TMU-Joint Institutional Review Board

Consent Form for Human Specimen Collection for Research/Trial (Non-Genetic Testing)

Hello:

Thank you for voluntarily becoming a subject in this research/trial. To ensure that you fully understand the specimen collection procedures of this research/trial and to protect your rights, please carefully read the following information. If you have any questions regarding this research/trial, the principal investigator will be more than willing to provide further explanations to help you understand fully. Your consent or lack thereof will not affect your current treatment and rights.

Research/Trial Name: The Effect of Fermented Milk Containing Lactobacillus casei Strain Shirota on Sarcopenia in Elderly Taiwanese: Interactions with the Nutrients Utilization, Diversity of Gut Microbiota, Microbiota-derived Metabolites and Muscle loss

Executive unit: Huang Huiyu Laboratory, Taipei Medical University
Tel: (02)26972036#138
Entrusted by/Pharmaceutical Factory: Yakult Co., Ltd

PI: Huang Huiyu	**Job Title: Professor**
Co-PI: Wu Jiexin	**Job Title: Professor**
Co-PI: Zhang Shixin	**Job Title: Director**
Co-PI: Liu Canhong	**Job Title: Professor/Vice-President**
Co-PI: Liao Kaiwei	**Job Title: Assistant Professor**
Co-PI: Yang Kunche	**Job Title: Attending Physician**
Co-PI: Lin Zhengqing	**Job Title: Attending Physician**

24-hour contact: Gao Heqing & Hu Enqi **Job Title: Case Receiving Researcher**
Contact Number : 0918075319 / 0920573659

Subject's Name: **Gender:**
Date of birth: **Age:**
Medical Record Number:
Address : **Phone:**

Contact Name/Relationship with Respondent:
Mailing address: Telephone:

1. Purpose of specimen collection, importance of the trial/research, and expected outcomes of the trial/research:

This study will collect your blood and stool samples to assess your nutritional status, inflammation levels, antioxidant capacity, hormone levels related to anabolic metabolism, the content of trace elements in your body, biochemical values, the ratio of blood cells, as well as the composition of gut microbiota and the levels of their metabolites. The results of this analysis will be used to evaluate the effects of a fermented beverage containing Lactobacillus casei strain Shirota on sarcopenia in elderly individuals in Taiwan. This study anticipates that after supplementing with the fermented beverage containing Lactobacillus casei strain Shirota, improvements in your gastrointestinal function, gut microbiota composition, and gut metabolites will enhance your immune and nutritional status, ultimately alleviating chronic inflammation associated with aging and slowing the progression of muscle loss or sarcopenia. Sarcopenia refers to the loss of muscle quality and quantity associated with aging. Elderly individuals with sarcopenia have a higher likelihood of developing metabolic-related diseases such as diabetes compared to other elderly individuals, and they also face increased risks of disability and mortality. Previous research has confirmed that the L. casei strain Shirota YIT9029 (LCS) can effectively improve gut microbiota and regulate immune and inflammatory responses. Therefore, this study aims to provide long-term supplementation of fermented beverages containing Lactobacillus casei strain Shirota to elderly patients with sarcopenia in Taiwan, in order to improve nutritional status, balance inflammatory phenomena, enhance gut microbiota, and microbial metabolites, thereby delaying the onset of sarcopenia. This study adopts an open-labeled experimental design, with half of the sarcopenia participants receiving the intervention product, while the other half do not. The allocation of participants to either the intervention or non-intervention group will be determined by random drawing. The expected number of participants is 40 to 60 in each group. The intervention beverage is a live fermented milk containing the L. casei strain Shirota YIT9029 (LCS), produced by Yakult Taiwan Co., Ltd. This beverage must be stored at 0-10℃. Each 100 ml bottle of live fermented milk contains over 30 billion CFU of the LCS strain. Participants are required to consume two bottles of live fermented milk daily (totaling 104 Kcal), and they will receive 14 bottles of live fermented milk each week. The nutritional labeling is as follows: Nutritional Component Analysis of the Sample

Item: Contains LCS live bacteria fermented milk

Calories: 52 Kcal/100mL

Fat: 0 g/100mL

Protein: 1.3 g/100mL

Carbohydrates: 14.5 g/100mL

Sugar: 10 g/100mL

Dietary Fiber: 3.3 g/100mL
Sodium: 17 mg/100mL
Calcium: 60 mg/100mL
Vitamin C: 28 mg/100mL
Vitamin D: 0.9 mg/100mL
Vitamin E: 3.4 mg/100mL
Total Lactic Acid Bacteria: 30 billion CFU/100mL
Allergen: This product contains milk.

