Effects of valproic acid on gene expression during human embryonic stem cell differentiation into neurons.

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Abstract

The widely used antiepileptic drug valproic acid (VPA) is known to exhibit teratogenicity in the form of a failure of the neural tube in humans. Embryonic stem cells (ESCs) are reported to be a promising cell source for evaluating chemical teratogenicity, because they are capable of reproducing embryonic developmental model and enable reduction in the number of experimental animals used. We previously investigated 22 genes for which expressions are altered by teratogens, specifically focusing on neural differentiation of mouse ESCs. In the present study, expressions of the investigated genes were evaluated by quantitative real-time PCR and compared during differentiation of human ESCs into neurons with or without VPA. Under the conditions, almost all gene expressions significantly changed in VPA-containing culture. Specifically, in neural development-related genes such as DCX, ARX, MAP2, and NNAT, more than 2-fold expression was observed. The findings suggest that the genes focused on in this study may help to elucidate the teratogenic effects of VPA and might be a useful tool to analyze embryotoxic potential of chemicals in humans.