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TYPE I AND TYPE III INTERFERONS DIFFER IN THEIR ADJUVANT ACTIVITIES FOR INFLUENZA VACCINES

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Type I and type III interferons (IFN) can promote adaptive immune responses in mice and improve vaccine-induced resistance to viral infections. The adjuvant effect of type III IFN (IFN-») specifically boosts mucosal immunity by an indirect mechanism, involving IFN-»-induced production of thymic stromal lymphopoietin (TSLP), a cytokine that activates immune cells. To date it remained unclear whether the previously described adjuvant effect of type I IFN (IFN-±/²) would also depend on TSLP and whether type I IFN stimulates different antibody subtypes. Here we show that after infection with a live-attenuated influenza virus, mice lacking functional type I IFN receptors failed to produce normal amounts of virus-specific IgG2c and IgA antibodies. In contrast, mice lacking functional IFN-» receptors contained normal levels of virus-specific IgG2c but had reduced IgG1 and IgA antibody levels. When applied together with protein antigen, IFN-± stimulated the production of antigen-specific IgA and IgG2c to a greater extent than IgG1, irrespective of whether the mice expressed functional TSLP receptors and irrespective of whether the vaccine was applied by the intranasal or the intraperitoneal route. Taken together, these results demonstrate that the adjuvant activities of type I and type III IFNs are mechanistically distinct.