## Stimulation of LXA₄ receptor alleviates motor dysfunction in intracerebral hemorrhage model mice

## Risa Futokoro, Masanori Hijioka, Yoshihisa Kitamura

Lab. Pharmacol. and Neurobiol., Col. Pharm. Sci., Ritsumeikan Univ.

Intracerebral hemorrhage (ICH), a bleeding into the brain parenchyma, is a devastating neurologic disease with the highest mortality among all stroke subtypes. In ICH brain, thrombin induces activation of microglia/macrophages followed by neuroinflammation. Furthermore, ICH leads to infiltration of numerous leukocytes. Recent report shows the arachidonic acid metabolite, leukotriene B<sub>4</sub> (LTB<sub>4</sub>), participates pathological progression of ICH (Hijioka *et al.*, 2017). In this study, we focused on lipoxin A<sub>4</sub> (LXA<sub>4</sub>), synthesized from arachidonic acid as same as LTB<sub>4</sub>. Treatment of murine microglial cell line BV-2 cells with thrombin (30 U/mL) increased mRNA expression level of inducible NO synthase (iNOS) and interleukin-6 (IL-6). Pretreatment with LXA<sub>4</sub> (100  $\mu$ M) suppressed thrombin-induced increases in iNOS and IL-6 mRNA expression. Moreover, immunocytochemical analysis revealed the translocation of nuclear factor-  $\kappa$  B (NF-  $\kappa$  B) into the nucleus induced by thrombin, and thrombin-induced nuclear translocation of NF-  $\kappa$  B was suppressed by LXA<sub>4</sub>. Finally, daily intravenous administration of LXA<sub>4</sub> receptor agonist, BML-111 (1 mg/kg) attenuated the motor dysfunction of mouse model of ICH. These data suggest that LXA<sub>4</sub> may be the novel therapeutic agent for ICH.