

*e-ASIA Joint Research Program
Progress Report*

1. Project Title: Elucidating the contribution of HBV/HDV co-/super-infection to hepatocellular carcinoma genome and biology

2. Joint Research Period: October 2, 2017 ~ March 31, 2021

3. Principal Investigators:

- Country 1: Taro Yamashita, Associate Professor, Kanazawa University Hospital, Japan.
 - Planned Funding Period: October, 2, 2017 – March, 31, 2021
- Country 2: Xin Wei Wang, Lab Chief, National Cancer Institute, USA.
 - Planned Funding Period: October, 2, 2017 – March, 31, 2021
- Country 3: Pham Van Thuc, Professor, Haiphong University of Medical and Pharmacy, Vietnam.
 - Planned Funding Period: In-kind

4. Summary of the Progress of the Joint Research:

Hepatocellular carcinoma (HCC), the most prominent form of liver cancer, represents the second most lethal cancer worldwide. It has become the fastest-rising cause of cancer-related deaths in the United States and is among the leading causes of cancer mortality in Asian countries, including Japan, Mongolia, and Vietnam. Most HCCs develop in the background of liver cirrhosis caused by the infection with hepatitis B virus (HBV) or hepatitis C virus (HCV). Furthermore, hepatitis D virus (HDV) infection, an incomplete RNA virus that requires chronic HBV infection for replication, accelerates the liver fibrosis and HCC development, but its epidemiology and pathogenesis is still equivocal and not clarified. We performed a collaborative study to perform whole RNA-seq analysis to clarify the potential gene expression changes in Japanese and Mongolian HCC cases, infected with HBV, HCV, and HBV/HDV. We further searched the potential fusion genes detected in Mongolian HCC samples. We found that some genomic regions are specifically expressed in Mongolian HCCs, suggesting the differential expression of genes in HCC, potentially related to the different ethnicities.

5. Scientific Achievements and Implemented Activities (Research Exchange, Workshop, Publication, etc. if any):

**For this item, please fill in the attached Excel file.*

Research Exchange:

Research meeting at Haiphong University, Haiphong, Vietnam. March 6th 2018.

Research meeting at NCI Bethesda, MD, USA. June 4th 2018.

NCI seminar “Reversal of Liver Cancer Progression from Preneoplastic Lesions”, June 4th 2018, 10:00 – 11:00 AM.

MEXT scholarship for research student (Dr. Doan Thi Bich Phuong, Haiphong University) from 2020 to 2024.

Research meeting and seminar at Kanazawa University, Kanazawa, Japan. July 22-August 4, 2019. Invited surgeons: Dr. BAATARJAV GAN-ERDENE, Dr. ENKHBAATAR ANKHBAYAR, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia.

Workshop:

The 4th international symposium on viral hepatitis, Haiphong, Vietnam. November 16, 2018

The international symposium on viral hepatitis, Ulaanbaatar, Mongolia. May 16-17, 2019

Publication:

Hashiba T, Yamashita T, Okada H, Nio K, Hayashi T, Asahina Y, Terashima T, Iida N, Takatori H, Shimakami T, Kawaguchi K, Arai K, Sakai Y, Yamashita T, Mizukoshi E, Takamura H, Ohta T, Honda M and Kaneko S: Inactivation of Transcriptional Repressor Capicua Confers Sorafenib Resistance in Human Hepatocellular Carcinoma. Cell Mol Gastroenterol Hepatol 2020.in press. doi: 10.1016/j.jcmgh.2020.02.009.

6. Future Goals and Plan of Activities within and after the project period:

We are currently investigating the potential transcriptomic cancer traits in HBV/HDV-related HCC. We will discuss the potential useful biomarkers and molecular targets through international collaboration among Japan, USA, Vietnam, and Mongolia within and after the project period.

7. Recommendations and Comments to the Program (if any):
(ex. Any support to request from the Program in order to achieve item 6.)

We hope if we could get the support about RNA-seq data analysis especially for the detection of RNA sequences not detected in human genome database, by AMED.

Lists of Achievements and Implemented Activities

1. Original Publication of Articles etc.

1. 1 Original Publications (Articles co-authored among Research Teams)

All Authors' Names, Title, Journal Name, Volume, Edition, Page, Year of Publication	DOI Code	Publication Status	Remarks (e.g. publication in top level journals etc.)