2. Reasons for being selected as a subject and inclusion/exclusion criteria:

Inclusion criteria:

1. Age between 65-85 years
2. No use of hormone therapy
3. No history of hospitalization in the past three months
4. Presence of sarcopenia symptoms (meeting at least one of the following)
   (1) Low muscle mass
   - Male: SMI <7.0 kg/m2
   - Female: SMI <5.7 kg/m2

   (2) Upper limb muscle strength (grip strength)
   - Male: <28 kg
   - Female: <18 kg

   (3) Lower limb muscle strength
   - Time to stand up and sit down five times: ≧12s

Exclusion criteria:

1. Currently undergoing cancer treatment or treatment within the last three months
2. Weight change greater than 5% or more than five kilograms in the past three months
3. BMI >35 kg/m2
4. Long-term use of corticosteroids for any condition
5. History of ischemic or hemorrhagic stroke
6. Uncontrolled hypertension (>180/110 mmHg)
7. Blood or peritoneal dialysis in the past three months
8. Engaged in exercise training in the past two years (exercise that causes faster breathing and heart rate than usual and sweating), use of muscle gain supplements, or medications affecting bone metabolism (e.g., corticosteroids, bisphosphonates, vitamin D, calcium supplements, etc.)
9. Use of antibiotics in the past three months
10. Use of probiotic-related products in the past two weeks
11. Resided abroad for more than one month in the past three months

12. Hyperthyroidism without medication control
13. Milk allergy

3. The examinations and steps you need to cooperate with for this trial/research:

This trial will first ask you whether you meet the inclusion and exclusion criteria, followed by signing the consent form and grouping for sarcopenia screening. The non-sarcopenia group will proceed directly to the post-test phase (including nutritional education, dietary recording, blood draw of 30ml, one stool sample collection, and a questionnaire survey). The sarcopenia group will undergo a pre-test before the supplementation drink (including nutritional education, dietary recording, blood draw of 25ml, one stool sample collection, and a questionnaire survey); after starting the supplementation drink, nutritional education and dietary recording will be conducted every 4 weeks. After 12 weeks of continuous supplementation, a post-test will be conducted (including nutritional education, dietary recording, blood draw of 30ml, one stool sample collection, and a questionnaire survey). Blood: This trial will provide you with a blood draw order; please have a medical technician or nurse collect a total of 55ml of blood from your arm, with one draw before the trial and two draws after the trial, totaling three draws (25ml/25ml/5ml respectively). Stool: This trial will distribute stool collection tubes to participants; please follow the instructions included in the bag of the stool collection tube to collect approximately the size of a small fingertip of stool into the collection tube, and store it in the freezer. Please return it to the collection staff on the day of the blood draw.

3. The inspection and steps required for you to participate in this experiment/study:

After asking you if you meet the inclusion conditions and exclusion conditions, the asarcopenia group will sign the consent form and the sarcopenia screening group, and the sarcopenia group will directly conduct the post-test part (including nutrition and health education, record diet, blood draw 30ml, stool collection once and questionnaire), and the sarcopenia group will conduct a pre-test (including nutrition and health education, Record diet, draw 25ml of blood, collect stool once and questionnaire); After starting to replenish drinks, nutrition education and diet will be recorded every 4 weeks; After 12 consecutive weeks of supplementation, a post-test will be conducted (including nutrition and health education, diet recording, blood collection of 30ml, stool collection and questionnaire).

Blood: This test will give you a blood drawsheet, ask the medical examiner or nurse to collect a total of 55ml of blood from the arm, before the test (once) and after the test (twice), a total of three times (25ml/25ml/ respectively) (25ml/25ml/ 5ml)。

Feces: This test will distribute a fecal collection tube to the subject, please follow the instructions attached to the collection tube bag to take it home for an appointment

1 section of feces the size of a little finger was put into the fecal collection pipe, stored in the refrigerator and frozen, and handed over to the person receiving the case for collection on the day of blood drawing.

4. Possible side effects, risks, and inconveniences you may experience from participating in this trial/research:

(1) The risks of this program are very low and will not cause you physical or psychological harm.

