Title of Research:

13_PT01-01

Development of in vivo fluorescent imaging of neuronal differentiation in zebrafish for developmental neurotoxicity testing

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Summary of Research:

Various chemicals may affect the differentiation of neurons, oligodendrocytes and astrocytes, which may cause neurodevelopmental disorders such as autism and attention deficit hyperactive disorder. *In vivo* models that can be used in both visualization of the neuronal differentiation and quantitative assessment of behavior are highly valuable for developmental neurotoxicity testing. Recently, zebrafish has emerged as an alternative non-mammalian animal model that allows testing of large numbers of subjects while reducing expenses and minimizing the use of mammalian subjects. In this study, we have developed three-color zebrafish exhibiting blue, yellow and red fluorescence in neurons, oligodendrocytes and astrocytes, respectively. Using the zebrafish, we evaluated the developmental neurotoxicity of four positive control chemicals, valproic acid, methyl mercury, nicotine, and bisphenol A. We were able to detect the toxicity of these chemicals on the neuronal differentiation. We will use more positive and negative chemicals to examine the sensitivity and specificity of the *in vivo* fluorescent imaging of neuronal differentiation in zebrafish for developmental neurotoxicity testing.

Timeline:

Mar 2016 ~ Feb 2017

Publications:

1) **Activation of Sterol Regulatory Element Binding Factors by Fenofibrate and Gemfibrozil Stimulates Myelination in Zebrafish**. Ashikawa, Y., Nishimura, Y., Okabe, S., Sasagawa, S., Murakami, S., Yuge, M., Kawaguchi, K., Kawase, R., and Tanaka, T. *Frontiers in pharmacology* 7, 206 (2016)
2) **EP300 protects from light-induced retinopathy in zebrafish.** Kawase, R., Nishimura, Y., Ashikawa, Y., Sasagawa, S., Murakami, S., Yuge, M., Okabe, S., Kawaguchi, K., Yamamoto, H., Moriyuki, K., Yamane, S., Tsuruma, K., Shimazawa, M., Hara, H., and Tanaka, T. *Frontiers in pharmacology* 7, 126 (2016).
3) **E2F4 promotes neuronal regeneration and functional recovery after spinal cord injury in zebrafish.** Sasagawa, S., Nishimura, Y., Hayakawa, Y., Murakami, S., Ashikawa, Y., Yuge, M., Okabe, S., Kawaguchi, K., Kawase, R., and Tanaka, T. *Frontiers in pharmacology* 7, 119 (2016).
4) **Downregulation of GSTK1 Is a Common Mechanism Underlying Hypertrophic Cardiomyopathy.** Sasagawa, S., Nishimura, Y., Okabe, S., Murakami, S., Ashikawa, Y., Yuge, M., Kawaguchi, K., Kawase, R., Okamoto, R., Ito, M., and Tanaka, T. *Frontiers in pharmacology* 7, 162 (2016).
5) **Comparative transcriptome analysis identifies CCDC80 as a novel gene associated with pulmonary arterial hypertension.** Sasagawa, S., Nishimura, Y., Sawada, H., Zhang, E., Murakami, S., Ashikawa, Y., Yuge, M., Okabe, S., Kawaguchi, K., Kawase, R., Mitani, Y., Maruyama, K., and Tanaka, T. *Frontiers in pharmacology* **7**, 142 (2016).
6) **Integrated Approaches to Drug Discovery for Oxidative Stress-Related Retinal Diseases.** Nishimura, Y., and Hara, H. *Oxid Med Cell Longev.* 2370252 (2016).