**Analysis of particle and cellular uptake characteristics of neuron- or microglia-derived EVs for microglia-targeted therapy**

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**Background and aims.** In recent years, the development of novel therapies targeting microglia, which plays a role in maintaining homeostasis in the brain, has been promising for cranial neurological diseases. On the other hand, extracellular vesicles (EVs) have been reported as a biological intercellular regulation system with tropism to specific organs and cells in a body. In this study, to investigate the development of novel microglia-targeted therapy, neuron- and microglia-derived EVs with focus on particle and cellular uptake characteristics were analysed.

**Methods.** EVs were collected by ultracentrifugation from acclimation medium of mouse neuroblast (Neuro2a) and microglia (BV2). The expression of exosomal markers in each EVs was confirmed by Western blot analysis. Particle properties and protein amounts of EVs were analysed by NTA and BCA protein assay. Cellular uptake into Neuro-2a and BV2 was evaluated by observation of fluorescently labelled EVs by fluorescence microscopy. EVs derived from each cell stimulated with LPS were also analysed to investigate the effects of inflammation.

**Results.** Collected EVs were confirmed as expressing CD9, CD63, CD81 and Tsg101 and showed 100-150 nm. The protein content of BV2-derived EVs was about 2-fold higher than that of Neuro2a-derived EVs. Both EVs exhibited higher uptake into Neuro2a than into BV2. The uptake into Neuro2a was about 1.7-fold higher in BV2-derived EVs than in Neuro2a-derived EVs. In contrast, the uptake into BV2 stimulated by LPS was significantly increased of both EVs than that into non-stimulated BV2, and the highest uptake was observed by Neuro2a-derived EVs. These results indicate that EVs secreted from neurons would be a useful tool for microglia-targeted therapy.