ELUCIDATION OF MOLECULAR MECHANISMS OF ALLERGIC ASTHMA AND DEPRESSION

Eri SEGI-NISHIDA
Graduate School of Pharmaceutical Sciences, Kyoto University
e-mail: eri.segi.nishida@pharm.kyoto-u.ac.jp

To elucidate the pathophysiological responses for chronic diseases, careful examination is needed at the level of molecular, cellular, tissue and whole body. Here we focus on the allergic asthma and depression, and show some pathophysiological aspects of each disease.

1) The suppressive role of the prostaglandin E receptor subtype EP3 in allergic inflammation

Aspirin-like drugs that inhibit prostaglandin synthesis induce life-threatening attacks in about 10% of adults with asthma, suggesting the existence of a prostaglandin-dependent process that suppresses the allergic reactions. We found that mice lacking EP3 developed severe allergic inflammation than wild-type mice. Conversely, an EP3-selective agonist suppressed the inflammation. This suppression was associated with inhibition of allergy-related gene expression. Thus, the PGE_2-EP3 pathway is an important negative modulator of allergic reactions.

2) The proliferation of neural stem-like cells induced by electroconvulsive seizure and VEGF in rat hippocampus.

All classes of antidepressants increase hippocampal cell proliferation and neurogenesis, which contributes, in part, to the behavioral actions of these treatments. Electroconvulsive seizure (ECS) is the most robust stimulator of hippocampal cell proliferation and the most efficacious treatment for depression, but the cellular mechanisms underlying the actions of ECS are unknown. To address this question, we investigated the effect of ECS on proliferation of neural stem-like and/or progenitor cells in the rat hippocampus. We found that at an early mitotic phase ECS increases the proliferation of neural stem-like cells and then at a later phase increases the proliferation of amplifying progenitors. We further demonstrate that VEGF signaling is necessary for ECS induction of stem-like cell proliferation and is sufficient to produce this effect.