Functional evaluation of the patient-derived iPS cells from *PDGFB*-variants in idiopathic basal ganglia calcification

Naoki Shibuya, Tomohiko Masaka, Hisaka Kurita, Masatoshi Inden, Isao Hozumi

Lab. Med. Therap. Mol. Therap., Gifu Pharm. Univ.

Idiopathic basal ganglia calcification (IBGC) is an intractable disease characterized by bilateral calcification in basal ganglia and other regions. The causative genes have been identified. Among them, the variant frequency of *PDGFB* in familial IBGC is about 10%. *PDGFB* encode platelet-derived growth factor B (PDGF-B). Previous studies showed PDGF-B is expressed in endothelial cells and neurons in the brain and PDGF-BB, a homodimer of PDGF-B, stimulates pericytes which are abundant in the brain and the Pi transport in the vascular smooth muscle cells. In this study, variant analyses of *PDGFB* for IBGC patients showed four novel pathogenic variants, c.160 + 2T > A, c.457 −1G > T, c.33_34delCT and c.342_343insG. The iPS cells (iPSCs) from three patients with novel *PDGFB* variant were established and endothelial cells were induced. Enzyme-linked immunoassay analysis showed that the levels of PDGF-BB in the blood sera of patients with *PDGFB* variants were decreased to 34.0% of that of the control levels. Those in the culture media of the endothelial cells derived from iPSCs of patients decreased to 58.6% of the control levels. As the endothelial cells developed from iPSCs of the patients showed a phenotype of the disease, IBGC-specific iPSCs will give us more information on the pathophysiology and the therapy of IBGC in the future.