[서식] C-05 심의결과 통지서(영문) (V7.0) (01-MAR-2017)

CNUHIRB
Chungnam National University Hospital Institutional Review Board
Tel :82-42-280-6715
FAX:82-42-280-6716 282 Munhwa-ro , Jung-Gu, Daejeon, 35015, Korea

Certificate of Approval

THE FOLLOWING WERE APPROVED:

BOARD ACTION DATED: 08/JUL/2024
STUDY NO : N/A
IRB File No. CNUH 2024-05-009

INVESTIGATOR: HyukSoo Eun

SPONSOR: N/A

PROTOCOL NO: N/A

TITLE: Exploration of liver-gut axis through identification of liver disease-specific microbiome

ALL CONDITIONS OF APPROVAL PREVIOUSLY ESTABLISHED BY THE CNUHIRB FOR THIS RESEARCH PROJECT CONTINUE TO APPLY.

CONTINUING REVIEW REPORT INTERVAL: 1 Year

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IF YOU HAVE ANY QUESTIONS, CONTACT THE CNUH IRB (Tel: 82-42-280-6715)

This is to certify that the information contained herein is true and correct as reflected in the records of the CNUH Institutional Review Board. **We certify that the CNUH IRB is in full compliance with Good Clinical Practice as defined under the Ministry of Food and Drug Safety (MFDS) regulations and the International Conference on Harmonisation (ICH) guidelines.**

Chairperson

19 July 2024
Date

ALL CNUH IRB APPROVED INVESTIGATORS MUST COMPLY WITH THE FOLLOWING:

1. Conduct the research as required by the protocol.
2. Use only the Consent Form bearing the CNUH IRB" APPROVED" stamp.
3. Provide non-Korean speaking subjects with a certified translation of the approved Consent Form in the subject's first language. The translated version must be approved by the CNUH IRB.
4. Obtain pre-approval from the CNUH IRB of any changes in the research activity (except when necessary to protect human subjects; immediately report to the CNUH IRB any such emergency changes for the protection of human subjects).
5. Report to the CNUH IRB the death, hospitalization, or serious illness of any study subject.
6. Promptly report to the CNUH IRB any new information that may adversely affect the safety of the subjects or the conduct of the trial.
7. Provide reports to the CNUH IRB concerning the progress of the research, when requested.
8. Obtain pre-approval of study advertisements from the CNUH IRB before use.
9. Conduct the informed consent process without coercion or undue influence, and provide the potential subject sufficient opportunity to consider whether or not to participate.

Korea MFDS regulations require that the CNUH IRB conduct review of approved research. You will receive Continuing Review Report forms from the CNUH IRB. These reports must be returned even though your study may not have started.

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Protocol		
Title	**영문**	Exploration of liver-gut axis through identification of liver disease-specific microbiome
Principal Investigator	HyukSoo Eun (Associate Professor of Gastroenterology, Chungnam National University Hospital)	
Researcher from an institution	**Principal Investigator :** HyukSoo Eun(Associate Professor of Gastroenterology, Chungnam National University Hospital) **Collaborator:** Eun-Kyeong Jo (Department of Microbiology, College of Medicine, Chungnam National University) In Soo Kim (Department of Pharmacology, College of Medicine, Chungnam National University) **Research manage :** SoonOK Kim (Chungnam National University Hospital)	
Collaborating research institution and researcher's name	[None]	
Medical device manage	[None]	
Monitoring officer in charge	[None]	
Contracting agency	[None]	
Funding agency for research	[None]	
Research period	After IRB approval, 60 months	
Disease under investigation	Autoimmune liver diseases (Autoimmune hepatitis, Primary biliary cholangitis, Primary sclerosing cholangitis), Metabolic liver diseases (Non-alcoholic fatty liver disease) Infectious liver diseases (Liver abscess)	

1. Background

■ Importance of Microbiome Research

▷ The gut microbiome is a vast community of microorganisms residing in the digestive system, including bacteria, viruses, fungi, and other microbes that play a crucial role in maintaining overall health.

▷ Research on the microbiome is known to be associated with a wide range of health conditions, including obesity, diabetes, autoimmune diseases, and even mental health disorders such as depression and anxiety.

