Azacitidine blockade of local B-cell switching to IgE synthesis

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Type I respiratory allergy is mediated by the formation of IgE to harmless proteins entering through the nasal and oral mucosa. The amount of the protein passing through the mucosal barrier is exceptionally low. Based on these data, we developed a low-dose allergy model that showed that prolonged administration of 50-300 ng/mouse/injection of protein in saline to the withers of mice causes significantly more pronounced IgE production than administration of 2-10 ug/mouse, which indicates the presence of a special microenvironment in the withers. In humans, the formation of extrafollicular zones in nasal polyps, bronchial mucosa, oral cavity and esophageal wall, in which IgE transcripts were detected, is shown. It can be assumed that in mice, too, B cells switch to IgE synthesis locally, in the withers region. Recombination of B-cell immunoglobulin genes is regulated by the activation-induced cytidine deaminase (AID) protein. AID stops switching B cells to synthesize other classes of immunoglobulins, including IgE. 5-Azacitidine (Aza) is an analog of the pyrimidine nucleoside cytidine. Molecular docking methods and *in vitro* experiments have shown that Aza effectively blocks AID synthesis. This paper analyzes the effect of local administration of Aza in a low-dose model of allergy to meadow timothy protein Phl p1.

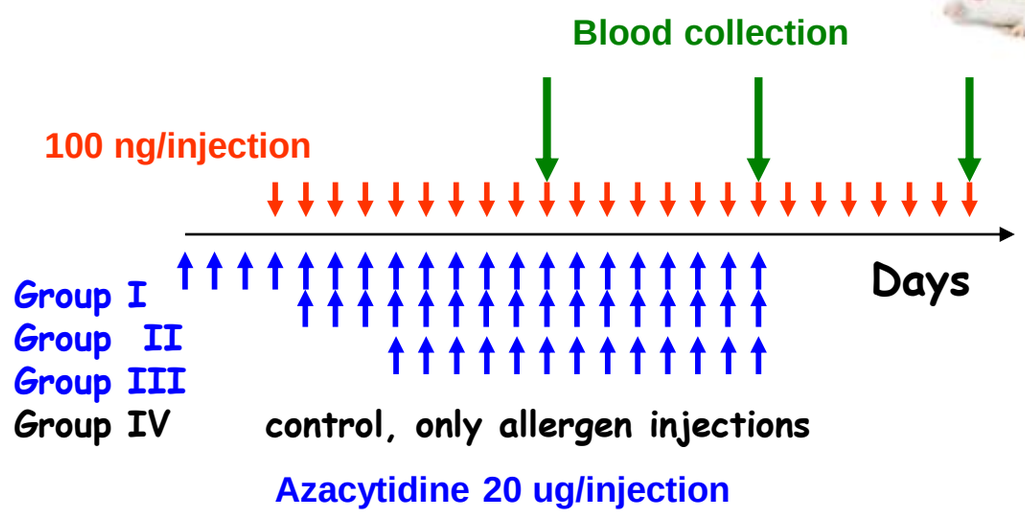
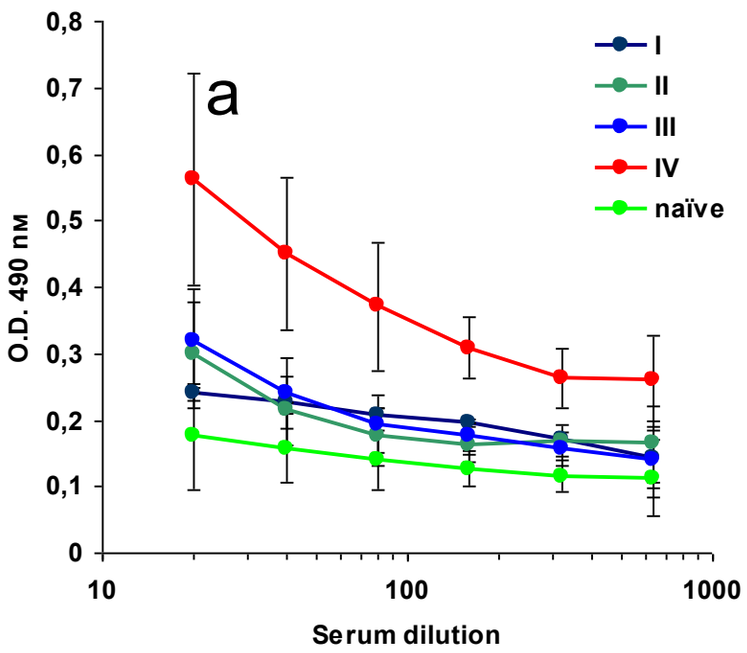
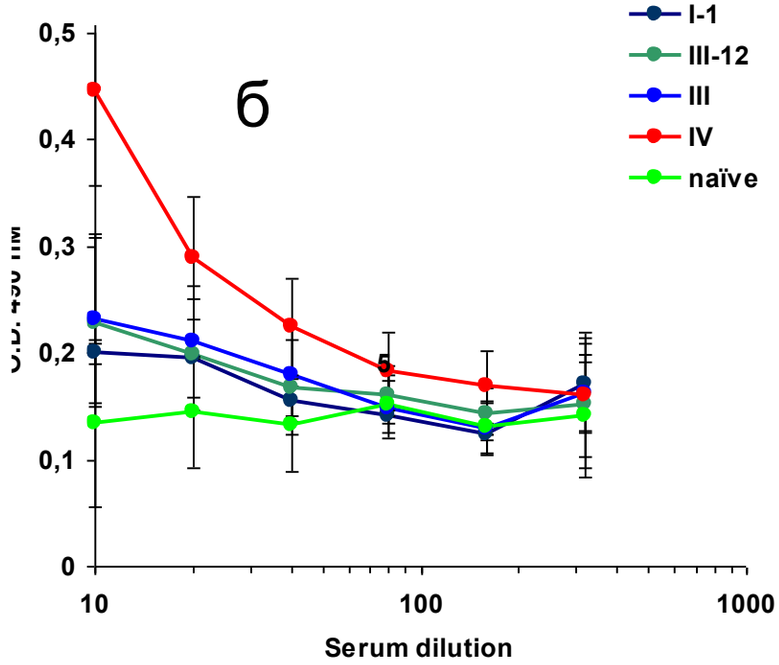


Fig. 1. Scheme of the experiment. BALB/c mice were injected with recombinant Phl p1 at a dose of 100 ng/mouse/injection (red arrows). Azacitidine was administered at a dose of 50 ug/mouse mixed with an allergen (blue arrows). Blood was collected in dynamics of response (green arrows).





It was shown that in all groups Aza blocks the switching of B cells to IgE synthesis (Fig. 2). no Significant differences in IgG titers were found.

Thus, local administration of Aza at the early stages of allergic sensitization leads to a decrease in IgE titers and, accordingly, can be used for allergy therapy.

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Fig. 2. IgE production in the groups with azacitidine (groups I-III) and in the control group (group IV), which was administered only Phl p1 at the end of Aza administration (a) and a month later without Aza administration (b).