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Effect of a LAT1-inhibitor on T cell-mediated allergic inflammation

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Activated T cells are crucial for the development of allergic diseases. We have recently clarified that L-type amino acid transporter 1 (LAT1) plays a functional role in activated T cells. Here, we comparatively investigated the effect of a LAT1 inhibitor, JPH203, on allergic inflammation induced in multiple organs, such as the skin, lungs, and nose of antigen-specific Th2 cell-transferred mice. The local antigen provocation to those mice evoked tissue-specific eosinophilic inflammation, especially accompanied by bronchial and nasal hyperresponsiveness (BHR and NHR) in the lungs and nose, respectively. Antigen-induced ear thickness, BHR, and NHR were significantly suppressed by the administration of JPH203, though the attenuation of eosinophil accumulation was only seen in the skin and nose. The infiltration of antigen-specific T cells determined in the lungs and nasal-associated lymphoid tissue was not affected by the JPH203 treatment. Activation-induced amino acid incorporation, oxidative phosphorylation, glycolysis, cyclin-related protein expression, and resulting cytokine synthesis in Th2 cells were suppressed by JPH203. JPH203 is potentially effective for treating allergic diseases through attenuating the function of activated T cells. However, the mechanisms may not involve the suppression of eosinophil or T cell infiltration in some target organs.