Form 3

Report for Joint/Usage Research Program for Endocrine/Metabolism (Fiscal Year 2020)

Date: 2021/4/30

To Director of Institute for Molecular and Cellular Regulation, Gunma University

Principal Applicant			
Institution	Ajou University		
Position	Professor		
Name	Bum-Ho, Bin		
Address	206, World cup-ro, Yeongtong-gu, Suwon-si, Gyeonggi-do, 16499, Korea		
TEL	+31-219-2618	E-mail	bhb@ajou.ac.kr

We report on the results of joint research in fiscal 2020 as below.

（Program No. 19004）

1． Research Title	Targeting ZIP13 prevents fibrosis progression.
2． Purpose and Significance of the research project	Based on our previous data that ZIP13 is a regulator of TGF-β signaling, targeting ZIP13 may prevent general fibrosis progression in liver and skin. The object of our study is to assess the underlying mechanism how ZIP13 is involved in fibrosis in liver and skin, and to develop the therapeutic strategy to treat fibrosis by controlling ZIP13.
3． Period of The Program	April 1, 2020 ～ March 31, 2021

4． Project Members

Name	Age	Gender	Institution/Department	Position	Role
(Principal Applicant) Bum-Ho, Bin	39	M	Ajou University, Department of Biological Sciences	Professor	Project director
(Research Collaborators) Hantae, Jo	36	M	Ajou University, Department of Applied Technology	Research Professor	Researcher
(Research Collaborators) Byungsun, Cha	28	M	Ajou University, Department of Biological Sciences	Ph. D. Candidate	Researcher

※If additional space is required, attach a separate sheet.

5． Collaborative Researcher of IMCR	Name of the Laboratory	Developmental Biology and Metabolism	Name	Ayako Fukunaka

6 . Research Plans

<At IMCR>
- Experimental research
- Material supplementation
- Discussion and analysis of data
- Generation of hepatic stellate cell-specific deleted mice
- Fibrosis induction in mice

<At Ajou University>
- Fibrosis mice model:

Two experimental methodologies were designed, including toxic and genetic-based models:
- Toxic model (Dimethylnitrosamine-based model, etc.) with Wild type mice (Test)
- Liver or Skin imaging (Sirius red / H&E / Azan staining)

- Expression of ZIP13 in mice and human:

Analysis of ZIP13 expression in skin and liver of healthy individual and fibrosis patients. In this step, human samples will be used, or existing data from a global database in combination with computational and biological experiments.

- Mechanism analysis:

Molecular mechanisms will be addressed to uncover the specific pathway involved in ZIP13-related fibrosis, which is crucial for global acceptance by the research community. Considering the inherent difficulties in pathway mechanism studies, below are listed some of the possible approaches to answer this question:
- Next generation sequencing
- Analyzing the TGF-β responses
- Molecular biological experiments

- Therapeutical strategy:

After demonstrating the mechanism, a strategy will be developed and tested *in vivo*. This step is crucial to elucidate the potential application of our study in clinical therapy:
- Targeting ZIP13 in fibrosis induced wild type mice by siRNA-based (LNA) technology
- Monitoring skin and liver fibrosis progression

7 . Research results:

- Transfer of the ZIP13 KO mice to Ajou University

- Liver fibrosis model mice
  - Established with Dimethylnitrosamine

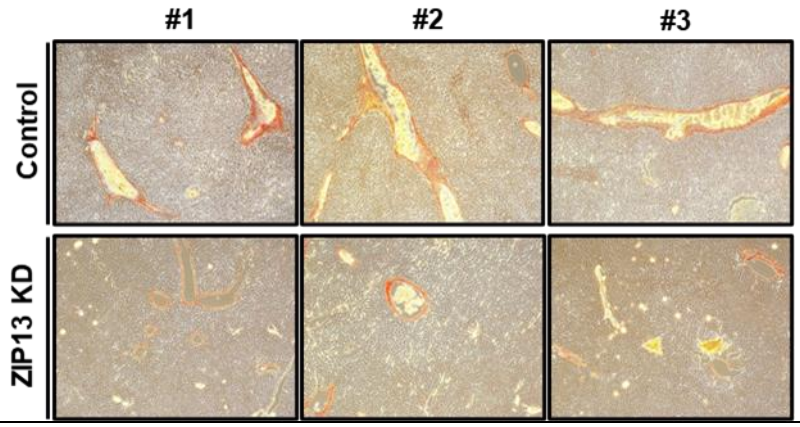
- Liver or Skin imaging
  - Established with Sirius red / H&E / Azan staining

- Next generation sequencing
  - In preparation

- Analysis of the TGF-β signaling in liver from ZIP13 KO mice
  - ZIP13 was highly expressed in hepatic stellate cells
  - ZIP13 deficiency leaded dysregulation of TGF-β signaling

- Molecular biological experiments
  - In preparation

- Targeting ZIP13 in fibrosis induced wild type mice by siRNA-based (LNA) technology
  - LNA targeting slc39a13 improved liver fibrosis (below)



8. Publications and/or Presentations resulting from Joint Research Program with IMCR.
Exchange of information on joint research with faculty members.

①Please describe a list of publications in which the name of the collaborative researcher of IMCR appears and send one paper reprints of each publication to IMCR.
None.

②Please describe a list of publications which include the description that the research is supported by Joint Research Program with IMCR and send one copy of each publication to IMCR.
None.

③Enter the name of the conference, the date of the conference, and the title of the presentation of the conference.(up to 3 cases)
None.

④Implementation status of information exchange with faculty members in charge of joint research.
We keep in touch with Dr. Fukunaka for further study.