PARTICIPANT INITIALS _____

Consent to Participate in Research

Sponsor / Study Title:	**Lung Institute Dallas / "An Observational Outcomes Study For Autologous Cell Therapy Among Patients With COPD And Interstitial Lung Disease: Cohort B Study Investigator(s)"**
Protocol Number:	**LI-002**
Principal Investigator:	**Melissa Rubio, PhD, FNP**
Telephone:	**(214) 299-8118 (24hr)**
Address:	**Lung Health Institute Dallas** **8140 Walnut Hill Lane, Suite 570** **Dallas, TX 75231**

General Information

Please read this form carefully. To be in a research study you must give your informed consent.

"INFORMED CONSENT" INCLUDES:

- Having the study doctor or study staff explain the research study to you
- Asking questions about anything that is not clear, and
- Taking home an unsigned copy of this consent form. This gives you time to think about it and talk to family or friends before you make your decision.

YOU SHOULD NOT JOIN THIS RESEARCH STUDY UNTIL ALL OF YOUR QUESTIONS ARE ANSWERED. THINGS TO KNOW BEFORE DECIDING TO TAKE PART IN A RESEARCH STUDY:

- The main goal of regular medical care is to help each patient.
- No one can promise that this study treatment or research study will help you.
- Taking part in a research study is entirely voluntary. No one can make you take part.
- During your study treatment, you will receive standard medical care. Standard care is the treatment normally given for a certain condition, such as a medical emergency.
- Your medical records may become part of the research record. If that happens, your medical records may be looked at and/or copied by the sponsor of this study and government agencies or other groups associated with the study.

AFTER READING AND DISCUSSING THE INFORMATION IN THIS CONSENT FORM YOU SHOULD KNOW:

- Why this research study is being done and why this consent is required
- What will happen during the research
- What study treatment procedures will be used
- Any possible benefits to you
- The possible risks to you
- The other medical procedures, drugs or devices that could be used instead of being in this research study
- How potential problems will be treated during the study and after the study is over.

If you are pregnant, or have reason to believe that you may be pregnant, you must notify the Lung Institute Principal Investigator immediately.

If you take part in this research study, you will be given a copy of this signed and dated consent form.

Any significant new findings developed during the course of the research study which may relate to your willingness to participate will be provided to you.

Study Description

Sponsor: Lung Health Institute **Protocol Number:** LI-002

Title: An Observational Outcomes Study for Autologous Cell Therapy Among Patients with COPD and Interstitial Lung Disease

This study involves exploring the outcomes of study treatment using your body's own, minimally manipulated cells to promote repair of damaged lung tissue from chronic lung disease. The aim of the study is an improvement in your pulmonary (lung) function and quality of life after study treatment.

THIS STUDY INVOLVES RESEARCH

Because this study uses cells from your own body, we are exempt from Food and Drug Administration (FDA) oversight. In the state of Texas, whenever stem cell treatment is used it is considered investigative and strict procedures and oversight of your study treatment are required and ensured. In addition, we will be tracking data on the outcomes of all of our treated participants in order to inform future patients and the future of cellular medical therapy.

Study Procedures

HOW MANY PARTICIPANTS WILL BE ENROLLED IN THE STUDY?

Patients may be enrolled in the study throughout the duration of the study, no approximate amount of participants have been set. Duration of study is set one year from approval date.

WHAT WILL I BE ASKED TO DO IF I PARTICIPATE IN THE STUDY?

Participants in this study are asked to provide Lung Institute with feedback regarding your progress, specifically as it relates to your quality of life improvements and PFT (lung function test) results. Feedback will be obtained over the course of six months, and up to a year.

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to obtain information regarding the efficacy of cell treatments for treating chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD). The application of autologous (participant's own) cells is performed to diminish inflammation and improve pulmonary function. The application of cells can be utilized as a stand-alone procedure or as an adjunct (in addition) to other procedures.

HOW LONG WILL I BE ASKED TO PARTICIPATE IN THIS STUDY?

