

US-Mongolia Pilot Project Evaluation

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Symposium Rationale

- Mongolia has the highest rate of liver cancer mortality (8x global average) in the world.
- The prevalence of chronic viral hepatitis B, C, and D in Mongolia are at an endemic level and constitutes the dominant cause for Mongolia's world leading liver cancer mortality rate.
- Liver cirrhosis and liver cancer mortalities account for 15% of all annual mortalities.
- The Ministry of Health and Sports of Mongolia, the Mongolian Society of Hepatology, and Onom Foundation were implementing the Hepatitis Prevention, Control, and Elimination (HPCE) Program.
 - The US - Mongolia Scientific Symposium was intended to bring together US and Mongolian scientists and specialists interested in conducting collaborative, multi-disciplinary research within the Hepatitis Prevention, Control and Elimination Program.

Methods

- Review CRDF reports and bilateral evaluation to (1) evaluate the content that CRDF provides, and (2) understand successes and accomplishments of each pilot project.
- Contact US and Mongolian PIs to better understand longevity in partnerships and other accomplishments not mentioned in the CRDF reports.
- Search for additional publications/conference posters that stemmed from these collaborations.

Evaluation of CRDF Global Resources

Reports: Progress status reports, final technical reports, and final report assessments

These resources provided by CRDF are challenging to navigate as some lacked identifying information or were labeled incorrectly. Below are my observations when navigating the report documents from CRDF.

- Six folders were provided, which included various reports, however, there were seven funded projects.
- Some of the documents were not filed in the correct folder (i.e. award No. on documents did not match the folder it was filed within)
- There is no consistency in what documents are included within each project (i.e. some may have Progress Status Reports, Final Technical Reports, and Final Reports, while others may have just one document) This, however, may be a result of PI responsiveness.
- Some of the documents that were provided had incomplete information (i.e. there was an award No. but there was no PI or institution information) therefore I could not match the documents to the appropriate project.
- Some reports have no identifying information (i.e. no PI information & no award number).
- Some reports are without a second award number and PI, even though each award has two PIs and two award numbers.
- Some reports have the wrong award number listed. (*i.e. Final Technical Report for proposal No. 23662 (Pis: N. Dashdorj and R. Allison) has award No. 62998 on the actual document, which is the award No. associated with proposal No. 23665*)

As a result of these inconsistencies, I chose to read the reports and sort them under their associated proposal number based on content. Each folder is now named after the proposal numbers as opposed to the award numbers.

CRDF Bilateral Evaluation Survey

The bilateral evaluation survey questions essentially fell into three categories; personal information (i.e. affiliation, email), collaboration partner and partnership, and experience with CRDF staff. Three researchers responded to the CRDF survey; one US PI (Dr. Allison) and two project collaborators (Dr. Bayarsaikhan and Dr. Dashdorj). These responses represented two of the seven pilot projects.

I was able to obtain contact information (email addresses) for ten of the twelve project PIs. I proposed four questions that stemmed from CRDF's bilateral evaluation survey that I found relevant to understanding project accomplishments and ongoing collaboration efforts. The following questions were proposed to the ten PIs whose contact information I was able to obtain.

1. *What is the current status of your joint research project?*
2. *How would you describe the achievement of the project's goals outlined in the original proposal?*
3. *Describe the greatest benefit(s) from participating in the joint research project.*
4. *Has the joint research project led to any publications or additional collaboration opportunities?*

Dr. Xin Wei Wang, a project PI from NCI, was the only one to respond. Below you will a summary of his responses in addition to the responses from those who completed CRDF's bilateral evaluation survey to the four proposed questions.