0 Total

1. 2 Original Publications (Articles by Single Team only)

All Authors' Names, Title, Journal Name, Volume, Edition, Page, Year of Publication	DOI Code	Publication Status	Remarks (e.g. publication in top level journals etc.)	Country name of the team
Tomomi Hashiba, Taro Yamashita, Hikari Okada, Kouki Nio, Takehiro Hayashi, Yoshiro Asahina, Takeshi Terashima, Noriho Iida, Hajime Takatori, Tetsuro Shimakami, Kazunori Kawaguchi, Kuniaki Arai, Yoshi Sakai, Tatsuya Yamashita, Eishiro Mizukoshi, Hiroyuki Takamura, Tetsuo Ohta, Masao Honda, and Shuichi Kaneko.	10.1016/j.jcmgh.2020.02.009.	in press		Japan

1 Total

Lists of Achievements and Implemented Activities

2. presentations at Academic Conferences etc. (Seminars, Workshops, Symposia)

2. 1 Conference Presentations (Joint Presentations among Research Teams)

Date	Type of Presentation	Speaker, "Title", Conference Name, Location, etc.
May 16, 2019	Guest/Invited Speaker	Taro Yamashita, "Whole RNA-seq Analysis of Hepatocellular Carcinoma in Mongolian and Japanese", The international symposium on viral hepatitis, Ulaanbaatar, Mongolia

1 Total

2. 2 Conference Presentations (by Single Team)

Date	Type of Presentation	Speaker, "Title", Conference Name, Location etc.	Country name of the team
June 4, 2018	Guest/Invited Speaker	Taro Yamashita "Reversal of Liver Cancer Progression from Preneoplastic Lesions", NCI seminar, Bethesda, MD.	Japan

1 Total

Lists of Achievements and Implemented Activities

3. Workshops, Seminars, Symposia and Other Events (Organized by the Project)

Event duration	Name of Organizer	Title of the Event	Location (Country, City, Venue)	Number of Participants (Including Team Members)	Overview
November 16, 2018	Phan Van Thuc	The 4th international symposium on viral hepatitis	Vietnam, Haiphong, Haiphong University of Medical and Pharmacy	50	Presentation of the data of sorafenib-resistant HCC and introduction of MEXT application program.
May 16–17, 2019	Duger Davaadorj	International symposium on viral hepatitis	Mongolia, Ulaanbaatar, Novotel Ulaanbaatar	50	Presentation of the data of Japanese and Mongolian HCCs infected with HBV, HCV, and HBV/HDV.

2 Total

Lists of Achievements and Implemented Activities

4. Record of Research Exchanges

Date of Departure	Date of Return	Last Name & First Name	Country of Affiliation	Affiliation	Position	Exchange Destination (Country, City, Research Organization etc)	Description of Exchange Content/Purpose	Duration of Exchange (autocompleted)
H30.3.5	H30.3.9	Taro Yamashita	Japan	Kanazawa University	Associate Professor	Vietnam, Haiphong, Haiphong University of Medical and Pharmacy	To confirm the study design and collcet the samples of the collaborative study.	5
H30.3.5	H30.3.9	Testuro Shimakami	Japan	Kanazawa University	Professor	Vietnam, Haiphong, Haiphong University of Medical and Pharmacy	To confirm the study design and collcet the samples of the collaborative study.	5
R1.7.22	R1.8.4	BAATARJAV GAN-ERDENE	Mongolia	Mongolian National University of Medical Sciences	Fellow	Japan, Kanazawa, Kanazawa University	To confirm the study design and collcet the samples of the collaborative study.	14
R1.7.22	R1.8.4	ENKHBAATAR ANKHBAYAR	Mongolia	Mongolian National University of Medical Sciences	Fellow	Japan, Kanazawa, Kanazawa University	To confirm the study design and collcet the samples of the collaborative study.	14
Total (Person)					4	Total (Person-day)		38

Lists of Achievements and Implemented Activities

5. Patent Applications

5. 1 Independent Applications by Single Team

Application Number	Name of Patent/ Patent Name	Application Date	Patent Applicants (Fill in All Members)	Publication Number (leave blank if unpublished)	Inventor	Country of Application	Registration Number (leave blank if unregistered)	Country Name of the Team

0

Total (Number of Application)

0

Total (Number of Registration)

5. 2 Joint Applications

Application Number	Name of Patent/ Patent Name	Application Date	Patent Applicants (Fill in All Members)	Publication Number (leave blank if unpublished)	Inventor	Country of Application	Registration Number (leave blank if unregistered)

0

Total (Number of Application)

0

Total (Number of Registration)

Lists of Achievements and Implemented Activities

6. Awards

Date of Award	Name of Award	Recipient	Remarks	Country Name of the Team

0

Total