Species comparison of interleukin-13 induced airway hyperreactivity as model for allergic asthma

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Introduction

High effort has been put into development of new therapeutic targets for allergic asthma. Currently there is a need for translational models with improved predictivity in respect to efficacy and safety. Interleukin-13 as a key cytokine of asthma is widely used to induce airway hyperreactivity in laboratory rodents. We assessed IL-13 induced hyperreactivity in PCLS of mice, rats, and humans.

Methods

PCLS were prepared from Balb/c mice, Brown Norway rats, and humans. Airways were pre-incubated with 100 ng/mL IL-13 of the corresponding species. Subsequently, bronchoconstriction was induced by addition of methacholine (MCh) and visualized by videomicroscopy. IL-13 receptor was stained in the airways of mouse, rat and human PCLS by immunohistochemistry.

Results

Human IL-13 receptor

The presence and location of the IL-13 receptor in PCLS of mouse, rat and human was investigated to confirm presence of the receptor in lung sections used for functional ex vivo studies (Figure 3).

IL-13 induced hyperreagibility

Methacholine-induced bronchoconstriction in mouse and rat PCLS exhibited an EC_{50} of 70 nM and 200 nM, respectively (Figure 4). Pre-incubation with rodent IL-13 decreased EC_{50} to 45 nM (mouse) and 140 nM (rat). In general, pre-incubation of rodent PCLS in the presence of IL-13 resulted in 20 % stronger bronchoconstriction at maximum methacholine concentration compared to untreated tissue. Contrary, IL-13 pre-incubation didn’t induce airway hyperresponsiveness in the human PCLS.

Summary & Conclusion

IL-13 induces AHR has been studied in rodents to mimic human asthma. Pre-incubation with IL-13 resulted in stronger bronchoconstriction and AHR in rodent PCLS had however not the same effect in human. Some human donors showed AHR as well but the diversity in human didn’t show conclusive results.

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