▷ It has also been shown to play a significant role in the onset of allergies and asthma. ▷ One of the key ways the gut microbiome influences health is by interacting with the immune system, helping to train it to recognize and respond to threats such as harmful bacteria and viruses. Therefore, disruptions in the balance of gut microbes can increase the risk of immune dysfunction, infections, and other health issues.

▷ Additionally, the microbiome is involved in the digestion and absorption of nutrients, breaking down complex carbohydrates and other compounds that cannot be digested by the body on its own to facilitate nutrient absorption.

▷ Therefore, research on the gut microbiome is essential for understanding the underlying mechanisms contributing to disease onset and identifying potential therapeutic approaches. Changes in diet and lifestyle can alter the composition of the gut microbiome, highlighting the potential for therapeutic interventions targeting this microbial community.

■ Importance of Research on Intractable Liver Diseases

▷ Chronic intractable liver diseases such as non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), and cirrhosis are characterized by progressive liver damage, which can lead to the necessity of liver failure and transplantation. However, there are currently no approved therapies that can effectively halt or reverse the progression of liver damage in patients with progressive diseases, resulting in high unmet medical needs.

▷ To address these issues, it is crucial to better understand the underlying mechanisms that cause liver damage. Liver fat accumulation in NAFLD and NASH is believed to induce inflammation and oxidative stress, leading to the death of liver cells and their replacement with scar tissue. However, the exact molecular pathways mediating these processes are not fully understood.

▷ Additionally, there is a need to identify biomarkers that can accurately predict disease progression and response to treatment. Current methods such as liver biopsy, while necessary for diagnosing liver diseases and staging, are invasive and not suitable for monitoring disease progression over time.

▷ From a therapeutic perspective, there is an urgent need for therapies that can effectively halt or reverse liver damage in patients with progressive diseases. Current treatments for NAFLD and NASH, such as weight loss and

lifestyle modifications, are effective for some patients but often insufficient once the disease has progressed. Therefore, there is a critical need to target specific pathways associated with liver damage and develop therapies capable of halting or reversing disease progression.

▷ Primary sclerosing cholangitis (PSC) and primary biliary cholangitis (PBC) also represent chronic cholestatic liver diseases with significant unmet medical needs. Despite relatively low prevalence, they have high morbidity and mortality rates, and there are currently no approved therapies capable of effectively halting or reversing liver damage.

▷ In PSC, the immune system attacks the bile ducts, leading to inflammation and fibrosis, but the exact triggering factors are poorly understood, necessitating research into the molecular pathways involved. Similarly, in PBC, immune-mediated attacks on small bile ducts cause inflammation and fibrosis, and while autoimmune involvement appears critical, exact triggering factors remain unclear.

▷ Current treatments for PSC and PBC involve ursodeoxycholic acid and immunosuppressants; however, effective therapies that can effectively halt or reverse liver damage are needed. Moreover, given the variability in disease severity and treatment response, a more personalized approach to treatment is warranted.

■ The Utility of Gut-Liver Axis Research for Chronic Intractable Liver Diseases

▷ The gut-liver axis refers to bidirectional communication between the liver and gastrointestinal tract mediated by various signaling molecules and cellular pathways. The gut microbiome can regulate liver function and metabolism through the production of diverse metabolites such as short-chain fatty acids and bile acids. Conversely, the liver generates bile secreted into the intestine to aid in fat digestion and absorption, and bile acids also act as signaling molecules that can modulate gut microbiota and intestinal immune function.

▷ Dysregulation of the gut-liver axis has been implicated in the onset of non-alcoholic fatty liver disease (NAFLD) and inflammatory bowel disease (IBD), and understanding the underlying mechanisms mediating this interaction could lead to the development of novel therapies targeting specific pathways associated with the gut-liver axis.

▷ Therefore, this study aims to identify specific gut microbiome profiles unique to patients with chronic intractable liver diseases and to conduct gut-liver axis research related to etiology and disease progression.

2. Data collection method

We will collect a total of 20cc of venous blood and 5cc of stool (using a stool collection kit) from each consenting participant (patients and cohabitants living together) at three time points: at the time of the patient's disease diagnosis, 3-6 months after the patient's disease treatment, and 6-12 months after the patient's disease treatment.

