Abnormal cell differentiation of human microglial cells and neuropsychiatric disorders: Translational research using human induced microglia-like (iMG) cells

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Postmortem brain analysis and PET imaging analysis are two major methods to estimate microglial activation in human subjects, and these studies have suggested activation of human microglia in the brain of patients with various psychiatric disorders. However, by using the above methods, only a limited aspect of microglial activation can be measured. We have originally developed a technique to create directly induced microglia-like (iMG) cells from fresh human peripheral blood monocytes adding GM-CSF and IL-34 for 2 weeks, instead of brain biopsy and iPS technique (Ohgidani, Kato et al. Sci Rep 2014). Using the iMG cells, dynamic morphological and molecular-level analyses such as phagocytosis and cytokine releases after cellular-level stress exposures are applicable. We believe that abnormal cell differentiation could be revealed using patient-derived iMG cells.

We have already revealed previously-unknown dynamic pathophysiology of microglia in patients with Nasu-Hakola disease (Sci Rep 2014), fibromyalgia (Sci Rep 2017) and rapid-cycling bipolar disorder (Front Immunology 2017). The iMG cells can analyze both state- and trait- related microglial characteristics of human subjects by repeated blood collection, which is especially valuable because majority of psychiatric disorders express situation- and time- oriented symptoms.

We believe that the iMG techniques shed new light on clarifying dynamic molecular pathologies of microglia in a variety of neuropsychiatric disorders.