Title of Research:

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Chip device for in vitro systemic toxicology

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Summary of Research:

The aim of this study is to develop microdevices, so-called Body on a chip, for *in vitro* drug testing to evaluate systemic toxicity of chemicals. This device may enable to replicate *in vivo* kinetics and interactions between several tissues including the skin, the small intestine, and the lung for drug absorption, liver and myocardial tissues for drug metabolism and exposure. The point of our device is to engineer cell layer and spherical tissues on a chip as tissue models to acquire more physiological responses.

In the second year of the project, we improved functionalities of spherical tissues. Data we obtained last year indicated that when cells form tissues and sufficient oxygen is supplied, not only positive effects but also adverse effects were observed, probably due to generation of reactive oxygen species. To alleviate the negative effects, we examined antioxidants. Indeed, the addition of antioxidants in culture medium further improved insulin secretion on pancreatic spheroids. Permeability testing was performed with skin and intestine models that we fabricated last year. In addition, interactions between two model tissues, liver and breast cancer, were evaluated on a seesaw-like stage, with which culture medium were perfused in the microdevice without any external pump and air pressure supply. In this setup, a pro-drug was metabolized with the liver model and inhibited growth of the cancer cells. Furthermore, we demonstrated that the modified h-CLAT testing shows a positive reaction to a positive control substrate.

Timeline:

March 1, 2018 – February 28, 2019

Topics:

Junji Fukuda, “Chip device for in vitro systemic toxicology”, JCIA LRI Research Conference, Tokyo, Japan, Aug 2017

Publications:

D. Myasnikova, T. Osaki, K. Onishi, T. Kageyama, B. Zhang, J. Fukuda, Synergic effects of oxygen supply and antioxidants on pancreatic β-cell spheroids, *Scientific Reports*, 9, 1802 (2019)