(2) Blood draws may cause minor effects, such as localized pain at the blood draw site, bruising, bleeding, swelling, or infection at the blood draw site. You can apply pressure with a sterilized cotton ball to stop any bleeding. If you experience any unexpected or uncomfortable conditions, you can inform the staff at any time to stop immediately, and please notify your trial principal investigator right away. If a participant feels unwell or experiences dizziness during the fitness testing process, they can stop the test at any time and lie down to rest. On-site medical staff will monitor their breathing, heart rate, and blood pressure, and assess whether further action is needed.

(3) The trial beverage contains milk; if you are allergic to milk, please do not participate.

(4) The trial beverage is a probiotic fermented drink, and this probiotic strain has been certified by the FDA to high standards. If you have a specific medical condition that your doctor advises against consuming, please do not participate.

(5) The trial beverage contains live probiotics, which may improve the gut microbiota and may cause normal reactions such as gas or more frequent bowel movements in participants. If you have any questions, you may raise them, and a doctor will respond.

5. Handling and storage location of specimens:

All specimens collected for this trial will be stored in the -80℃ freezer of Professor Huang Hui-Yu's laboratory at Taipei Medical University. Professor Huang Hui-Yu will be responsible for their custody, and after the trial is completed (within 5 years), they will be immediately destroyed as infectious waste.

6. Possible personnel involved in specimen custody, specimen usage, and related information:

Specimens will be managed exclusively by the research team of Professor Huang Hui-Yu's laboratory at Taipei Medical University. Except for certain blood tests that will be analyzed by Pochi Biochemical Co., Ltd. and fecal specimens that will be analyzed by a testing company, all analyses will be conducted by our team. The vendors to whom specimens are entrusted have all committed to returning any remaining specimens to our laboratory research team after analysis or disposing of them as infectious waste.

7. Data and Specimen Handling Methods During and After the Trial/Study Period:

Regarding the preservation and handling of specimens/data during the trial/study period, the Huang Hui-Yu Laboratory at the Institute of Metabolism and Obesity Sciences, Taipei Medical University, will treat your data as confidential to the extent required by law. You also understand that the study sponsors (companies), the Ministry of Health and Welfare, and the Joint Human Research Ethics Committee of Taipei Medical University and its affiliated hospitals have the right to review your data and will adhere to confidentiality ethics. The researchers will collect data using a research number to replace your name for the examination results and physician diagnoses obtained during the study. Aside from the aforementioned institutions that have the legal right to review, we will take care to protect your privacy. Even if the results of the trial/study are published, your identity will remain confidential. After the completion of this trial, all specimens will be immediately destroyed as infectious waste. After the trial/study concludes, the relevant data regarding your participation will be stored at the Huang Hui-Yu Laboratory of the Institute of Metabolism and Obesity Sciences, Taipei Medical University, and will be maintained by the principal investigator, Huang Hui-Yu, for 20 years. After the retention period expires, we will handle your trial/study-related data according to your preferences.

Do you agree to have your data used for other medical trials/research?

□ Agree □ Willing to continue providing for Professor Huang Hui-Yu's other related research (the research plan must first be approved by the Joint Human Research Ethics Committee of Taipei Medical University and its affiliated hospitals, which will decide whether you need to sign another consent form).

□ Disagree □ The data will be destroyed by Professor Huang Hui-Yu's laboratory at the Institute of Metabolism and Obesity Science, Taipei Medical University.

8. Expected benefits of the trial/research:

(1) This trial/research provides a cash payment of 800 NT dollars as transportation expenses, which includes the cost of one self-registration. The transportation fee will be provided along with the test report after the trial concludes. If you withdraw midway or refuse to allow your samples and data to be used in this trial/research, you will receive a stationery or daily necessities gift package instead.

(2) If you have any questions or issues now or during the trial/research period, please feel free to contact Professor Huang Hui-Yu's research team at the Institute of Metabolism and Obesity Sciences at Taipei Medical University (phone: 0987335297/0987338713).

(3) During the trial/research process, any significant findings related to your health or illness that may affect your willingness to continue participating in this research will be communicated to you promptly.

(4) If you have any doubts about your rights or suspect that you have been harmed due to your participation in the trial/research, please feel free to contact the Joint Human Research

Ethics Committee of Taipei Medical University and its affiliated hospital (phone: (02) 66382736 ext. 1728 or email: tmujirb@gmail.com).