Study treatments are conducted over the course of 2 days; thereafter, you will be expected to provide Lung Institute with feedback regarding your progress, specifically as it relates to your quality of life improvements and PFT results. Feedback will be obtained over the course of six months, and up to a year. Outreach to obtain results will be conducted at a minimum of 2 weeks, 3 months, and 6 months.

PARTICIPANT INITIALS _____

Consent

I understand that Lung Health Institute (LHI) will perform the following type(s) of study procedure:

VENOUS STUDY TREATMENT

- Drawing of blood
- Processing blood to separate cells
- Administration of PRP-PC (Platelet Rich Plasma-Platelet Concentrate) to participant

Data will be collected on your medical diagnosis, pulmonary function test results before and after study treatment, and your perceived quality of life scores before and after study treatment. We will follow up with you by phone two weeks, three months and six months after your study treatment to collect this information.

Risks and Minimizing Risks

What risks will I face by participating in this study?
Although there are risks associated with the application of cell treatments, the risks are minimized by applying your autologous cells in the same day that they are extracted and minimally processed. Additional risk factors may be mitigated with appropriate protocols focused on participant safety; therefore, the overall risk to benefit relationship results in a study treatment with minimal risks which may or may not improve a participant's quality of life.

- **Adverse reaction to cells** - There is a possibility of an adverse reaction to the application of cells. This risk is minimized by using autologous (your own) minimally manipulated cells.
- **Anemia** - There have been reports of anemia with harvesting of cells from the circulation. This risk is low. To minimize this risk we request blood work (CBC).
- **Bleeding** - It's possible, though unusual, to experience an episode of bleeding, which may be excessive, during or after a procedure or study treatment. Bleeding may require additional treatment or transfusion of blood or blood products. Certain medications, such as aspirin, anti-inflammatory drugs or blood thinners may increase the risk of bleeding. This risk will be minimized by a review of your medical history and medications prior to your procedure as well as the application of appropriate pressure to the study treatment site whenever bleeding could occur.
- **Blood clot development** - Blood clots may occur with any type of procedure or treatment. Clots can block blood flow and cause complications, including pain, swelling, inflammation, tissue damage, pulmonary emboli (a blood clot causing blockage of an artery in the lungs) or death. We will minimize this risk by utilizing safe and appropriate treatment modalities.
- **Death** - Although the risk is remote, death may occur during or soon after any procedure or surgical procedure. We will minimize this risk by using safe and appropriate treatments.
- **Dizziness** - Dizziness may occur after harvesting of cells. It usually responds to IV fluids. You can minimize this risk by ensuring that you are well-hydrated and have eaten the day of your procedure.
- **Embolus development** - An embolus is a clot that can be from blood or cells. There is a chance that an embolus or emboli (plural) may develop with cell procedures. This risk is low and is minimized due to our cell processing protocols.
- **Failure of the procedure** - There is a chance that undergoing cell application will not alleviate symptoms, reduce inflammation or improve lung function. Recurrence of pulmonary (lung) symptoms may recur.
- **Fever** - Fever associated with cell harvesting usually responds to acetaminophen (for example, Tylenol). If fevers persist, a work-up for infection must be completed.