3. Selection and Exclusion Criteria for Study Participants (Samples), Target Sample Size, and Justification

A. Selection Criteria

Adults aged 19 years and older diagnosed with autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, non-alcoholic fatty liver disease, or liver abscess, who have consented to participate in this study at Chungnam National University Hospital.

Adults aged 19 years and older, who are cohabitants of patients diagnosed with autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, non-alcoholic fatty liver disease, or liver abscess, and have consented to participate in this study at Chungnam National University Hospital.

B. Exclusion Criteria

Individuals under the age of 19.

Patients or guardians who do not consent to participate in the study

C. Sample Size and Justification

1) Sample Size: Total of 3,000 cases

Autoimmune Liver Diseases (patients diagnosed with autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis): Experimental group 500 cases, Cohabitants control group 500 cases.

Metabolic Liver Diseases (patients diagnosed with non-alcoholic fatty liver disease): Experimental group 500 cases, Cohabitants control group 500 cases

Infectious Liver Diseases (patients diagnosed with liver abscess): Experimental group 500 cases, Cohabitants control group 500 cases

2) Justification:

The calculation of the sample size was conducted using G*Power (version 3.1.9.7) to enable comparative studies among patient groups with statistical significance. For this study, we aimed for an effect size of 0.25, significance level α error probability of 0.05, and power (1-β error probability) of 0.95. This calculation resulted in a required sample size of 417 cases per group, totaling 834 samples. Considering a potential loss rate of 20% in the collection of the primary sample, feces, we aimed for 500 cases per group, resulting in a total of 3,000 samples across the three liver disease groups.

4. Method

1) Sample Collection and Storage

[Fecal Samples]

Participants who have consented to this study will provide 5cc of feces using the following kit: Samples obtained from patients and cohabitants will be stored in a designated freezer maintained at -80°C, equipped with a security device, at a specific location. Each sample will be assigned an encrypted sample number. Upon usage, the entry and exit of samples will be recorded by a designated manager. Once the experiment objectives are achieved, all samples will be disposed of appropriately.

[Blood Samples]

Participants who have consented to this study will provide 20cc of blood via venipuncture from the arm into EDTA and SST bottles as follows: Samples obtained from patients will undergo peripheral blood mononuclear cell isolation within 24 hours using plasma and Ficoll density gradient separation. These samples will be stored in a designated freezer maintained at -80°C, equipped with a security device, at a specific location. Each sample will be assigned an encrypted sample number. Upon usage, the entry and exit of samples will be recorded by a designated manager. Once the experiment objectives are achieved, all samples will be disposed of appropriately.

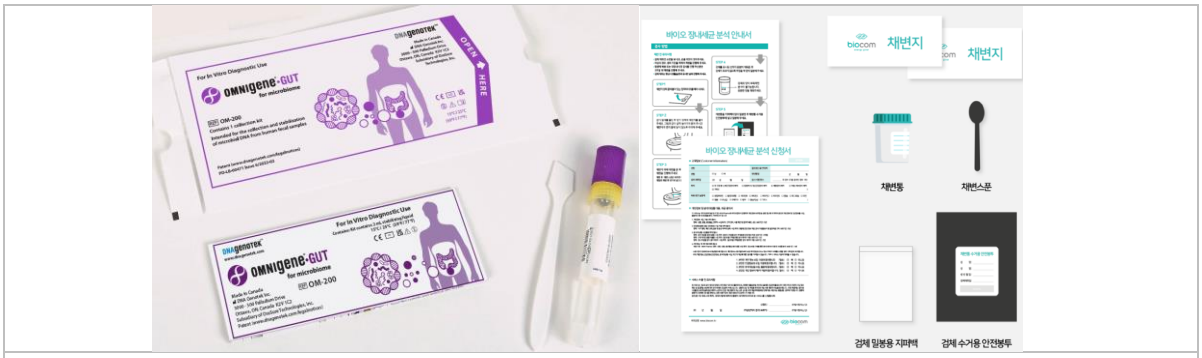

Fig 1. Stool kit

2) Analytical Methods

From collected fecal samples, bacterial DNA will be extracted using a DNA extraction kit, followed by 16S ribosomal RNA gene amplicon sequencing. Peripheral blood mononuclear cells will undergo total RNA extraction using an RNA extraction kit, followed by RNA sequencing. Plasma samples will undergo metabolite measurement using LC-MS or NMR.