9. Costs to be borne by the subjects:

There are no additional costs for the subjects in this trial.

10. Other potential benefits derived from the trial/research:

The results of this trial/research will be published in international scientific journals for academic use and for health food application purposes.

11. Mechanism to Protect Your Personal Privacy:

Huang Hui-Yu will treat your data as confidential to the extent regulated by law. You also understand that the Ministry of Health and Welfare and the Joint Human Research Ethics Committee of Taipei Medical University and its affiliated hospitals have the right to review your data and will adhere to confidentiality ethics. This research is regulated by the U.S. FDA, which may inspect relevant records and post trial-related information on the ClinicalTrials.gov website (http://www.ClinicalTrials.gov). The content on ClinicalTrials.gov will not include any identifiable information, and the website will provide a summary of the research results. You can search this website at any time. Regarding the examination of the samples you provide and the data collected and analyzed during and after the trial/research process, the principal investigator Huang Hui-Yu will comply with confidentiality obligations and be responsible for maintaining your privacy. Your samples will be labeled with a code (coding: using numbers or letters to replace your name, initials, national identification number, medical record number, phone number, address, and other identifiable personal information), and no other sample testers will be able to identify the source of the samples. Without your consent, the principal investigator will not disclose any information that may identify you. If information obtained from the samples is provided to third parties or made public, it will be processed in a way that does not identify your personal data.

12. If the participant decides to withdraw from the trial/research midway, the handling of samples and data is as follows:

You may refuse to participate in the trial/research, and you may also withdraw your consent unconditionally at any time during the trial/research. If you decide to withdraw from this trial/research, please contact the personnel listed on the consent form immediately to inform them of your decision. Your withdrawal will not affect the doctor-patient relationship or any legitimate medical rights. Your samples will be handled according to your choice; however, you will be informed that your data will be retained and analyzed, and if it is to be used beyond the original scope, your informed consent will be required again. Additionally, any use beyond the original scope must first be approved by the Joint Human Research Ethics Committee of Taipei Medical University and its affiliated hospitals. Samples:

□ I agree to continue providing samples for the principal investigator to use in this trial/research, and if the use exceeds the original scope, I will need to provide my informed consent again, and such use must first be approved by the Joint Human Research Ethics Committee of Taipei Medical University and its affiliated hospitals. Please process or destroy the samples according to the scheduled timeline after the project ends.

□ Destroyed upon the principal investigator's suggestion to withdraw or upon my notification of withdrawal.

13. Other important matters related to specimen collection or use:

Your specimen will be used in accordance with the information provided in this consent form. If the use of the specimen exceeds the original scope, your informed consent will be required again, and any use beyond the original scope must first be approved by the Joint Human Research Ethics Committee of Taipei Medical University and its affiliated hospitals.

14. Source of funding for the trial/research and all institutions participating in the trial/research:

This trial is sponsored by Yakult Honsha Co., Ltd. (Japan) and is coordinated by Professor Huang Hui-Yu from the Institute of Metabolism and Obesity Sciences at Taipei Medical University as the principal investigator. Recruitment of subjects will be conducted by Taipei Medical University, Shuang Ho Hospital of the Ministry of Health and Welfare, Taipei Medical University Hospital, and Wan Fang Hospital of Taipei City.

15. Compensation for Damages and Insurance:

(1) The collection steps for this specimen will be conducted according to the doctor's recommendations, with a guideline of not extracting more than 25ml within one day.

(2) Professor Huang Hui-Yu from the Institute of Metabolism and Obesity Sciences at Taipei Medical University will make every effort to protect your rights during the trial/research period and will exercise necessary medical care. If any injury occurs due to the execution of the planned steps of this trial/research, the principal investigator will provide relevant information and consultation, and Taipei Medical University will be legally responsible for compensation for damages.

(3) This project is insured under a plan named "Fubon Property Clinical Trial Liability Insurance." Fubon Life Insurance is responsible for compensating the insured for any injuries or death suffered by the trial subjects (hereinafter referred to as subjects) due to adverse reactions from the insured drug during the insurance period while conducting the clinical trial of the insured drug (compensation for damages caused by expected side effects of the insured drug; however, damages caused by side effects exceeding expectations are not included). According to the terms of the "Subject Consent Form," the insurer shall bear the liability for compensation for damages, and Fubon Life Insurance will be responsible for compensating the insured for claims made by the subjects during the trial period.

