Clinical Safety Evaluation and Preliminary Efficacy Study of Subcutaneous Myografts Transplantation

Informed Consent Form

Protocol Version: V1.0; Protocol Date: January 20, 2026

We are conducting a research study entitled "Clinical Safety Evaluation and Preliminary Efficacy Study of Subcutaneous Transplantation of Autologous Differentiated Myocytes." Based on your medical condition, you may be eligible to participate in this study. We would like to invite you to take part. This informed consent form provides information about the purpose, procedures, potential benefits, risks, inconveniences, and discomforts of the study. Please read it carefully before deciding whether to participate. During the consent discussion, you may ask questions at any time and request clarification from the investigator. You are encouraged to discuss participation with your family members, friends, and your physician before deciding. If you are currently participating in another clinical study, please inform the study doctor or research staff.

Principal Investigator: Professor Yin Pengbin

Leading Institution Investigator: Professor Yin Pengbin

Site Principal Investigator: Professor Yin Pengbin

1. Why Is This Study Being Conducted?

This study is funded by the National Natural Science Foundation of China and aims to evaluate the safety and preliminary efficacy of subcutaneous transplantation of autologous differentiated myocytes in patients with long-term bed rest. Prolonged bed rest or loss of mobility leads to skeletal muscle disuse, reduced protein synthesis, and rapid fiber loss. Importantly, skeletal muscle is not only a motor organ but also an endocrine organ that secretes myokines, which regulate energy metabolism, inflammatory responses, and multi-organ homeostasis. Muscle atrophy significantly reduces myokine secretion, thereby aggravating insulin resistance, chronic inflammation, systemic metabolic disorders, and degenerative changes. Current interventions, such as passive exercise, physical therapy, and nutritional support, have limited effectiveness and cannot maintain long-term muscle mass. Therefore, there is a clinical need for a substitute muscle tissue that can survive long term, mimic "exercise-like" activity, and exert endocrine regulatory effects. Mature myocytes are terminally differentiated cells and represent a safe and programmable cell therapy platform. Our

previous studies have developed a novel technique for subcutaneous transplantation of autologous differentiated myocytes, creating muscle grafts with spontaneous contractile activity and good vascularization. These grafts can continuously secrete myokines and may fundamentally improve muscle atrophy, sarcopenia, and systemic metabolic disorders in long-term bedridden patients.

二、Who will be invited to participate in this study?

This study plans to invite participants aged 18–80 years, of any sex, who have long-term bed rest or marked activity restriction, show signs of muscle atrophy/sarcopenia, and are deemed eligible by the study physician. A history of long-term bed rest is defined as continuous bed rest for ≥4 weeks, due to causes including neurological injury (e.g., brain death, stroke, spinal cord injury), recovery after major orthopedic surgery, intensive care, or activity limitation related to chronic diseases. Evidence of muscle atrophy includes a significant decrease in muscle volume or muscle strength confirmed by clinical evaluation and imaging. Based on dual-energy X-ray absorptiometry (DXA), the appendicular skeletal muscle mass index (ASM/height²) is < 7.0 kg/m² in men and < 5.4 kg/m² in women (EWGSOP2). Written informed consent must be obtained from the patient's immediate family member or legal guardian, including consent for muscle biopsy, and the general health condition must permit subcutaneous transplantation. The underlying disease must be stable (APACHE II score 0–20), with no acute exacerbation or contraindications to surgery/transplantation. Detailed inclusion and exclusion criteria will be explained by the study physician during screening and will be determined according to the study protocol and screening results.

3. How many people will take part in this study?

A total of 6 participants are planned to be enrolled, and this study center plans to recruit approximately 6 participants.

4. How will the study be conducted?

After signing the informed consent form, screening will be performed. The research team will collect baseline information, including age, sex, and body mass index (BMI), and will complete laboratory tests such as complete blood count, CRP, liver and kidney function tests, and creatine kinase (CK). Dual-energy X-ray absorptiometry (DXA) will be used to assess appendicular skeletal muscle mass, providing baseline data for subsequent comparisons.

After confirming that the participant meets health requirements and has no contraindications, a qualified surgeon will obtain a small piece of muscle tissue (approximately the size of a grain of rice)

using a minimally invasive method during a routine clinical procedure (e.g., surgery). The tissue will be immediately sent to a GMP-compliant cell preparation laboratory for isolation of muscle satellite cells, in vitro expansion, and induced differentiation, ultimately yielding mature autologous differentiated myocytes. Before implantation, all cells must pass strict quality testing, including sterility, cell viability, purity, and secretory function assessment, to ensure safety and suitability for implantation.