3) Integrated Analysis with Clinical Data

Clinical data will be utilized to stratify or classify patient groups, and sequencing results will be integrated to identify disease-specific gut bacteria.

*** Observational Items, Clinical Examination Items, and Observation Methods**

- Basal characteristics (age, gender, chief complaints, weight, past medical history, present illness, family history, alcohol consumption, smoking history)
- Hematological and serological/immunological markers (complete blood count results, serum alkaline phosphatase, AST, ALT, gamma-GT, total bilirubin, glycated hemoglobin, fasting blood glucose, lipid profile, IgM, IgG, antinuclear antibodies, anti-smooth muscle antibodies, anti-mitochondrial antibodies, HBsAg, HBeAg, HBcAg, HBs-Ab, anti-HBe, anti-HCV status)
- Imaging findings (CT scan, MRI, abdominal ultrasound, endoscopic retrograde cholangiopancreatography (ERCP) if applicable)
- Histopathological findings (pathological findings of liver biopsy tissue if applicable)

4) Statistical Analysis Methods

Statistical analysis for the results of microbial species and distribution will involve Taxonomic profiling using the Galaxy platform, followed by LDA analysis. Grouping by primary diagnosis and deriving LDA Effect Size or utilizing MaAsLin2 functionality to identify taxa showing significant compositional changes between diseases. For transcriptome and metabolome results, categorical variables will be analyzed using the Chi-square test, while continuous variables will undergo t-tests. Correlation analysis will employ Pearson’s coefficient.

5) Criteria for Suspension and Withdrawal

(1) If the research subject (or legal representative, if applicable) requests withdrawal of consent during the study.
(2) If contamination or other issues are discovered in the human-derived samples rendering them unusable.
(3) If it is determined that interpretation of the test results is not feasible.
(4) If there is insufficient human-derived material to proceed with repeat or confirmatory testing.
(5) If the subject is found to have been registered in violation of selection/exclusion criteria.

6) Evaluation Criteria, Methods, and Reporting Procedures for Safety, Including Adverse Event

This study involves research using human-derived materials obtained through natural defecation of research subjects. Therefore, it is deemed that there will be no direct harm to the subjects' bodies. Consequently, there are no safety evaluations related to adverse events, including side effects, anticipated for this study.

7) Benefits and Risks of the Study

Benefits of the Study

This study, conducted using human samples, does not offer direct benefits to the participants. However, it will contribute to the accumulation of knowledge aimed at treating patients with similar conditions.

Risks of the Study

- The blood collection procedure in this study is conducted similarly to routine clinical practices, typically involving approximately 30ml of blood (20ml for research and 10ml for routine tests). This amount is minimal and poses little risk to the patient's safety (less than 1/500th of the total blood volume in the body, equivalent to less than 1/25th of a typical blood donation).
- However, depending on the individual condition of the participant, symptoms such as dizziness, nausea, or vomiting may occur during blood collection. In such cases, the collection will be immediately discontinued, and measures such as intravenous hydration and bed rest will be provided to ensure stability.
- Additionally, for elderly participants aged 65 and above, the study protocol will involve explaining the research purpose, background, and methods in simple terms and allowing sufficient time to obtain informed consent.
- Furthermore, if applicable, guardians or representatives will also be provided with detailed explanations of the study's purpose, background, and procedures to obtain their consent.

5. Measures for Ensuring Participant Safety

A. Basic Measures to Ensure Ethical Conduct of the Study

We will adhere to clinical research regulations such as the Helsinki Declaration (2013 revised edition) and ICH-GCP after obtaining IRB approval.

B. Consent Process for Research Participants

▷ Research participants will be explained and consent will be obtained before collecting human specimens for the study.

-Person providing consent: Research participants
-Waiting time between explanation and consent process: 1-2 hours
-Language used by the researcher during the explanation and consent process: Korean
Research participants will be provided with a research information sheet and consent form.

▷ We will conduct the study on those who have signed the consent form for this study among those who visited Chungnam National University Hospital, and explain that there will be no coercion or compulsion to participate and that there will be no undue influence on treatment even if they do not participate.

