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IL-7 as a mucosal adjuvant in pulmonary immunization protocols

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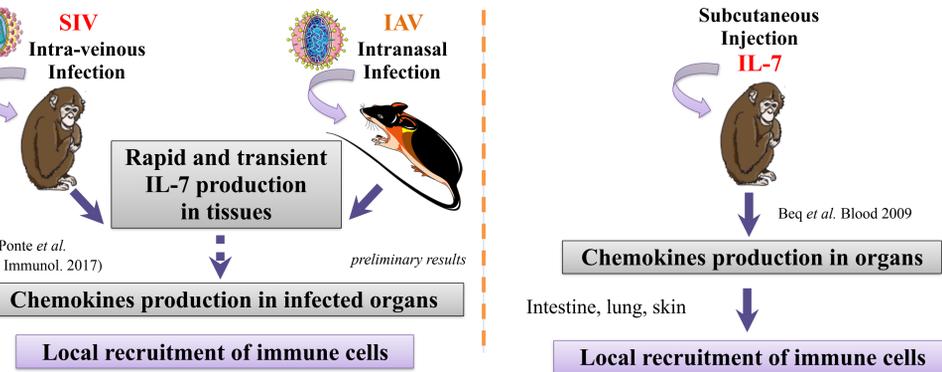
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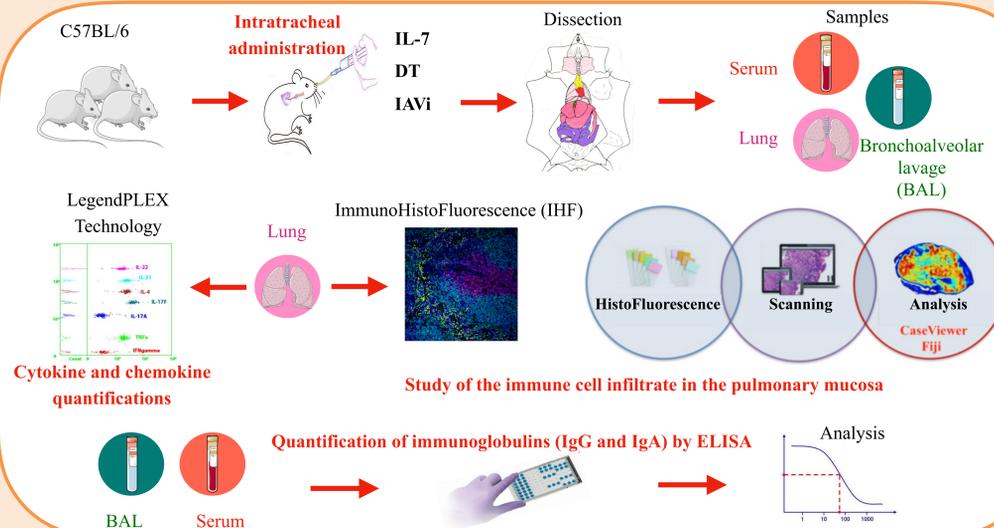
Background

IL-7, is a cytokine produced by stromal cells of lymphoid and non-lymphoid organs, is essential during thymopoiesis as well as for T lymphocyte homeostasis (survival and proliferation of LT). IL-7 is also important for B lymphopoiesis. But our data argue for another function.



Could IL-7 act as an adjuvant in mucosal immunization protocols ?