16. Your Rights:

(1) This trial/research

■ Provides

■Transportation allowance of 800 NT dollars in cash (for those who complete the trial, this amount includes one registration fee) / a stationery gift pack (for those who withdraw midway or refuse to allow the use of specimen data).

☐ Nutritional allowances

☐ gifts

We will be provided according to your participation progress/ratio, and there is no need to return anything upon withdrawal.

☐No other subsidies or gifts are provided; please assist without compensation.

(2) If you have any questions or issues now or during the trial/research period, please feel free to contact the research staff of Professor Huang Hui-Yu's team at the Institute of Metabolism and Obesity Sciences at Taipei Medical University (phone: 0987335297 / 0987338713).

(3) During the trial/research process, any significant findings related to your health or illness that may affect your willingness to continue participating in this research will be communicated to you promptly.

(4) If you have any doubts about your rights during the trial/research process or suspect that you have been harmed due to your participation in the trial/research, please feel free to contact the Joint Human Research Ethics Committee of Taipei Medical University and its affiliated

hospital (phone: (02) 66382736 ext. 1728 or email: tmujirb@gmail.com).
(5) Aside from the situations mentioned above, if the participant or their legal representative, guardian, assistant, or anyone with the right to consent has any misunderstandings or areas of unfamiliarity regarding the current, future, or past research and wishes to discuss or clarify any questions, please feel free to contact the Joint Human Research Ethics Committee of Taipei Medical University and its affiliated hospital. We will provide a staff member who is not involved in the research to offer information. If needed, please contact the Joint Human Research Ethics Committee of Taipei Medical University and its affiliated hospital (Phone: (02) 6638-2736 ext. 1728 or Email: tmujirb@gmail.com).
(6) If you wish to withdraw your consent after providing a specimen, you can contact Professor Huang Hui-Yu's research team at the Institute of Metabolism and Obesity Sciences at Taipei Medical University (the principal investigator or their representative) at the phone numbers 0987335297/0987338713.
(7) You have the right to refuse or withdraw from this trial/research at any time, and this will not affect your medical care or other rights.

17. Signature

Researcher Declaration:

I assure that I or a member of my trial/research team (an authorized representative for this step) has explained this trial/research to the subjects, including the purpose, procedures, and potential risks and benefits associated with participating in this trial/research. All questions raised by the subjects have been answered.

Explanation of the Consent Form by the Researcher

Name (block letters)_____
Signature_____
Date_____

Subject's Declaration

The information above has been explained to me, and I have had the opportunity to ask questions regarding this trial/research. I understand and agree to participate in this trial/research program, and a copy of the consent form has been provided. If I have any questions in the future, who can I contact ?

Subject

Name (block letters)_____
Date of birth _____
Signature_____
Date_____

Legal representative/Guardian/Assistor

Name (block letters)_____(if applicable)
Relationship between you and subject: _____
Signature_____
Date_____

If you are not the subject or their legal representative, but due to factual circumstances, the subject or their legal representative is temporarily unable to sign this consent form and you need to sign on their behalf as a person with consent authority, please write your name in block letters and indicate your relationship to the subject:

Name (block letters)_____
Relationship between you and subject:(Those who have the right to consent should check according to the laws and regulations of the trial/study)

National identity cards number_____
Contact phone number_____
Contact address_____
Signature_____
Date_____

Witness of Verbal Consent

(If the subject is unable to read the above content and the explanation is provided verbally by the researcher, another witness must be present) hereby certifies that the principal investigator and research personnel have fully explained the content of this trial/research to the subject.

Witness
Name (block letters) **(Research-related personnel cannot be witnesses)**_____
National identity cards number_____
Contact phone number_____
Contact address_____
Signature_____
Date_____

◎ If the subject, legal representative, assistant, or person with consent rights is unable to read, a witness must be present to participate in all discussions regarding the subject's consent. After ensuring that the consent of the subject, legal representative, guardian, assistant, or person with consent rights is given freely, they should sign the subject's consent form and indicate the date. Research personnel cannot be witnesses.

PI signature
PI/Co-PI
Name (block letters)_____
Signature_____
Date_____