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LUNG ALERT

A novel form of receptor interaction may contribute to β-agonist resistance in asthma

▲ McGraw DW, Mihlbachler KA, Schwarb MR, *et al*. Airway smooth muscle prostaglandin-EP_1 receptors directly modulate β_2-adrenergic receptors within a unique heterodimeric complex. *J Clin Invest* 2006;**116**:1400–9

In attempting to elucidate the hitherto poorly understood action of the prostanoid-EP_1 receptor, researchers in the US have uncovered a new type of receptor interaction and demonstrated its action on murine airway smooth muscle contraction.

Prostaglandin E_2 (PGE_2) produces its diverse biological effects by acting on four endogenous receptor subtypes (EP_1–EP_4). The authors set out to define the action of the EP_1 receptor. In a series of experiments they first showed that activation of EP_1 receptors by PGE_2 failed to cause contraction of mouse tracheal ring, as might have been expected, but did cause a marked reduction in β_2 adrenergic receptor (β_2AR) mediated relaxation. This was shown to be mediated at the level of the receptor itself. This suggested an interplay between the EP_1 receptor and the β_2AR, with activation of the former resulting in decreased function of the latter. They went on to demonstrate coupling of the two receptors into a heterodimer. Activation of the EP_1 receptor within the heterodimer causes a conformational change in the β_2AR, uncoupling it from its G protein with resultant desensitisation to β_2AR agonists.

This study demonstrates a novel modulatory function of the EP_1 receptor in regulating the action of the β_2AR. This may contribute to the reduced response to β_2AR agonists in severe asthma, when there may be increased concentrations of endogenous PGE_2.

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LUNG ALERT

Short course antibiotics in community acquired pneumonia

▲ El Moussaoui R, de Borgie CA, van den Broek P, *et al*. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study. *BMJ* 2006;**332**:1355–8

This Dutch study, undertaken between November 2000 and July 2003, took adults with a pneumonia severity index score of $\leqslant 110$ and randomly assigned those who substantially improved after 72 hours of intravenous amoxicillin to either 750 mg oral amoxicillin (n = 63) or placebo (n = 56) three times daily for 5 days thereafter.

Clinical, bacteriological and radiological outcomes were assessed. The clinical success rate at day 10 (per protocol analysis) was 93% in both groups (50/54 in the 3 day treatment group and 56/60 in the 8 day treatment group: difference 0.1% (95% CI −9 to 10)). At day 28 clinical success rates were 90% (47/52) in the 3 day treatment group and 88% (49/56) in the 8 day treatment group (difference 2% (95% CI −9 to 15)). There was therefore little difference between the two groups.

This study suggests that a short course of antibiotic therapy is not inferior to a longer course in patients with mild to moderate-severe uncomplicated community acquired pneumonia who show clinical improvement after 3 days of intravenous antibiotics.

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