Human induced pluripotent stem cell (hiPSC)-derived astrocytes are functional in hiPSC-derived neural networks

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hiPSC-derived neural networks (hiPSC-networks) on dish are expected to provide the improvement of human predictability in the drug development. To date, we have established the stable protocol to reproduce hiPSC-networks. However, little data are available whether astrocytes are also functional or not in these hiPSC-networks. In this study, we examined the role of astrocytes in hiPSC-networks. qRT-PCR study indicated that the mRNA levels of GFAP, AQP4 and L-glutamate (L-Glu) transporter were increased along with culture days and their expression changes were obtained later than those of neuronal genes. GFAP(+)Nestin(-) astrocytes appeared at DIV 49 and L-Glu transporters were detected in these cells immunohistochemically at DIV 63. We examined whether L-Glu transporters were functional or not at DIV 63. When we applied 100 microM of L-Glu to the sample, the concentration was decreased to less than 15 microM in 1hr. In microelectrode array experiments at DIV 63, the treatment with non-specific EAAT blocker TFB-TBOA decreased firing activities. These results suggest that astrocytes are functionally differentiated and indispensable for homeostatic control of extra-synaptic L-Glu concentrations of hiPSC-networks. Currently we are identifying EAATs subtypes in the hiPSC-networks used in this study.