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POSTER PRESENTATION Open Access

Examining the role of arginase in air pollution-induced exacerbation of asthma

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Background

The arginase isozymes (arginase 1 and 2), convert L-arginine into L-ornithine and urea, and thus compete with the nitric oxide synthase isozymes for substrate. We have previously shown that arginase 1 expression is upregulated in human asthma and plays a functional role in airways hyperresponsiveness (AHR) in an animal model of allergic airways inflammation. Ambient particles and ozone are major constituents of urban air pollution and contribute to asthma exacerbations. However, the mechanisms underlying the exacerbation of allergic airways disease by air pollution remain to be elucidated. There is evidence that arginase expression is augmented in cigarette smoking asthmatics. We tested the hypothesis that arginase is involved in the exacerbation of respiratory symptoms in response to air pollution in animal models of allergic airways inflammation.

Methods

We used sub-acute (16-day) and chronic (12-week) murine models of ovalbumin (OVA)-induced allergic airways inflammation as models of asthma. All mice were sensitized to OVA, and then randomized to aerosol challenge with PBS (control; OVA/PBS) or OVA (allergic airways inflammation; OVA/OVA). Twenty-four hours after the final OVA or PBS challenge, mice underwent a combined exposure to concentrated ambient fine particles plus ozone (CAP+O_3), or filtered air. Following exposure, mice were treated with either the arginase inhibitor *S*-boronoethyl l-cysteine (BEC; 40 μg/g b.w.), or vehicle (PBS), by direct nebulization into the airways. After determination of the airways responsiveness to methacholine using the flexiVent, tissues were harvested for Western blotting, activity testing and immunohistochemistry.

Results

Exposure to CAP+O_3 augmented the AHR in the OVA/OVA mice with no significant effect on the OVA/PBS controls in both the sub-acute and chronic models. Expression of arginase 1 and total arginase activity were significantly augmented in OVA/OVA mice exposed to CAP+O_3, compared to filtered air. Immunohistochemistry revealed that arginase 1 expression was specifically up-regulated in the peribronchiolar region following CAP+O_3 exposure in OVA/OVA mice. Treatment with BEC significantly reduced the pollution-induced AHR in CAP+O_3-exposed OVA/OVA mice in both the sub-acute and chronic murine models to control levels.

Conclusions

This study demonstrates that arginase 1 is up-regulated following environmental exposures in murine models of allergic airways inflammation. Attenuation of airways hyperresponsiveness by arginase inhibition suggests that this pathway is a promising candidate for future therapies to prevent or treat air pollution-induced exacerbation of allergic symptoms.

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