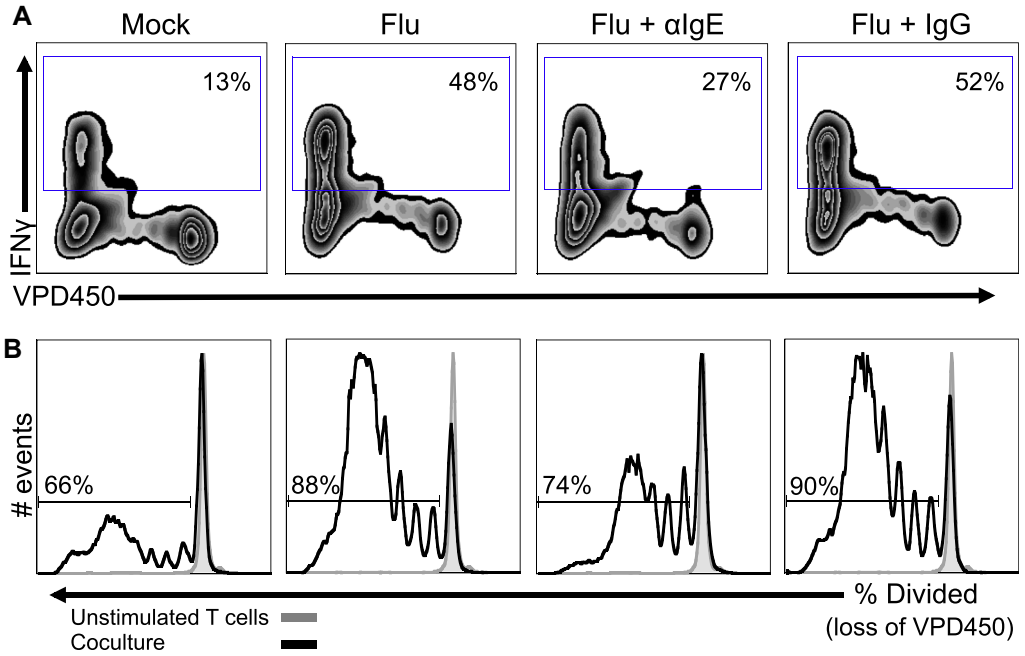

FIG E1. IgE cross-linking inhibits virus-driven monocyte T-cell priming and proliferation. Representative flow cytometry plots for Fig 1. Naive CD4 T cells polarized with monocytes exposed to no virus (mock) or influenza A virus (Flu) ± IgE cross-linking antibody (αIgE) or isotype IgG control. T cells were labeled with the cell proliferation dye, VPD450, before coculture. **A,** Zebra plots for IFN-γ expression versus VPD450 show decreased IFN-γ–positive cells in the presence of IgE cross-linking. **B,** Histograms show cell proliferation (measured by loss of VPD450 intensity, x-axis) of T cells stimulated with monocytes (black line) compared with unstimulated T cells in gray.

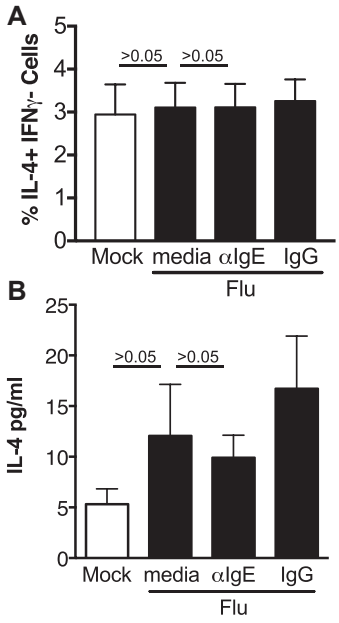

FIG E2. IgE cross-linking does not alter T_H2 polarization. Naive CD4 T cells polarized with monocytes exposed to no virus (mock) or influenza A virus (Flu) ± IgE cross-linking antibody (αIgE) or isotype IgG control. Graphs shown are **(A)** mean percentages of IL-4+ IFN-γ− cells for the indicated conditions. N = 15 donor pairs. **B,** Mean IL-4 concentration in monocyte-T-cell coculture supernatants. N = 5 donor pairs; error bars represent SEM, and *P* values represent results of 2-way ANOVA.

