Assessment of Developmental Neurotoxicity during Neuronal Differentiation using a Triple-Transgenic Zebrafish Line

Adachi Yuka[1], Junko Koiwa[1], Takashi Shiromizu[1], Toshio Tanaka[2], Yuhei Nishimura[1]

[1]Dept. Integrative Pharm., Mie Univ. Grad. Sch. Med. 2-174 Edobashi, Tsu, Mie 514-8507, [2]Dept. Systems Pharm., Mie Univ. Grad. Sch. Med. 2-174 Edobashi, Tsu, Mie 514-8507

The developing brain is extremely sensitive to many chemicals. Various screening methods have been used to assess the developmental neurotoxicity (DNT) of chemicals. However, assessment of toxicity during progenitor cell differentiation into neurons, astrocytes, and oligodendrocytes often requires immunohistochemistry, which is a reliable but labor-intensive and time-consuming assay. Here, we report the development of a triple-transgenic zebrafish line that expresses distinct fluorescent proteins in neurons (Cerulean), astrocytes (mCherry), and oligodendrocytes (mCitrine), which can be used to detect DNT during neuronal differentiation. Using in vivo fluorescence microscopy, we could detect DNT by 6 of the 10 neurotoxicants tested after exposure to zebrafish from 12 h to 5 days' post-fertilization. Moreover, the chemicals could be clustered into three main DNT groups based on the fluorescence pattern: (i) inhibition of neuron and oligodendrocyte differentiation and stimulation of astrocyte differentiation; (ii) inhibition of neuron and oligodendrocyte differentiation; and (iii) inhibition of neuron and astrocyte differentiation, which suggests that reporter expression reflects the toxicodynamics of the chemicals. Thus, the triple-transgenic zebrafish line developed here may be a useful tool to assess DNT during neuronal differentiation.