



Title of Research:

22-1-04

Establishment of Human iPSC Reporter-Based Developmental Toxicity Assay that Detects FGF Signal Disruption

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Summary of Research:

In this study, a real-time luminescence measurement system was introduced to improve the accuracy of the kinetic assay, which has been a hallmark of the signal disruption assay. Although this system enabled continuous measurements over a 3-day period and captured more detailed changes in developmental toxicity than conventional manual measurements, it also raised several issues. The measurement system revealed the edge effect of the culture plate and experimental errors in each run. Therefore, a protocol to reduce these problems was investigated in detail and reconstructed in this study. This includes optimization of the pre-culture schedule, reduction of evaporation of culture medium, and concentration of luminescent substrates. In the Wnt signal disruption test, we prepared Wnt signal reporter cells and examined for the signal disruption assay. In addition, we tested Wnt ligands to FGF/SRF signal reporter cells. In particular, the latter showed that intracellular signaling network links may be responsible for the high probability of teratogen detection in this assay, suggesting that the number of signaling pathways in the future battery assay could be reduced.

Timeline: March 1, 2023 –

Topics:

Y. Okubo and J. Fukuda, Evaluation of developmental toxicity analyzing by dynamics of signal disruption, *Seikagaku Mini Review*, 95, 2, 1-6, 2023, Doi: 10.14952/SEIKAGAKU.2023.95

Presentation Award, K. Mizota, Y. Okubo, M. Shibata, R. Ohara, Y. Nakajima, J. Fukuda: Developmental toxicity testing of chemicals based on long-term signal disruption using human iPSC reporter cells, 61st Japanese Society for Artificial Organs, Nov. 9-11, Tokyo

Publications:

Invited talk. Y. Okubo: Developmental toxicity detection via dynamics of FGF-SRF signal disruption in human iPSC-based assay. 13TH Global Summit on Regulatory Science (GSRS23) In-Person Annual conference. Sep. 27, 2023.

Y. Okubo, K. Mizota, M. Shibata, R. Ohara, S. Kitajima, Y. Hirabayashi, Y. Nakajima, J. Fukuda: Developmental toxicity test using human iPS cells based on signal disruptions induced by chemical substances. 12th World Congress on Alternatives and Animal Use in the Life Sciences (WC12), Niagara Falls, Canada. (Aug. 30, 2023). Oral presentation.

K. Mizota, Y. Okubo, M. Shibata, R. Ohara, S. Kitajima, Y. Hirabayashi, Y. Nakajima, J. Fukuda: Developmental toxicity testing of chemicals based on long-term signal disruption using human iPSC reporter cells. 12th World Congress on Alternatives and Animal Use in the Life Sciences (WC12), Niagara Falls, Canada. (Aug. 30, 2023). Poster presentation.