Quantification of phosphorylated TrkB in human blood extracellular vesicles and effect of food-derived antioxidant

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Food-derived antioxidant ergothioneine (ERGO) is not synthesized in mammals, but ingested from daily diet. After oral administration, ERGO is efficiently absorbed in gastrointestinal tract and distributed to the brain parenchyma via transporter SLC22A4, implying its fundamental role in the brain. Oral administration of ERGO actually enhances learning and memory in mice at least in part through activation of tropomyosin receptor kinases B (TrkB), a receptor for neurotrophins. Therefore, we hypothesized that amount of phosphorylated-TrkB (p-TrkB), the activated form in extracellular vesicles (EVs) in blood may reflect the ERGO-induced enhancement of cognitive function, since EVs may contain brain-derived exosomes and might be useful as a liquid biopsy for verifying the effect on brain function even in humans. We first evaluated expression of p-TrkB by western blot in EVs which were isolated from human serum by ultracentrifugation method. There was a significant correlation between blood ERGO concentration and expression of p-TrkB in EVs. We also confirmed expression of SNAP25, a neuron-derived protein in the isolated EVs. These results suggest that expression of p-TrkB in EVs in circulation is associated with ERGO exposure and might be a possible biomarker useful for assessment of ERGO-induced beneficial effect in the human brain.