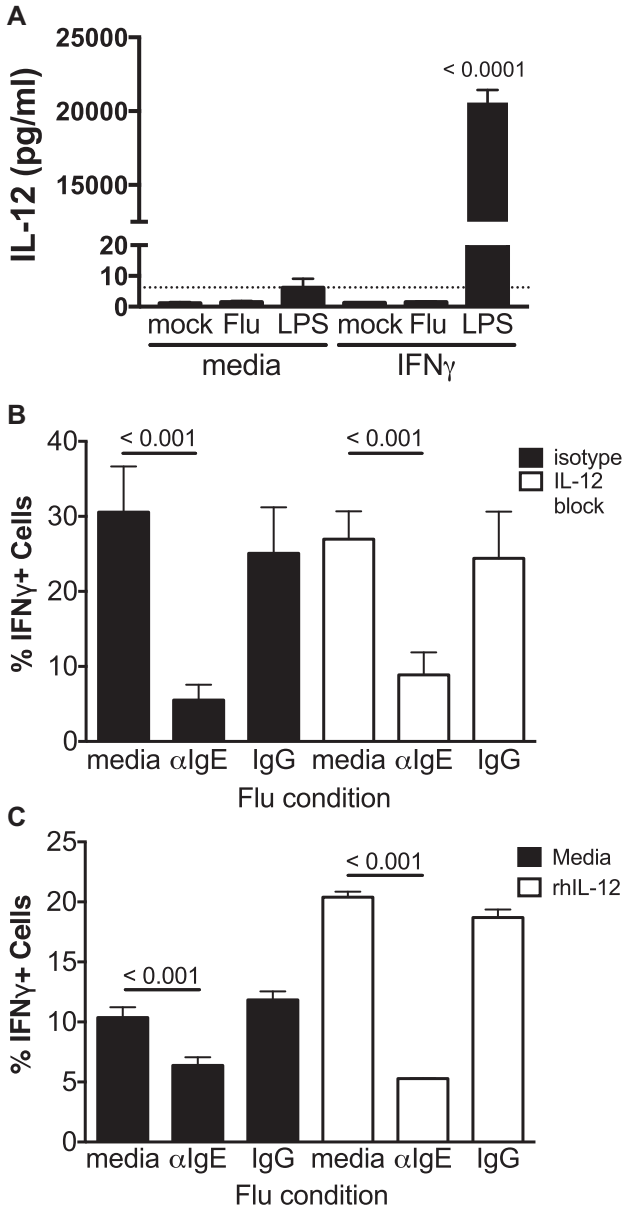

FIG E3. IL-12 is not involved in T_H1 polarization by influenza-exposed monocytes. IL-12 is a critical factor in T_H1 development.[E21] Neither blocking antibodies nor exogenous addition of IL-12 restored the IgE-mediated defect in T_H1 differentiation. **A,** IL-12p70 production was measured in supernatants from monocytes treated ± IFN-γ for 18 hours followed by 24-hour incubation with media alone (mock), influenza A virus (Flu), or LPS. IL-12p70 was not detectable after influenza exposure, despite robust production under positive control conditions. Dashed line denotes the limit of detection. **B,** Monocyte-induced T_H1 priming; mean % IFN-γ+ T cells in depicted conditions treated ± isotype control (black bars) or neutralizing IL-12 antibody (white bars). N = 3. **C,** % IFN-γ+ T cells ± rh IL-12. Representative data (of N = 3 experiments) is shown; error bars represent SEM and *P* values represent results of 1-way ANOVA.