▷ For research subjects aged 65 and older (patients and patients' cohabitants), we will explain the purpose, background, and methods of the study in simple terms and with sufficient time to obtain their consent. In addition, we will obtain

consent from guardians or representatives after explaining the purpose, background, and methods of the study sufficiently to them.

▷ If a patient's cohabitant who cannot visit the hospital refuses to participate in the study or if the patient lives alone, only the patient will be registered as a research subject.

C. Compensation Plan for Research Subjects

Research subjects (patients and patients' cohabitants) will be reimbursed KRW 50,000 for each stool sample collected, deposited into the patient's account, with funding from the Korea Research Foundation [Chungnam University Industry-Academia Collaboration Foundation].

D. Measures for Ensuring the Safety of Research Subjects

If symptoms such as dizziness, nausea, or vomiting occur during the blood collection process for research subjects (patients and patients' cohabitants), we will immediately stop the collection and implement hydration therapy and bed rest to ensure stability.

E. Personal Information Protection Measures for Research Subjects

(1) The ultimate responsibility for all information collected in the research process lies with the principal investigator. All personal information collected in this study will comply with the Personal Information Protection Act and related regulations, strictly maintaining and protecting the privacy of research subjects.
(2) Personal identifying information of research subjects will be coded or anonymized to prevent identification.
(3) All documents related to the research will be encrypted and stored in the principal investigator's locked personal research office where access is restricted to authorized personnel only. However, the principal investigator will take measures to allow access within the scope defined by regulations to government agencies, sponsors or their delegated institutions' monitors, inspectors, and IRB upon request.
(4) After the completion of the research, documents will be kept for 3 years from the end of the research in accordance with Article 15 of the Enforcement Rules of the Life Ethics and Safety Act, and documents containing personal information will be destroyed in compliance with Article 16 of the Enforcement Decree of the Personal Information Protection Act.

6. Storage and Disposal Methods of Human Specimens

The human specimens used in this study will be disposed of after the completion of the research in accordance with Article 39 of the Law on Bioethics and Safety, Article 36 of its enforcement rules, and Article 13 of the Waste Management Act. Specimens will be stored for the duration agreed upon by the donors, and upon expiration of the

storage period, they will be disposed of. If a donor requests disposal during the storage period, their request will be honored. When disposing of human specimens, records including the date, quantity disposed, and disposal method will be maintained for 5 years from the date of disposal.

7. Publication and reporting of research finding

The results of this study are planned to be reported in an SCI(E) academic journal

8. Reference

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2. Cani PD. Gut microbiota - at the intersection of everything? Nat Rev Gastroenterol Hepatol. 2017 Jun;14(6):321-322. doi: 10.1038/nrgastro.2017.54.

3. Spor A, Koren O, Ley R. Unravelling the effects of the environment and host genotype on the gut microbiome. Nat Rev Microbiol. 2011 Apr;9(4):279-90. doi: 10.1038/nrmicro2540.

4. Norman JM, Handley SA, Baldridge MT, Droit L, Liu CY, Keller BC, Kambal A, Monaco CL, Zhao G, Fleshner P, Stappenbeck TS, McGovern DP, Keshavarzian A, Mutlu EA, Sauk J, Gevers D, Xavier RJ, Wang D, Parkes M, Virgin HW. Disease-specific alterations in the enteric virome in inflammatory bowel disease. Cell. 2015 Jan 29;160(3):447-60. doi: 10.1016/j.cell.2015.01.002.

5. Kau AL, Ahern PP, Griffin NW, Goodman AL, Gordon JI. Human nutrition, the gut microbiome and the immune system. Nature. 2011 Jun 15;474(7351):327-36. doi: 10.1038/nature10213.

6. Leung C, Rivera L, Furness JB, Angus PW. The role of the gut microbiota in NAFLD. Nat Rev Gastroenterol Hepatol. 2016 Jul;13(7):412-25. doi: 10.1038/nrgastro.2016.85.

7. Dickson I. Gut microbiota-mediated liver inflammation in PSC. Nat Rev Gastroenterol Hepatol. 2019 Mar;16(3):140-141. doi: 10.1038/s41575-019-0116-z.

