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The increased susceptibility to adult-onset asthma through the inhibition of the development of respiratory tolerance by early life stress**Tasuku Kawano, Ryusuke Ouchi, Tomomitsu Miyasaka, Yuichi Ohkawara, Tomoko Takahashi, Motoaki Takayanagi and Isao Ohno**
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Statement of the Problem: Allergic asthma is characterized by Th2 type inflammation, essentially due to a breakdown of immune tolerance to an environmental allergen. Etiologically, experiences of early-life stress have been demonstrated to be associated with heightened prevalence of adult asthma. However, mechanisms underlying the stress leading to the development of asthma are poorly understood. Therefore, we examine if early-life stress increases the susceptibility to adult-onset asthma through the inhibition of the development of the respiratory tolerance.

Methodology & Theoretical Orientation: Female BALB/c pups were sensitized by intraperitoneal injections of ovalbumin (OVA)/Al(OH)₃ on postnatal days (PND) 24 and 29. Respiratory tolerance was induced by the inhalation of OVA on PNDs 18 and 21 before the sensitization. Maternal separation (MS) was used as a model of early-life stress and repeated from PND 17 to 22. On PND 76, the mice were challenged with OVA aerosol. Airway inflammation was evaluated with numbers of inflammatory cells in bronchoalveolar lavage fluid (BALF). The contents of IFN- γ , IL-4, IL-5 and IL-13 in BALF were measured by ELISA. The airway hyper-responsiveness (AHR) was assessed by methacholine-induced airflow obstruction.

Conclusion & Significance: In tolerized mice, the numbers of inflammatory cells, the cytokine contents and AHR were remarkably decreased compared with those in non-tolerized mice. However, these effects of the tolerance were significantly reduced by MS exposure. These results suggested that early-life stress exposure has a potential to increase the risk of adult-onset asthma through the inhibition of the development of immune tolerance.

Biography

Tasuku Kawano completed his PhD at Tohoku Medical and Pharmaceutical University in 2009. He is presently working as an Assistant Professor in the Department of Pathophysiology at Tohoku Medical and Pharmaceutical University. He aims to reduce asthma patients. He studies elucidation of asthmatic onset mechanism based on nerve-endocrine-immunity axis. He has been trying for the creation of new fields for the development of novel medicines and preventive drugs in asthma. He has published a paper, "The involvement of central nervous system histamine receptors in psychological stress-induced exacerbation of allergic airway inflammation in mice" in *Allergol Int.* 2016 Sep; 65 Suppl:S38-44.

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