- **Hypotension** - Hypotension or low blood pressure has been reported after harvesting of cells. It usually responds to IV fluids. This risk can be minimized by ensuring that you are well-hydrated and have eaten the day of the procedure.
- **Infection** - Infection may occur at the IV site and the site of application of your cells. To minimize risk infection prevention protocols are maintained and followed during the study treatment process and participant education is provided on post study treatment cleaning and wound care.
- **Pain** - Any procedure can result in pain. To minimize this risk, we ask that our participants communicate any discomfort so that we can reduce or mitigate (lessen).
- **Nausea/vomiting** - Nausea and vomiting have been reported with cell harvesting. This is usually temporary and responds to supportive care. Again, this can be minimized with good hydration and nutrition the day of the procedure.
- **Numbness/tingling** - Although a low risk, this has been reported with leukapheresis (the process of separating cells from peripheral blood in the vein). Laboratory analysis may be required along with calcium infusion.
- **Respiratory difficulties** - Breathing difficulties (which are usually temporary) or post-operative pneumonia, may occur as a result of any procedure or surgery. Pulmonary embolus, a blood clot causing blockage of an artery in the lungs may occur as a result of any procedure or surgery. Pulmonary embolus may be fatal.
- **Scar Formation** - Scar tissue forms as a part of the natural healing process after any procedure, surgery or injury. In rare circumstances, some patients can form excessive amounts of scar tissue that can be a source of pain. Scarring can by minimized by massage and applying vitamin E oil to the site after the incision has healed completely. Unfortunately, not all scarring can be prevented.
- **Soreness** - Pain at the site of cell harvesting or site of application will occur. It is unlikely to be permanent. We will minimize this risk using local anesthetic during the procedure.
- **Stroke** - Though a low risk and unlikely, there is a possibility that a stroke will occur during the procedure or in the recovery period.
- **Transfers of undiagnosed cancer** - There is a risk that undiagnosed cancer in the area where the cells are harvested may be transferred to the participant's area of transplantation. To minimize risks, cells will not be altered in any way, thereby reducing the risk of tumor induction by carcinogens.
- **Administration of incorrect cells** - The cells administered are the participant's own cells. There is a low risk of administration errors. Materials are clearly marked before they leave the procedure room, eliminating the risk of a participant receiving someone else's cells in error.
- **Tumorigenicity** - There is no evidence that point-of-care adult cellular therapy cause tumors. Initial concerns on tumorigenicity (formation of tumors) after adult cellular therapy decreased as experimental and clinical data have revealed no such complication reported to date. Human mesenchymal stem cells can undergo spontaneous transformation following long-term in vitro (out of the body) culture of approximately 4-5 months. Your cells will not be cultured and will be used immediately during the procedure, thereby minimizing this risk.
- **Unintended differentiation** – Stem cells and progenitor cells are cells that have the ability to develop into one of several different types of cells. The cells may transplant into an area of the body and start to grow into certain types of cells that we do not want them to grow into. Although rare, in a single study it was found that bone-marrow harvested stem cells transplanted into rats caused a calcification, or hardening, of the cells of the rat's heart that was not intended. Though a low risk, unintended differentiation could occur in areas of stem cell implantation.
- **If Pregnant** - Or may become pregnant, there may be risks to you, the embryo or fetus that are unforeseeable. If you are pregnant, or have reason to believe that you may be pregnant, you must notify the Lung Health Institute Principal Investigator immediately.

Potential Benefits

You may or may not benefit as a result of your participation in this study.

- Increased Activity - Ability to be more physically active; walking greater distances.
- PFT - Improvement in FEV1 of 5-10% or more.
- Oxygen - Ability to reduce use of oxygen and possibly to stop it.
- Reduction in Medications - Ability to function well without the use of bronchodilator inhalers and Prednisone.
- Increased Pulmonary Health - Reduction or ceasing of secondary pulmonary infections.

Source of Funding for the Study

WILL I BE CHARGED ANYTHING FOR PARTICIPATING IN THIS STUDY?

There is no cost to you to participate in the data collection and investigation of your response to study treatment.

At this time, insurance companies are not covering the cost of cellular therapy for chronic pulmonary diagnosis; therefore, the cost of study treatment is the responsibility of the participant. It will likely be a few more years before insurance covers the cost of this cellular therapy. If you have questions about this, a patient coordinator will be able to help.

WHAT SERVICES ARE COVERED UNDER PAYMENT OF INVESTIGATIVE CELLULAR THERAPY?

Payment in full for investigative cellular therapy accounts for medical, surgical, facility, and office services rendered by Lung Health Institute (LHI) for consented procedures. Additional medical services rendered by external providers and facilities are not covered under your investigative cell therapy payment, and therefore fall under participant's financial responsibility. Should additional medical services be required due to injury sustained at an LHI facility, LHI will agree to review the case and make a determination for possible reimbursement of related, reasonable, and necessary medical expenses not routinely covered by insurance for the required tests and study treatments; however, participants should assume they will not receive reimbursement for study-related injuries.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and social security number or Medicare Health Insurance Claim Number. This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

You will not lose any of your legal rights or release the sponsor, the Investigator, the study staff, or study site from liability for mistakes by signing this consent document.

