Expression of glucocorticoid receptors (GRs) in eosinophils derived from steroid-resistant asthma model of mice

Kennosuke Hashimoto, Maki Matsuo, Ayaka Mori, Hayato Shimora, Momo Utsumi, Rina Ano, Masaya Matsuda, Kazuyuki Kitatani, Takeshi Nabe

Lab. of Immunopharmacol., Fac. of Pharm. Sci., Setsunan Univ., Osaka, Japan

[Background] It has been known that 5-10% of asthmatic patients are resistant to the steroid therapy. However, mechanisms underlying the acquisition of steroid resistance have been unclear. GRs consist of two alternatively spliced isoforms: GR α , which activates gene transcription, and GR β , a dominant-negative receptor. Objective of this study is to elucidate whether mRNA levels of GR α and GR β in eosinophils are increased in steroid-resistant asthma mice.

[Methods] Ovalbumin (OVA)-sensitized BALB/c mice were intratracheally challenged with OVA at 5 or 500 μ g/animal 4 times. Dexamethasone (1 mg/kg) was i.p. administered during the multiple challenges. One day after the 4th challenge, eosinophils in the lung were purified by FACS. mRNA levels of GR α and GR β in the eosinophils were quantified by real-time RT-PCR. Airway remodeling was evaluated by staining with PAS and Masson trichrome.

[Results] (1) Infiltration of eosinophils and development of airway remodeling in 5 μ g OVA model were suppressed by dexamethasone, whereas those in 500 μ g OVA model were not. (2) GR β mRNA level in eosinophils from 500 μ g OVA model was higher than that from 5 μ g OVA model. No difference in GR α mRNA level was detected between the two models.

[Conclusion] ☒ The increased expression of GR β may account for the acquisition of steroid resistance.