ICF template(3)_인체유래물연구용

Informed Consent Statement

Title	**Exploration of liver-gut axis through identification of liver disease-specific microbiome**
Principal Investigator	**HyukSoo Eun(Associate Professor of Gastroenterology, Chungnam National University Hospital)**

You have been invited to participate in this study. This document is designed to provide you with relevant information to help you decide whether or not to participate. It explains the purpose, content, risks, and benefits of the study. It is important that you fully understand why this study is being conducted and what your involvement will entail. If there are any parts of this document that are unclear or if you have additional questions about the study, you may request further explanation from the Principal Investigator or the research staff.

Your decision to participate is completely voluntary, and you are free to decline participation even after hearing about the study. Please take sufficient time to consider your decision before agreeing to participate. You may discuss your participation with your family or others before making a decision. Your decision to participate or not will be respected without any consequences.

You have the right to withdraw from the study at any time without any negative consequences. If you decide to participate, you will be asked to sign the Participant Consent Form, and you will receive a copy for your records.

1. Purpose

The purpose of this study is to identify specific biomarkers related to liver disease and gut microbiota that are anticipated to be critical in the occurrence and progression of liver diseases.

2. Participation period and number of study participants

This study is planned to be conducted with 3,000 participants at our institution. The anticipated study period is 60 months from the IRB approval date. With your consent, we will use collected blood and stool samples to conduct the research. Your participation in the study will be approximately 12 months from the time of study enrollment.

3. Method

This study involves analyzing blood and stool samples from patients diagnosed with liver diseases and their cohabitants. The targeted liver diseases include autoimmune liver diseases (autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis), metabolic liver diseases (non-alcoholic fatty liver disease), and infectious liver diseases (liver abscess). To participate in this study, you (patients and cohabitants) must first listen to and fully understand the purpose and methods of the study explained by the researchers, and then sign the consent form. Upon agreeing to provide information, the researcher will verify if you (patients and cohabitants) meet the study criteria. If deemed suitable, you will be enrolled as a study participant. The researcher will collect your blood and stool samples for research purposes and gather your medical record information, including age, gender, underlying conditions, diagnosis, treatment details, and blood test results. Blood and stool samples will be collected three times: at the time of patient's disease diagnosis, 3-6 months after treatment, and 6-12 months after treatment. Each blood sample (venous blood) will be approximately 20cc, and each stool sample (collected using a stool collection kit) will be approximately 5cc. Blood samples will undergo metagenomic and metabolomic analyses, while stool samples will undergo bacterial identification analysis. The study aims to identify quantitative differences in gut microbiota, metabolomes, and transcriptomes statistically from the results obtained.

4. Storage and Disposal of Research Specimens

This study involves the collection of blood and fecal specimens for research purposes using human-derived materials. Specimens will be collected three times: at the time of patient diagnosis, 3-6 months after treatment, and 6-12 months after treatment. Approximately 20cc of venous blood and 5cc of feces (using a stool collection kit) will be collected each time.
Records identifying you (patients and patients' cohabitants) will be kept confidential. Any identifiable records and genetic information will be encoded with a research participant identification code for anonymization. Other information collected for research purposes will be encrypted for transmission and storage.
Before signing the Informed Consent Form for Human-Derived Materials Research provided in the following pages, please review and fill in the consent details yourself. You may decide the preservation period for the human-derived materials collected for this study. Additionally, the human-derived materials collected for this study will not be used for other purposes. Any remaining materials after the study will be stored and disposed of according to the Life Ethics and

Safety Act and hospital regulations.
The human-derived materials collected in this study may be used for future research purposes and possibilities. If you agree to this, please review and sign the consent section of the Human-Derived Materials Research Consent Form on the following pages. You may also decide on the preservation period for your human-derived materials. Furthermore, you have the right to decide whether to consent to the use of your human-derived materials for secondary research (secondary use) within the preservation period, and if you agree, you can also choose the scope of the research (similar and comprehensive studies). Other than the period and scope determined by you, the materials will not be used, and any remaining human-derived materials will be stored and disposed of according to the Life Ethics and Safety Act and hospital regulations.

5. Voluntary participation and withdrawal of consent

Your participation in this study (patient and patient's cohabitant) is voluntary. You may choose not to participate in the study at any time and may also withdraw from the study. Even if you decide not to participate in this study, your attending physician will continue to treat your illness as usual, so you will not suffer any disadvantages. Your decision will not affect your future medical care. Additionally, after you decide not to participate in this study, your biological samples will be disposed of according to hospital regulations, and no further information will be collected about your biological samples.