After completion of in vitro preparation, in a sterile environment, 1×10^8 mature differentiated myocytes will be mixed with 6 mL of collagen to prepare an injectable muscle graft. Bilateral multi-point subcutaneous injections will then be administered into the abdominal region (≤1 mL per injection point; depth 1–2 cm) to form an evenly distributed cell layer. After injection, local compression dressing will be applied, and the participant will be observed for at least one hour to ensure that there is no obvious bleeding, allergic reaction, or other acute adverse event. Participants will be advised to avoid strenuous activity, compression, or immersion of the injection area for 72 hours after the procedure.

After implantation, participants will enter a standardized follow-up phase. The research team will conduct follow-up evaluations on postoperative Day 1, Day 7, Day 14, and at Months 1, 3, 6, and 12. Assessments include monitoring of vital signs; evaluation of redness, swelling, or induration at the injection site; changes in complete blood count and inflammatory markers; liver and kidney function; and CK levels. In addition, graft survival, angiogenesis, and structural integration will be dynamically assessed by ultrasound or MRI. DXA will be repeated at specific time points (Months 3, 6, and 12) to evaluate improvements in muscle mass. If necessary, handgrip strength testing, energy metabolism assessment, and other measures will be used for comprehensive evaluation.

Throughout the study, all biological samples and clinical data will be managed using an anonymized coding system. Identifying information and test data will be stored separately, and access will be restricted to authorized study personnel only. The research team will continuously monitor potential risks, such as minor bleeding, infection, or allergic reactions, and a 24-hour emergency management mechanism will be in place. The study protocol has been reviewed and approved by an independent ethics committee (approval number attached to the informed consent form). Your voluntary participation and right to withdraw at any time will be fully respected.

Your participation will help promote the development of subcutaneous transplantation of

autologous differentiated myocytes and support future precision treatment strategies. Study results will provide you with a personalized health report to help you better understand your health status.

If you participate, you will be asked to:

Participate voluntarily and sign the informed consent form before the study begins; follow the clinical research protocol and the unified arrangements of the investigators. You will cooperate with the research team in clinical data collection, including medical history, physical examination, neuropsychological assessment, necessary neuroimaging examinations, and collection of blood, urine, or other biological samples. Some examinations may take time or cause inconvenience, such as multiple hospital visits, blood draws, and imaging tests, and may cause mild discomfort. If you have any questions about study examinations or procedures, you may consult the study physician.

Before entering the study, you should prepare as required. For example, avoid coffee and alcohol for 24 hours before assessments or interventions; do not smoke; do not take unapproved medications; and ensure adequate sleep the night before assessments. During the study, your treating physician will inform you which medications may be continued and which should be paused or avoided. If you need to use any new prescription drugs, over-the-counter drugs, herbal medicines, or nutritional supplements during the study, please inform the study physician in advance and use them only after approval to ensure data accuracy and safety.

In addition, during participation in this study, you may not concurrently participate in any other clinical trials involving drugs, cell therapies, or medical devices. This is because other studies may affect objective assessment of your condition, interfere with study results, or increase unnecessary health risks. If you have questions about any procedures, medication restrictions, or lifestyle precautions, you may ask the research team at any time, and we will provide clear explanations and necessary assistance.

5. How might participation affect your daily life?

When deciding whether to participate, please carefully consider how the examinations and follow-up visits listed above may affect your daily work and family life, including the time and transportation required for each visit. If you have any questions about the examinations or procedures involved, you may contact us.

During the study, please follow the study physician's arrangements. If you need to use new prescription drugs, over-the-counter drugs, herbal medicines, or nutritional supplements, please

inform the study physician first. For your safety and to ensure valid study results, you may not participate in any other clinical studies involving drugs or medical devices during the study period.

6. What Are the Risks and Possible Adverse Effects of Participating in This Study?

The research staff will closely monitor any side effects during the study. If you experience any side effects or discomfort at any time during the trial, it is very important that you report them to the research team immediately. If you or the investigators believe that you cannot tolerate these side effects, you may withdraw from the study.

