appointment with *(staff member name)* on Tuesday from 10:00am to 1:00pm. Please let us know if you will be able to make it!".
"We've been trying to reach out to you about your participation in the research project". Please give *(staff member name)* a call at (xxx) xxx-xxxx".

Any cell phone number or email address that specifically identifies you will not be used to report information about the project. We will store this information separately from other data you give us to protect your identity to the maximum extent possible. However, although every reasonable effort will be taken to protect your confidentiality, the confidentiality of internet communication cannot be guaranteed, and text messages are not encrypted or secure during their transmission.

Thus, it is possible that this information may be captured or intercepted and used by others not associated with this study.
If you agree to be contacted via text message, please be aware that charges may be incurred by your cellular provider if your usage plan limits the number of text messages you are allowed. If this may be a problem for you, you may wish to only allow us to contact you via email.

- ❑ I give the study staff permission to contact me via text messaging at the following cell phone number: (__ __ __) __ __ __ - __ __ __ __

- ❑ I give the study staff permission to contact me via email at the following address: _____@_____
- ❑ I do not wish to be contacted via text or email messages.

Might I be contacted after this study is over?

With your permission, we may contact you after the conclusion of this study to ask if you would like to participate in other studies. This is optional and you can still participate in this study even if you do not want to be contacted after it is over.

- ❑ YES – you may contact me about future studies.
- ❑ NO – you may not contact me about future studies.

A signed copy of this consent form will be given to you.

Assessment of Understanding: Before you sign this consent form, you will be asked to complete a brief questionnaire to make sure you understand the key points of this study. A member of the research team will review the questionnaire with you.

Summation/Signature

You have read the above description of the research study. You have been told of the risks and benefits involved, and all your questions have been answered to your satisfaction. A member of the research team will answer any future questions you may have. You voluntarily agree to join this study and know that you can withdraw from the study at any time without penalty. By signing this form, you have not given up any of your legal rights.

For subjects 18 or older:

_____	_____	_____
Printed Participant's Legal Name	Subject's signature	Date
_____	_____	_____
Witness's Printed Name	Witness's Signature	Date

For subjects 15-17 years old:

_____

Printed Participant's Legal Name

_____
Parent's or Legally Authorized Representative's printed name

_____ _____
Parent's or Legally Authorized Representative's signature Date

_____
Description of signer's authority to act on behalf of the participant

_____ _____ _____
Witness's Printed Name Witness's Signature Date

Investigator's Statement

In addition to advising the above participant of other forms of treatment and therapy which are appropriate, I have offered an opportunity for further explanation of the risks and discomforts which are or may be associated with this study and to answer any further questions relating to it.

_____ _____ _____
Investigator's signature Investigator's printed name Date