Methods



Results

Local administration of IL-7 changes the pulmonary physiology

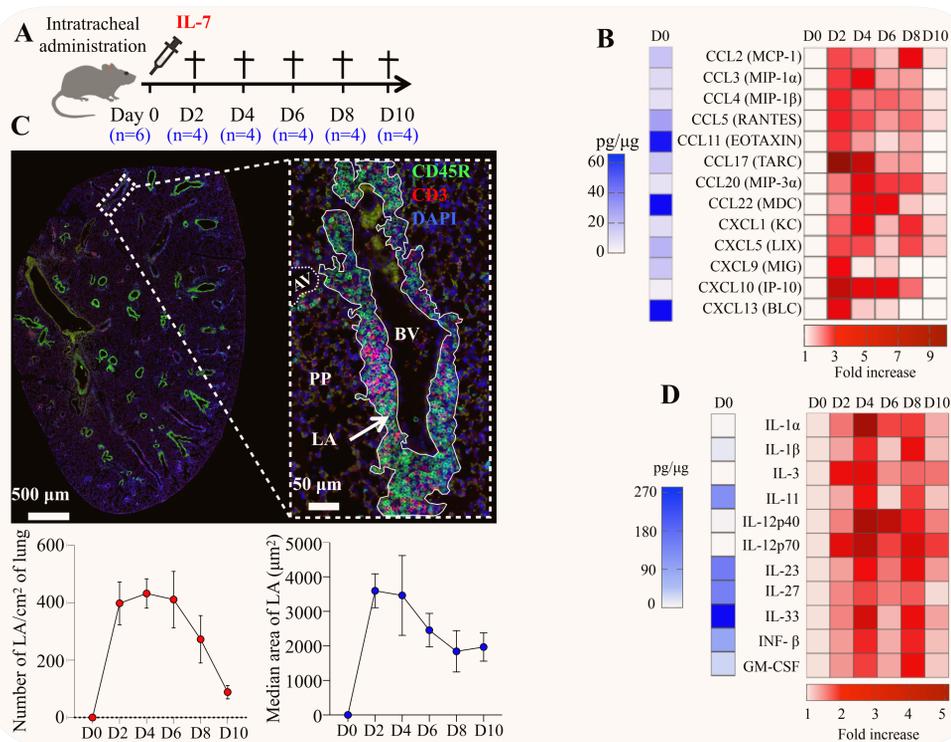


FIG 1. (A) Mice were intratracheally administered with IL-7 and then sacrificed at different time points (D2, D4, D6, D8, D10). D0 represents control mice that have not been treated with IL-7. From lung homogenates, both pro-inflammatory chemokines (B) and cytokines (D) were assayed using a liquid-phase multiplex ELISA. (C) Lung sections were labeled for CD3 (LT, red) and CD45R (LB, green). Nuclei were DAPI-stained (blue). Lymphoid aggregates evidenced in the pulmonary mucosa were analyzed with the CaseViewer software allowing to estimate their number (left panel) and surface (right panel). LA: lymphoid aggregate, PP: pulmonary parenchyma, BV: blood vessel, AV: pulmonary alveoli.

IL-7 promotes the production of cytokines involved in both T and B immune responses rather than tolerogenic cytokines

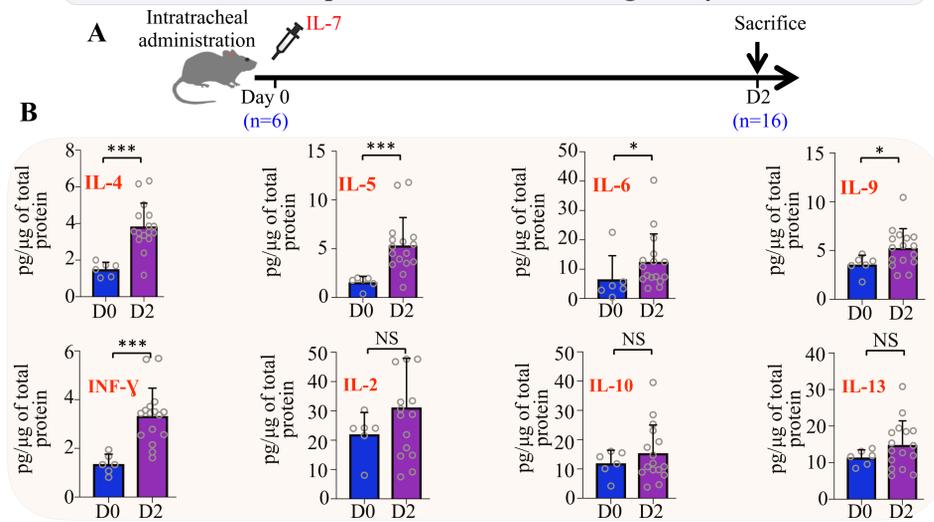


FIG 2. (A) Mice were intratracheally administered with IL-7 at D0 then sacrificed at D2. Control mice were not treated with IL-7 (D0). (B) Lung homogenates were assayed for different immune response polarizing cytokines using a liquid phase ELISA. Bars and error bars represent means ± SD.

IAV immunized mice that previously received IL-7 as an adjuvant are more resistant to influenza pathology