1. What is the current status of your joint research project?

Dr. Wang indicated that their Mongolian Fellow, Dr. Enkjargal Bayarsaikhan, has completed training and is now the Director of Laboratory of Medicine at the National Cancer Center of Mongolia. Additionally, they have completed a pilot study, which involved completing an entire exome sequencing and transcriptome sequencing analysis of tumors and adjacent tumors from National Cancer Center of Mongolia. All three survey respondents indicated that the current status of their joint research project was 'ongoing'. Dr. Bayarsaikhan and Dr. Dashdorj also indicated that they intend to apply for a new project or grant with their collaborating partner.

2. How would you describe the achievement of the project's goals outlined in the original proposal?

Dr. Wang stated that the goals in the initial proposal had been reached and the project itself was complete. The three survey respondents also indicated positive result. Dr. Bayarsaikhan and Dr. Allison stated that projects goals were fully accomplished, while Dr. Dashdorj indicated that their achievement exceeded initial project goals.

3. Describe the greatest benefit(s) from participating in the joint research project.

Dr. Wang stated they were able to determine possible mechanisms related to hepatitis D virus-related hepatocarcinogenesis in Mongolia and to identify drivers responsible for Mongolian liver cancer. Dr.

Bayarsaikhan indicated that laboratory experience at NIH as their greatest benefit. Dr. Allison said the greatest benefit of their project was the ability to build research and laboratory capacity in the collaborator's country. Lastly, Dr. Dashdorj indicated great collaboration as their greatest benefit as it enabled better research.

4. Has the joint research project led to any publications or additional collaboration opportunities?

Dr. Wang stated that they have a manuscript currently being revised for Nature Communications. Additionally, he plans to continue collaboration with Dr. Bayarsaikhan and the efforts of the original project by performing additional tumor specimens to validate their initial findings. Dr. Bayarsaikhan indicated that this collaborative experience led to both publications and development of research protocols. Dr. Allison indicated that publications and conferences stemmed from his joint research project. Lastly, Dr. Dashdorj indicated that both research protocols and conferences resulted from his research collaboration.

Although Dr. Wang and Dr. Dr. Bayarsaikhan represent the same project, it was beneficial to obtain more detailed information from Dr. Wang around project accomplishments and longevity as the CRDF survey evaluation questions appear to be limited with regards to response options.

Accomplishments

As Indicated in Reports Provided by CRDF

Proposal No 23665: Implementing Project ECHO for Viral Hepatitis in Mongolia

The aim of the project was accomplished, which was to develop a learning tool for primary care physicians and hepatitis specialists through establishment of tele-medicine platform known as Project ECHO. Project ECHO is described as it is the first ever viral hepatitis specific training for primary care doctors. The goal was to involve 300 participants, but they were only able to enroll 60. CRDF did not consider this to be a notable success story.

Publication:

1. **Batdelger, D., Dagvadorj, A.**, Zulkhuu, G. (May 2015) Experience of distance learning in viral hepatitis training. INNOVATION magazine of the Academy of Sciences of Mongolia (In Press, in Mongolian)

Conference: Academic Conference of the Academy of Sciences of Mongolia

Proposal No 23664: Hepatitis survey among Mongolian children and adolescences

Initially proposed to enroll 750 subjects, however, they we were able to expand the enrollment to 2419 subjects.

Publications + Conference Posters:

1. Sereenendorj, K., Enkhbat, M., Eichner, M., Boldbaatar, K., Dashtseren, B., Bat-Ulzii, P., Genden, Z., Enkhbat, A., Budeebazar, M., **Dashdorj, N.**, Dashdorj, N., & **Yagaanbuyant, D.** (April 19, 2019). THU-419- Prevalence of hepatitis B and C virus infections in Mongolian children and adolescents. *Journal of Hepatology*, 70(1, Supplement), e341. [https://doi.org/10.1016/S0618-8278\(19\)30666-8](https://doi.org/10.1016/S0618-8278(19)30666-8)

Conferences: **(1)** XVII Congress Pediatric Infectious Disease Specialists, Russia **(2)** International Liver Meeting, Vienna Austria 2019