6. Risk and benefit

In this study, blood collection from you (patient and patient's cohabitant) will be conducted similarly to routine clinical procedures. Approximately 30ml of research blood will be collected, which includes 20ml for research purposes in addition to the standard 10ml drawn for routine testing. The research blood collection volume (approximately 30ml) poses minimal risk to patient safety (less than 1/500th of the total blood volume in our body) and is unlikely to cause any issues (equivalent to less than 1/25th of a typical blood donation of 500ml). However, if you experience dizziness, nausea, vomiting, or any other discomfort during the blood collection procedure due to personal condition, the medical staff will promptly halt the collection and provide fluid therapy and bed rest to ensure stability.
Furthermore, this study utilizes your biological samples (blood and feces) for research purposes, which will not directly benefit you. However, it may contribute to accumulating knowledge for the

treatment of patients with similar conditions as yours.

7. Rewards

In this study, there may be potential side effects associated with blood collection from you (patient and patient's cohabitant). If you experience any discomfort, please inform us immediately. The principal investigator will provide the best medical care possible. However, we do not compensate for any damage caused by your intentional or negligent actions.

8. Information and expenses related to participation in the study

If you (patient or patient's cohabitant) participate in this study and provide a stool sample, you will receive transportation expenses (equivalent to approximately 50,000 KRW) for one collection. The principal investigator will cover the costs of tests and medical expenses incurred during your participation in this study. There will be no cost to you (patient or patient's cohabitant) for participating in this study. However, any unrelated expenses such as hospitalization, consultation fees, or medication costs will be your responsibility. Additionally, transportation expenses for additional clinic visits related to stool collection will be reimbursed.

9. Collection, use, disclosure, and protection of personal informatio

Your (patient or patient's cohabitant) personal information will be kept confidential and will not be disclosed without your written permission, except as described herein or as required by law. The data you provide will not be used to personally identify you. Medical confidentiality and privacy regarding personal information in this study will comply with legal requirements.

All appropriate measures will be taken to protect your personal information collected during the study. Information collected during your participation will be stored securely in locked facilities and encrypted. Access will be restricted to the principal investigator and research team only. When transmitted over information networks or auxiliary storage media, this information will be encrypted. Any records identifying you will be maintained in confidence when the study results are reported in reports, publications, or presentations.

Furthermore, records of this study may be accessed directly by authorized personnel for the purposes of ensuring the proper conduct of the study and verifying the accuracy of collected data,

within the limits defined by relevant regulations, without compromising your confidentiality.

-Internal auditors

-Government regulatory agencies (such as the Ministry of Food and Drug Safety or the Ministry of Health and Welfare)

-Institutional Review Board (IRB) within an organization reviewing the ethical and scientific validity of research

10. Questions

If you have any questions or need assistance regarding participation in this study, please feel free to contact the appropriate contact person listed for your inquiry.

Principal Investigator: HyukSoo Eun	**042-280-7418**
Research coordinator: SoonOk Kim	**042-280-6717**
Chungnam National University Hospital 282 Munhwa-ro, Jung-gu Daejeon, 35015 South Korea	

※ **If you have any questions regarding your rights as a research participant or if you need to discuss general aspects of the study as a participant or representative, please contact the following**

Clinical Research Ethics Center	**042-280-6781**
	e-mail: hrpp@cnuh.co.kr
266 Munhwa-ro, Jung-gu Chungnam National University Hospital Biomedical Research Center 2nd Floor Clinical Research Ethics Center Daejeon, 35015 South Korea	

Only the IRB-stamped informed consent form and description are valid for medical research ethics review

Informed Consent Form

Title	Exploration of liver-gut axis through identification of liver disease-specific microbiome

※ If you fully understand and agree to the following, please mark (√) in the square box	
☐	I have listened to and understood sufficient explanations regarding the purpose, methods, and potential risks of this study through the participant information sheet.
☐	I have had enough time to consider participating in this study, have asked all questions I have had, and have received satisfactory answers from the research team.
☐	I understand that even if I agree to participate in this study, I am free to withdraw my consent at any time and receive appropriate alternative treatment thereafter.
☐	I am aware that I will receive one copy of this consent form.
☐	I consent to participate in this study freely and voluntarily, according to my own will.
☐	By signing this consent form, I agree to the collection and use of the personal information listed below for medical research purposes.
☐	By signing this consent form, I agree to the collection and use of the sensitive information listed below for medical research purposes

* By signing this page, you confirm the following:

*By signing the informed consent form for this research study, you have received explanations about the purpose of the study and satisfactory answers to all your questions. You have also been informed of your right to withdraw consent at any time. Therefore, based on your understanding, you voluntarily agree to participate in this study. You understand that this consent form will be kept for **3 years,** and you will receive a copy of it.

