

# Novel mechanism of action of corticosteroids in allergic diseases

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Research by Peter Barnes (Imperial College, London) and colleagues may explain the effectiveness of common treatments for allergic inflammation and may point the way to targets for new treatments for allergic diseases, according to a study published in this week's open-access journal *PLoS Medicine*.

Allergic diseases - which affect about 50 million people a year in the US alone - are triggered when the immune system responds to a normally harmless material by activating a specific type of T lymphocyte called a T helper-2 cell (Th2). The Th2 cells make three [cytokines](#), which are responsible for the inflammation associated with allergies.

[Corticosteroids](#) are often used to treat allergic inflammation but it is not well understood how these corticosteroids work to inhibit the expression of Th2 cytokines.

Using laboratory experiments and tests in seven patients with mild [asthma](#), Peter Barnes and colleagues suggest that corticosteroids inhibit the expression of Th2 cytokines and thus reduce allergic inflammation through two interacting mechanisms which both prevent the nuclear translocation of GATA-3, a key regulator of cytokine expression. Firstly, they suggest that corticosteroids compete with GATA-3 for binding to the nuclear import protein importin- $\alpha$ . Secondly, they suggest that corticosteroids prevent the phosphorylation of GATA-3, further preventing GATA-3 from binding to importin- $\alpha$ .

According to the authors, "This novel mechanism of action of

corticosteroids may account for the striking clinical efficacy of corticosteroids in the treatment of allergic diseases", although further experiments are needed to show that the lymphocytes at the sites of allergic infection respond to corticosteroids in the same way as lymphocytes in the blood. In addition, these findings suggest that interaction between phosphorylated GATA-3 and importin- $\alpha$  may represent an important target for the development of new therapies for the treatment of [allergic diseases](#).

More information: Maneechotesuwan K, Yao X, Ito K, Jazrawi E, Usmani OS, et al. (2009) Suppression of GATA-3 Nuclear Import and Phosphorylation: A Novel Mechanism of Corticosteroid Action in Allergic Disease. PLoS Med 6(5): e1000076.  
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