Poster: [https://www.postersessiononline.eu/173580348_eu/Baatarsuren1 congressos/ILC2019/aula/-THU 419 ILC2019.pdf](https://www.postersessiononline.eu/173580348_eu/Baatarsuren1%20congresos/ILC2019/aula/-THU_419_ILC2019.pdf)

Poster journal: [https://www.journal-of-hepatology.eu/article/S0618-8278\(19\)30666-8/pdf](https://www.journal-of-hepatology.eu/article/S0618-8278(19)30666-8/pdf)

**The manuscript stemming from this conference poster was to be published in the Journal of Viral Hepatitis in Dec. 2018.*

Proposal No 23663: Estimation of the rate of mother to child transmission of hepatitis B

CRDF only provided a project status report, therefore, it is lacking content on long-term accomplishments.

Proposal No 23659: Analysis of IL28B polymorphisms relationship with HDV clearance in Mongolian population

It was stated that this study was the first statistically significant analysis including appropriate amount of sample size to give an unarguable answer for the question about the association of HDV infection and SNP rs12979860. Additionally, capacity of molecular and cell biology studies was dramatically increased in New Mongol Institute of Technology. By collaborating in this project, researchers from the National Center for Communicable Diseases and the Liver Center are well familiarized with molecular biology applications including genetic diagnostic technologies and they have gained their experience for further establishment of genetic diagnostics.

Conference Poster:

1. Batsuuri, Z., Bat-Ulzii, P., Enkhbat, E., **Dashdorj, N.**, Chimed, G., **Perenlei, E.**, **Oidovsambuu, O.** (April 01, 2019)

Analysis of interleukin 28B rs12979860 polymorphism relationship with spontaneous clearance of hepatitis D virus infection in Mongolian population. *Journal of Hepatology*, 70(1), Supplement, e253

DOI: [https://doi.org/10.1016/S0618-8278\(19\)30477-3](https://doi.org/10.1016/S0618-8278(19)30477-3)

Conference: *International Liver Meeting, Vienna Austria 2019*

Proposal No 23656: The Genomic Landscape of Hepatitis D-related Hepatocellular Carcinoma among Mongolian Patients

CRDF provided no reports pertaining to proposal 23656.

Proposal No 23662: HCV and HBV-Mediated B-Cell Malignant Transformation and Prioritization of HCV Treatment in Mongolia

It was stated that the group in Mongolia have fully accomplished their preliminary aims of the proposal as it relates to the establishment of a B-NHL registry combined with subsequent determination of HBB and HBC status. The most immediate result of the work to date is improved patient care for lymphoma patients in Mongolia. CRDF did not consider this to be a notable success story.

Publication + Conference Posters:

1. Мянмаржав, Б., Khishigjargal, Б., Myadagsuren, S., Erdenetsogt, D., **Dagvadorj, A.**, Даваадорж3, Д., Д. Наранжаргал (April 8, 2016) Non-Hodgkin's Lymphoma, Hepatitis Virus in combined cases-results of chemotherapy. INNOVATION OF SCIENCE Magazine. (In Mongolian)

2. Budeebazar, M., Batsukh, K., Boldbaatar, D., Norov, O., Dungubat, E., **Yagaanbuyant1, D.**, Mordorj, A., Bungert, A., Duger, D., **Dashdorj, N.**, Dashdorj, N. (June 2016) Chronic hepatitis C prevalence among patients diagnosed with B-Non-Hodgkin lymphoma. *Journal of Viral Hepatitis*, 25, 90-91

3. Budeebazar, M., Boldbaatar, D., Myadagsuren, S., Saruul, T., Baatarsuren, U., Batsukh, K., Dungubat, E., Bungert, A., Mordorjyn, A., **Yagaanbuyan, D.**, Davaadorj, D., **Dashdorj, N.**, Dashdorj, N. (April 12, 2019). Contribution of HBV and HCV infection in mortality of B-NHL subjects. *Journal of Hepatology*, 70(1), Supplement, e1-e952 DOI: [https://doi.org/10.1016/S0168-8278\(19\)30968-5](https://doi.org/10.1016/S0168-8278(19)30968-5)

Proposal No 23657: Circulating Tumor DNA (ctDNA) and liver cancer: Building capacity for cancer prevention in Mongolia

CRDF only provided a project status report, therefore, it is lacking content on long-term accomplishments.