Research participant	Name :	Sign		Date	
Researcher	Name :	Sign		Date	
If necessary Legal guardian	Name :	Sign		Date	
	Relationship: Research participant ( )			Consent rationale	
If necessary Witness	Name :	Sign		Date	

Only the IRB-stamped informed consent form and description are valid for medical research ethics review

■ Regulations on Enforcement of the Act on Bioethics and Safety [Appendix Form No. 34]

Consent Form for Human Biological Materials Research

No	

Research participant	Name	Date of Birth
	Adress	
	Phone number	Sex

Legal guardian	Name	Relationship
	Phone number	

Principal Investigator	HyukSoo Eun
	042-280-7418

By signing this consent form, you agree to the following:

This consent is for the use of your human biological materials (including tissues, cells, blood, body fluids, serum, plasma, chromosomes, DNA, RNA, proteins, etc., collected or extracted from your body) for research purposes such as disease diagnosis and development of treatments. Your consent is voluntary, and you should have the opportunity to ask questions and receive adequate explanations from a counselor before making a decision. Your decision to consent or not will not affect your future medical care or treatment.

1. Human biological materials refer to components obtained from the human body, including tissues, cells, blood, body fluids, and substances isolated from these, such as serum, plasma, chromosomes, DNA, RNA, and proteins. You must receive sufficient explanation about the collection methods and procedures before your biological materials are collected.

2. If you agree to the use of your human biological materials for the research purposes described below, you can decide on the preservation period of your biological materials, whether to provide them to others or for other research purposes, and the handling of personal information when provided. You may withdraw your consent at any time. Depending on the nature of the research, there may be different methods of handling your biological materials, records, and information until your withdrawal, for which you will receive separate explanations or documents from the researcher.
3. You have the right to access records regarding your consent, provision, and disposal of your biological materials through yourself or your legal guardian at any time related to your participation in this research.
4. Human biological materials that have exceeded the agreed preservation period will be disposed of according to Article 13 of the Waste Management Act, and in cases of temporary closure, closure, or abnormal termination of the relevant research, the biological materials will be transferred according to the procedures prescribed by law
5. Research using your human biological materials will proceed after approval by the Institutional Review Board (IRB) of the institution in accordance with the Act on Bioethics and Safety, and the institution and researchers will take necessary measures to protect your personal information.
6. You cannot claim rights to new drugs, diagnostic tools, patent applications, or product developments resulting from research using your biological materials. Research using your provided biological materials will be presented at conferences and published in journals under the researcher's name without revealing your personal information.

※ You must receive sufficient explanation for all of the above and receive one copy of the signed consent form.

	Purpose	Aim to study the specific gut bacteria associated with liver diseases and their relevance to liver disease."
	Types and quantities	Blood 20cc* 3 / Stool 5cc* 3
	Preservation period	1. Research preservation[ ] 2. After ( ) years of consent
	Consent for secondary use within the preservation period	1. I consent to providing it only within the scope of similar research [ ] 2. I consent to providing it for comprehensive research purposes [ ] 3. I do not consent[ ]
	Inclusion of personal identifying information for secondary us	1. Inclusion of personally identifiable information [ ] 2. Exclusion of personally identifiable information [ ]

(뒤쪽)

I voluntarily consent to donate my biological materials, as described above, having understood the contents of the consent form regarding the collection methods, procedures, and purposes of the research under Article 37 of the Bioethics and Safety Act and Article 34 of the implementing regulations thereo

Consent form date

Human biological material donor (Sign)

Legal guardian (Sign)

Research counselor (Sign)

Document	In the case of a legal representative, a document proving that the person is a legal representative