ARE PARTICIPANTS PAID OR GIVEN ANYTHING FOR BEING IN THE STUDY?

No. You are not given any payments for your participation during or after the study.

Confidentiality

WHAT HAPPENS TO THE INFORMATION COLLECTED?

All information collected about you during the course of this study will be kept confidential to the extent permitted by law. We may decide to present what we find to others, or publish our results in scientific journals or at scientific conferences. Only the Principal Investigator and clinic study staff will have immediate access to the information. However, the Institutional Review Board or appropriate federal agencies like the Office for Human Research Protections may review your records.

WHY IS MY INFORMATION COLLECTED?

It is important to us and to the future of cellular therapy that we track your response to study treatment over time. This information will be used to inform future patients and the medical community of the results of cellular treatment for chronic lung disease.

HOW IS MY INFORMATION PROTECTED?

The protection of confidential health information is of the highest importance. Your electronic medical record is protected by safeguards to ensure that only the study staff that are required to view your records do so. Oversight of clinic study staff and of your protected health information is enforced by the Compliance Department of Regenerative Medicine Solutions and by the Institutional Review Board.

HOW AM I PROTECTED?

Clinic study staff are trained in the protection of human participants in research. The Compliance Department and Institutional Review Board ensure that clinic study staff protects both you and your health information during your study treatment.

Department of Health and Human Services (DHHS) Required Statement

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 Web site at any time.

Alternatives

ARE THERE ALTERNATIVES TO PARTICIPATING IN THE STUDY?

- Using medication to assist with symptoms;
- Lung Transplant/Lung Reduction Surgery;
- Undergoing physical therapy (Pulmonary Rehabilitation);
- Acupuncture;
- Mind-body medicine;
- Chiropractic treatment;
- Lifestyle modification;
- Nutritional modification/supplements;
- Hypnosis; and
- Interactive guided imagery.

The study doctor will discuss the risks and benefits of alternate treatments with you.

Voluntary Participation and Withdrawal

WHAT HAPPENS IF I DECIDE NOT TO BE IN THIS STUDY?

Your participation in this study is entirely voluntary. You may choose not to take part in this study, or if you decide to take part, you can change your mind later and withdraw from the study. There is no penalty or loss of benefits to you. If you decide not to participate in the study, it will not affect the resources available to you, your care received at the clinic nor your relationship with the clinic.

PARTICIPANT INITIALS _____

Involuntary Withdrawal

UNDER WHAT CIRCUMSTANCES WOULD MY PARTICIPATION IN THE STUDY BE WITHDRAWN WITHOUT MY CONSENT?

If you decide not to participate in the feedback portion of this study, your participation may be terminated due to Lung Institute's inability to gather information regarding your progress which would be necessary to gather results data and to identify the efficacy of our study treatments. If you decide to leave the study, please contact the study doctor or study staff at the telephone number listed on the first page of this form.

Questions

Whom to contact about this study

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document or **mrubio@lunginstitute.com**.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00022039.

WHO DO I CONTACT FOR COMPLAINTS ABOUT LUNG INSTITUTE AND MY CELLULAR THERAPY TREATMENT?

At the Lung Institute, you may contact our Compliance Department at (855) 469-5864. By law, you cannot be penalized for filing a complaint.

Signatures

RESEARCH PARTICIPANT'S CONSENT TO PARTICIPATE IN RESEARCH:

To voluntarily agree to take part in this study, you must sign and date on the line below. You are not giving up any of your legal rights by signing this form. Your signature below indicates that you have read or had read to you this entire consent form, including the risks and benefits, and have had all of your questions answered, and that you are 18 years of age or older.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

PRINCIPAL INVESTIGATOR (OR Study DESIGNEE)

I have given this research participant information on the study that is accurate and sufficient for the participant to fully understand the nature, risks and benefits of the study.

_____ _____

Printed Name of Person Obtaining Consent Study Role

_____ _____

Signature of Person Obtaining Consent Date