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# Functional analysis of Gpnmb gene in Alzheimer's disease model mice

Kohichi Kawahara, Natsuki Kumakura, Yukina Kojima, Takuya Hasegawa, Takehiko Maeda

*Dept. Pharmacol., Fac. Pharm. Sci., Niigata Univ. Pharm. Appl. Life. Sci.*

The onset and progression of Alzheimer's disease (AD) correlate with neuroinflammatory processes, and inflammatory microglia (MG) are associated with AD-like pathology in a transgenic mouse model. We recently developed a novel monoclonal antibody, 9F5, against one subtype (type 1) of rat primary MG, and identified the antigen molecule for 9F5: truncated form of rat GPNMB/osteoactivin (Kawahara et al., GLIA, 2016). However, the distribution and function of GPNMB+ type 1 MG in AD brain are largely unknown. In the present study, we observed GPNMB+Iba1+ MG surrounding A$\beta$ plaque in neocortex of amyloid precursor protein (APP23) transgenic mice. In addition, GPNMB+Iba1+ MG were observed in non-plaque areas of hippocampus of APP23 mice. We generated Gpnmb knockout mice to investigate the functional relevance of GPNMB for microglia *in vivo*. Homozygous Gpnmb-KO mice did not show any growth retardation including body weight loss, and the fertility was normal. We observed that AD-related brain dysfunction in APP23 and 5xFAD mice were regulated by Gpnmb gene dosage. These finding suggest that GPNMB-positive type 1 MG may play a role in regulation of neuropathological process of AD.