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INTRINSIC ACTIVITY

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MEETING ABSTRACT

A2.1

Apolipoprotein A-IV potently suppresses eosinophil responsiveness *in vitro* and alleviates house dust mite-induced airway hyperreactivity in mice

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Background: Eosinophil accumulation orchestrated by allergic sensitization and T_h2-mediated immune response is a hallmark of allergic inflammation as observed in allergic rhinitis and severe asthma. Recent studies pointed out a crucial role for apolipoproteins in the pathogenesis of inflammatory diseases. However, the role of apolipoprotein A-IV (apoA-IV) in allergic inflammation has not been addressed thus far. Here, we explored the signaling mechanism and anti-inflammatory effects of apoA-IV on eosinophil effector function *in vitro* and *in vivo*.
Methods: *In vitro* studies included apoA-IV measurement in serum of healthy and allergic individuals, as well as migratory responsiveness, respiratory burst and calcium mobilization of human peripheral blood eosinophils. Allergen-driven airway inflammation was assessed in a mouse model of acute house dust mite (HDM)-induced asthma.
Results: ApoA-IV levels were significantly decreased in serum from allergic patients compared to healthy controls. Recombinant apoA-IV potently inhibited eosinophil responsiveness by means of shape change, integrin expression and chemotaxis. We were able to elucidate the underlying molecular mechanism, which was independent of ABCAI and SRBI binding but involved Rev-ErbA-α. Moreover, apoA-IV induced the PI3K/PDK1-dependent activation of PKA. Of note, systemic application of apoA-IV clearly prevented AHR and reduced the influx of inflammatory cells into the airways in a murine model of HDM-induced allergic asthma.
Discussion: ApoA-IV is an endogenous anti-inflammatory protein that potently suppresses eosinophil effector function. Here, we provide new insights into the molecular mechanisms underlying the apoA-IV-induced signaling in eosinophils. Our data indicate that exogenously added apoA-IV may represent a novel pharmacological approach for the treatment of allergic inflammation and other eosinophil-driven disorders.
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