Neutrophils from atopic mice attenuate post-viral airway hyper-responsiveness

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RATIONALE: Severe respiratory viral infections drive development of atopic disease and asthma. It is unclear how pre-existing atopy affects the antiviral immune response. Using Sendai virus (SeV; murine parainfluenza virus), we found pre-existing atopy prevented post-viral airway hyper-reactivity (AHR). Neutrophils (PMN) are critical in our SeV model, and we hypothesized that PMN from atopic mice were responsible for the protection against post-viral airway disease.

METHODS: Mice were given 1µg house dust mite extract i.n. (HDM; "atopic") or PBS ("non-atopic") and 1 week later 10µg daily for 5 days. Three days later 2x105 pfu SeV given i.n. and airway hyper-responsiveness to methacholine (AHR) determined by invasive measurement. To deplete PMN 100µg of anti-Ly6G or isotype control was given intraperotoneally 24 hours before SeV inoculation. As a second PMN depletion method, we crossed ROSA-iDTRKI with MRP8-Cre+ mice to generate PMNDTR (MRP8-Cre+;ROSA-iDTR), in which PMN are depleted by diptheria toxin (DT) administration. Controls were littermate mice lacking MRP8-Cre (PMNWT). PMN were depleted in these mice with 500ng/20gm DT given i.p. 24h before SeV infection. In all experiments, AHR was determined 21 days post SeV inoculation.

RESULTS: Atopic mice failed to develop AHR compared to non-atopic mice ($p=0.005$, $n=4$). Atopic mice with PMN depleted developed significantly increased AHR regardless of method used to deplete PMN ($p=0.0005$, $n=3$ Ly6G vs isotype; $p=0.002$ PMNDTR vs PMNWT).

CONCLUSIONS: PMN in atopic mice are necessary 24 hours before viral inoculation to suppress the development of post-viral airway disease. Studies are underway to determine the PMN mechanism involved.