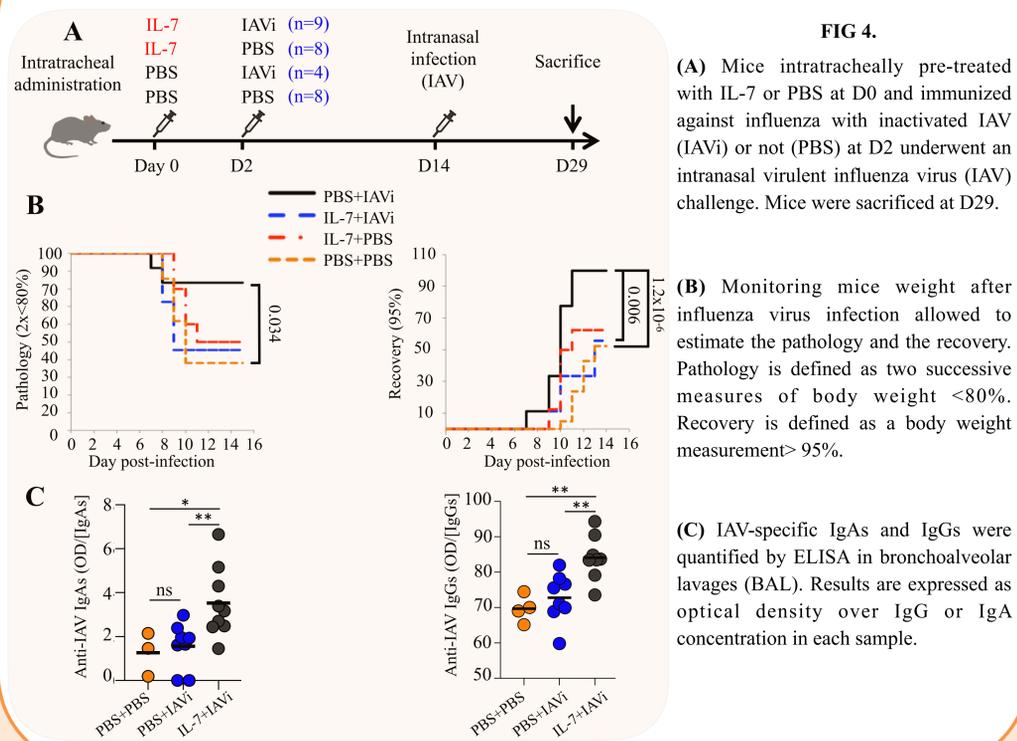


FIG 3. (A) Mice intratracheally pre-treated with IL-7 or PBS at D0 and immunized against influenza with inactivated IAV (IAVi) or not (PBS) at D2 underwent an intranasal virulent influenza virus (IAV) challenge. Mice were sacrificed at D29. (B) Monitoring mice weight after influenza virus infection allowed to estimate the pathology and the recovery. Pathology is defined as two successive measures of body weight < 80%. Recovery is defined as a body weight measurement > 95%. (C) IAV-specific IgAs and IgGs were quantified by ELISA in bronchoalveolar lavages (BAL). Results are expressed as optical density over IgG or IgA concentration in each sample.

IL-7 enhances the specific antibody response in a mucosal immunization protocol against diphtheria toxoid (DT)

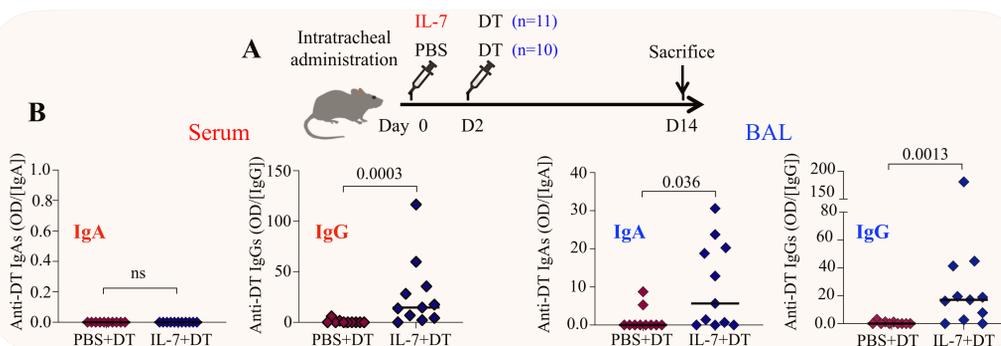


FIG 4. (A) At D0, mice were intratracheally treated with IL-7 or PBS (control) then at D2, immunized against DT, used as a model antigen. At D14, mice were sacrificed for the analysis. (B) DT-specific IgAs and IgGs were quantified by ELISA in serum and bronchoalveolar lavages (BAL).

Conclusion

Intratracheal administration of IL-7 changes the pulmonary physiology by inducing chemokine production and immune cell infiltration. These modifications seem to prepare the pulmonary mucosa to better respond to a subsequent administration of antigen by the same route. Indeed, following mucosal immunization against DT, mice pretreated with IL-7 developed stronger specific mucosal immune response than mice not treated with IL-7. In particular, IL-7 pre-treatment promoted a robust production of DT-specific IgAs in the BAL but not in the serum, as detected by ELISA. Moreover, only mice pretreated with IL-7 before immunization against IAV (inactivated IAV) were protected from the pathology caused by an intranasal influenza infection. Taken together, these data argue for IL-7 being a good candidate to be further evaluated as a mucosal adjuvant.