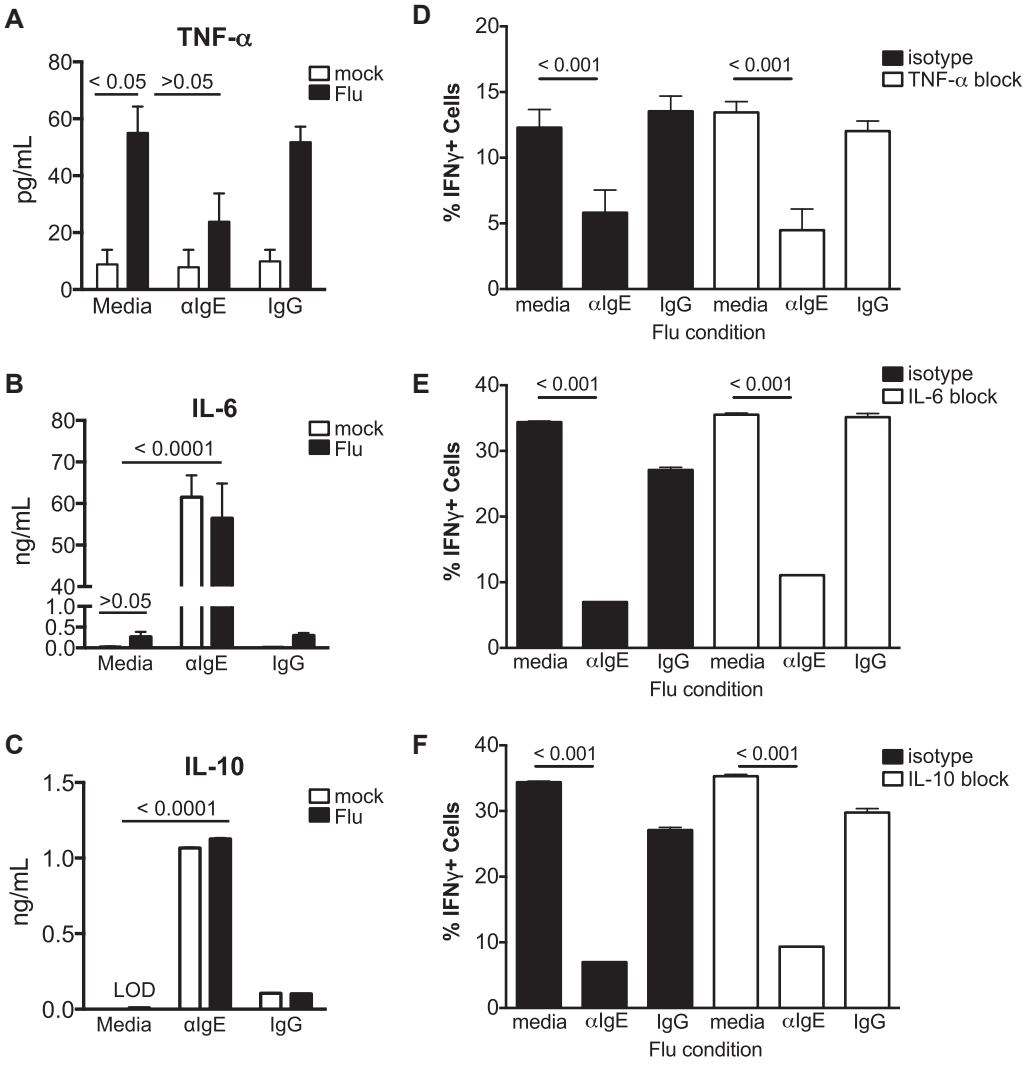

FIG E4. IgE cross-linking suppresses T_H1 priming independently of TNF-α, IL-6, and IL-10. Cytokine secretion from monocyte supernatants at 18 hours after influenza virus (Flu) ± IgE cross-linking was measured for **(A)** TNF-α, **(B)** IL-6, or **(C)** IL-10. These were secreted by monocytes upon IgE cross-linking,[7] and in the presence of both IgE cross-linking and influenza. **D-F,** Neutralization of these cytokines did not impact influenza-induced T_H1 priming or restore inhibition by IgE cross-linking. Mean percentages of IFN-γ+ T cells in monocyte-T-cell cocultures treated with isotype controls (black bars) or neutralizing antibodies (white bars) to (Fig E4, *D*) TNF-α, (Fig E4, *E*) IL-6, or (Fig E4, *F*) IL-10. Representative data from N = 3 experiments are shown; error bars represent SEM, and *P* values represent results of 1-way ANOVA.

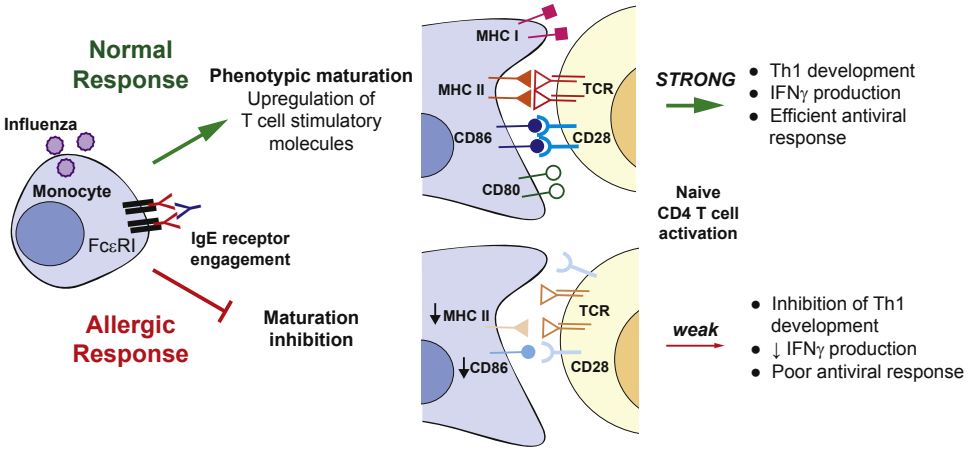

FIG E5. Model of IgE-mediated inhibition of monocyte-driven T_H1 priming. Upon monocyte influenza exposure, the normal antiviral response results in phenotypic maturation and upregulation of monocyte cell surface molecules, downstream antigen presentation, and strong TCR signal culminating in T_H1 differentiation. In the setting of allergic stimulation, via IgE receptor (FcεRI) engagement, virus-induced monocyte maturation is inhibited, resulting in weak TCR signal and poor T_H1 differentiation. Impaired T_H1 production would have significant downstream effects, including decreased antiviral cytokine secretion (eg, IFN-γ), cytotoxic $CD8^+$ T-cell development, and antigen-specific antibody production.

TABLE E1. Influenza virus associations with allergic disease

- Influenza viruses are associated with severe disease in individuals with allergic asthma, and have been linked to exacerbations.[E4-E6]
- During the 2009 influenza pandemic, increased disease severity was observed in patients with asthma, with many requiring intensive level care.[E7,E8]
- However, other comorbidities besides asthma have higher rates of severe outcomes, including death, among hospitalized individuals with influenza.[E9-E11]
- The Centers for Disease Control and Prevention reports that asthma is the most common underlying comorbidity in children and in the top 5 for adults hospitalized with influenza.[E12]
- More severe infections have been noted in atopic vs nonatopic children in general.[E13]
- Influenza is also isolated more frequently from adults with allergic rhinitis compared with healthy controls.[E14]
- Murine models of allergic sensitization demonstrate enhanced allergic phenotypes after influenza infection.[E15,E16]

Investigating IgE-mediated effects on antiviral immune responses to influenza virus may shed light on key mechanisms modulating allergen-virus interactions.