Additional Relevant Publications and Posters

1. Baatarsuren, U., Munkh-Erdene, T., Myanganbayar, M., Batsukh, M., Jamsranjav, A., Dugerjav, D., Tseren, O., Janchiv, C., Bungert, A., **Dagvadorj, A.**, Enkhbayar, E., Dashdorj, N., Genden, Z., & **Dashdorj, N.** (September 2017). Correlation between prevalence of hepatitis B and C virus infection and mortality of hepatocellular carcinoma in Uvs province, Mongolia. *Journal of Hepatology*, 66(1), S710.

[https://doi.org/10.1016/S0168-8278\(17\)31902-5](https://doi.org/10.1016/S0168-8278(17)31902-5)

Poster: <https://www.globalhep.org/sites/default/files/content/programs/files/2019-11/Poster-%20Correlation%20between%20hepatitis%20prevalence%20and%20mortality%20from%20HCC.pdf>

2. Chen, X., **Oidovsambuu, O.**, Liu, P., Grosely, R., Elazar, M., Winn, V. D., Fram, B., Boa, Z., Dai, H., Dashtseren, B., **Yagaanbuyant, D.**, Genden, Z., **Dashdorj, N.**, Bungert, A., Dashdorj, N., & Glenn, J. S. (2017). A novel quantitative microarray antibody capture assay identifies an extremely high hepatitis delta virus prevalence among hepatitis B virus-infected Mongolians. *Hepatology* (Baltimore, Md.), 66(6), 1739–1749. <https://doi.org/10.1002/hep.28957>

3. Dashdorj, N., **Dashdorj, N.**, Bungert, A. S., Genden, Z., **Dendev, B.**, Duger, D., **Dagvadorj, A.**, & **Yagaanbuyant, D.** (January 2017). Hepatitis prevention, control, and elimination program in Mongolia: National hepatitis elimination program in a country with the highest burden of viral hepatitis in the world. *Journal of Hepatology*, 66(1), S412–S413. [https://doi.org/10.1016/S0168-8278\(17\)31184-4](https://doi.org/10.1016/S0168-8278(17)31184-4)
Conference: *The International Liver Congress 2017 — 52nd Annual meeting of the European Association for the Study of the Liver*

4. Dashtseren, B., Bungert, A., Bat-Ulzui, P., Enkhbat, M., Lkhagva-Ochir, O., Jargalsaikhan, G., Enkhbat, A., **Oidovsambuu, O.**, Klemen, J., Dashdorj, **N.**, **Dashdorj, N.**, Genden, Z., & **Yagaanbuyant, D.** (September 2017). Endemic Prevalence of Hepatitis B and C in Mongolia: A Nationwide Survey Amongst Mongolian Adults. *Journal of Viral Hepatitis*, 24(9). <https://doi.org/10.1111/jvh.12697>

For clarity, this chart was created as a means of having all relevant project information in one place. It includes PI and funding information as well as information on complementary resources, such as CRDF reports and CDRF survey completion.