This study involves subcutaneous transplantation of autologous differentiated myocytes derived from your own muscle tissue. Overall, the risk is relatively low; however, some discomfort or medical risks may still occur. During muscle tissue collection, although the procedure is minimally invasive and performed under local anesthesia, adverse effects such as mild pain, transient bleeding, subcutaneous bruising, or infection may occur. In rare cases, local treatment or antibiotic therapy may be required. During the cell implantation procedure, the transplanted cells are derived from your own body; therefore, the theoretical risk of immune rejection is low. However, local reactions at the injection site may occur, including redness, swelling, induration, fluid exudation, localized pain, or mild inflammatory responses. In a small number of participants, subcutaneous nodules or fibrosis may develop. In addition, collagen, used as a carrier material, has occasionally been reported to cause mild allergic reactions or local swelling, which are usually relieved with symptomatic treatment. In very rare cases, more serious adverse events may occur, such as deep infection, hematoma formation, graft necrosis, anaphylactic shock, or abnormal local tissue proliferation. If any of these occur, the research team has a 24-hour emergency response mechanism to provide prompt medical management and will terminate the study intervention if necessary.

Furthermore, as autologous differentiated myocyte transplantation is a novel therapeutic approach, its efficacy is not guaranteed. It is possible that the graft may not survive or that the expected improvement in muscle mass may not be observed. Participation in this study will not affect your existing treatment plan.

You may experience adverse reactions during the study. All adverse events will be monitored. If you experience any adverse effects between scheduled visits, please contact your study physician promptly. Some questionnaire items may make you feel uncomfortable; you may choose not to answer them. At any time during the study, including data collection, you have the right to withdraw.

We will make every effort to protect your personal information from disclosure. All study procedures will strictly comply with relevant clinical practice standards, ethical principles, and applicable laws and regulations. If you have any questions regarding the examinations or procedures involved in this study, please consult the study physician.

Known Risks: Muscle biopsy will be performed by qualified physicians and is generally safe and controllable. However, short-term discomfort may occur in a small number of participants. For example, mild pain or soreness at the biopsy site may last for 1–2 days and can be relieved with physician-recommended analgesics. Some individuals may experience local bruising or swelling, which usually improves with cold compresses. Infection is rare, with an estimated incidence of less than 1%. After subcutaneous injection, local redness, induration, mild pain, serous exudation, or slight fever may occur. These symptoms usually resolve with observation or symptomatic treatment. If fever (body temperature >38.5°C) or worsening redness and swelling occur, please contact the research team immediately.

Unknown Risks: There may be risks or adverse effects that are currently unforeseeable. Despite strict protective measures, medical research may involve unpredictable risks, such as individual variability in recovery or unknown long-term effects during follow-up. If you experience any abnormal symptoms, regardless of whether they are described above, please contact the study physician immediately. Thank you for your understanding and contribution.

7. What Are the Possible Benefits of Participating in This Study?

If you agree to participate, you may or may not receive direct medical benefits. If you choose not to participate, your current and future medical care will not be affected. Even if you consent to participate, you may change your mind and withdraw at any time without affecting your access to standard medical services.

Direct Benefits: The autologous differentiated myocyte subcutaneous transplantation technique used in this study is designed to mimic sustained mild exercise and to secrete myokines. Some participants may experience positive changes after treatment, such as increased skeletal muscle mass, improved local muscle strength, enhanced physical endurance, reduced inflammatory markers, or improved metabolic function (e.g., blood glucose or lipid levels). These potential benefits may help delay or improve sarcopenia, frailty, and metabolic disorders associated with long-term bed rest.

In addition, all participants will receive comprehensive health assessments, including DXA-based muscle mass evaluation, inflammatory and metabolic marker monitoring, and nutritional and exercise guidance. These assessments may help you better understand your overall health status and potentially optimize subsequent rehabilitation or treatment strategies.

Potential Benefits: Data generated from this study will provide clinical evidence regarding the safety, feasibility, and preliminary efficacy of autologous differentiated myocyte transplantation. This may support the development of future precision therapies for sarcopenia, muscle loss due to long-term bed rest, metabolic disorders, and age-related frailty. Such advances may benefit you or other patients with similar conditions in the future.

Any study-related findings that may affect your or your family's health will be communicated to you in a timely manner.

8. Are There Alternative Treatment Options If You Do Not Participate?

You may choose not to participate in this study without any impact on your access to standard medical care. Conventional interventions for muscle atrophy related to long-term bed rest include rehabilitation training or passive exercise, physical therapy, nutritional support, and standardized treatment of underlying diseases. Please discuss specific options with your treating physician.

9. Is Participation and Completion of This Study Mandatory?

Your participation in this study is entirely voluntary. You may refuse to participate, and this decision will not negatively affect your current or future medical care. Even after consenting, you may withdraw at any time without discrimination, retaliation, or loss of medical benefits. When you decide to withdraw, please inform your study physician, who can provide appropriate medical advice and guidance.

