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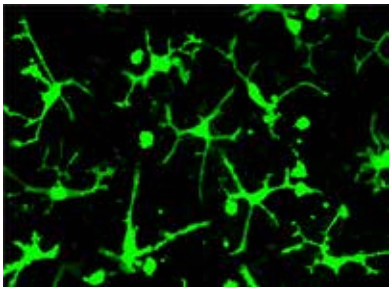
Project Leader **Hiroshi Sakuma** Developmental Neuroimmunology Project

Towards a Better Understanding of Neuro-immune Interactions in the Developing Brain

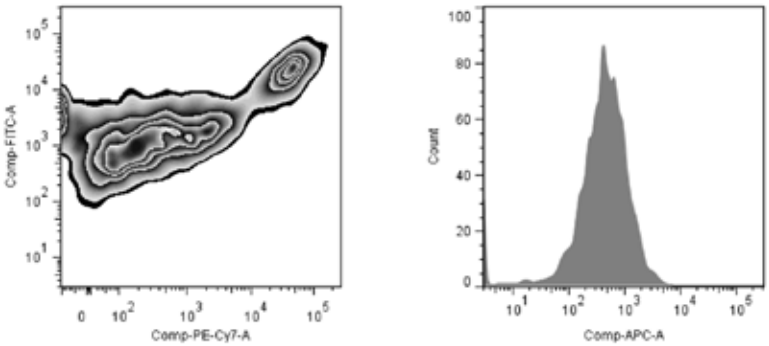


Our research focuses on the role of immune system in the developing brain. Immune and inflammatory responses not only combat pathogens but also play a variety of physiological roles in the central nervous system. Microglia are brain-resident immune cells and play multiple roles in the protection from pathogens and the clearance of debris. In addition, recent studies have shed light on unexpected functions of microglia in the physiological condition. For example, microglia actively participate in the brain development by modulating synapses.

"We are investigating the mechanisms by which microglia maintain homeostasis in the developing brain."

Our main research areas include:

1) Development and differentiation of microglia
2) Neuron-microglia interaction
3) In-vitro differentiated myeloid cells for cell therapy
4) Autoantibodies associated with neurological diseases
5) New biomarkers for pediatric immune-mediated neurological diseases



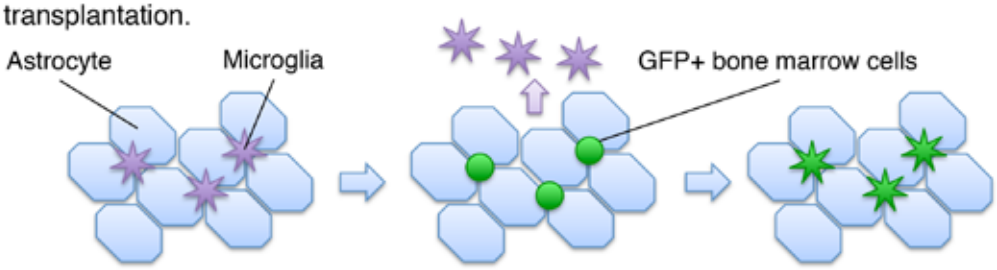
Flow cytometric analysis of microglia

Developmental Neuroimmunology

Research topic

Astrocytes nurture microglia?

Microglial progenitors originate from yolk sac and develop into mature microglia in the fetal brain. This observation suggests that non-microglial brain cells support microglial development. We speculated that astrocyte-microglia interaction, both contact-dependent and -independent, is critical for phenotype acquisition of microglia. Based on this hypothesis, we have tried to induce microglia from hematopoietic stem-cells by co-culture with astrocyte. When bone-marrow lineage negative cells were co-cultured on astrocyte monolayer for one week, they develop into microglia-like cells characterized by process-bearing morphology and the expression of microglial markers including CX3CR1 and TREM-2. Differentiation of microglia-like cells was further facilitated by interleukin-34 and TGF-β. These findings provide theoretical basis for optimizing treatment of neurological diseases by hematopoietic cell transplantation.



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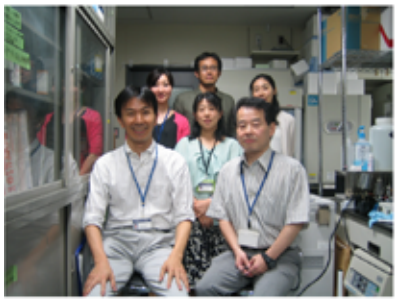

Developmental Neuroimmunology