Form 3

Report for Joint/Usage Research Program for Endocrine/Metabolism (Fiscal Year 2019)

Date: 2020/03/31

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

Principal Applicant	
Institution	Kyushu University
Position	Associate Professor
Name	Ka Fai William TSE

We report on the results of joint research in fiscal 2019 as below.

(Program No. 18003)

1. Research Title	Triclosan: a risk factor of fatty liver disease
2. Purpose and Significance of the research project	The project aims to understand the developmental toxicity of a common environmental pollutant, triclosan (TCS), on its stimulatory effects on developing the fatty liver disease. TCS and its degradation by-product, 2,4-Dichlorophenol (2,4-DP), can be found in the environment worldwide. Their potential toxicities on the lipid metabolism and liver development are not well known. We hypothesize that the exposure of TCS and 2,4-DP will promote the development of fatty liver. The transgenic zebrafish model will be used to perform functional assays; together with the next generation sequencing, the potential link between the TCS and fatty liver will be uncovered.
3. Period of The Program	April 1, 2019 ～ March 31, 2020

4. Project Members

Name	Age	Gender	Institution/Department	Position	Role
(Principal Applicant) Ka Fai William TSE	36	M	Kyushu University, Faculty of Agriculture	Associate Professor	Project director
(Research Collaborators) Yun-jin JIANG	55	M	National Health Research Institutes, Institute of Molecular and Genomic Medicine	Associate Investigator	Expert in zebrafish genetics / Advisor
Keng Po LAI	43	M	City University of Hong Kong, Department of Chemistry	Visiting Assistant Professor	Expert in RNA-sequencing and bioinformatics/ Advisor
May-su YOU	56	F	National Health Research Institutes, Institute of Molecular and Genomic Medicine	Senior Specialist	Expert in zebrafish genetics / Advisor

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

5. Collaborative Researcher of IMCR	Name of the Laboratory	Integrated Signaling Systems	Name	Tohru ISHITANI

6. Research Plans

The drastic advancement in industrialization and technology and the growth in human population in the past century have resulted in unprecedented environmental changes in human history. The production of large amounts of synthetic chemicals and pollutants has influenced our ecosystem and brings potential hazards to humans. Among the pollutants, the endocrine disrupting chemicals (EDCs) are the most concerning pollutants; as they can interfere with the synthesis, metabolism, and action of endogenous hormones. EDC has been widely used in personal-care products, such as triclosan (TCS). It is an antimicrobial agent that can be accumulated in fatty tissue. Our previous students have shown that TCS could affect lipid metabolism during early development in zebrafish embryos. Zebrafish has been widely used in the developmental studies as an excellent *in vivo*, high-throughput and scalable system for decades. The fatty liver mutant (*trappc11*$^{-/-}$) induced ER stress and altered the protein trafficking that resulting in hepatic steatosis. Here, we would like to investigate if the TCS and 2,4-DP could stimulate the disease development. The project will uncover the underlying mechanism by various biological functional assays, next-generation sequencing, and bioinformatics analysis.

7. Research results:

In the past two years, we have identified the general toxicity of TCS and its degradation by-product 2,4-DP in the wild-type and liver- GFP labeled zebrafish. In addition, we have applied the fatty liver mutant line to perform the general characterization of metabolic genes and enzymes under the acute TCS and 2,4-DP exposure. Furthermore, we have identified the development functional time window of the *trappc11* gene and started to investigate its relationship with the pollutants. Results suggested that the TCS and 2,4-DP could influence the lipid metabolism during early embryogenesis. In this year, we are preparing the samples for the next generation sequencing. The sequencing will dissect the genetic information of the TCS/ 2,4-DP exposed embryos. Various bioinformatics analysis will be done and the data validation/ functional experiments will be performed to confirm the sequencing data. We expected that we could have the full picture of the toxicogenomics of TCS and 2,4-DP exposure in the project.

8. Publications and/or Presentations resulting from Joint Research Program with IMCR.

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.

N/A

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.

N/A