Proposal No.	Award No.	CRDF Docs	Completed CRDF Survey	Title	Mongolian PI	Mongolian Institute	US PI	US Institute	NIH IC	Amount
23665		FTR, FRA		<i>Implementing Project ECHO for Viral Hepatitis in Mongolia</i>	Dendev Batdelger D.Batdelger@onomfoundation.org	Mongolian Society of Hepatology	Norah Terrault norah.terrault@ucsf.edu	University of California San Francisco	NIAID	\$50,000
23664		PSR, FTR		<i>Hepatitis survey among Mongolian children and adolescences</i>	Ayush Dagvadorj	Onom Foundation	Norah Terrault norah.terrault@ucsf.edu	University of California San Francisco	NIAID	\$50,000
23663		PSR x2		<i>Estimation of the rate of mother to child transmission of hepatitis B</i>	Dahgwahdorj Yagaanbuyant	Mongolian Society of Hepatology	Kenrad Nelson knelson3@jhu.edu	John Hopkins University	NIAID	\$50,000
23659		PSR/FTR		<i>Analysis of IL28B polymorphisms relationship with HDV clearance in Mongolian population</i>	Odgerel Oidovsambuu o.odgerel@onomfoundation.org	New Mongol Technology Institute	Perenlei Enkhbaatar peenkhba@utmb.edu	University of Texas, Medical Branch	NIAID	\$50,000
\$200,000										
23656	62997	N/A	(1) Enkhjargal Bayarsaikhan	<i>The Genomic Landscape of Hepatitis D-related Hepatocellular Carcinoma among Mongolian Patients.</i>	Dendev Batdelger D.Batdelger@onomfoundation.org	National Cancer Center of Mongolia	Xin Wei Wang wangx@intra.nci.nih.gov	NCI-NIH	NCI	\$49,800
23662		PSR, FTR, FRA	(1) Naranjargal Dashdorj (2) Robert Allison	<i>HCV and HBV-Mediated B-Cell Malignant Transformation and Prioritization of HCV Treatment in Mongolia</i>	Naranbaatar Dashdorj n.dashdorj@onomfoundation.org	Liver Center	Robert Allison traveldoc365@gmail.com	National Institute of Health Clinical Center	NCI	\$50,000
23657		PSR		<i>Circulating Tumor DNA (ctDNA) and liver cancer: Building capacity for cancer prevention in Mongolia</i>	Batmunkh Munkhbat munkhbatb@mnums.edu.mn	Mongolian National University of Medical Sciences	Ann Hsing annhsing@stanford.edu	Board of Trustees of the Leland Stanford Junior University	NCI	\$49,025
\$148,825										
PSR=Project Status Report FRA=Final Report Assessment FTR=Final Technical Report										

Next Steps

1. Further understand sustainability and longevity
 - It may be worth looking further into what new partnerships have been developed from these projects. Between CRDF's bilateral evaluation and Dr. Wang's response, we only have information around ongoing collaboration from two of the seven projects. Attempting to connect with PIs again could be beneficial, or possibility other collaborators from these projects.
 - Search each of the PIs on a database like PubMed may provide better insight into the publications that stemmed from these projects.
 - Obtaining contact information for the PIs whose information I was not able to locate and prompting them with the same questions as mentioned above.
2. Explore ongoing research efforts in Mongolia as they pertain to liver cancer and hepatitis
 - While there are currently no active NIAID-funded grants pertaining to liver cancer and/or hepatitis research in Mongolia, it may be worth looking into what other US agencies are involved in research on these diseases.
 - Utilizing QVR to explore NIH's collaboration presence in Mongolia, as opposed to just NIAID's presence.
3. Explore the current health status and research efforts in Mongolia
 - When the symposium took place in 2016, the Hepatitis Prevention, Control, and Elimination (HPCE) Program (MISSION 2020) was newly developed and it's aims were to eliminate cancer-causing hepatitis C virus in Mongolia by 2020 and to reduce mortalities related to liver cirrhosis and liver cancer by 50% in Mongolia by 2020. The program's 2030 goal is a 90% reduction in hepatitis B and C incidence and mortality. It may be worth looking into ongoing efforts to eliminate hepatitis and liver cancer in the country since 2016, as a means of identifying areas of additional collaboration. It may also be worth connecting with other researchers in the field who were not PIs on these pilot projects for additional perspectives and insight into these diseases.