Your participation may be terminated under certain circumstances, including but not limited to: The investigator determines, based on safety considerations and examination results, that continuation is not in your best interest; Significant deviation from the study protocol as judged by the investigators; Loss to follow-up. If you require other diagnostic or therapeutic interventions, fail to comply with the study plan, or for any other reasonable reason, the investigator may terminate your participation.

The sponsor or regulatory authorities may also terminate the study during its conduct. If the

study is terminated early, you will be notified promptly, and the investigators will provide recommendations for subsequent care based on your health status.

For participants who withdraw early, a final follow-up visit may be planned for safety reasons; you have the right to decline this visit. If new information relevant to your health or rights becomes available after withdrawal, the research team may contact you again.

In principle, after withdrawal, your information will be securely stored until final destruction and will not be further used or disclosed. However, in rare circumstances, your information may continue to be used or disclosed even after withdrawal or study completion, including: When removal of your data would compromise the scientific validity of the study or data safety evaluation; When limited, non-identifiable information is used for research, teaching, or related activities;

When regulatory authorities require access to study records for oversight purposes, which may include information related to your participation.

10. Costs of Participation

You will not receive any payment for participating in this study, nor will you be required to pay any trial-related expenses. All costs arising from study-related examinations, tests, and assessments will be covered by the hospital's research funding.

11. Management of Research-Related Injury

If you experience any injury or health problems during participation in this study, please inform the research staff immediately (Contact: Xiang Honglin, Tel: 18482610634). If an adverse event occurs during the study, the investigator will determine whether the event is related to the research. In the event that a research-related adverse event causes injury, the clinical research institution and investigators will provide adequate and timely medical treatment and management. The research institution will cover the medical expenses related to the research-induced injury and provide appropriate financial compensation in accordance with applicable regulations.

12. Will Your Personal Information Be Kept Confidential?

If you decide to participate in this study, your participation and all personal information collected during the study will be kept confidential. Your blood, urine, and other biological samples will be identified using study identification numbers rather than your name. Information that can identify you will not be disclosed to individuals outside the research team without your permission. All study personnel are required to maintain confidentiality regarding your identity. Your records

will be stored in locked file cabinets and will be accessible only to authorized research staff. To ensure that the study is conducted in accordance with regulatory requirements, authorized representatives of government regulatory authorities or members of the ethics committee may review your personal records at the study site when necessary. When study results are published, no information that could identify you personally will be disclosed.

13. New Information Related to the Study

During the study, new information related to the treatment may become available. If this information may affect your willingness to continue participation, you will be informed in a timely manner so that you can decide whether to continue in the study or withdraw.

14. Who Should You Contact If You Have Questions or Concerns?

If you have any questions related to this study, please contact:

Xiang Honglin; Tel: 18482610634

If you have questions regarding your rights as a research participant, please contact:

Medical Ethics Review Committee, Fourth Medical Center of the PLA General Hospital; Tel: 010-66848312

Informed Consent Signature Page

Participant Informed Consent Statement

I have been informed about the background, purpose, procedures, potential risks, and possible benefits of the study entitled "Clinical Safety Evaluation and Preliminary Efficacy Study of Subcutaneous Transplantation of Autologous Differentiated Myocytes." I have been given sufficient time and opportunity to ask questions, and all of my questions have been answered to my satisfaction. I have also been informed whom to contact if I have questions or wish to obtain additional information. I have read this informed consent form and agree to participate in this study. I understand that I may withdraw from the study at any time during the study period without providing any reason. I have been informed that I will receive a copy of this informed consent form, which will include the signatures of both me and the investigator.

Participant Signature: _____ Date: _____

Contact Telephone Number: _____

Legal Representative Signature **(if applicable)**: _____ Date: _____

Relationship to Participant: _____

I confirm that the information contained in this informed consent form has been accurately explained, and that the participant and/or the participant's legal representative has fully understood this information. The participant has voluntarily agreed to participate in this study.

Impartial Witness Signature (if applicable): _____ Date: _____

Investigator Disclosure Statement

I confirm that I have explained to the participant (and/or the participant's legal representative) the background, purpose, procedures, potential risks, and possible benefits of the study entitled "Clinical Safety Evaluation and Preliminary Efficacy Study of Subcutaneous Transplantation of Autologous Differentiated Myocytes." I have provided sufficient time for the participant to read the informed consent form, discuss participation with others, and have answered all questions related to the study. I have informed the participants of the appropriate contact information in case of questions or concerns, and I have explained that the participant (or legal representative) may withdraw from the study at any time without providing any reason.

Investigator Signature: _____ Date: _____

Contact Telephone Number: _____